

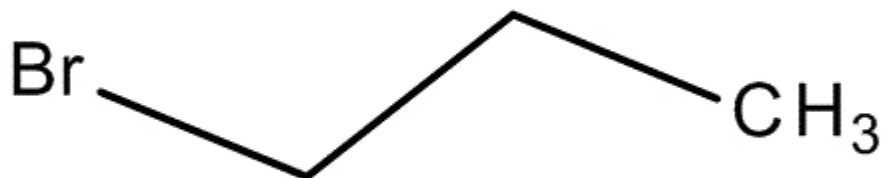


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**Draft Risk Evaluation for
1-Bromopropane
(*n*-Propyl Bromide)**

CASRN: 106-94-5



August 2019

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Docket

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Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

ABBREVIATIONS

AC	Acute concentration
ACGIH	American Conference of Government Industrial Hygienists
ACH	Air changes per hour
ADAF	Age-Dependent Adjustment Factor
ADC	Average daily concentration
ADR	Acute dose rate
ADR _{pot}	Potential acute dose rate
AEGL	Acute exposure guideline level
AER	Air exchange rate
APF	Assigned protection factor
Apx	Appendix
AT	Averaging time
Atm	Atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BL	Baseline
BMCL	Benchmark concentration, lower confidence limit(s)
BMD	Benchmark dose
BMDL	Benchmark dose, lower confidence limit(s)
BMR	Benchmark response level
BLS	Bureau of Labor Statistics
BOD	Biochemical oxygen demand
BOP	3-bromo-1-hydroxypropanone
BW	Body weight
C	Contaminant concentration
C _{air}	Air concentration
°C	Degree Celsius
CAA	Clean Air Act
C _{FF}	Average far field concentration
C _{FFTWA}	Time weighted average far field concentration
CNF	Average near field concentration
CN _F TWA	Time weighted average near field concentration
C _p _{pot}	Modeled peak concentration
CASRN	Chemical Abstracts Service Registry Number
CBI	Confidential business information
CCD	Chemical Control Division
CCRIS	Chemical Carcinogenesis Research Information System
CDR	Chemical Data Reporting
CEM	Consumer exposure module
CESSD	Chemistry, Economics, and Sustainable Strategies Division
CI	Confidence interval
cm	Centimeter(s)
cm ³	Cubic meter(s)
CNS	Central nervous system
CO ₂	Carbon dioxide

CYP	Cytochrome P450
DEv	Duration of an event
DIY	Do-it-yourself
DNA	Deoxyribonucleic acid
EC	Engineering controls
ECA	Enforceable consent agreement
ED	Exposure duration
EF	Exposure frequency
E-FAST2	Exposure and Fate Assessment Screening Tool version 2
EFH	Exposure Factors Handbook
EMIC	Environmental Mutagens Information Center
EPA	Environmental Protection Agency
ERG	Eastern Research Group, Inc.
EU	European Union
EvapTime	Evaporation time
FF	Far field
FQ	Frequency of product use
FSA	Free surface area
ft	Foot/feet
ft ²	Square foot/feet
ft ³	Cubic foot/feet
g	Gram(s)
g/cm ³	Grams per cubic centimeters
g/L	Grams per liter
G	Average generation rate
GM	Geometric mean
GSD	Geometric standard deviation
GD	Gestational day
GENE-TOX	Genetic Toxicology Data Bank
GSH	Glutathione (reduced)
H _{NF}	Near field height
HAPs	Hazardous air pollutants
HCV	Human cancer value
HEC	Human equivalent concentration
HED	Human equivalent dose
HHE	Health Hazard Evaluation
hr	Hour(s)
HSDB	Hazardous Substances Data Bank
HSIA	Halogenated Solvents Industry Alliance
IA	Indoor air
IARC	International Agency for Research on Cancer
IMIS	Integrated Management Information System
InhR	Inhalation rate
IRIS	Integrated Risk Information System
IUR	Inhalation unit risk
k	Emission rate
K _{ow}	Octanol: water partition coefficient

kg	Kilogram(s)
K _{oc}	Soil organic carbon-water partitioning coefficient
L	Liter(s)
lb	Pound(s)
L _{NF}	Near field length
LADC	Lifetime average daily concentration
LADD	Lifetime average daily dose
LEV	Local exhaust ventilation
LT	Lifetime
LOAEL	Lowest-observed-adverse-effect level
MA	Model-averaging
m	Meter(s)
m ²	Square meter(s)
m ³	Cubic meter(s)
MCCEM	Multi-Chamber Concentration and Exposure Model
µg/m ³	Microgram(s) per cubic meter
mg	Milligram(s)
mg/kg-bw	Milligram(s) per kilogram body weight
mg/L	Milligram(s) per liter
mg/m ³	Milligram(s) per cubic meter
mg/mL	Milligram(s) per milliliter
min	Minute(s)
MITI	Ministry of International Trade and Industry
Mlbs	Million of pounds
mm Hg	Millimeters of mercury
MMOA	Mutagenic Mode of Action
MOE	Margin of exposure
MOE _{acute}	Margin of exposure for acute exposures
MOE _{chronic}	Margin of exposure for chronic exposures
MOU	Memorandum of understanding
MW	Molecular weight
NAICS	North American Industry Classification System
NAPL	Nonaqueous phase liquid
NAS	National Academies of Science
NCEA	National Center for Environmental Assessment
NCI	National Cancer Institute
NEI	National Emissions Inventory
NESHAP	National Emissions Standards for Hazardous Air Pollutants
NF	Near field
NF/FF	Near field/far field
NHANES	National Health and Nutrition Examination Survey
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
nm	Nanometer(s)
NOAEL	No-observed-adverse-effect level

NOES	National Occupational Exposure Survey
NOHSC	National Occupational Health and Safety Commission
NJDEP	New Jersey Department of Environmental Protection
NPS	Nonpoint source
NTP	National Toxicology Program
OAR	Office of Air and Radiation
OCSPP	Office of Chemical Safety and Pollution Prevention
OECD	Organization for Economic Co-operation and Development
ONU	Occupational non-user
OPPT	Office of Pollution Prevention and Toxics
OR	Odds ratio
OSHA	Occupational Safety and Health Administration
OSWER	Office of Solid Waste and Emergency Response
OW	Office of Water
oz	Ounce(s)
PA	Personal air
PBZ	Personal breathing zone
PEL	Permissible exposure limit
PESS	Potentially exposed or susceptible subpopulations
PERC	Perchloroethylene
PID	Photoionization detector
PND	Postnatal day
POD	Point of departure
POTW	Publicly Owned Treatment Works
ppb	Parts per billion
ppm	Parts per million
PS	Point Source
PVC	Polyvinyl chloride
Q _{FF}	Far field ventilation rate
QNF	Near field ventilation rate
QA	Quality assurance
QC	Quality control
RAD	Risk Assessment Division
RCRA	Resource Conservation and Recovery Act
REACH	Registration Evaluation Authorization and Restriction of Chemicals
RfC	Reference concentration
RfD	Reference dose
RR	Rate ratio
RTECS	Registry of Toxic Effects of Chemical Substances
s	Second(s)
SAB	Science Advisory Board
SARA	Superfund Amendments and Reauthorization Act
SCG	Scientific Consulting Group, Inc.
SD	Standard deviation
SDS	Safety data sheet(s)
SNAP	Significant New Alternative Policy for ozone depleting substances
SVHC	Substance of Very High Concern

t	Time
TCA	Trichloroacetic acid
TCE	Trichloroethylene
TOXLINE	Toxicology Literature Online
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TSCATS	Toxic Substance Control Act Test Submission database
TWA	Time-weighted average
UF	Uncertainty factor
UF _S	Subchronic to chronic uncertainty factor
UF _A	Interspecies uncertainty factor
UF _H	Intraspecies uncertainty factor
UF _L	LOAEL to NOAEL uncertainty factor
UF _D	Database uncertainty factor
US EPA	United States Environmental Protection Agency
V _{FF}	Far field volume
v_{NF}	Indoor wind speed
V _{NF}	Near field volume
VOC	Volatile organic compound
VP	Vapor pressure
WWTP	Waste Water Treatment Plant
WNF	Near field width
WY	Working years
Yr (s)	Year(s)

EXECUTIVE SUMMARY

This draft risk evaluation for 1-Bromopropane (1-BP) was performed under the auspices of the Frank R. Lautenberg Chemical Safety for the 21st Century Act and disseminated for public comment and peer review. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act, the Nation's primary chemicals management law, on June 22, 2016. As per EPA's final rule, [Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act](#) (82 FR 33726), EPA is taking comment on, and will also obtain peer review on, this draft risk evaluation for 1-BP. All conclusions, findings, and determinations in this document are subject to comment.

The Agency published the Scope of the Risk Evaluation for 1-BP ([U.S. EPA, 2017d](#)) in June 2017, and the Problem Formulation in June 2018 ([U.S. EPA, 2018c](#)), which represented the analytical phase of risk evaluation in which "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" as described in Section 2.2 of the [Framework for Human Health Risk Assessment to Inform Decision Making](#). EPA received comments on the published problem formulation for 1-BP and has considered the comments specific to 1-BP, as well as more general comments regarding EPA's chemical risk evaluation approach for developing the draft risk evaluations for the first 10 chemicals.

TSCA § 26(h) requires EPA to use scientific information, technical procedures, measures, methods, protocols, methodologies and models consistent with the best available science and base its decisions on the weight of the scientific evidence. To meet the TSCA § 26(h) science standards, EPA used the TSCA systematic review process described in the Application of Systematic Review in TSCA Risk Evaluations document ([U.S. EPA, 2018a](#)). The process complements the risk evaluation process in that the data collection, data evaluation and data integration stages of the systematic review process are used to develop the exposure, fate and hazard assessments.

EPA has identified the conditions of use for 1-BP (Chemical Abstracts Service Registry Number [CASRN] 106-94-5), including manufacturing and processing; and industrial, commercial, and consumer activities and uses. The primary use of 1-BP is as a solvent for cleaning and degreasing (including vapor degreasing, cold cleaning, and aerosol degreasing). Several other categories determined not to be conditions of use that were excluded during problem formulation ([U.S. EPA, 2018c](#)) include non-pesticidal agricultural products (since 1-BP is only used in the processing of such products and is not present in the final non-pesticidal agricultural products), adhesives in consumer products (except as an adhesive accelerant for arts and crafts), and engine degreasing or brake cleaning in consumer products (since these are only commercial products).

According to data collected in EPA's 2016 Chemical Data Reporting (CDR) Rule, 25.9 million pounds of 1-BP were manufactured in or imported into the United States in 2015 ([U.S. EPA, 2016a](#)). Data publicly reported indicate that there are two domestic manufacturers and eight importers of 1-BP in the United States.

Total production volume (domestic manufacture plus import) of 1-BP has increased from 2012 to 2015 ([U.S. EPA, 2016a](#)). 1-BP's volume has increased because it has been an alternative to ozone-depleting substances and chlorinated solvents. Import volumes for 1-BP reported to the 2016 CDR are between 10 million and 25 million pounds per year ([U.S. EPA, 2016a](#)). In past years, import data from 1-BP were claimed as CBI, but import data from other public sources indicate that

import volumes of brominated derivatives of acyclic hydrocarbons (which includes 1-BP as well as other chemicals) were 10.9 million pounds in 2007, which dropped to 10.3 million pounds in 2011 ([NTP, 2013b](#)).

In the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)), EPA identified the conditions of use (COUs) and presented conceptual models and an analysis plan for this draft risk evaluation. The conditions of use evaluated for 1-BP, as further described in Section 1.4.1 of the draft risk evaluation for 1-BP, include:

- Manufacturing, including domestic manufacturing of 1-BP and import of 1-BP
- Processing: as a reactant/intermediate in all other basic inorganic chemical manufacturing; all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing
- Processing: incorporating into formulation, mixture, or reaction products for solvents for cleaning and degreasing
- Processing: incorporating into article
- Repacking solvents for cleaning or degreasing in all other basic organic chemical manufacturing
- Recycling
- Distribution in commerce
- Industrial and commercial use as solvent for cleaning and degreasing, including vapor degreaser (batch vapor degreaser – open top and closed loop, inline vapor degreaser), cold cleaner aerosol spray degreaser/cleaner
- Industrial and commercial use as adhesives and sealants
- Industrial and commercial use as cleaning and furniture care products, including dry cleaning, spot cleaner and other liquid, spray and aerosol cleaners.
- Other industrial and commercial uses: arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner, refrigerant flush); anti-adhesive agents (mold cleaning and release product); building/construction materials not covered elsewhere (insulation); electronic and electronic products and metal products; functional fluids (close/open-systems) – refrigerant/cutting oils; asphalt extraction; laboratory chemicals; and temperature indicator – coatings
- Consumer uses: as a solvent (for cleaning or degreasing) in the form of aerosol spray degreaser or cleaner; as a cleaning and furniture care product in the form of: spot cleaner or stain remover, liquid cleaner (e.g., coin and scissor cleaner), and liquid spray or aerosol cleaner; as arts, crafts and hobby materials in the form of adhesive accelerant; as automotive care products in the form of refrigerant flush; as anti-adhesive agents in the form of mold cleaning and release product; and as insulation in building/construction material - insulation.
- Disposal: municipal waste incinerator

In this draft risk evaluation, EPA quantitatively evaluated the risk to the environment and human health for the conditions of use described in Section 1.4.1 of this draft risk evaluation using both monitoring data and modeling approaches. EPA evaluated risk to workers and occupational non-users (ONUs are workers who do not directly handle 1-BP but perform work in an area where 1-BP is present) from inhalation and dermal exposures by comparing the estimated exposures to acute and chronic human health hazards. EPA also evaluated the risk to consumer populations

from inhalation and dermal exposures. Lifestages from infants to adults were included in the draft evaluation, by comparing the estimated exposures to acute and chronic human health hazards.

The manufacturing, processing, use and disposal of 1-BP can result in releases to the environment via air, water, sediment, biosolids and soil. EPA quantitatively evaluated risk to aquatic species from exposure to surface water, which was determined to be the only relevant route of exposure to environmental receptors under the conditions of use of this assessment. EPA did not conduct additional analysis of exposures to sediment-dwelling or terrestrial species beyond what was presented in the Problem Formulation ([U.S. EPA, 2018c](#)).

Approach

EPA used reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation, in a fit for purpose approach, to develop risk evaluations that rely on the best available science and are based on the weight of scientific evidence. EPA used previous analyses as a starting point for identifying key and supporting studies to inform the fate, exposure, and hazard assessments. EPA evaluated other studies that were published since these reviews. EPA reviewed the information and evaluated the quality of the methods and reporting of results of the individual studies using the evaluation strategies described in the Application of Systematic Review in TSCA Risk Evaluations document ([U.S. EPA, 2018a](#)).

As described in the Problem Formulation ([U.S. EPA, 2018c](#)), an aquatic exposure assessment was conducted using EPA's Toxics Release Inventory (TRI) release information to model predicted surface water concentrations near discharging facilities. To examine whether near-facility surface water concentrations could approach aquatic concentrations of concern for 1-BP, EPA employed a conservative approach, using available modeling tools and data to estimate near-facility surface water concentrations resulting from reported releases of 1-BP to surface water. High-end surface water concentrations (i.e., those obtained assuming low receiving water body stream flows) from all [E-FAST 2014](#) runs were compared to the acute and chronic aquatic concentrations of concern derived from available data characterizing the environmental hazards of 1-BP to fish, aquatic invertebrates, and aquatic plants.

In the human hazard section, EPA evaluated reasonably available information and identified hazard endpoints including non-cancer and cancer effects, associated with inhalation exposures. EPA used an approach based on the Framework for Human Health Risk Assessment to Inform Decision Making ([U.S. EPA, 2014c](#)) to evaluate, extract and integrate 1-BP's human health hazard and dose-response information. EPA reviewed key and supporting information from previous hazard assessments as well as the existing body of knowledge on 1-BP's human health hazards. These data sources¹ included published and non-published data sources, including key and supporting studies identified in and evaluated in the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)). EPA relied heavily on the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)) to inform hazard characterization.

¹ 1-BP does not have an existing EPA IRIS Assessment.

EPA considered adverse effects for 1-BP across organ systems. EPA considered data on toxicity following acute and chronic exposures, for irritation, sensitization, genotoxicity, reproductive, developmental and other systemic toxicity and carcinogenicity. From these effects, EPA selected endpoints supported by the evidence for non-cancer and cancer that were amenable to quantitative analysis for dose-response assessment as discussed in more detail in Section 3.2.5. Based on the weight of the scientific evidence evaluation, six adverse health effect domains were selected for dose-response analysis: (1) liver toxicity, (2) kidney toxicity, (3) reproductive toxicity, (4) developmental toxicity, (5) neurotoxicity, and (6) carcinogenicity. For non-cancer endpoints, emphasis was placed on acute/short term inhalation, and repeated-dose inhalation studies identified as most appropriate for hazard characterization and dose-response analysis. As discussed in Section 3.2.2, dermal HEDs for dermal exposures were derived by extrapolating from the inhalation PODs. Given the different 1-BP exposure scenarios considered (both acute and chronic), different endpoints were used based on the expected exposure durations.

Potentially Exposed or Susceptible Subpopulations

TSCA § 6(b)(4) requires that EPA conduct a risk evaluation to “determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use.” TSCA § 3(12) states that “the term ‘potentially exposed or susceptible subpopulation’ means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly.”

In developing the draft risk evaluation, EPA analyzed the reasonably available information to ascertain whether some human receptor groups may have greater exposure or susceptibility than the general population to the hazard posed by a chemical.

For occupational exposures, EPA assessed exposures to workers and ONUs from all 1-BP conditions of use. In Section 2.4, EPA calculated the percentage of employed workers and ONUs whom may be susceptible subpopulations within select industry sectors relevant to 1-BP conditions of use. The percentages were calculated using Current Population Survey (CPS) data for 2017. CPS is a monthly survey of households conducted by the Bureau of Census for the Bureau of Labor Statistics and provides a comprehensive body of data on the labor force characteristics. Statistics for the following subpopulations of workers and ONUs are provided: adolescents, men and women of reproductive age,² and the elderly. For the purpose of this assessment, EPA considers “reproductive age” as age 16 to 54. As shown in Section 2.4.1, men make up the majority of the workforce in manufacturing sectors. In other sectors, women (including those of reproductive age and elderly women) make up nearly half of the workforce.

Adolescents, or persons between 16 and 19 years in age, are generally a small part of the total workforce. As shown in Section 2.4, this age group comprises less than two percent of the workforce, with the exception of the repair and maintenance subsector, where 1-BP may be used in

² While statistics on pregnant women are not available, CPS provides data on the number of employed female workers by age group, which allows for determination of the number of employed women of reproductive age.

aerosol degreasing; and the dry cleaning subsector, where 1-BP may be used for dry cleaning and spot cleaning.

For consumer exposures, EPA assessed exposures to users and non-users (bystanders). EPA assumes, for this evaluation, consumer users are male or female adults (between 16 and 21 years of age and greater than 21 years of age), including woman of reproductive age. Non-users could be any age group ranging from infants to adults (Section 2.3.2.3).

Risk Characterization

In each risk evaluation under TSCA section 6(b), EPA determines whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use. In making this determination, EPA considered relevant risk-related factors, including, but not limited to: the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any potentially exposed or susceptible subpopulations); the severity of hazard (including the nature of the hazard, the irreversibility of the hazard); and uncertainties. EPA considered the confidence in the data used in the risk estimates and whether estimates might be over estimates or underestimates of risk.

EPA identifies a single human health adverse effect as the “unreasonable risk driver” for a particular condition of use. This is the effect that is most sensitive, and it is expected that managing risks for this effect will address other identified risks. As described in Section 4, additional significant risks associated with more than one adverse effect (e.g. developmental, reproductive, liver, kidney, nervous system) were identified for many conditions of use.

Environmental Risks

EPA integrated relevant pathways of environmental exposure with available hazard data to estimate risk to terrestrial environmental receptors. A qualitative consideration of the high volatility, high water solubility and low Log K_{oc} of 1-BP, as well as a consideration of the conditions of use of this assessment suggest that 1-BP will only be present at low concentrations in the sediment and terrestrial environmental compartments, so these pathways were not further analyzed in this risk evaluation since risk from these exposure pathways are not expected. In this risk evaluation, EPA utilized a conservative screening level approach to calculate risk to the aquatic organisms. For all conditions of use, EPA did not identify any exceedances of benchmarks to aquatic organisms from exposures to 1-BP in surface waters, indicating that the exposure concentrations of 1-BP are less than the concentrations that would cause an effect to organisms in the aquatic pathways (See Section 4.1).

As a result, EPA determined that 1-BP does not present unreasonable risk to the environment under the identified conditions of use.

Human Health Risks

Workers and Occupational Non-Users (ONUs)

The impact of respirator use based on respirator APF of 10, 25, and 50 was evaluated. The calculated MOE with respirator use was then compared to the Agency's benchmark MOE to determine the level of APF that would be needed to mitigate risk for all health domains. The MOE estimates for these respirator scenarios assume workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity where there is potential exposure to 1-BP. For some occupational conditions of use, respirators with an APF of 50 do not reduce worker exposure to levels where the calculated MOE is greater than the benchmark MOE. Respirator use for occupational non-users was not evaluated because they do not directly handle 1-BP and are unlikely to wear respirators. In addition, small commercial facilities performing dry cleaning and spot cleaning are unlikely to have a respiratory protection program. Non-cancer inhalation and dermal Margins of Exposure (MOEs) for acute and chronic exposure scenarios in workers were derived from monitoring and modeling (with and without engineering controls) for each COU.

Calculated MOEs were above the Agency's benchmarks in most cases for non-cancer effects following acute and chronic inhalation exposures in workers using monitoring data and modeling for the following COUs:

- Manufacturing (domestic manufacturing and import)
- Processing: as a reactant/intermediate
- Processing: incorporation into article
- Repackaging
- Recycling
- Disposal

Calculated MOEs were below the Agency's benchmarks in most cases for non-cancer effects following acute and chronic inhalation exposures in workers using respirators and in ONUs without the use of respirators using monitoring data and modeling for the following COUs:

- Processing: incorporation into formulation, mixture, or reaction product
- Industrial and commercial use as solvent for cleaning and degreasing, including batch vapor degreasers, in-line vapor degreasers, cold cleaner and aerosol spray degreaser/cleaner
- Industrial and commercial use as cleaning and furniture care products, including dry cleaning, spot cleaner and other liquid, spray and aerosol cleaners
- Industrial and commercial use as adhesives and sealants, including spray adhesives

Calculated MOEs were above the Agency's benchmarks for manufacture, import, processing, and disposal activities for both acute and chronic dermal exposure scenarios for all glove protection factors (PFs) for all COUs.

Cancer inhalation risk estimates for chronic occupational exposure values were derived from monitoring data and modeling (with and without engineering controls). The benchmark cancer risk estimate of 1×10^{-4} was exceeded for all of the uses in workers and occupational non-users for both central tendency and high-end exposure estimates for both monitoring and modeling data without considering the use of a respirator. When respirators were assumed to be used by the workers, the risk estimates did not exceed the benchmark for the following conditions of use:

- Manufacturing (domestic manufacturing and import)

- Repackaging
- Recycling
- Processing: incorporating into article
- Industrial and commercial use as solvent for cleaning and degreasing, including vapor degreasing closed loop
- Disposal

In the case of the solvent for cleaning and degreasing vapor degreasing closed loop, the cancer inhalation risk remains for ONUs, since EPA is not anticipating that ONUs would be wearing respirators. In most cases, benchmark cancer risk estimates were similar between monitoring and modeling within each use. The following COUs have cancer inhalation risk estimates that exceeded the benchmark even after considering that respirators were used by workers:

- Processing: Incorporation into formulation, mixture, or reaction products
- Industrial and commercial use as a solvent for cleaning and degreasing, including vapor degreaser (batch vapor degreaser – open top and closed loop, inline vapor degreaser), cold cleaner, and aerosol spray degreaser/cleaner
- Industrial and commercial use as cleaning and furniture care products, including dry cleaning, spot cleaner, and other liquid, spray, and aerosol sealants
- Other industrial and commercial uses (e.g., adhesive accelerant, automotive care products, etc.)

Cancer dermal risk estimates were derived for chronic occupational exposures. The benchmark cancer risk estimate (1×10^{-4}) was exceeded for all COUs when no gloves were used (PF=1); however, as the PF increased between 5 and 20, the benchmark cancer risk estimate (1×10^{-4}) was not exceeded.

Consumers and Bystanders

Calculated MOEs were below the Agency's benchmark for non-cancer effects following acute inhalation and dermal exposures to all users evaluated (except for the insulation condition of use), even during low intensity use conditions. The number of consumers at risk is not known but would be any consumer purchasing and using the products containing 1-BP within a residence.

Calculated MOEs were below the Agency's benchmark for non-cancer effects following acute inhalation exposures to all bystanders evaluated (except for the insulation condition of use), although under certain low intensity use conditions, the calculated MOEs were above the Agency's benchmark. The number of bystanders at risk is not known but would be any bystander located in a residence where a consumer has used the products containing 1-BP.

Calculated MOEs were below the Agency's benchmark for non-cancer effects following acute dermal exposures to all users evaluated under the three conditions of use evaluated for dermal exposure in this evaluation, although under low intensity use of general cleaners/degreasers, the calculated MOEs were above the Agency's benchmark. The number of users at risk for dermal exposure is not known but would be any consumer purchasing and using the products containing 1-BP within the residence.

Risk Determination

After considering the relevant risk-factors, EPA determined that the following conditions of use of 1-BP do not present an unreasonable risk of injury to human health (including consumers and/or bystanders) or the environment:

- Manufacturing (Domestic Manufacturing and Import)
- Processing: as a reactant/intermediate
- Processing: incorporation into articles
- Repackaging
- Recycling
- Distribution in commerce
- Disposal
- Consumer uses of insulation

The following conditions of use of 1-BP present an unreasonable risk of injury to human health (including workers, ONUs, consumers, and/or bystanders):

- Processing: Incorporation into formulation, mixture, or reaction products
- Industrial and commercial use as solvent for cleaning and degreasing, including vapor degreaser (batch vapor degreaser – open top and closed loop, inline vapor degreaser), cold cleaner and aerosol spray degreaser/cleaner
- Industrial and commercial use as adhesives and sealants
- Industrial and commercial use as cleaning and furniture care products, including dry cleaning, spot cleaner and other liquid, spray and aerosol cleaners.
- Other industrial and commercial uses: arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner, refrigerant flush); anti-adhesive agents (mold cleaning and release product); building/construction materials not covered elsewhere (insulation); electronic and electronic products and metal products; functional fluids (close/open-systems) – refrigerant/cutting oils; asphalt extraction; laboratory chemicals; and temperature indicator – coatings
- Other consumer uses: as a solvent (for cleaning or degreasing) in the form of aerosol spray degreaser or cleaner; as a cleaning and furniture care product in the form of: spot cleaner or stain remover, liquid cleaner (e.g., coin and scissor cleaner), and liquid spray or aerosol cleaner; as arts, crafts and hobby materials in the form of adhesive accelerant; as automotive care products in the form of refrigerant flush; and as anti-adhesive agents in the form of mold cleaning and release product

1 INTRODUCTION

This document presents for comment the draft risk evaluation for 1-bromopropane (1-BP) under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016.

The Agency published the *Scope of the Risk Evaluation for 1-BP* ([U.S. EPA, 2017d](#)) in June 2017, and the problem formulation in June 2018 ([U.S. EPA, 2018c](#)), which represented the analytical phase of risk evaluation in which “the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined” as described in Section 2.2 of the [Framework for Human Health Risk Assessment to Inform Decision Making](#). EPA received comments on the published problem formulation for 1-BP and has considered the comments specific to 1-BP, as well as more general comments regarding EPA's chemical risk evaluation approach for developing the draft risk evaluations for the first 10 chemicals EPA is evaluating. The problem formulation ([U.S. EPA, 2018c](#)), presented a conceptual model and an analysis plan. Based on EPA's analysis of the conditions of use, physical-chemical and fate properties, environmental releases, and exposure pathways, the preliminary conclusions of the problem formulation were that further analysis of exposure pathways, e.g., to workers and consumers was necessary in this risk evaluation; and that further analysis for environmental release pathways leading to surface water, sediment, or land-applied biosolid exposures to ecological receptors was not necessary in this risk evaluation.

After further consideration, EPA determined that the listing of 1-BP as a Hazardous Air Pollutant (HAP) will address the inhalation exposure pathway via ambient air to the general population, which eliminated the need for evaluation. The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For all major source categories emitting HAP, the CAA requires issuance of technology-based standards and, 8 years later, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.

As referenced in the 1-BP Problem Formulation ([U.S. EPA, 2018c](#)), in December 2016, EPA, through its Office of Air and Radiation (OAR), issued a draft notice of the Agency's rationale for granting the petition to add 1-BP to the list of HAPs contained in section 112(b)(1) of the Clean Air Act (CAA), 42 U.S.C. 7412. Under Section 112 of the CAA, EPA is required to regulate and control emissions of listed hazardous air pollutants. Based upon consultation, OCSPP understands from OAR that the Agency is finishing review of comments on this draft notice and intends to finalize an action before the end of 2019. After further consideration of the likely future applicability of EPA regulations to 1-BP, EPA has determined that the Clean Air Act adequately assesses and effectively manages risks to the population via the ambient air pathway.

The draft risk evaluation for 1-BP is based on the best available science. The risk evaluation is structured such that Section 1 presents the basic physical-chemical properties of 1-BP, as well as a background on uses, regulatory history, conditions of use and conceptual models, with particular

emphasis on any changes since the publication of the problem formulation. Section 1 also includes a discussion of the systematic review process utilized in this draft risk evaluation. Section 2 provides the analysis and discussion of the exposures, both human and environmental, that can be expected based on the conditions of use for 1-BP. Section 3 discusses environmental and human health hazards of 1-BP. Risk characterization is presented in Section 4, which integrates and assesses the best available science and “reasonably available information”³ on human health and environmental hazards and exposures, as required by TSCA (15 U.S.C. 2605(b)(4)(F)). This section also includes a discussion of any uncertainties and how they impact the risk evaluation. In Section 4.4.2, the agency presents the draft risk determination of whether risks posed by the chemical substance under the conditions of use are “unreasonable” as required under TSCA (15 U.S.C. 2605(b)(4)).

As per EPA’s final Risk Evaluation Rule, [*Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*](#) (82 FR 33726), this draft risk evaluation will be subject to both public comment and peer review, which are distinct but related processes. EPA is providing 60 days for public comment on all aspects of this draft risk evaluation, including the submission of any additional information that might be relevant to the science underlying the risk evaluation. This satisfies TSCA section 6(b)(4)(H) which requires EPA to provide public notice and an opportunity for comment on a draft risk evaluation prior to publishing a final risk evaluation.

Peer review will be conducted in accordance with EPA's regulatory procedures for chemical risk evaluations, including using the [*EPA Peer Review Handbook*](#) and other methods consistent with section 26 of TSCA (See 40 CFR 702.45). As explained in the Risk Evaluation Rule, the purpose of peer review is for the independent review of the science underlying the risk assessment. Peer review will therefore address aspects of the underlying science as outlined in the charge to the peer review panel such as hazard assessment, assessment of dose-response, exposure assessment, and risk characterization.

As EPA explained in the Risk Evaluation Rule (82 Fed. Reg. 33726 (July 20, 2017)), it is important for peer reviewers to consider how the underlying risk evaluation analyses fit together to produce an integrated risk characterization, which forms the basis of an unreasonable risk determination. EPA believes peer reviewers will be most effective in this role if they receive the benefit of public comments on draft risk evaluations prior to peer review. For this reason, and consistent with standard Agency practice, the public comment period will precede peer review on this draft risk evaluation. The final risk evaluation may change in response to public comments received on the draft risk evaluation and/or in response to peer review, which itself may be informed by public comments. EPA will respond to public and peer review comments received on the draft risk evaluation and will explain changes made to the draft risk evaluation for 1-BP in response to those comments in the final risk evaluation.

³ “Reasonably available information means information that EPA possesses or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines specified in TSCA section 6(b)(4)(G) for completing such evaluation. Information that meets the terms of the preceding sentence is reasonably available information whether or not the information is confidential business information, that is protected from public disclosure under TSCA Section 14.”

EPA solicited input from the public and stakeholders (including other government agencies) on the first 10 chemicals as it developed use dossiers, scope documents, and problem formulations. At each step, EPA has received information and comments specific to individual chemicals and of a more general nature relating to various aspects of the risk evaluation process, technical issues, and the regulatory and statutory requirements. EPA has considered comments and information received at each step in the process and factored in the information and comments as the Agency deemed appropriate and relevant including comments on the published problem formulation of 1-BP. In addition to any new comments on the draft risk evaluation, the public should re-submit or clearly identify any previously filed comments, modified as appropriate, that are relevant to this risk evaluation and that the submitter feels have not been addressed. EPA does not intend to further respond to comments submitted prior to the publication of this draft risk evaluation unless they are clearly identified in comments on this draft risk evaluation.

1.1 Physical and Chemical Properties

1-BP is a colorless liquid with a sweet odor. It is a brominated hydrocarbon that is slightly soluble in water. 1-BP is a volatile organic compound (VOC) that exhibits high volatility, a low boiling point, low flammability and no explosivity. Figure 1-1 presents the chemical structure and Table 1-1 summarizes the physical-chemical properties of 1-BP.

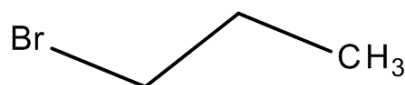


Figure 1-1. Chemical Structure of 1-Bromopropane

Table 1-1. Physical-Chemical Properties of 1-BP

Property	Value ^a	Reference
Molecular formula	C ₃ H ₇ Br	O'Neil (2013)
Molecular weight	122.99	O'Neil (2013)
Physical form	Colorless liquid; sweet hydrocarbon odor	O'Neil (2013)
Melting point	-110°C	O'Neil (2013)
Boiling point	71°C at 760 mmHg	O'Neil (2013)
Density	1.353 g/cm ³ at 20°C	O'Neil (2013)
Vapor pressure	146.26 mmHg (19.5 kPa) at 20°C	Boublík et al. (1984)
Vapor density	4.25 (relative to air)	Patty et al. (1963)
Water solubility	2.450 g/L at 20°C	Yalkowsky et al. (2010)
Octanol/water partition coefficient (Log K _{ow})	2.10	Hansch (1995)
Henry's Law constant	7.3x10 ⁻³ atm-m ³ /mole (estimated)	U.S. EPA (2012c)
Flash point	22°C	O'Neil (2013)

Property	Value ^a	Reference
Autoflammability	490°C	NEPA (2010)
Viscosity	5.241 mPa·s at 20°C	Haynes and Lide (2010)
Refractive index	1.4341	O'Neil (2013)
Dielectric constant	8.09 at 20°C	Haynes and Lide (2010)
^a Measured unless otherwise noted.		

1.2 Uses and Production Volume

The information on the conditions of use is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: “industrial use” means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. “Commercial use” means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. “Consumer use” means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use ([U.S. EPA, 2016a](#)).

CDR, information from commenters, and types of available products show that the primary use of 1-BP is degreasing. The exact use volumes associated with degreasing is CBI⁴ in the 2016 CDR ([U.S. EPA, 2016a](#)). EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, consumer use, disposal) rather than as a single distribution scenario. EPA expects that some commercial products containing 1-BP are also available for purchase by consumers, such that many products are used in both commercial and consumer applications/scenarios.

The 2016 CDR reporting data on the production volume for 1-BP are provided in Table 1-2 and come from EPA’s CDR database ([U.S. EPA, 2016a](#)). This information has not changed from that provided in the [Scope Document \(EPA-HQ-OPPT-2016-0741-0049\)](#).

⁴ It is important to note that EPA does have access to and does review all CBI information in this process. EPA has also reviewed all CBI claims referred to in this draft risk evaluation, and these claims have been substantiated and approved by EPA.

Table 1-2. Production Volume of 1-BP in CDR Reporting Period (2012 to 2015) ^a

Reporting Year	2012	2013	2014	2015
Total Aggregate Production Volume (lbs)	18,800,000	24,000,000	18,500,000	25,900,000

^a The CDR data for the 2016 reporting period is available via ChemView (<https://chemview.epa.gov/chemview>) ([U.S. EPA, 2016a](#)). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the Scope Document ([EPA-HQ-OPPT-2016-0741-0049](#)) is more specific than currently in ChemView.

According to data collected in EPA's 2016 Chemical Data Reporting (CDR) Rule, 25.9 million pounds of 1-BP were manufactured in or imported into the United States in 2015 ([U.S. EPA, 2016a](#)). Data publicly reported indicate that there are two domestic manufacturers and eight importers of 1-BP in the United States.

Total production volume (domestic manufacture plus import) of 1-BP has increased from 2012 to 2015, as can be seen in Table 1-2 ([U.S. EPA, 2016a](#)). 1-BP's volume has increased because it has been an alternative to ozone-depleting substances and chlorinated solvents. Import volumes for 1-BP reported to the 2016 CDR are between 10 million and 25 million pounds per year ([U.S. EPA, 2016a](#)). In past years, import data from 1-BP were claimed as CBI, but import data from other public sources indicate that import volumes of brominated derivatives of acyclic hydrocarbons (which includes 1-BP as well as other chemicals) were 10.9 million pounds in 2007, which dropped to 10.3 million pounds in 2011 ([NTP, 2013b](#)).

1.3 Regulatory and Assessment History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to 1-BP. EPA compiled a regulatory summary from federal, state, international and other government sources, as cited in Appendix A.

Federal Laws and Regulations

1-BP is subject to federal statutes or regulations, in addition to TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

State Laws and Regulations

1-BP is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

Laws and Regulations in Other Countries and International Treaties or Agreements

1-BP is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-3). Depending on the source, these assessments may include information on conditions of use, hazards, exposures, and potentially exposed or susceptible subpopulations. EPA found no additional assessments beyond those listed in the Scope Document ([Scope Document; EPA-HQ-OPPT-2016-0741-0049](#)).

In addition to using this information, EPA conducted a full review of the relevant data and information collected in the initial comprehensive search (see *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0048](#)) using the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). Thus, EPA considered data and information that has been made available since these assessments were conducted.

Table 1-3. Assessment History of 1-BP

Authoring Organization	Assessment
EPA Assessments	
Office of Chemical Safety and Pollution Prevention (OCSPP)/Office of Pollution Prevention and Toxics (OPPT)	TSCA work plan chemical risk assessment: Peer review draft 1-bromopropane: (n-Propyl bromide) spray adhesives, dry cleaning, and degreasing uses CASRN: 106-94-5 [2016 Draft Risk Assessment (U.S. EPA, 2016d)]
Office of Air Quality Planning and Standards (OAQPS)	Draft notice to grant the petition to add 1-BP to the list of HAPs (https://www.regulations.gov/document?D=EPA-HQ-OAR-2014-0471-0062)
Other U.S.-Based Organizations	
National Institute for Occupational Safety and Health (NIOSH)	Criteria for a Recommended Standard: Occupational Exposure to 1-Bromopropane (2016)
Agency for Toxic Substances and Disease Registry (ATSDR)	Toxicological Profile for 1-Bromopropane (2017)

1.4 Scope of the Evaluation

1.4.1 Conditions of Use Included in the Risk Evaluation

TSCA § 3(4) defines the conditions of use as “the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.” Conditions of use have not changed since the issuance of the 1-BP Problem Formulation ([U.S. EPA, 2018c](#)) on June 11, 2018; thus, the conditions of use described in the 1-BP problem formulation, and reproduced below in Table 1-4, remain the same. No additional information was received by EPA following the publication of the problem formulation that would require updating the conditions of use (Table 2-2) or the life cycle diagram as presented in the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)).

The life cycle diagram in Figure 1-2 depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period ([U.S. EPA, 2016a](#)). EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, consumer use, disposal) rather than as a separate distribution scenario.

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Manufacture	Domestic manufacture	Domestic manufacture	U.S. EPA (2016a)
	Import	Import	U.S. EPA (2016a)
Processing	Processing as a reactant	Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing	U.S. EPA (2016a)
	Processing - incorporating into formulation, mixture or reaction product	Solvents for cleaning or degreasing in manufacturing of: - all other chemical product and preparation - computer and electronic product - electrical equipment, appliance and component - soap, cleaning compound and toilet preparation - services	U.S. EPA (2016a)
	Processing - incorporating into articles	Solvents (which become part of product formulation or mixture) in construction	U.S. EPA (2016a) ; Public Comment, EPA-HQ-OPPT-2016-0741-0017
Processing	Repackaging	Solvent for cleaning or degreasing in all other basic organic chemical manufacturing	U.S. EPA (2016a)
	Recycling	Recycling	U.S. EPA (2016a) ; Use Document, EPA-HQ-OPPT-2016-0741-0003
Distribution in commerce	Distribution	Distribution	U.S. EPA (2016a) ; Use Document, EPA-HQ-OPPT-2016-0741-0003

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Industrial/ commercial/ use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (e.g., open-top, closed-loop)	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0015 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		In-line vapor degreaser (e.g., conveyORIZED, web cleaner)	Kanegsberg and Kanegsberg (2011) ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Cold cleaner	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Aerosol spray degreaser/cleaner	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0018 ; Public Comment, EPA-HQ-OPPT-2016-0741-0020
	Adhesives and sealants	Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
Industrial/ commercial/use	Cleaning and furniture care products	Dry cleaning solvent	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0005 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Spot cleaner, stain remover	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0022
		Liquid cleaner (e.g., coin and scissor cleaner)	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Liquid spray/aerosol cleaner	Use Document, EPA-HQ-OPPT-2016-0741-0003

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Industrial/ commercial/use (continued)	Other uses	Arts, crafts and hobby materials - adhesive accelerant	U.S. EPA (2016d)
		Automotive care products - engine degreaser, brake cleaner	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Anti-adhesive agents - mold cleaning and release product	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0015 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0018
		Building/construction materials not covered elsewhere - insulation	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0027
		Electronic and electronic products and metal products	U.S. EPA (2016a) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0024
		Functional fluids (closed systems) - refrigerant	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Functional fluids (open system) - cutting oils	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0014
		Other - asphalt extraction	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Other - Laboratory chemicals ^c	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-2016-0741-0059
		Temperature Indicator – Coatings	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
Consumer uses	Solvent (for cleaning or degreasing)	Aerosol spray degreaser/cleaner	U.S. EPA (2016d) ;
	Cleaning and furniture care products	Spot cleaner, stain remover	U.S. EPA (2016d) ; Public Comment, EPA-HQ-OPPT-2016-0741-0022
		Liquid cleaner (e.g., coin and scissor cleaner)	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Liquid spray/aerosol cleaner	Use Document, EPA-HQ-OPPT-2016-0741-0003

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Consumer uses (continued)	Other uses	Arts, crafts and hobby materials - adhesive accelerant	U.S. EPA (2016d)
		Automotive care products – refrigerant flush	U.S. EPA (2016d)
		Anti-adhesive agents - mold cleaning and release product	U.S. EPA (2016d)
		Building/construction materials not covered elsewhere - insulation	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0027
Disposal (Manufacturing, Processing, Use)	Disposal	Municipal waste incinerator	2016 TRI Data (updated October 2017) U.S. EPA (2017g)
		Off-site waste transfer	

^aThese categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of 1-BP in industrial and/or commercial settings.

^bThese subcategories reflect more specific uses of 1-BP.

^c“Other – Laboratory Chemicals” was changed from “Temperature Indicator – Laboratory Chemicals” since the problem formulation because other uses of 1-BP as a laboratory chemical were identified.

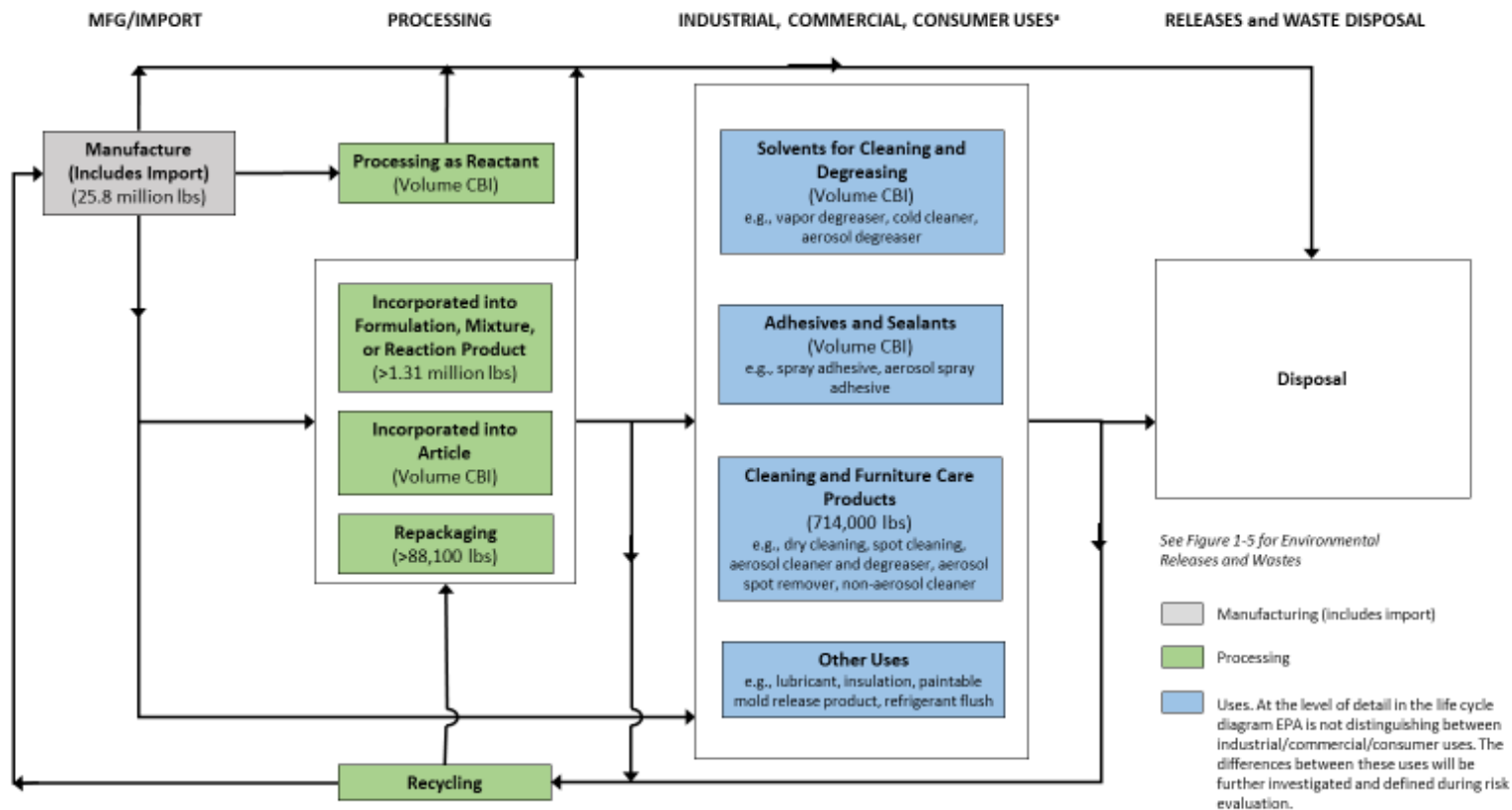


Figure 1-2. 1-BP Life Cycle Diagram

^a See Table 1-4 for additional uses not mentioned specifically in this diagram.

1.4.2 Conceptual Models

The conceptual models for this draft risk evaluation are shown in Figure 1-3, Figure 1-4, and Figure 1-5. EPA considered the potential for hazards to human health and the environment resulting from exposure pathways outlined in the preliminary conceptual models of the 1-BP scope document ([U.S. EPA, 2017d](#)). These conceptual models indicate where potential exposures to 1-BP may result from industrial and commercial activities, consumer activities and uses, and environmental releases and wastes. The problem formulation documents refined the initial conceptual models and analysis plans that were provided in the scope documents ([U.S. EPA, 2018c](#)).

The pathways that are included in the risk evaluation but received no additional analysis beyond the results of a screening level analysis or consideration of chemical specific properties that were presented in the problem formulation are: air (inhalation) for ecological terrestrial species, water (drinking water; wastewater; surface water and resulting exposures to ecological aquatic species); biosolids, sediments, and soils. These are included in this risk evaluation so that EPA can carry the findings forward to a risk determination.

Review and evaluation of the data available for 1-BP in this draft risk evaluation supported the preliminary conclusions as described in the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)). However, as referenced in the problem formulation (and in Appendix A.1 in this draft risk evaluation), in December 2016, EPA, through its Office of Air and Radiation (OAR), issued a draft notice of the agency's rationale for granting petitions to add 1-BP to the list of HAPs contained in section 112(b)(1) of the CAA. Under Section 112 of the CAA, EPA is required to regulate and control emissions of listed hazardous air pollutants. After further consideration of the likely future applicability of EPA regulations to 1-BP EPA has determined that the Clean Air Act adequately assesses and effectively manages risks to the general population and the environment for terrestrial receptors via the ambient air pathway. As a result, EPA has modified the conceptual models since the problem formulation. Based upon consultation within the Agency, OCSPP understands from OAR that the Agency is finishing review of comments on this draft notice and intends to finalize an action before the end of 2019. The revised conceptual models are shown below in Figure 1-3, Figure 1-4, and Figure 1-5.

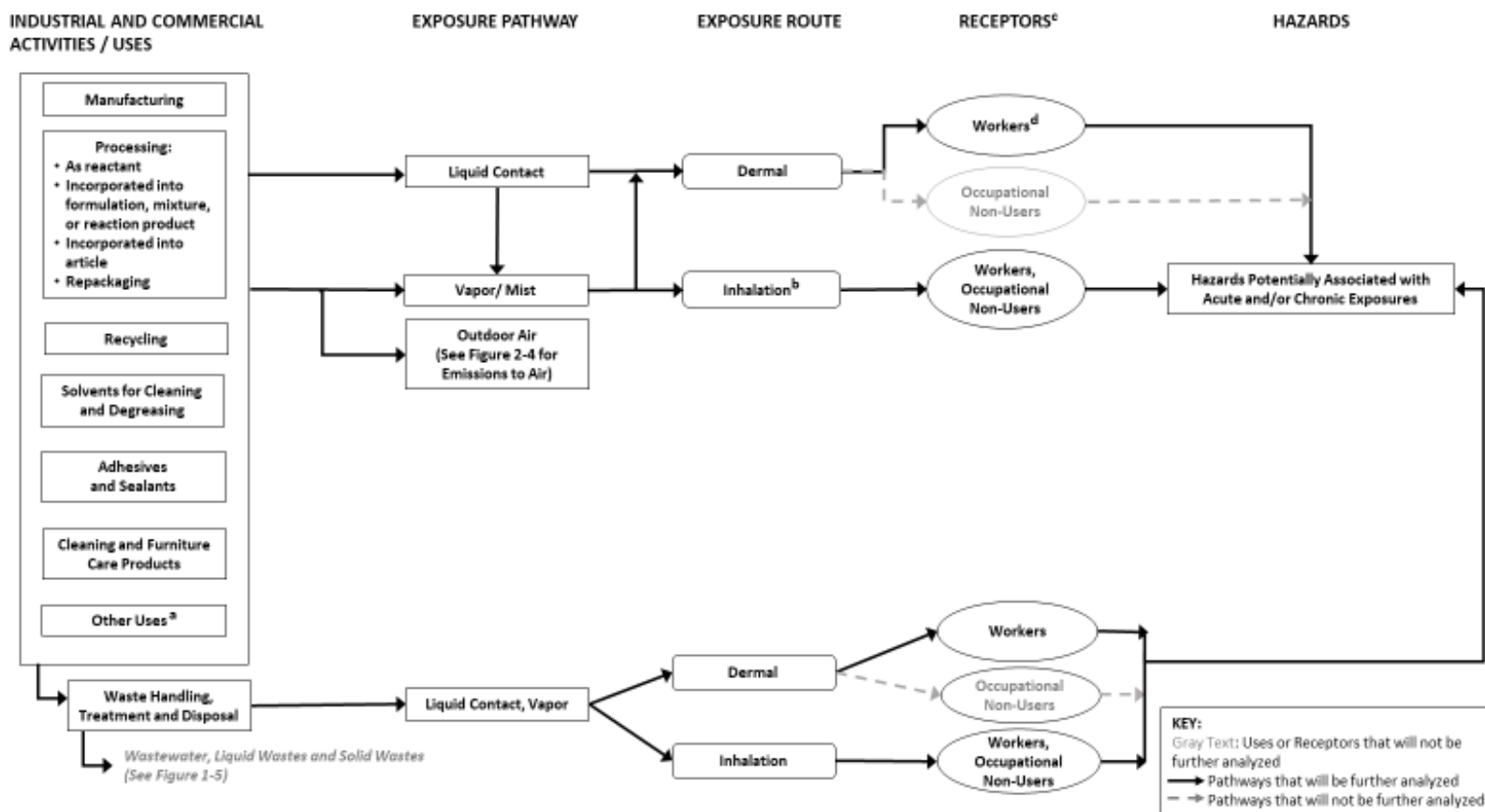


Figure 1-3. 1-BP Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of 1-BP that EPA analyzed in this draft risk evaluation.

^aSome products are used in both commercial and consumer applications. Additional uses of 1-BP are included in Table 1-4.

^bExposure may occur through mists that deposit in the upper respiratory tract, however based on physical-chemical properties, mists of 1-BP will likely be rapidly absorbed in the respiratory tract or evaporate and were considered in the inhalation exposure assessment.

^cReceptors include potentially exposed or susceptible subpopulations.

^dEPA also considered the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

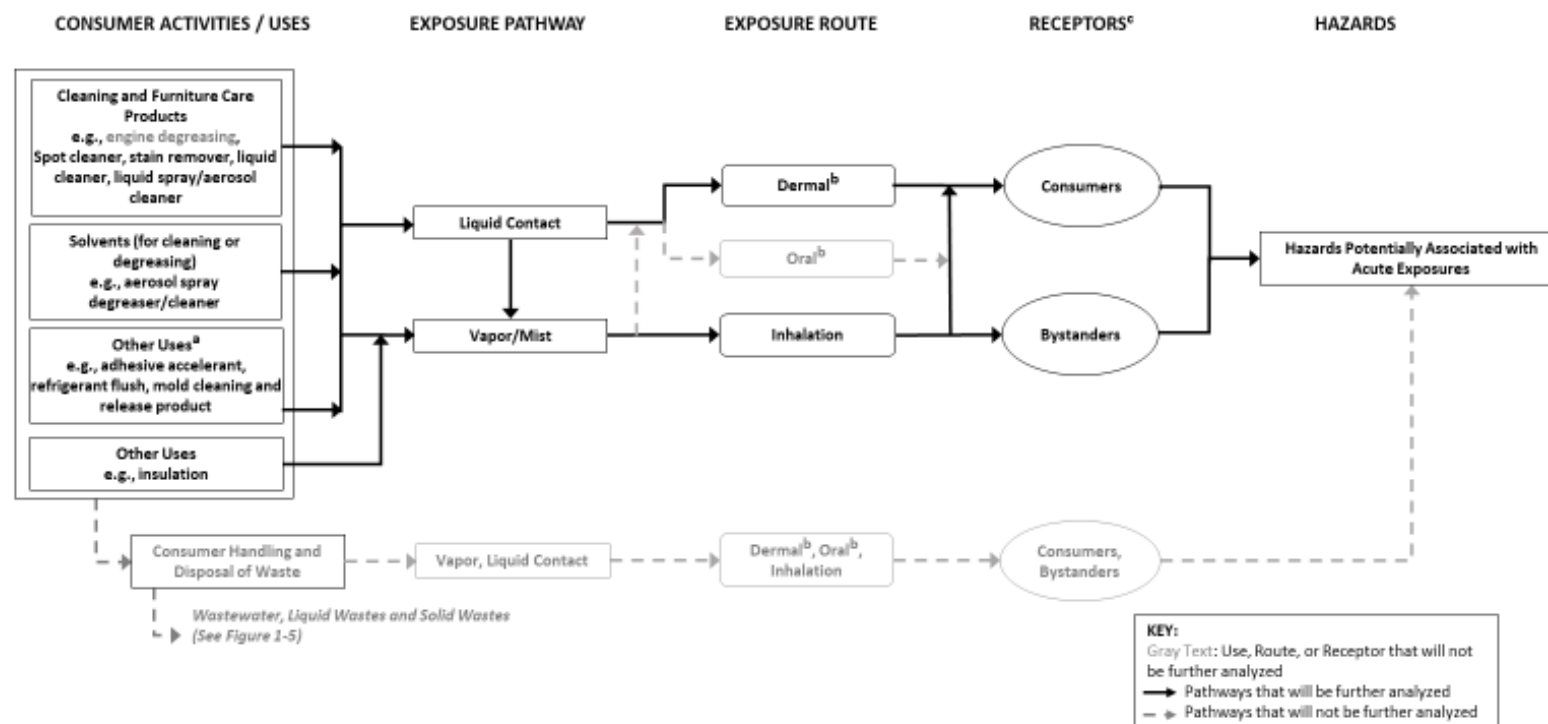


Figure 1-4. 1-BP Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of 1-BP that EPA analyzed in this draft risk evaluation.

^aSome products are used in both commercial and consumer applications. Additional uses of 1-BP are included in Table 1-4.

^b Dermal exposure may occur through skin contact with liquids; ingestion is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed.

^cReceptors include potentially exposed or susceptible subpopulations.

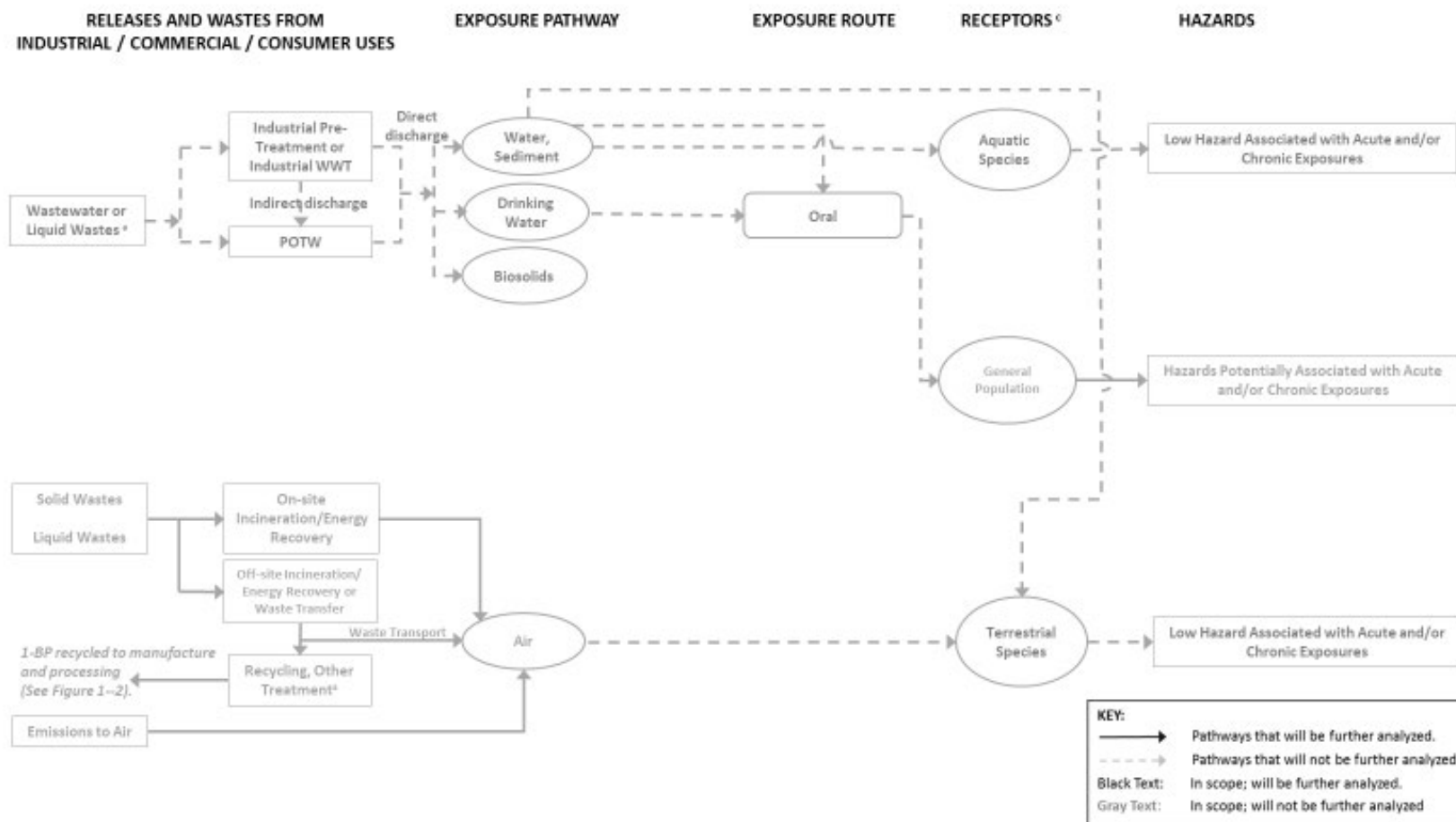


Figure 1-5. 1-BP Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes and hazards to environmental receptors from environmental releases and wastes of 1-BP that EPA analyzed in this draft risk evaluation.

^aIndustrial wastewater may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to publicly owned treatment works (POTW) (indirect discharge).

^bPresence of mist is not expected. Dermal and oral exposures are expected to be low.

^cReceptors include potentially exposed or susceptible subpopulations.

1.5 Systematic Review

TSCA requires EPA to use scientific information, technical procedures, measures, methods, protocols, methodologies and models consistent with the best available science and to base decisions under Section 6 on the weight of scientific evidence. Within the TSCA risk evaluation context, the weight of the scientific evidence is defined as “a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance” (40 C.F.R. 702.33).

To meet the TSCA science standards, EPA was guided by the systematic review process described in the *Application of Systematic Review in TSCA Risk Evaluations* document ([U.S. EPA, 2018a](#)). The process complements the risk evaluation process in that the data collection, data evaluation and data integration stages of the systematic review process are used to develop the exposure and hazard assessments based on reasonably available information. EPA defines “reasonably available information” to mean information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation (Citation to Final Rule).

EPA is implementing systematic review methods and approaches within the regulatory context of the amended TSCA. Although EPA will make an effort to adopt as many best practices as practicable from the systematic review community, EPA expects modifications to the process to ensure that the identification, screening, evaluation and integration of data and information can support timely regulatory decision making under the aggressive timelines of the statute.

1.5.1 Data and Information Collection

EPA planned and conducted a comprehensive literature search based on key words related to the different discipline-specific evidence supporting the risk evaluation (e.g., environmental fate and transport; engineering releases and occupational exposure; exposure to general population, consumers and environmental exposure; and environmental and human health hazard). EPA then developed and applied inclusion and exclusion criteria during the title and abstract screening to identify information potentially relevant for the risk evaluation process. The literature and screening strategy as specifically applied to 1-BP is described in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)), and the results of the title and abstract screening process were published in the *Strategy for Conducting Literature Searches for 1-BP (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0047](#)).

For studies determined to be on-topic after title and abstract screening, EPA conducted a full text screening to further exclude references that were not considered relevant to the risk evaluation. Screening decisions were made based on eligibility criteria documented in the form of the “populations, exposures, comparators, and outcomes (PECO) framework or a modified framework”⁵. Data sources

⁵ A PESO statement was used during the full text screening of environmental fate and transport data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. A RESO statement was used during the full text screening of the engineering and occupational exposure literature. RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes.

that met the criteria were carried forward to the data evaluation stage. The inclusion and exclusion criteria for full text screening for 1-BP are available in Appendix F of the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)).

Although EPA conducted a comprehensive search and screening process as described above, EPA made the decision to leverage the literature published in previous assessments⁶ when identifying relevant key and supporting data⁷ and information for developing the 1-BP risk evaluation. This is discussed in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). In general, many of the key and supporting data sources were identified in the comprehensive *Strategy for Conducting Literature Searches for 1-BP (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0047](#)). However, there were instances wherein EPA missed relevant references that were not captured in the initial categorization of the on-topic references. EPA found additional data and information using backward reference searching, a technique that will be included in future search strategies. This issue was discussed in Section 4 of the *Application of Systematic Review for TSCA Risk Evaluations* document ([U.S. EPA, 2018a](#)). Other relevant key and supporting references were identified through targeted supplemental searches to support the analytical approaches and methods in the 1-BP risk evaluation (e.g., to locate specific information for exposure modeling) or to identify new data and information published after the date limits of the initial search.

EPA used previous chemical assessments to quickly identify relevant key and supporting information as a pragmatic approach to expedite the quality evaluation of the data sources, but many of those data sources were already captured in the comprehensive literature as explained above. EPA also considered newer information not taken into account by previous chemical assessments as described in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). EPA then evaluated the confidence of the key and supporting data sources as well as newer information instead of evaluating the confidence of all the underlying evidence ever published on 1-BP fate and transport, environmental releases, environmental and human exposure and hazard potential. Such a comprehensive evaluation of all of the data and information published for 1-BP would be extremely labor intensive and could not be achieved under the TSCA statutory deadlines for most chemical substances especially those that have a data rich database. EPA also considered how this evaluation of the key and supporting data and newer information would change the previous conclusions presented in the previous assessments.

Using this pragmatic approach, EPA evaluated the confidence of the key and supporting data sources as well as newer information instead of evaluating the confidence of all the underlying evidence published on 1-BP's fate and transport, environmental releases, environmental and human exposure and hazards. This allowed EPA to maximize the scientific and analytical efforts of other regulatory and non-regulatory agencies by accepting for the most part the relevant scientific knowledge gathered and analyzed by others except for influential information sources that may have an impact on the weight of the scientific evidence and ultimately the risk findings. The influential information (i.e., key/supporting)

⁶ Examples of existing assessments are EPA's chemical assessments (e.g. previous work plan risk assessments, problem formulation documents), ATSDR's Toxicological Profiles, EPA's IRIS assessments and ECHA's dossiers. This is described in more detail in the *Strategy for Conducting Literature Searches for 1-BP: Supplemental File for the TSCA Scope Document* ([U.S. EPA, 2017e](#))

⁷ Key and supporting data and information are those that support key analyses, arguments, and/or conclusions in the risk evaluation.

came from a smaller pool of sources subject to the rigor of the TSCA systematic review process to ensure that the risk evaluation uses the best available science and the weight of the scientific evidence.

Figure 1-6 to Figure 1-9 depict the literature flow diagrams illustrating the results of this process for each scientific discipline-specific evidence supporting the draft risk evaluation. Each diagram provides the total number of references at the start of each systematic review stage (i.e., data search, data screening, data evaluation, data extraction/data integration) and those excluded based on criteria guiding the screening and data quality evaluation decisions.

EPA made the decision to bypass the data screening step for data sources that were highly relevant to the draft risk evaluation as described above. These data sources are depicted as “key/supporting data sources” in the literature flow diagrams. Note that the number of “key/supporting data sources” were excluded from the total count during the data screening stage and added, for the most part, to the data evaluation stages depending on the discipline-specific evidence. The exception was the engineering releases and occupational exposure data sources that were subject to a combined data extraction and evaluation step (Figure 1-7).

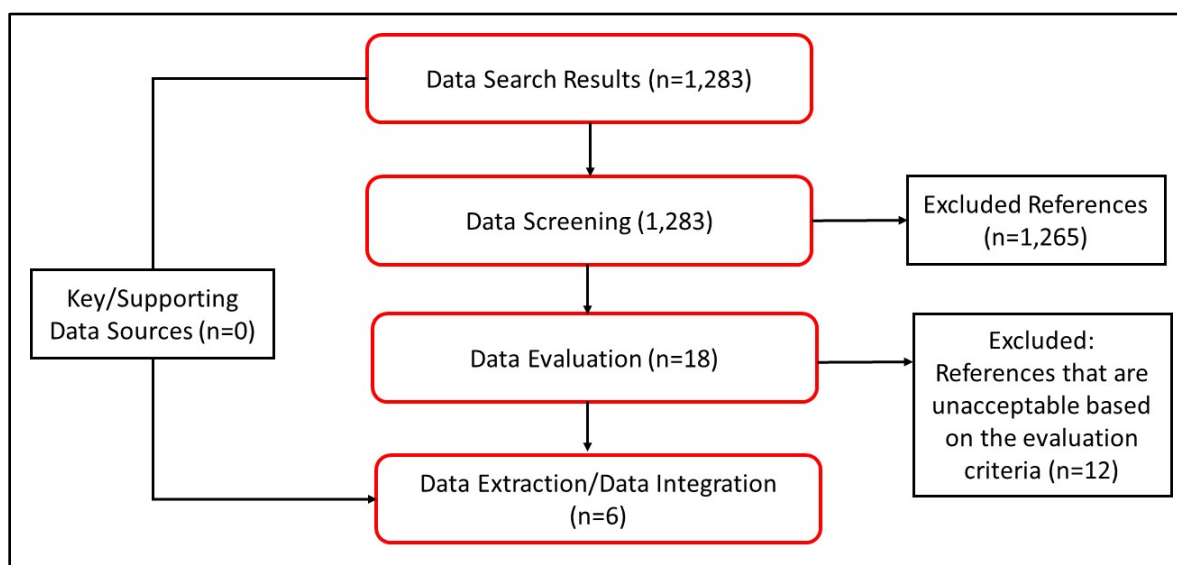


Figure 1-6. Literature Flow Diagram for Environmental Fate and Transport Data Sources

Note: Literature search results for the environmental fate and transport of 1-BP yielded 1,283 studies. Only the environmental fate and transport pathway for air was identified in the conceptual model. Other fate studies moving forward were used to inform general discussion of the environmental fate of 1-BP but were not used directly in the risk evaluation. 1,265 studies were determined to be off topic. The remaining 18 studies entered full text screening for the determination of relevance to the risk evaluation. All remaining studies were determined to be relevant and entered data evaluation. Twelve studies were deemed unacceptable based on the evaluation criteria for fate and transport studies and the remaining six studies were carried forward to data extraction.

* These are key and supporting studies from existing assessments (e.g., EPA IRIS assessments, ATSDR assessments, ECHA dossiers) that were considered highly relevant for the TSCA risk evaluation. These studies bypassed the data screening step and moved directly to the data evaluation step.

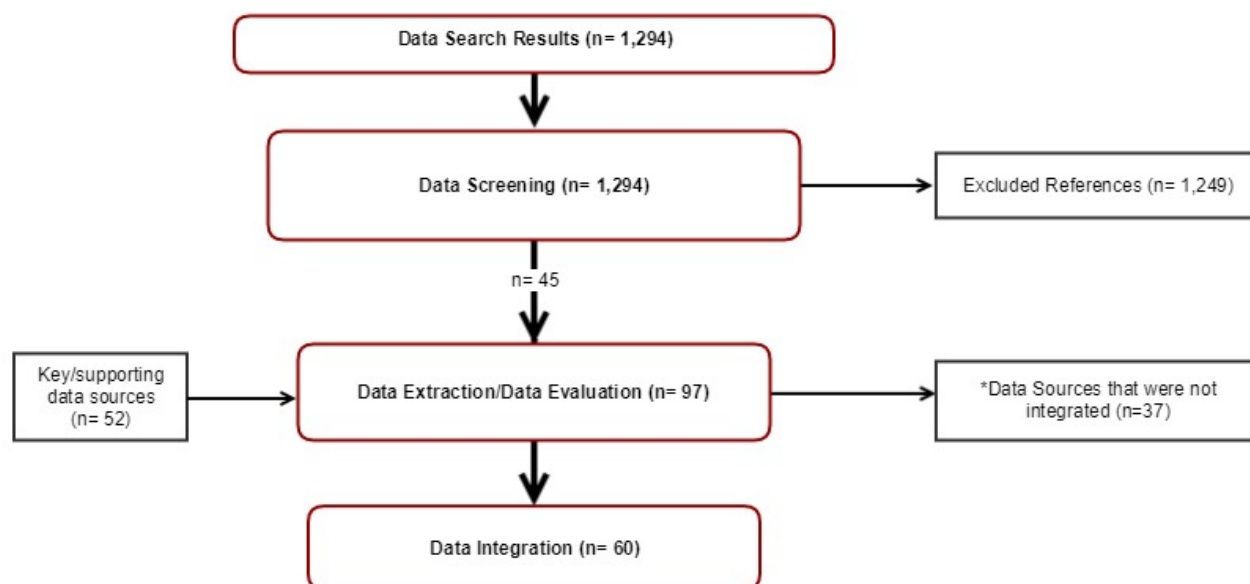


Figure 1-7. Literature Flow Diagram for Environmental Release and Occupational Exposure Data Sources

Note: Literature search results for environmental release and occupational exposure yielded 1,294 data sources. Of these data sources, 45 were determined to be relevant for the risk evaluation through the data screening process. In addition, EPA identified several data gaps and performed a supplemental, targeted search to fill these gaps (e.g. to locate information needed for exposure modeling). The supplemental search yielded 52 relevant data sources that bypassed the data screening step and were evaluated and extracted.

*The quality of data in these sources (n=37) were acceptable for risk assessment purposes, but they were ultimately excluded from further consideration based on EPA's integration approach for environmental release and occupational exposure data/information. EPA's approach uses a hierarchy of preferences that guide decisions about what types of data/information are included for further analysis, synthesis and integration into the environmental release and occupational exposure assessments. EPA prefers using data with the highest rated quality among those in the higher level of the hierarchy of preferences (i.e., data > modeling > occupational exposure limits or release limits). If warranted, EPA may use data/information of lower rated quality as supportive evidence in the environmental release and occupational exposure assessments. Sources that contain only environmental release data for the air pathway were evaluated but not integrated, because this pathway was determined to be out of scope during development of the risk evaluation.

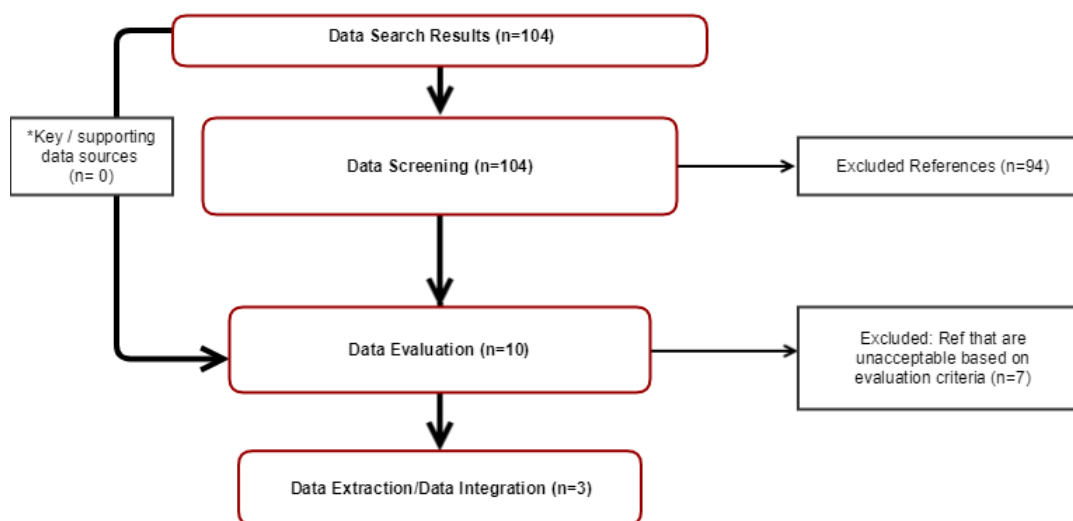


Figure 1-8. Literature Flow Diagram for Consumer and Environmental Exposure Data Sources

Note: EPA conducted a literature search to determine relevant data sources for assessing exposures for 1-BP within the scope of the risk evaluation. This search identified 104 data sources. Of these, 94 were excluded during the screening of the title, abstract, and/or full text and 10 data sources were recommended for data evaluation. Following the evaluation process, 3 references were forwarded for further extraction and data integration.

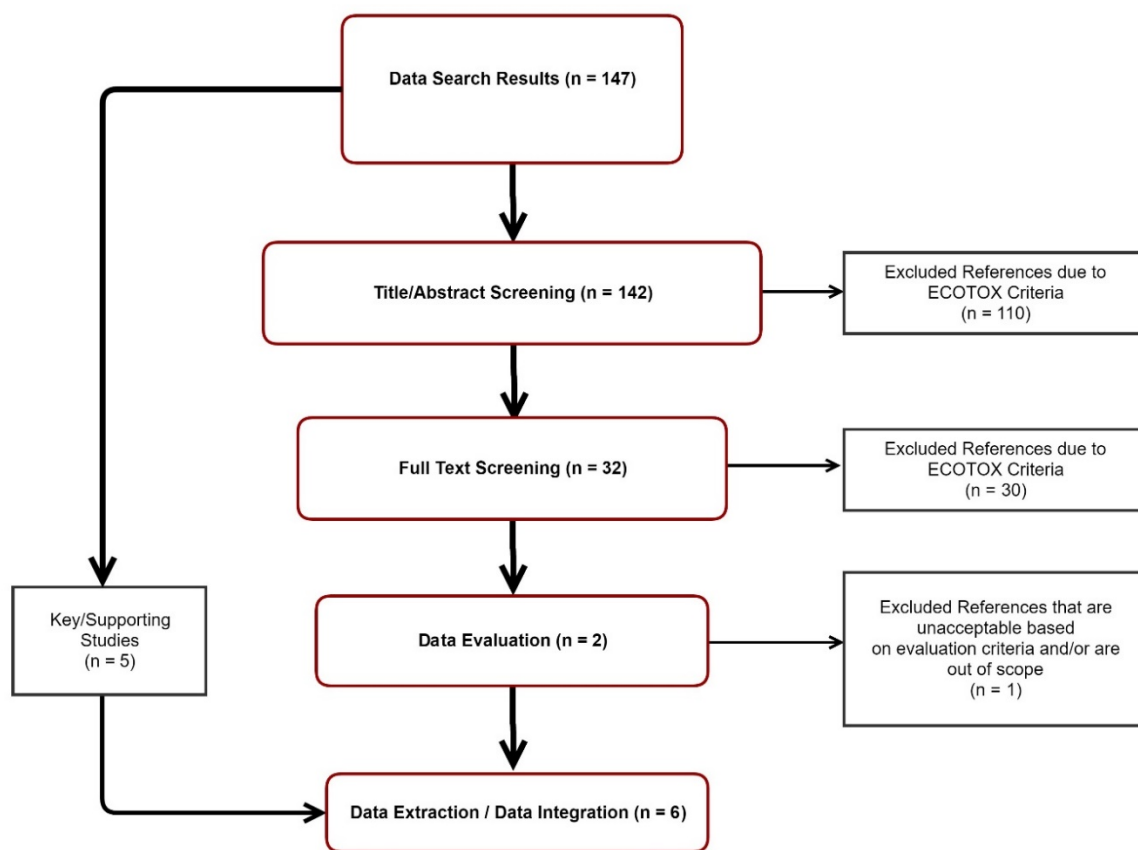


Figure 1-9. Literature Flow Diagram for Environmental Hazard Data Sources

Note: The environmental hazard data sources were identified through literature searches and screening strategies using the ECOTOXicology Knowledgebase System (ECOTOX) Standing Operating Procedures. For studies determined to be on-topic after title and abstract screening, EPA conducted a full text screening to further exclude references that were not relevant to the risk evaluation. Screening decisions were made based on eligibility criteria as documented in the ECOTOX User Guide ([U.S. EPA, 2018b](#)). Additional details can be found in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017c](#)).

The literature search process for environmental hazard data found 147 citations for 1-BP. At the title and abstract screening phase, 110 citations were excluded as off-topic using ECOTOX criteria. The remaining 32 citations underwent a more thorough full text screening using the same criteria to determine which citations should undergo data evaluation. Several studies were considered “out of scope” after the screening steps, and therefore excluded from data evaluation, due to the elimination of exposure pathways during the risk evaluation process. For data evaluation, EPA developed data quality evaluation criteria based on a combination of EPA’s ECOTOX criteria and the Criteria for Reporting and Evaluating ecotoxicity Data (CRED). There were 2 citations that went to data evaluation. Only one study was used for data extraction/data integration.

Data depicted in the “Key/Supporting Studies” represent 5 environmental hazard studies summarized in the ECHA database for 1-BP. As the full study reports for these summaries could not be obtained by EPA, these were not evaluated during the data evaluation stage. These citations were found independently from the ECOTOX process. During problem formulation, EPA made refinements to the conceptual models resulting in the elimination of the terrestrial exposure pathway from further analysis. Thus, environmental hazard data sources on terrestrial organisms were considered out of scope and excluded from data quality evaluation.

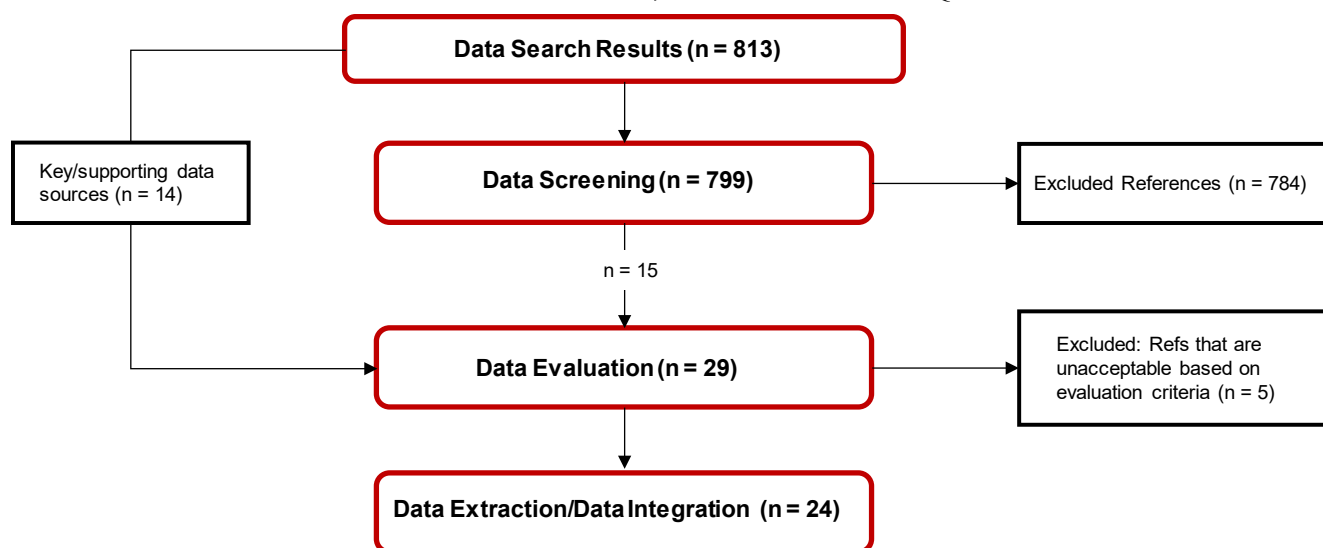


Figure 1-10. Literature Flow Diagram for Human Health Hazard Data Sources

Note: The literature search results for human health hazard of 1-BP yielded 813 studies. This included 14 key and supporting studies identified from previous EPA assessments. Of the 799 new studies screened for relevance, 784 were excluded as off topic. The remaining 15 new studies together with the 14 key and supporting studies entered data evaluation. Five studies were deemed unacceptable based on the evaluation criteria for human health hazard data sources and the remaining 24 studies were carried forward to data extraction/data integration. Additional details can be found in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)).

1.5.2 Data Evaluation

During the data evaluation stage, EPA assesses the quality of the data sources using the evaluation strategies and criteria described in *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)). For the data sources that passed full-text screening, EPA evaluated their quality and each data source received an overall confidence of high, medium, low or unacceptable.

The results of these data quality evaluations are provided in Sections 2.1 (Fate and Transport), 2.2 (Environmental Exposures), 2.3 (Human Exposures), 3.1 (Environmental Hazards) and 3.2 (Human Health Hazards). Additional information is provided in the appendices of the main document.

Supplemental files⁸ also provide details of the data evaluations including individual metric scores and the overall study score for each data source.

1.5.3 Data Integration

Data integration includes analysis, synthesis, and integration of information for the risk evaluation. During data integration, EPA considers quality, consistency, relevancy, coherence and biological plausibility to make final conclusions regarding the weight of the scientific evidence. As stated in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a), data integration involves transparently discussing the significant issues, strengths, and limitations as well as the uncertainties of the reasonably available information and the major points of interpretation (U.S. EPA, 2018d).

EPA used previous assessments to identify key and supporting information and then analyzed and synthesized available lines of evidence regarding 1-BP's chemical properties, environmental fate and transport properties, potential for exposure and hazard. EPA's analysis also considered recent data sources that were not considered in the previous assessments (Section 1.5.1) as well as reasonably available information on potentially exposed or susceptible subpopulations.

The exposures and hazards sections describe EPA's analysis of the influential information (i.e., key and supporting data) that were found acceptable based on the data quality reviews as well as discussion of other scientific knowledge using the approach described in Section 1.5.1. The exposure section also describes whether aggregate or sentinel exposures to a chemical substance were considered under the conditions of use within the scope of the risk evaluation, and the basis for that consideration.

⁸ The supplemental files accompanying the risk evaluation are listed in Appendix B.

- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Updates to the Data Quality Criteria for Epidemiological Studies. (EPA, 2019r).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies. (EPA, 2019m).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Consumer Exposure (EPA, 2019k).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data. (EPA, 2019n).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data for Common Sources. (EPA, 2019o).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies. (EPA, 2019l).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiologic Studies. (EPA, 2019q).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies. EPA-HQ-OPPT-2019-0235 (EPA, 2019p).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction Tables for Environmental Fate and Transport Studies. (EPA, 2019j).
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction for Consumer Exposure (EPA, 2019i).

2 EXPOSURES

This section describes EPA's approach to assessing environmental and human exposures. First, the fate and transport of 1-BP in the environment is characterized. Then, releases of 1-BP into the environment are assessed. Last, this information is integrated into an assessment of occupational, consumer, and environmental exposures for 1-BP. For all exposure-related disciplines, EPA screened, evaluated, extracted, and integrated reasonably available empirical data. In addition, EPA used models to estimate exposures. Both empirical data and modeled estimates were considered when selecting values for use in the exposure assessment.

Exposure equations and selected values used in the exposure assessment are presented in the following sections. More specific information is provided in Supplementary Files (see Appendix B).

Following the inclusion of 1-BP on EPA's workplan list in 2012, EPA published a 2016 Draft Risk Assessment ([U.S. EPA, 2016d](#)) prior to passage of the Lautenberg Act amendments to TSCA. Since that time, EPA has published a Scope of the Risk Evaluation for 1-BP in 2017 ([Scope Document; EPA-HQ-OPPT-2016-0741-0049](#)), and Problem Formulation in 2018 ([U.S. EPA, 2018c](#)). EPA has incorporated the following refinements based on public comments and review of data since work began on 1-BP:

- Refined parameters for occupational exposure models;
- Expanded consumer uses evaluated for inhalation exposure
- Included evaluation for dermal exposure from industrial, commercial, and consumer use scenarios

2.1 Fate and Transport

The environmental fate studies considered for this assessment are summarized in Table 2-1 and were supplemented by an updated literature search following problem formulation.

2.1.1 Fate and Transport Approach and Methodology

EPA also used the previous 1-BP assessment to identify key and supporting fate information that would be influential in the risk evaluation, as described in Section 1.5.1. For instance, EPA assessed the quality of a study on the ready biodegradability of 1-BP ([Sakuratani et al., 2005](#)) based on the data quality criteria described in the Application of Systematic Review in TSCA Risk Evaluations ([U.S. EPA, 2018a](#)) and the study was rated 'medium' confidence. Other fate estimates were based on modeling results from EPI Suite™ ([U.S. EPA, 2012b](#)), a predictive tool for physical-chemical and environmental fate properties. The data evaluation tables describing their review can be found in the supplemental document, Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies ([EPA, 2019m](#)).

The 1-BP environmental fate characteristics and physical-chemical properties used in fate assessment are presented in Table 2-1 and Table 1-1, respectively. EPA used EPI Suite™ estimations and reasonably available fate data to characterize the environmental fate and transport of 1-BP. As part of problem formulation, EPA also analyzed the air, water, sediment, land application and biosolids pathways and determined no further analysis would be conducted on these pathways. The results of the analyses are described in the problem formulation in June 2018 ([U.S. EPA, 2018c](#)) and presented again in Appendix C. Please note that this section and Appendix C may also cite other data sources as part of the reasonably available evidence on the fate and transport properties of 1-BP. EPA subjected these other data sources to the later phases of the systematic review process (i.e., data evaluation and integration).

2.1.2 Summary of Fate and Transport

1-BP is a volatile liquid with high vapor pressure, moderate water solubility, and high mobility in soil. It is expected to exhibit low adsorption to soils and thus can migrate rapidly through soil to groundwater. 1-BP is slowly degraded by hydroxy radical oxidation when released to the atmosphere (half-life 9-12 days). Based on this estimated half-life in air, long range transport via the atmosphere is possible (see Appendix C). Volatilization and microbial degradation influence the fate of 1-BP when released to water, sediment, or soil. Biotic and abiotic degradation rates ranging from days to months have been reported ([U.S. EPA, 2012c](#); [Sakuratani et al., 2005](#); [Mabey and Mill, 1978](#)).

1-BP does not meet criteria to be classified as persistent or bioaccumulative ([Federal Register, 1999](#)). Biotic and abiotic degradation studies have not shown this substance to be persistent (overall environmental half-life of less than two months). No measured bioconcentration studies for 1-BP are available. An estimated bioaccumulation factor of 12 ([U.S. EPA, 2012b](#)) suggests that bioconcentration and bioaccumulation in aquatic organisms are low (i.e., bioconcentration/bioaccumulation factors of less than 1000).

Table 2-1. Summary of Environmental Fate and Transport Properties

Property or Endpoint	Value ^a	References	Study Quality
Direct photodegradation	Not expected to undergo direct photolysis	HSDB (2017)	High
Indirect photodegradation	9-12 days (estimated for atmospheric degradation)	EPI Suite Version 4.10 (U.S. EPA, 2012b)	High
Hydrolysis half-life	26 days	U.S. EPA (2016d) (Mabey and Mill, 1978)	Low
Biodegradation	70% in 28 days (OECD 301C)	(Sakuratani et al., 2005)	Medium
Bioconcentration factor (BCF)	11 (estimated)	EPI Suite Version 4.10 (U.S. EPA, 2012b)	High
Bioaccumulation factor (BAF)	12 (estimated)	EPI Suite Version 4.10 (U.S. EPA, 2012b)	High
Organic carbon:water partition coefficient (Log K _{oc})	1.6 (estimated)	EPI Suite Version 4.10 (U.S. EPA, 2012b)	High
^a Measured unless otherwise noted			

2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport

The EPI Suite™ model (Version 4.1) ([U.S. EPA, 2012b](#)) was used to estimate several environmental fate properties for 1-BP in the absence of data (see Table 2-1). A full discussion of the performance of the individual property estimation methods used in EPI Suite is available in the EPI Suite™ help files. No data on the bioconcentration or bioaccumulation potential of 1-BP was found. These properties were used to inform decisions on whether 1-BP has the potential to build up in aquatic and terrestrial species via exposure to water and diet and whether fish ingestion pathways of exposure should be included in

the risk evaluation. EPA compared measured BCF values for a series of halogenated ethanes and propanes and EPI Suite™ estimated BCF values. The largest observed error for BCF estimation was 0.56 log units and none of the chemicals had measured Log BCF values greater than 1.6. Thus, even if the estimate for 1-BP was subject to the maximum observed error its log BCF would be expected to fall in the range of 0.5 to 1.5, indicating low bioconcentration potential (BCF <1000).

2.2 Environmental Exposures

2.2.1 Environmental Exposures Approach and Methodology

The manufacturing, processing, use and disposal of 1-BP can result in releases to the environment. Environmental exposures via air, water, sediment, biosolids and soil are all discussed in the environmental risk characterization section (Section 4.1). The predominance of these exposures is via the air pathway as reported releases to water was limited to 5 pounds in 2017 (See Appendix G). EPA did not conduct additional analysis of exposures to aquatic or terrestrial exposures beyond what was presented in the 2018 Problem Formulation ([U.S. EPA, 2018c](#)).

As described in the problem formulation ([U.S. EPA, 2018c](#)), an aquatic exposure assessment was conducted using 2016 TRI release information ([U.S. EPA, 2017g](#)) to model predicted surface water concentrations near discharging facilities. To examine whether near-facility surface water concentrations could approach aquatic concentrations of concern for 1-BP, EPA employed a conservative approach, using available modeling tools and data to estimate near-facility surface water concentrations resulting from reported releases of 1-BP to surface water. High-end surface water concentrations (i.e., those obtained assuming low receiving water body stream flows) from all [E-FAST 2014](#) runs ranged from 0.19 µg/L to 77.9 µg/L. The E-FAST results were compared to the acute and chronic aquatic concentrations of concern of 4,860 µg/L and 243 µg/L, respectively (see Table 4-1). This aquatic exposure analysis and additional details about the approach and results are presented in Appendix G. The analysis and determination of risk are presented in the risk characterization and risk determination sections, respectively.

2.3 Human Exposure Assessment

2.3.1 Occupational Exposures

EPA assessed occupational exposures following the analysis plan published in the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)). Specific assessment methodology is described in further detail below for each type of assessment. Additional details of EPA's occupational exposure assessment can be found in the *1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)). Table 2-2 presents a crosswalk of the industrial and commercial conditions of use (see Table 1-4) and the section of the risk evaluation in which occupational exposure for that use is assessed.

For the purpose of this assessment, EPA assumes workers and occupational non-users (ONU) are men and women of reproductive age (16 or older), including adolescents (16 to <21 years old). EPA also considers exposure to children who may be present at the workplace, such as small family-owned dry cleaners, an occupational exposure scenario recommended for assessment from the peer review of the 2016 Draft Risk Assessment of 1-BP ([U.S. EPA, 2016d](#)).

Table 2-2. Crosswalk of Subcategories of Use Listed in the Problem Formulation Document to Occupational Conditions of Use Assessed in the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	Assessed Condition of Use
Manufacture	Domestic manufacture	Domestic manufacture	Section 2.3.1.5 – Manufacture
	Import	Import	Section 2.3.1.6 – Import
Processing	Processing as a reactant	Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing	Section 2.3.1.7 – Processing as a Reactant
Processing	Processing - incorporating into formulation, mixture or reaction product	Solvents for cleaning or degreasing in manufacturing of: - all other chemical product and preparation - computer and electronic product - electrical equipment, appliance and component - soap, cleaning compound and toilet preparation - services	Section 2.3.1.8 – Processing – Incorporation into Formulation, Mixture, or Reaction Product
	Processing - incorporating into articles	Solvents (which become part of product formulation or mixture) in construction	Section 2.3.1.9 – Processing – Incorporation into Articles
	Repackaging	Solvent for cleaning or degreasing in all other basic organic chemical manufacturing	Section 2.3.1.10 – Repackaging
	Recycling	Recycling	Section 2.3.1.20 – Disposal, Recycling
Distribution in commerce	Distribution	Distribution	Not assessed as a separate operation; exposures/releases from distribution are considered within each condition of use.

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Life Cycle Stage	Category ^a	Subcategory ^b	Assessed Condition of Use
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (e.g., open-top, closed-loop)	Section 2.3.1.11 – Batch Vapor Degreaser (Open-Top) Section 2.3.1.12– Batch Vapor Degreaser (Closed-Loop)
		In-line vapor degreaser (e.g., conveyORIZED, web cleaner)	Section 2.3.1.13 – In-line Vapor Degreaser
		Cold cleaner	Section 2.4.1.13 – Cold Cleaner
		Aerosol spray degreaser/cleaner	Section 2.3.1.15 – Aerosol Spray Degreaser/Cleaner
	Adhesives and sealants	Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses	Section 2.3.1.18 – Adhesive Chemicals (Spray Adhesives)
	Cleaning and furniture care products	Dry cleaning solvent	Section 2.3.1.16 – Dry Cleaning
		Spot cleaner, stain remover	Section 2.3.1.17 – Spot Cleaner, Stain Remover
		Liquid cleaner (e.g., coin and scissor cleaner)	Section 2.3.1.19 – Other Uses
		Liquid spray/aerosol cleaner	Section 2.3.1.19 – Other Uses
	Industrial/ commercial use (continued)	Other uses	Arts, crafts and hobby materials - adhesive accelerant
Automotive care products - engine degreaser, brake cleaner			Section 2.3.1.15 – Aerosol Spray Degreaser/Cleaner
Anti-adhesive agents - mold cleaning and release product			Section 2.3.1.19 – Other Uses
Building/construction materials not covered elsewhere - insulation			
Electronic and electronic products and metal products			
Functional fluids (closed systems) - refrigerant			
Functional fluids (open system) - cutting oils			
Other - asphalt extraction			
Other - Laboratory chemicals			Section 2.3.1.19 – Other Uses
Temperature Indicator – Coatings			

Life Cycle Stage	Category ^a	Subcategory ^b	Assessed Condition of Use
Disposal (Manufacturing, Processing, Use)	Disposal	Municipal waste incinerator Off-site transfer	Section 2.3.1.20 – Disposal, Recycling
		Municipal waste incinerator	
		Off-site waste transfer	

^a These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of 1-BP in industrial and/or commercial settings.

^b These subcategories reflect more specific uses of 1-BP.

2.3.1.1 Number of Sites and Workers Approach and Methodology

Where available, EPA determined the number of sites and workers using data reported under the Chemical Data Reporting (CDR) Rule. The CDR Rule, issued under the TSCA, requires manufacturers and importers to report certain information on the chemicals they produce domestically or import into the United States. For the 2016 CDR cycle, manufacturers and importers of chemicals listed on the TSCA inventory were required to report if their production volume exceeded 25,000 pounds at a single site during any of the calendar years 2012, 2013, 2014 or 2015.

For conditions of use where CDR data are insufficient, EPA determined the number of sites that manufacture, process, and use 1-BP using readily available market data and data from Section 3 of the Toxics Release Inventory (TRI), “Activities and Uses of the Toxic Chemical at the Facility.” In addition, EPA determined the number of workers by analyzing Bureau of Labor Statistics (BLS) and U.S. Census data using the methodology described in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)).

Table 2-3 presents the confidence rating of data that EPA used to estimate number of sites and workers.

Table 2-3. Data Evaluation of Sources Containing General Facility Estimates

Source Reference	Data Type	Confidence Rating	Condition of Use
(U.S. EPA, 2017a)	Number of Sites and Workers	High	Manufacture, Import, Processing as a Reactant, Processing – Incorporation into Formulation
(U.S. BLS, 2016)	Number of Workers	High	Processing – Incorporation into Articles, all conditions of use involving industrial and commercial uses of 1-BP, Disposal
(Bureau, 2015)	Number of Workers	High	
(IRTA, 2016)	Number of Sites	Medium	Batch Vapor Degreaser (Closed-Loop), In-line Vapor Degreaser
(U.S. EPA, 2013c)	Number of Sites	Medium	Aerosol Spray Degreaser/Cleaner
(Enviro Tech International, 2017)	Number of Sites	High	Dry Cleaning
(CDC, 2016)	Number of Sites	Medium	Batch Vapor Degreaser (Open-Top), Adhesive Chemicals (Spray Adhesive)
(U.S. EPA, 2017b, 2016c)	Number of Sites	Medium	Disposal

2.3.1.2 Inhalation Exposures Approach and Methodology

To assess inhalation exposure, EPA reviewed reasonably available exposure monitoring data and mapped them to specific conditions of use. Monitoring data used in the occupational exposure assessment include data collected by government agencies such as OSHA and NIOSH, and data found in published literature. For each exposure scenario and worker job category (“worker” or “occupational non-user”), where available, EPA provided results representative of *central tendency* and *high-end* exposure levels. For datasets with six or more data points, central tendency and high-end exposures were estimated using the 50th and 95th percentile value from the observed dataset, respectively. For datasets with three to five data points, the central tendency and high-end exposures were estimated using the median and maximum values.⁹ For datasets with two data points, the midpoint and the maximum value were presented. Finally, datasets with only one data point were presented as-is. A dataset comprises the combined exposure monitoring data from all studies applicable to that condition of use.

EPA assumes workers are those who directly handle 1-BP at the facility. Occupational non-users are those who do not directly handle 1-BP but perform work in an area where the chemical is present.

For exposure assessment, personal breathing zone (PBZ) monitoring data were used to determine the time-weighted average (TWA) exposure concentration. TWA exposure concentrations are then used to calculate the Acute Concentration (AC), Average Daily Concentrations (ADC) and Lifetime Average Daily Concentration (LADC) using the approach and equations described in the *Supplemental Information on Occupational Exposure Assessment* (EPA, 2019g). Table 2-4 presents the confidence rating of monitoring data that EPA used to assess occupational exposures. EPA evaluated monitoring data using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). All exposure monitoring data, except for data from one source, have a “high” confidence rating.

For several conditions of use, EPA modeled exposure in occupational settings. The models were used to either supplement existing exposure monitoring data or to provide exposure estimates where measured data are unavailable. For example, EPA used the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* to estimate worker exposure during container and truck unloading activities that occur at industrial facilities. EPA also refined its exposure models from the 2016 draft Risk Assessment to address peer review comments.

Table 2-4. Data Evaluation of Sources Containing Occupational Exposure Data

Source Reference	Data Type	Confidence Rating	Condition of Use
(OSHA, 2013a)	PBZ Monitoring	High	Manufacture
(Hanley et al., 2010)	PBZ Monitoring	High	Processing -- Incorporation into Formulation
(Reh and Nemhauser, 2001)	PBZ Monitoring	High	Batch Vapor Degreaser
(OSHA, 2013b)	PBZ Monitoring	High	Batch Vapor Degreaser, Spot Cleaner, Adhesive Chemicals (Spray Adhesive), Cold Cleaner
(Osha, 2019)	PBZ Monitoring	High	Batch Vapor Degreaser, Spot Cleaner

⁹ If the median value is not available, EPA may use the mean (arithmetic or geometric), mode, or midpoint values of a distribution to represent the central tendency scenario.

Source Reference	Data Type	Confidence Rating	Condition of Use
(U.S. EPA, 2006b)	PBZ Monitoring	Medium	Batch Vapor Degreaser, Aerosol Spray Degreaser/Cleaner
(Eisenberg and Ramsey, 2010)	PBZ Monitoring	High	Dry Cleaning
(Blando et al., 2010)	PBZ Monitoring	High	Dry Cleaning
(NIOSH, 2002b)	PBZ Monitoring	High	Adhesive Chemicals (Spray Adhesive)
(Reh et al., 2002)	PBZ Monitoring	High	Adhesive Chemicals (Spray Adhesive)
(NIOSH, 2003b)	PBZ Monitoring	High	Adhesive Chemicals (Spray Adhesive)

2.3.1.3 Consideration of Engineering Control and Personal Protective Equipment

OSHA recommends employers utilize the hierarchy of controls for reducing or removing hazardous exposures. The most effective controls are elimination, substitution, or engineering controls. Example engineering controls include process enclosure, local exhaust ventilation (LEV), and general dilution ventilation. Where available, the occupational exposure assessment presents information on the specific controls employed. For most conditions of use, however, EPA does not have information on the effectiveness and prevalence of engineering controls.

Personal protective equipment, such as respirators and gloves, is the last means of worker protection in the hierarchy of controls and should only be considered when process design and engineering controls cannot reduce workplace exposure to an acceptable level. Few literature sources indicate the use of respirators in 1-BP conditions of use, and the inhalation exposure estimates do not account for respirators. The impact of potential respirator use on worker exposure is addressed in Section 4.2, Human Health Risk.

OSHA's Respiratory Protection Standard (29 CFR 1910.134) provides a summary of respirator types by their assigned protection factor (APF). OSHA defines APF to mean: the workplace level of respiratory protection that a respirator or class of respirators is expected to provide to employees when the employer implements a continuing, effective respiratory protection program according to the requirements of OSHA's Respiratory Protection Standard. If respirators are necessary in atmospheres that are not immediately dangerous to life or health, workers must use NIOSH-certified air-purifying respirators or NIOSH-approved supplied-air respirators with the appropriate APF. Respirators that meet these criteria include air-purifying respirators with organic vapor cartridges. Respirators must meet or exceed the required level of protection listed in Table 2-5. Based on the APF, inhalation exposures may be reduced by a factor of 5 to 10,000, if respirators are properly worn and fitted.

Table 2-5. Assigned Protection Factors for Respirators in OSHA Standard 29 CFR 1910.134

Type of Respirator	Quarter Mask	Half Mask	Full Facepiece	Helmet/Hood	Loose-fitting Facepiece
1. Air-Purifying Respirator	5	10	50	-	-
2. Power Air-Purifying Respirator (PAPR)	-	50	1,000	25/1,000	25
3. Supplied-Air Respirator (SAR) or Airline Respirator	-	-	-	-	-
• Demand mode	-	10	50	-	-
• Continuous flow mode	-	50	1,000	25/1,000	25

Type of Respirator	Quarter Mask	Half Mask	Full Facepiece	Helmet/Hood	Loose-fitting Facepiece
Pressure-demand or other positive-pressure mode	-	50	1,000	-	-
4. Self-Contained Breathing Apparatus (SCBA)	-	-	-	-	-
Demand mode	-	10	50	50	-
Pressure-demand or other positive-pressure mode (e.g., open/closed circuit)	-	-	10,000	10,000	-

Source: 29 CFR 1910.134(d)(3)(i)(A)

2.3.1.4 Dermal Exposures Approach and Methodology

Although the inhalation pathway is expected to be the primary exposure for 1-BP, dermal exposure may be important in contributing to the overall exposure. During the 2016 peer review of the draft 1-BP Risk Assessment, peer reviewers recommended that quantitative estimates of dermal exposure be included to address this pathway. Peer reviewers also noted the possible occupational exposure scenarios where dermal contact could be occluded.

EPA assessed dermal exposure to workers using the *Dermal Exposure to Volatile Liquids Model* (modified version of the peer reviewed *EPA/OPPT 2-Hand Dermal Exposure to Liquids Model*) ([U.S. EPA, 2013a](#)). The model estimates 0.16 percent dermal absorption for non-occluded exposures based on a 2011 *in vitro* dermal penetration study of 1-BP conducted by Frasch et al. ([2011](#)). The report presents several occupational dermal exposure scenarios, accounting for the potential for evaporation and glove use. The dermal exposure assessment is described in more detail in Section 2.3.1.22.

2.3.1.5 Manufacture

Process Descriptions

1-BP is produced by reacting n-propyl alcohol with hydrogen bromide and then removing the excess water that forms in the process ([NTP, 2013b](#)). The reaction product may then be distilled, neutralized with sodium hydrogen carbonate, stored, and packaged ([Ichihara et al., 2004a](#)). The purity of the final product may range from 96 percent ([Li et al., 2010](#)) to over 99.9 percent ([OSHA, 2013a](#)).

The manufacturing process may be either batch or continuous. Based on a site visit in 2013 conducted by PEC, Icarus Environmental, and OSHA representatives, one major U.S. manufacturer of 1-BP operates a continuous, closed production process for 24 hours per day and 7 days per week ([OSHA, 2013a](#)).

Number of Sites and Potentially Exposed Workers

The CDR Rule requires manufacturers and importers to provide EPA information on the chemicals they produce domestically or import into the United States. Based on CDR data, EPA identified two domestic 1-BP manufacturers, Albemarle Corporation and Chemtura Corporation, for calendar year 2015. Table 2-6 below summarizes the number of workers reasonably likely to be exposed to 1-BP at the two manufacturing facilities, as reported in the 2016 CDR ([U.S. EPA, 2017a](#)). The term “reasonably likely to be exposed,” for the purpose of CDR, means “an exposure to a chemical substance which, under foreseeable conditions of manufacture, processing, distribution in commerce, or use of the chemical

substance, is more likely to occur than not to occur.” These exposures would include activities such as charging reactor vessels, drumming, bulk loading, cleaning equipment, maintenance operations, materials handling and transfer, and analytical operations. The estimate also includes persons whose employment requires them to pass through areas where chemical substances are manufactured, processed, or used, i.e., those who may be considered “occupational non-users”, such as production workers, foremen, process engineers, and plant managers. There are 35 to 73 potentially exposed workers and ONUs at the two manufacturing sites.

Table 2-6. Number of Potentially Exposed Workers and Occupational Non-Users at Manufacturing Facilities

Company	Facility	Facility Location		Number of Workers ^a Likely to be Exposed	Basis for Manufacturing Determination
		City	State		
Albemarle Corporation	Albemarle Corp South Plant	Magnolia	AR	25 – <50	2016 CDR (Sec. 2.B.4)
Chemtura Corporation	Great Lakes Chemical - Central	El Dorado	AR	10 – <25	2016 CDR (Sec. 2.B.4)
Total				35 – 73	

Source: ([U.S. EPA, 2017a](#))

^a May include both workers and ONUs

Assessment of Inhalation Exposure Based on Monitoring Data

1-BP exposure monitoring data were identified for one manufacturing facility in the U.S. At this facility, workers were observed to spend most of their time in a control room monitoring the production process via a computerized system. QC samples are taken and analyzed inside a laboratory fume hood, and in some cases, in a nitrogen purge dry box. Product loading is controlled using a computerized system; smart-hoses and a vent line are used to minimize leaks and to capture vapors generated during loading. At this facility, employees wear safety glasses, nitrile gloves¹⁰, and steel toe shoes when performing product sampling and laboratory analysis. In addition, operators wear a full chemical suit¹¹ during truck loading, including a full-face respirator equipped with organic vapor cartridges ([OSHA, 2013a](#)).

Table 2-7 presents the exposure levels from an OSHA site visit to this facility. The purpose of the site visit was to collect information on 1-BP production processes, engineering controls, and potential exposures. OSHA performed personal sampling on one operator during the day shift, one operator during the night shift, and one laboratory technician; the company also collected simultaneous samples for result comparison and verification. EPA used the TWA results to assess worker exposures; EPA assumed the TWA exposures approximate 8-hr TWA because actual sampling time ranged from 429 to 449 minutes (7.2 to 7.5 hour). In the table, the high-end exposure value represents the maximum TWA exposure among the three workers sampled, and the central tendency value represents the median exposure. Exposure was highest during truck loading, which occurs once every 24 hours. The operator wore a full-face respirator during this activity ([OSHA, 2013a](#)).

For comparison purpose, Ichihara et al. ([Ichihara et al., 2004a](#)) noted that none of the workers surveyed at a Chinese facility wore PPE. These workers manually add chemicals into reaction pots, pour final

¹⁰ Nitril is not a recommended glove material for protection against 1-BP according to the OSHA/NIOSH Hazard Alert ([OSHA, 2013d](#)).

¹¹ Chemical resistant pants and jacket with hood, steel-toed rubber boots, chemical resistant gloves, and full-face respirator equipped with organic vapor cartridges.

product into drums, and adjust the final drum volume with hand scoops (Li et al., 2010). In comparison to the U.S. facility, exposure levels in China are more than two orders of magnitude higher, and the authors/investigators themselves complained of nasal and conjunctival irritation following visits to the facility. Exposure concentration was highest when workers transferred produced solvents into containers; in many cases, the TWA exposure concentration for workers exceeded 100 ppm. While the work practices at this facility may not be representative of U.S. operations, these data may be indicative of potential worst-case exposure levels in the absence of adequate engineering controls and workplace protection.

Table 2-7. Summary of 8-hr 1-BP TWA Exposures (AC, ADC and LADC) for Manufacture Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Data Points	Confidence Rating of Air Concentration Data
	Central tendency (Median)	High-end (Max)	Central tendency (Median)	High-end (Max)		
Worker ^a	0.09	0.27	0.04	0.14	3	High

Source: (OSHA, 2013a)

AC = Acute Concentration; ADC = Average Daily Concentration and LADC = Lifetime Average Daily Concentration.

a – Because OSHA and the company took simultaneous samples, two sets of exposure monitoring data are available for each worker. For the same worker, EPA used the higher of the two TWA exposure results. For the lab technician and the day shift operator, EPA used company results (OSHA experienced a pump malfunction while performing sampling on the lab technician, and OSHA results for the day shift operator were below the reporting limit of 0.007 ppm of OSHA’s sampling and analytical method PV2061). For the night shift operator, EPA used OSHA results. The workers worked 12-hour shifts but were not exposed to 1-BP for the entire shift; exposure data are available as 8-hr TWA exposures.

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data collected at workplaces directly applicable to this condition of use, and the data were determined to have a “high” confidence rating through EPA’s systematic review process. Specifically, the data were determined to be highly reliable, representative in geographic scope, and reflective of current operations. The source also provides complete metadata including sample type, sample duration, and exposure frequency.

The three data points come from a detailed site visit report and consider all sources of exposure at that manufacturing facility. It is not known whether these data points would also be representative of the worker exposure level at the other domestic manufacturing facility. Despite this uncertainty, EPA has a high level of confidence in the assessed exposures based on the strength of the monitoring data.

2.3.1.6 Import

Process Descriptions

Commodity chemicals such as 1-BP may be imported into the United States in bulk via water, air, land, and intermodal shipments (Kane, 2015). These shipments take the form of oceangoing chemical tankers, railcars, tank trucks, and intermodal tank containers. Chemicals shipped in bulk containers may be repackaged into smaller containers for resale, such as drums or bottles. The type and size of container will vary depending on customer requirement. In some cases, QC samples may be taken at import sites for analyses. Some import facilities may only serve as storage and distribution locations, and repackaging/sampling may not occur at all import facilities.

1-BP may be imported neat or as a component in a formulation. In the 2016 CDR, most companies reported importing 1-BP at concentrations greater than 90 percent; one company reported importing a formulation containing 1 to 30 percent 1-BP.

The total 1-BP import volume from the 2016 CDR is CBI. However, recent data from other public sources estimate an import volume of 10.3 million pounds of brominated derivatives of acrylic hydrocarbons, which includes 1-BP and other chemicals ([ATSDR, 2016](#)).

Number of Sites and Potentially Exposed Workers

In the 2016 CDR, seven companies reported importing 1-BP into the United States during calendar year 2015. In addition, Superior Oil Company, Inc. reported to the CDR but withheld its activity information in Section 2.B.4 of CDR Form U ([U.S. EPA, 2017a](#)). Based on its facility address, it is likely an import office, rather than industrial manufacturing facility.

Table 2-8 below summarizes the number of persons (including workers and ONUs) reasonably likely to be exposed to 1-BP at the import facilities, as reported in the 2016 CDR (where available). Of these import facilities, six facilities estimated that fewer than 10 employees per site are likely to be exposed, and one facility estimated 25 to up to 50 employees are likely to be exposed.

Table 2-8. Number of Potentially Exposed Workers and Occupational Non-Users at Import Facilities

Company	Facility	Facility Location		Number of Workers ^a Likely to be Exposed	Basis for Import Determination
		City	State		
CBI	CBI	CBI	CBI	<10	2016 CDR (Sec. 2.B.4)
Custom Synthesis, LLC	Custom Synthesis LLC	Anderson	SC	25 - <50	2016 CDR (Sec. 2.B.4)
Enviro Tech International Inc	Enviro Tech International Inc	Melrose Park	IL	<10	2016 CDR (Sec. 2.B.4)
ICL North America	ICL-IP America Inc.	St. Louis	MO	<10	2016 CDR (Sec. 2.B.4)
MC International, LLC	MC International, LLC	Miami	FL	<10	2016 CDR (Sec. 2.B.4)
Phoenix Chemical Co Inc	Phoenix Chemical Co	Calhoun	GA	<10	2016 CDR (Sec. 2.B.4)
Superior Oil Company, Inc.	Superior Oil Company, Inc.	Indianapolis	IN	Withheld	2016 CDR (Address)
WEGO Chemical Group	WEGO Chemical & Mineral Corp	Great Neck	NY	<10	2016 CDR (Sec. 2.B.4)
Total				31 - 103	

Source: ([U.S. EPA, 2017a](#))

a - May include both workers and ONUs

Assessment of Inhalation Exposure Based on Modeling

EPA has not identified exposure monitoring data for import. Therefore, EPA assessed exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model*, assuming 1-BP is present at 100 percent concentration when imported, as consistent with the import concentration reported to the 2016 CDR. The model provides inhalation exposure estimates to volatile liquid chemicals during outdoor loading and unloading activities at an industrial facility. The model accounts

for the emissions of saturated air containing the chemical of interest that remains in the loading arm, transfer hose, and related equipment, and emissions from equipment leaks from processing units such as pumps, seals, and valves. The model assumes industrial facilities use a vapor recovery system to minimize air emissions, such that vapor losses from displacement of saturated air inside the container is mitigated by the use of such systems. See the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)) for detailed description of this model.

For the central tendency scenario, the model assumes the use of a 12-foot transfer hose with two-inch diameter, with an average outdoor wind speed of 9 miles per hour (mph). For the high-end scenario, the model assumes the use of an engineered loading system, such as a loading arm, and that the operation occurs outdoor with a wind speed of 5 mph. For the purpose of this assessment, loading/unloading event is assumed to occur once per work shift. Combining published EPA emission factors and engineering calculations with EPA *Mass Balance Inhalation Model* (peer reviewed), this model estimates central tendency and high-end exposure concentrations for chemical unloading scenarios at industrial facilities. As shown in Table 2-9, the central tendency and high-end exposures are 0.01 ppm and 0.06 ppm as 8-hr TWA, respectively. Note the model does not estimate exposure levels for ONUs.

Table 2-9. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Import Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	1.14E-2	6.01E-2	4.55E-3	3.08E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.7 Processing as a Reactant

Process Descriptions

Processing as a reactant or intermediate is the use of 1-BP as a raw material in the production of another chemical, in which 1-BP is reacted and consumed. In the early to mid-1990s, 1-BP was used as an intermediate in the production of pesticides, quaternary ammonium compounds, flavors and fragrances, pharmaceuticals, and other chemicals ([HSIA, 2010](#)). According to the 2016 CDR, 1-BP is used as an intermediate in the production of other organic chemicals, inorganic chemicals, pharmaceuticals, pesticides, fertilizers, and other agricultural chemicals. The volume of these uses from CDR are CBI ([Enviro Tech International, 2017](#); [HSIA, 2010](#)).

Number of Sites and Potentially Exposed Workers

EPA identified the number of sites and workers using downstream industrial processing and use information reported by manufacturers and importers in Part III, Section A of the CDR Form U. As shown in Table 2-10, 1-BP is potentially used as a chemical intermediate at between three and 27 sites, where 30 to 72 workers and ONUs are potentially exposed. CDR does not differentiate between workers and ONUs. CDR also does not provide the identity of these downstream sites. Information reported under the TRI program indicates Dow Chemical's Midland, MI facility is a processing site ([U.S. EPA, 2016c](#)).

Table 2-10. Estimated Number of Sites and Workers and Occupational Non-Users for Industrial Intermediate Uses

Reporting Company	Type of Process	NAICS code	Industrial Sector	Industrial Function Category	Number of Sites	Number of Workers ^a	Basis for Processing Determination
Albemarle Corporation	Processing as a reactant	32518	All Other Basic Inorganic Chemical Manufacturing	Intermediates	<10	10 - <25	2016 CDR
Chemtura Corporation	Processing as a reactant	32519	All Other Basic Organic Chemical Manufacturing	Intermediates	<10	10 - <25	2016 CDR
Chemtura Corporation	Processing as a reactant	3253	Pesticide, Fertilizer, and Other Agricultural Chemical Manufacturing	Intermediates	<10	10 - <25	2016 CDR
Total					3 - 27	30 - 72	

Source: ([U.S. EPA, 2017a](#))

a - May include both workers and ONUs

Assessment of Inhalation Exposure Based on Modeling

See Section 2.3.1.6 for the assessment of worker exposure from chemical unloading activities. At industrial facilities, workers are potentially exposed when unloading 1-BP from transport containers into intermediate storage tanks and process vessels. Workers may be exposed via inhalation of vapor or via dermal contact with liquids while connecting and disconnecting hoses and transfer lines. EPA assumes the exposure sources, routes, and exposure levels are similar to those at an import facility. The exposure results are presented in Table 2-11.

Table 2-11. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Processing as a Reactant Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	1.14E-2	6.01E-2	4.55E-3	3.08E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, this activity may be only a small part of the worker's day. The model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities that can contribute to a worker's overall 8-hr daily exposure. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker 8-hr exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.8 Processing – Incorporation into Formulation, Mixture, or Reaction Product

Process Descriptions

After manufacture, 1-BP may be supplied directly to end-users, or may be incorporated into various products and formulations at varying concentrations for further distribution. Incorporation into a formulation, mixture, or reaction product refers to the process of mixing or blending several raw materials to obtain a single product or preparation. For example, formulators may add stabilizing packages to 1-BP for specialized vapor degreasing uses ([Enviro Tech International, 2017](#)), or mix 1-BP with other additives to formulate adhesives, sealants, and other products.

In a 2010 study, Hanley et al. describes the process of formulating adhesive products containing 1-BP at one facility:

“...a large variety of glues, sealants, and coatings were manufactured for a multitude of commercial and industrial applications using water-, epoxy-, and organic solvent-based formulas. When charging the batch mixers, large volume solvents (e.g. 1-BP) were dispensed through an enclosed piping manifold system. Solid chemicals were added manually through hatch openings, which otherwise remained closed during mixing. After blending, the finished product was pumped into buckets, drums, or bulk tanks using semi-enclosed methods. Local exhaust ventilation was not provided for the mixing vessels or packaging locations. Instead, each bay on the charging and packing floors were serviced with high volume dilution ventilation consisting of air supply and exhaust system located on opposite walls to produce directional air flow. A solvent blend containing over 96 percent 1-BP was used as the principal solvent in one product line. This adhesive was made approximately once every 45 days.” ([Hanley et al., 2010](#))

It is not known whether the specific equipment and engineering controls cited by Hanley et al. ([Hanley et al., 2010](#)) is representative of other facilities. However, the general process activities (e.g., unloading of raw materials into mixing vessels) are likely similar across different formulation facilities.

Number of Sites and Potentially Exposed Workers

EPA identified the number of sites and workers using downstream industrial processing and use information reported by manufacturers and importers in Part III, Section A of the CDR Form U. As shown in Table 2-12, the number of 1-BP formulation sites ranges from 33 to 99.¹² This range is

¹² CDR does not provide the identity of these formulation sites. However, some formulation sites can be identified using TRI data (see Section 2.3.1.8).

consistent with the estimate provided in the *Analysis of Economic Impacts of Final nPB [1-bromopropane] rulemaking for Cleaning Solvent Sector* of the SNAP program, which estimated that in 2007, there were seven companies that formulated solvent-based products containing 1-BP, three companies that formulated adhesive products containing 1-BP, an additional 60 small providers of specialty products¹³ that contained 1-BP, and approximately 20 or 25 companies that prepared aerosol formulations with 1-BP ([U.S. EPA, 2007a](#)). The number of workers and ONUs likely exposed ranges from 220 to 1,046. CDR does not differentiate between workers and ONUs.

Table 2-12. Estimated Number of Sites and Workers and Occupational Non-Users for Processing – Incorporation into Formulation, Mixture or Reaction Product

Reporting Company	Type of Process	NAICS Code	Industrial Sector	Industrial Function Category	Number of Sites	Number of Workers ^a
CBI	Processing - incorporation into formulation, mixture, or reaction product	11	Agriculture, Forestry, Fishing and Hunting	Agricultural chemicals (non pesticidal)	NKRA	NKRA
Albemarle Corporation	Processing - incorporation into formulation, mixture, or reaction product	325998	All Other Chemical Product and Preparation Manufacturing	Solvents (for cleaning or degreasing)	<10	10 - <25
Chemtura Corporation	Processing - incorporation into formulation, mixture, or reaction product	3256	Soap, Cleaning Compound, and Toilet Preparation Manufacturing	Solvents (for cleaning or degreasing)	10 - <25	100 - <500
Custom Synthesis, LLC	Processing - incorporation into formulation, mixture, or reaction product	335	Electrical Equipment, Appliance, and Component Manufacturing	Solvents (for cleaning or degreasing)	10 - <25	100 - <500
ICL	Processing - incorporation into formulation, mixture, or reaction product	334	Computer and Electronic Product Manufacturing	Solvents (for cleaning or degreasing)	10 - <25	NKRA
MC International, LLC	Processing - incorporation into formulation, mixture, or reaction product	32552	Adhesive Manufacturing	Solvents (which become part of product formulation or mixture)	<10	NKRA
Wego Chemical and Mineral Corp.	Processing - incorporation into formulation, mixture, or reaction product	51, 52, 53, 54, 55, 56, 61, 62, 71, 72, 81, 92	Services	Solvents (for cleaning or degreasing)	<10	10 - <25
Total					33 - 99	220 – 1,046

Source: ([U.S. EPA, 2017a](#))

^a May include both workers and ONUs

NKRA – Not known or reasonably ascertainable

¹³ In a 2017 public comment, Enviro Tech stated that most of these additional companies merely market the same products produced by one of the seven major solvent manufacturers, sometimes under a private label. Enviro Tech International is a major supplier of 1-BP and fluorinated solvents. ([International, 2017](#))

Assessment of Inhalation Exposure Based on Monitoring Data

For formulation of 1-BP into products, EPA assessed exposure using a Hanley et al. ([Hanley et al., 2010](#)) exposure study at an adhesive manufacturing facility. The study did not provide detailed data to allow determination of 50th and 95th percentile exposures, but stated that the geometric mean full-shift (8 to 10 hour) TWA measurement was 3.79 ppm for those who handled 1-BP products (workers), and 0.33 ppm for those who did not use 1-BP (i.e., ONUs). The maximum exposure value was 18.9 ppm TWA for those who directly used 1-BP, and 1.59 ppm TWA for those who did not use 1-BP ([Hanley et al., 2010](#)). Table 2-13 presents the central tendency (geometric mean) and high-end (maximum) exposure levels reported in this study. Exposure levels at other facilities will differ from those observed by Hanley et al ([Hanley et al., 2010](#)) depending on the process controls.

Table 2-13. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Processing/Formulation Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	Central tendency (mean)	High-end (Max)	Central tendency (mean)	High-end (Max)		
Worker	3.79	18.9	1.51	9.69	3	High
ONU	0.33	1.59	0.13	0.82	8	

Source: ([Hanley et al., 2010](#))

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data collected at one adhesive formulation facility. Although the data have a high confidence rating and are directly applicable to this condition of use, the data may not be representative of exposures across the range of facilities that formulates products containing 1-BP (e.g. degreasing and dry cleaning formulations). Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.9 Processing – Incorporation into Articles

Process Descriptions

According to EPA's Use Dossier, 1-BP is present at less than 5 percent concentration in the THERMAXTM brand insulation manufactured by Dow Chemical ([U.S. EPA, 2017c](#)). THERMAXTM is a polyisocyanurate rigid board insulation for interior and exterior applications, and can be used on walls, ceilings, roofs, and crawl spaces in commercial and residential buildings. The product is marketed to have superior durability and fire performance over generic polyisocyanurate insulations.¹⁴ EPA does not have information on the exact process for producing THERMAXTM and the function of 1-BP in the insulation material ([DOW, 2018](#)).

¹⁴ <https://www.dow.com/en-us/products/thermaxbrandinsulation#sort=%40gtitle%20ascending>

Number of Sites and Potentially Exposed Workers

Dow's website indicates insulation products containing 1-BP are produced at its Pennsauken, NJ facility ([DOW, 2018](#)). The number of potentially exposed workers at this specific facility is not known; however, EPA estimated the number of workers at facilities characterized under NAICS 326150,¹⁵ "Urethane and Other Foam Product (except Polystyrene) Manufacturing" using Bureau of Labor Statistics' OES data ([2015](#)) and ([2012](#)) U.S. Census SUSB. The method for estimating number of workers is detailed in Appendix A of the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)). The analysis indicates an average of 15 potentially exposed workers and 4 ONUs per site.

Table 2-14. Estimated Number of Workers and Occupational Non-Users Potentially Exposed during Incorporation of 1-BP into Articles for NAICS 326150

Exposed Workers	Exposed Occupational Non-Users	Total Exposed	Estimated Number of Establishments	Workers per Site	Occupational Non-Users per Site
15	4	19	1	15	4

Assessment of Inhalation Exposure Based on Modeling

EPA did not find monitoring data for this condition of use. As such, EPA modeled exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model*. The model provides estimates of high-end and central tendency exposure concentration for a chemical unloading scenario. See Section 2.3.1.6 for the assessment of worker exposure from chemical unloading activities. The exposure results are presented in Table 2-15.

Table 2-15. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Processing – Incorporation into Articles Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	1.14E-2	6.01E-2	4.55E-3	3.08E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgment to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

¹⁵ The Dow facility reports a primary NAICS of 326150 in the 2016 and 2017 TRI

2.3.1.10 Repackaging

Process Descriptions

Chemicals shipped in bulk containers may be repackaged into smaller containers for resale, such as drums or bottles. The type and size of container will vary depending on customer requirement. In some cases, QC samples may be taken at repackaging sites for analyses. Note repackaging could occur for both domestic and imported shipments of 1-BP; repackaging activities that occur at import facilities are addressed in Section 2.3.1.6.

Number of Sites and Potentially Exposed Workers

EPA identified the number of sites and workers using downstream industrial processing and use information reported by manufacturers and importers in Part III, Section A of the CDR Form U. As shown in Table 2-16, one company reported up to 10 downstream repackaging sites with 10 to up to 25 workers. Another company reported downstream repackaging activities but indicated the number of sites and workers were not known or reasonably ascertainable ([U.S. EPA, 2017a](#)). EPA does not know the identity of these sites. In addition, EPA does not know whether these sites are exclusive repackaging sites or whether they also fall under other 1-BP conditions of use.

Table 2-16. Number of Potentially Exposed Workers and Occupational Non-Users at Repackaging Facilities

Reporting Company	Type of Process	NAICS code	Industrial Sector	Industrial Function Category	Number of Sites	Number of Workers ^a
Albemarle Corporation	Processing – repackaging	325998	All other chemical product and preparation manufacturing	Solvents (for cleaning and degreasing)	<10	10 - <25
Phoenix Chemical Co Inc	Processing – repackaging	NKRA	NKRA	NKRA	NKRA	NKRA
Total					<10	10 - <25

Source: ([U.S. EPA, 2017a](#))

a - May include both workers and ONUs

Assessment of Inhalation Exposure Based on Modeling

EPA has not identified exposure monitoring data for repackaging. Therefore, EPA assessed exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model*. As shown in Table 2-17, the central tendency and high-end exposures are 0.01 ppm and 0.06 ppm as 8-hr TWA, respectively. Note the model does not estimate exposure levels for ONUs.

Table 2-17. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Repackaging Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	1.14E-2	6.01E-2	4.55E-3	3.08E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.11 Batch Vapor Degreaser (Open-Top)

Process Descriptions

Vapor degreasing is a process used to remove dirt, grease, and surface contaminants in a variety of industries. 1-BP is often used to replace chlorinated solvents, especially in applications where flammability is a concern ([CRC Industries Inc., 2017](#)). 1-BP is also desirable because of its low corrosivity, compatibility with many metals, and suitability for use in most modern vapor degreasing equipment. Vapor degreasing may take place in batches or as part of an in-line (i.e., continuous) system. In batch machines, each load (parts or baskets of parts) is loaded into the machine after the previous load is completed. With in-line systems, parts are continuously loaded into and through the vapor degreasing equipment as well as the subsequent drying steps. Vapor degreasing equipment can generally be categorized into one of the three categories: (1) batch vapor degreasers, (2) conveyORIZED vapor degreasers and (3) web vapor degreasers.

In batch open-top vapor degreasers (OTVDs), a vapor cleaning zone is created by heating and volatilizing the liquid solvent in the OTVD. Workers manually load or unload fabricated parts directly into or out of the vapor cleaning zone. The tank usually has chillers along the side of the tank to prevent losses of the solvent to the air. However, these chillers are not able to eliminate emissions, and throughout the degreasing process significant air emissions of the solvent can occur. These air emissions can cause issues with both worker health and safety as well as environmental issues. Additionally, the cost of replacing solvent lost to emissions can be expensive ([NEWMOA, 2001](#)). The use of 1-BP in OTVD has been previously described in EPA's [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#).

OTVDs with enclosures operate the same as standard OTVDs except that the OTVD is enclosed on all sides during degreasing. The enclosure is opened and closed to add or remove parts to/from the machine, and solvent is exposed to the air when the cover is open. Enclosed OTVDs may be vented directly to the atmosphere or first vented to an external carbon filter and then to the atmosphere ([U.S. EPA; ICF Consulting, 2004](#)). Figure 2-1 illustrates an OTVD with an enclosure. The dotted lines in Figure 2-1 represent the optional carbon filter that may or may not be used with an enclosed OTVD.

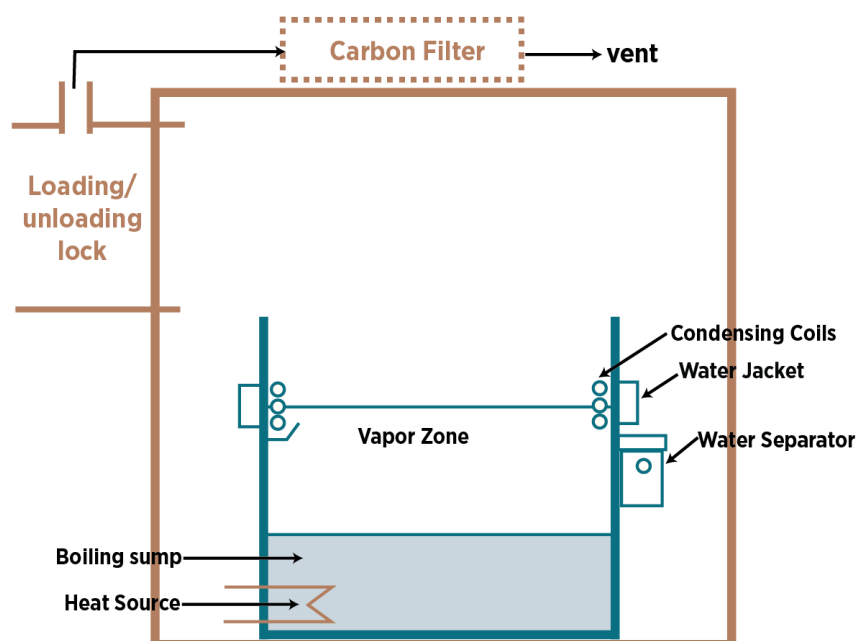


Figure 2-1. Open-Top Vapor Degreaser with Enclosure

Number of Sites and Potentially Exposed Workers

EPA estimated the number of workers potentially exposed to 1-BP in vapor degreasing using Bureau of Labor Statistics' OES data ([2015](#)) and U.S. Census SUSB ([2012](#)). The method for estimating number of workers is detailed in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)) and the 2016 draft Risk Assessment ([U.S. EPA, 2016d](#)). Table 2-18 presents the estimated number of workers and occupational non-users based on industry- and occupational-specific employment data.

The number of businesses that use 1-BP for vapor degreasing is estimated at 500 to 2,500 businesses ([CDC, 2016](#); [U.S. EPA, 2007c](#)). EPA assumes each business equates to one site and that each site has one degreasing unit. The total number of potentially exposed workers and occupational non-users is estimated at 4,712 to 23,558. Because EPA was unable to determine which industry sectors and occupations perform specific degreasing types (e.g., OTVD, conveyorized vapor degreasing, cold cleaning), these estimates likely cover a range of degreasing operations and are not specific to OTVD.

Table 2-18. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP in Degreasing Uses

Exposed Workers ^a	Exposed Occupational non-users ^a	Total Exposed ^a	Estimated Number of Establishments	Workers per Site	Occupational non-users per Site
Low-end					
3,200	1,500	4,700	500	6	3
High-end					
16,000	7,300	24,000	2,500	6	3

Note: Number of workers and occupational non-users per site are calculated by dividing the exposed number of workers or occupational non-users by the number of establishments. Values are rounded to the nearest integer.

a – Values rounded to 2 significant digits.

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-19 summarizes the 1-BP exposure data for vapor degreasing operations. EPA obtained exposure monitoring data from several sources, including journal articles, NIOSH Health Hazard Evaluations (HHEs), the OSHA Chemical Exposure Health Data (CEHD) database, and data submitted to EPA SNAP program. NIOSH HHEs are conducted at the request of employees, employers, or union officials, and provide information on existing and potential hazards present in the workplaces evaluated. OSHA CEHD are workplace monitoring data from OSHA inspections; EPA SNAP program data are collected as part of EPA's effort to identify substitutes for ozone-depleting substances. Some of these data, such as monitoring data conducted during OSHA inspections, are not intended to be representative of typical exposure levels.

Data from these sources cover exposure at a variety of industries that conduct vapor degreasing, including telecommunication device manufacturing, aerospace parts manufacturing, electronics parts manufacturing, helicopter transmission manufacturing, hydraulic power control component manufacturing, metal product fabrication, optical prism and assembly, and printed circuit board manufacturing. It should be noted that sources that only contain a statistical summary of worker exposure monitoring, but exclude the detailed monitoring results, are not included in EPA's analysis below.

Most of the gathered data were for batch open-top vapor degreasers, except for data from OSHA ([Osha, 2019, 2013b](#)) and EPA SNAP program, where the type of degreaser is typically not specified. EPA included these data in the analysis despite uncertainty in the degreaser type. Note the 2016 draft Risk Assessment ([U.S. EPA, 2016d](#)) previously categorized data as either pre- or post-Engineering Control. After further evaluation, EPA removed these categories because EPA determined there is insufficient information on engineering controls at all facilities to accurately characterize the dataset.

EPA defined a vapor degreasing "worker" as an employee who operates or performs maintenance tasks on the degreaser, such as draining, cleaning, and charging the degreaser bath tank. EPA defined "occupational non-user" as an employee who does not directly handle 1-BP but performs work in the surrounding area. Some data sources do not describe their work activities in detail, and the exact proximity of these occupational non-users to the degreaser is unknown. As shown in the table, workers are exposed to significant levels of 1-BP, with 50th and 95th percentile exposures of 6.70 ppm and 49.4 ppm as 8-hr TWA, respectively. For occupational non-users, the 50th and 95th percentile exposure levels are below 3 ppm as 8-hr TWA.

Table 2-19. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Vapor Degreaser Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker	6.70	49.4	2.66	25.3	153	Medium - High
ONU	0.02	2.15	0.01	1.10	18	

Source: ([Osha, 2019, 2013b](#); [U.S. EPA, 2006b](#); [Reh and Nemhauser, 2001](#))

Assessment of Inhalation Exposure Based on Modeling

Figure 2-2 illustrates the near-field / far-field model that can be applied to vapor degreasing ([AIHA, 2009](#)). This model, including all model input parameters, was previously peer reviewed as part of the 2016 draft 1-BP Risk Assessment. As the figure shows, volatile 1-BP vapors evaporate into the near-field, resulting in worker exposures at a concentration C_{NF} . The concentration is directly proportional to the evaporation rate of 1-BP, G , into the near-field, whose volume is denoted by V_{NF} . The ventilation rate for the near-field zone (Q_{NF}) determines how quickly 1-BP dissipates into the far-field, resulting in occupational non-user exposures to 1-BP at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the 1-BP dissipates out of the near-field. EPA assumes the far-field volume (V_{FF}) ranges from 300 m³ (10,594 ft³) to 2,000 m³ (70,629 ft³) for degreasing facilities ([Von Grote et al., 2003](#)). The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly 1-BP dissipates out of the surrounding space and into the outside air. See *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)) for the model equations, model parameters, parameter distributions, and associated assumptions.

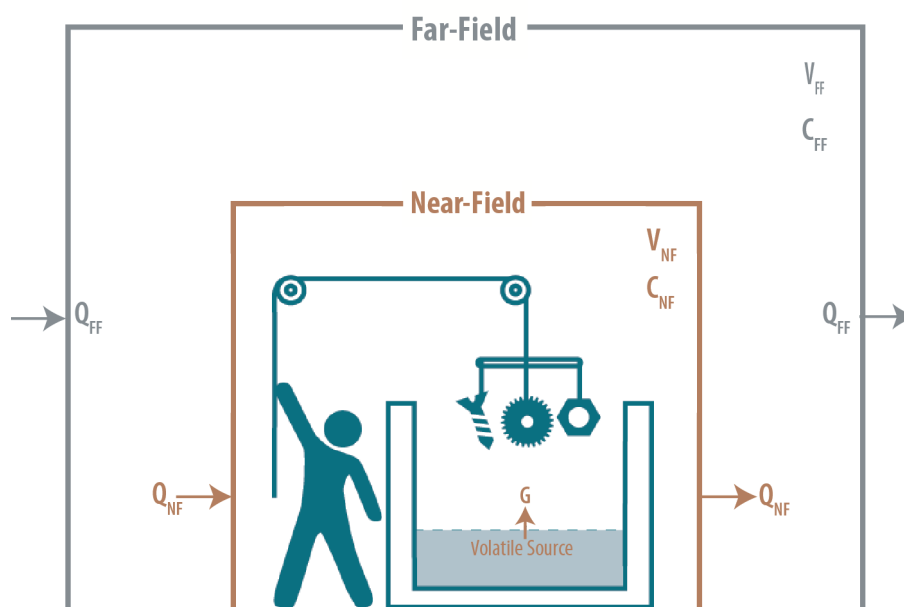


Figure 2-2. Schematic of the Near-Field/Far-Field Model for Vapor Degreasing

To estimate the 1-BP vapor generation rate, the model references an emission factor developed by the California Air Resources Board (CARB) for the California Solvent Cleaning Emissions Inventories ([CARB, 2011](#)). CARB surveyed facilities that conduct solvent cleaning operations and gathered site-specific information for 213 facilities. CARB estimated a 1-BP emission factor averaging 10.43 lb/employee-yr, with a standard deviation of 17.24 lb/employee-yr, where the basis is the total number of employees at a facility. The majority of 1-BP emissions were attributed to the vapor degreasing category.

It should be noted that the “vapor degreasing” category in CARB’s study includes the batch-loaded vapor degreaser, aerosol surface preparation process, and aerosol cleaning process. It is not known what percentage, if any, of the 1-BP emission factor is derived from aerosol applications. This modeling approach assumes the 1-BP emission factor is entirely attributed to vapor degreasing applications. The emission factor is expected to represent emissions from batch-loaded degreasers used in California at the time of study. *It is not known whether these are specifically open-top batch degreasers, although open-*

top is expected to be the most common design. The CARB survey data did not include emissions for conveyORIZED vapor degreasers.

The CARB emission factor is then combined with U.S. employment data for vapor degreasing industry sectors from the Economic Census.¹⁶ The 2016 1-BP draft Risk Assessment identified 78 NAICS industry codes that are applicable to vapor degreasing. For these industry codes, the Census data set indicates a minimum industry average of 8 employees per site, with a 50th percentile and 90th percentile of 25 and 61 employees per site, respectively. A lognormal distribution is applied to the Census data set to model the distribution of the industry-average number of employees per site for the NAICS codes applicable to vapor degreasing.

These nationwide Census employment data are comparable to the 2008 California employment data cited in CARB's study. According to the CARB study, approximately 90 percent of solvent cleaning facilities in California had less than 50 employees (whereas the national Census data estimate 90 percent of facilities have less than or equal to 61 employees). It is important to note that the Census data report an average number of employees per site for each NAICS code. The number of employees for each individual site within each NAICS code is not reported. Therefore, the distribution EPA calculated represents a population of *average* facility size for each NAICS code, and not the population of *individual* facility sizes over all NAICS codes.

The vapor generation rate, G (kg/unit-hr), is calculated *in-situ* within the model, as follows:

Equation 2-1. Equation for Calculating Vapor Degreasing Vapor Generation Rate

$$G = EF \times EMP / (2.20462 \times OH \times OD \times U)$$

Where

EF = emission factor (lb/employee-yr)

EMP = Number of employees (employee/site)

OH = Operating hours per day (hr/day)

OD = Operating days per year (day/yr)

U = Number of degreasing units (unit/site)

2.20462 = Unit conversion from lb to kg (lb/kg)

Batch degreasers are assumed to operate between two and 24 hours per day, based on NEI data on the reported operating hours for OTVD using TCE. EPA performed a *Monte Carlo* simulation with 100,000 iterations and the Latin Hypercube sampling method in [@Risk](#)¹⁷ to calculate 8-hour TWA near-field and far-field exposure concentrations. Near-field exposure represents exposure concentrations for workers who directly operate the vapor degreasing equipment, whereas far-field exposure represents exposure concentrations for occupational non-users (i.e., workers in the surrounding area who do not handle the degreasing equipment). Table 2-20 presents a statistical summary of the exposure modeling results. These exposure estimates represent modeled exposures for the workers and occupational non-users. For

¹⁶ For the purpose of modeling, EPA used data from the 2007 Economic Census for the vapor degreasing NAICS codes as identified in the TCE RA ([U.S. EPA, 2014d](#)). The 2012 Economic Census did not have employment data (average number of employees per establishment) for all vapor degreasing NAICS codes of interest.

¹⁷ A risk analysis software tool (Microsoft Excel add-in) using *Monte Carlo* simulation

workers, the baseline (pre-engineering control) 50th percentile exposure is 1.89 ppm 8-hr TWA, with a 95th percentile of 23.9 ppm 8-hr TWA. Compared to literature studies:

- Hanley et al. (2010) reported a geometric mean of 2.63 ppm 8-hr TWA exposure with a range of 0.078 to 21.4 ppm 8-hr TWA among 44 samples;
- NIOSH (Reh and Nemhauser, 2001) reported a range of 0.01 to 0.63 ppm 8-hr TWA among 20 samples;
- A 2003 EPA analysis suggested that 87 percent of the samples were less than 25 ppm 8-hr TWA among 500 samples at vapor degreasing facilities (U.S. EPA, 2003).

The modeled mean near-field exposure is found to be generally comparable to the exposures reported in literature. For occupational non-users, the modeled far-field exposure has a 50th percentile value of 0.99 ppm and a 95th percentile of 13.5 ppm 8-hr TWA. These modeled far-field results are somewhat higher than reported literature values. (Hanley et al., 2010) reported workers away from the degreasers are exposed at concentrations of 0.077 to 1.69 ppm 8-hr TWA, with a geometric mean of 0.308 ppm 8-hr TWA. *It should be noted that the modeled exposures represent the potential exposure associated with batch-loaded degreasers, which could include both OTVD and batch-loaded, closed-loop vapor degreasers.*

The model also presents a “post-Engineering Control” (post-EC) scenario by applying a 90 percent emission reduction factor to the baseline, pre-EC scenario. The estimate is based on a Wadden et al. (1989) study, which indicates a LEV system for an open-top vapor degreaser (lateral exhaust hoods installed on two sides of the tank) can be 90 percent effective (Wadden et al., 1989). The study covered only reductions in degreaser machine emissions due to LEV and did not address other sources of emissions such as dragout, fresh and waste solvent storage and handling. Furthermore, a caveat in the study is that most LEV likely do not achieve ACGIH design exhaust flow rates, indicating that the emission reductions in many units may not be optimized. Therefore, using this factor likely overestimates control technology efficiency, and underestimates exposures. Actual exposure reductions from added engineering controls can be highly variable and can only be verified by monitoring studies.

Table 2-20. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Batch Vapor Degreaser (Open-Top) Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm)		Chronic, Cancer Exposures (ppm)		Confidence Rating of Air Concentration Data
	AC _{1-BP} , 8-hr TWA	ADC _{1-BP} , 8-hr TWA	LADC _{1-BP} , 8-hr TWA		
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Workers (Near-Field)					
Pre EC	1.89	23.9	0.70	9.19	N/A – Modeled Data
Post EC 90%	0.19	2.39	0.07	0.92	
Occupational non-users (Far-Field)					
Pre EC	0.99	13.5	0.37	5.23	N/A – Modeled Data
Post EC 90%	0.10	1.35	0.04	0.52	

Pre-EC: refers to modeling where no reduction due to engineering controls was assumed

Post-EC: refers to modeling where engineering controls with 90% efficiency were implemented. The percent effectiveness is applied to the pre-EC exposure concentration to calculate post-EC exposure.

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data from several different sources, with confidence rating of the data ranging from medium to high, as determined through EPA's systematic review process. Some of the data sources do not clearly specify whether the vapor degreaser is a batch, open-top system or another system. Because OTVDs typically have the highest emissions among all vapor degreasers, the inclusion of data for other degreaser types may underestimate exposure for this condition of use.

The exposure data are supplemented with near-field/far-field exposure modeling using a *Monte Carlo* analysis, which incorporates variability in the model input parameters. This model was peer reviewed as part of the 2016 1-BP draft Risk Assessment ([U.S. EPA, 2016d](#)). Although there is some uncertainty on the CARB emission factor used in the model and whether the factor represents emissions exclusively for batch open-top systems, the model results are in general agreement with monitoring data. Based on reasonably available information, EPA has a high level of confidence in the assessed exposure for this condition of use.

2.3.1.12 Batch Vapor Degreaser (Closed-Loop)***Process Descriptions***

In closed-loop degreasers, parts are placed into a basket, which is then placed into an airtight work chamber. The door is closed, and solvent vapors are sprayed onto the parts. Solvent can also be introduced to the parts as a liquid spray or liquid immersion. When cleaning is complete, vapors are exhausted from the chamber and circulated over a cooling coil where the vapors are condensed and recovered. The parts are dried by forced hot air. Air is circulated through the chamber and residual solvent vapors are captured by carbon adsorption. The door is opened when the residual solvent vapor concentration has reached a specified level ([Kanegsberg and Kanegsberg, 2011](#)). Figure 2-3 illustrates a standard closed-loop vapor degreasing system.

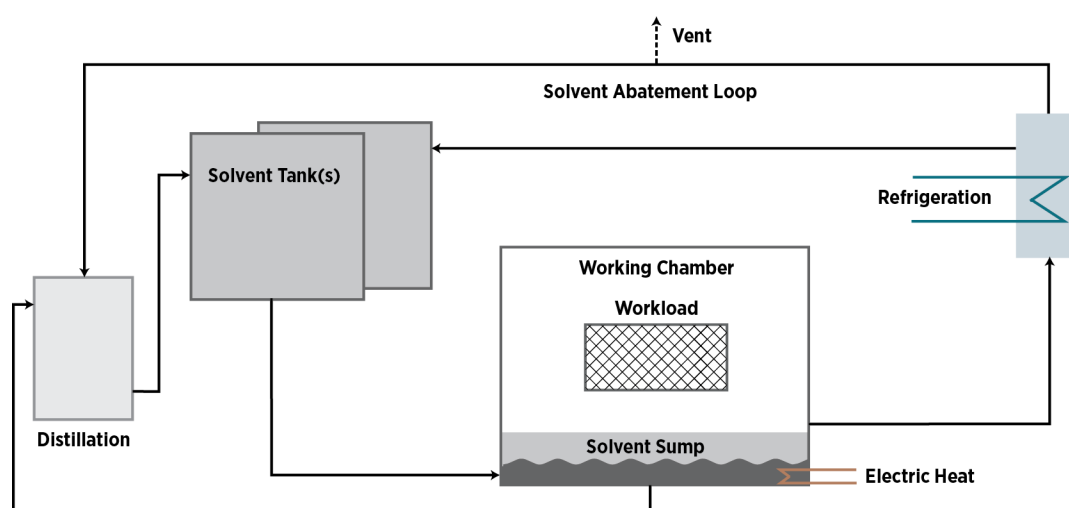


Figure 2-3. Closed-loop/Vacuum vapor Degreaser

Airless degreasing systems are also sealed, closed-loop systems, but remove air at some point of the degreasing process. Removing air typically takes the form of drawing vacuum but could also include purging air with nitrogen at some point of the process (in contrast to drawing vacuum, a nitrogen purge operates at a slightly positive pressure). In airless degreasing systems with vacuum drying only, the cleaning stage works similarly as with the airtight closed-loop degreaser. However, a vacuum is generated during the drying stage, typically below 5 torr (5 mmHg). The vacuum dries the parts and a vapor recovery system captures the vapors ([Kanegsberg and Kanegsberg, 2011](#); [ERG, 2001](#); [NEWMOA, 2001](#)).

Airless vacuum-to-vacuum degreasers are true “airless” systems because the entire cycle is operated under vacuum. Typically, parts are placed into the chamber, the chamber sealed, and then vacuum drawn within the chamber. The typical solvent cleaning process is a hot solvent vapor spray. The introduction of vapors in the vacuum chamber raises the pressure in the chamber. The parts are dried by again drawing vacuum in the chamber. Solvent vapors are recovered through compression and cooling. An air purge then purges residual vapors over an optional carbon adsorber and through a vent. Air is then introduced in the chamber to return the chamber to atmospheric pressure before the chamber is opened ([Durkee, 2014](#); [NEWMOA, 2001](#)). The general design of vacuum vapor degreasers and airless vacuum degreasers is similar as illustrated in Figure 2-3 for closed-loop systems except that the work chamber is under vacuum during various stages of the cleaning process.

Number of Sites and Potentially Exposed Workers

According to the Institute for Research and Technical Assistance (IRTA), there may be as many as 2,000 vacuum degreasers in the U.S., of which approximately 100 systems use 1-BP ([IRTA, 2016](#)).¹⁸ Table 2-21 presents the estimated number of workers and ONUs at 100 facilities, assuming one unit per facility, based on the average number of worker and ONU per site from the BLS data analysis. It is unclear whether these approximately 100 facilities are a subset of those facilities presented in Section 2.3.1.11.

Table 2-21. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP in Batch Closed-Loop Degreasing

Exposed Workers ^a	Exposed Occupational non-users ^a	Total Exposed ^a	Estimated Number of Establishments	Workers per Site	Occupational non-users per Site
650	290	940	100	6	3

Note: Number of workers and occupational non-users per site are calculated by dividing the exposed number of workers or occupational non-users by the number of establishments. Values are rounded to the nearest integer.

a – Values rounded to 2 significant digits.

Assessment of Inhalation Exposure Based on Modeling

There are no 1-BP monitoring data specific to closed-loop degreasers. A NEWMOA study states air emissions can be reduced by 98 percent or more when a closed-loop degreaser is used instead of an open-top vapor degreaser ([NEWMOA, 2001](#)). This reduction factor is applied to the vapor degreasing model results presented in Section 2.3.1.11 to estimate exposure to batch closed-loop vapor degreasers. The approach assumes the CARB emission factor primarily represents emissions from OTVDs, rather than other types of batch-loaded degreasers.

¹⁸ It is unclear whether the IRTA estimate includes other types of closed-loop degreasers.

Table 2-22 presents the exposure model results for batch closed-loop vapor degreasers. For workers, the 50th and 95th percentile exposure levels are 0.04 ppm and 0.48 ppm as 8-hr TWA. For occupational non-users, the 50th and 95th percentile exposure levels are 0.02 ppm and 0.27 ppm as 8-hr TWA, respectively.

Table 2-22. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Batch Closed-Loop Vapor Degreasing Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	0.04	0.48	0.01	0.18	N/A – Modeled Data
ONU	0.02	0.27	0.01	0.10	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

For this condition of use, EPA did not identify any exposure monitoring data. Exposure is assessed using the OTVD model and by assuming 98 percent exposure reduction when switching from open-top to closed-loop batch vapor degreasers. The model incorporates variability in the input parameters through a *Monte Carlo* approach, and the model was peer reviewed in 2016. However, the representativeness of the exposure reduction factor used in the model is not known, as actual exposure will likely differ depending on the specific equipment design and work practices. In addition, this model uses the CARB emission factor for batch-loaded degreasers to estimate average baseline emissions from open-top vapor degreasers, which could result in an underestimate. Based on reasonably available information, EPA has a medium level of confidence in the assessed exposure for this condition of use.

2.3.1.13 In-line Vapor Degreaser (Conveyorized)

Process Descriptions

In conveyorized systems, an automated parts handling system, typically a conveyor, continuously loads parts into and through the vapor degreasing equipment and the subsequent drying steps. Conveyorized degreasing systems are usually fully enclosed except for the conveyor inlet and outlet portals.

Conveyorized degreasers are likely used in shops where large number of parts need to be cleaned. There are seven major types of conveyorized degreasers: monorail degreasers; cross-rod degreasers; vibra degreasers; ferris wheel degreasers; belt degreasers; strip degreasers; and circuit board degreasers ([U.S. EPA, 1977](#)). See *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)) for detailed description of each type of conveyorized degreaser.

Continuous web cleaning machines are a subset of conveyorized degreasers but differ in that they are specifically designed for cleaning parts that are coiled or on spools such as films, wires, and metal strips ([Kanegsberg and Kanegsberg, 2011](#); [U.S. EPA, 2006a](#)). In continuous web degreasers, parts are uncoiled and loaded onto rollers that transport the parts through the cleaning and drying zones at speeds greater than 11 feet per minute ([U.S. EPA, 2006a](#)). The parts are then recoiled or cut after exiting the cleaning machine ([Kanegsberg and Kanegsberg, 2011](#); [U.S. EPA, 2006a](#)).

Number of Sites and Potentially Exposed Workers

According to IRTA, there are likely 1,000 conveyORIZED systems in use, of which 80 percent (800 systems) use 1-BP ([IRTA, 2016](#)). Table 2-23 presents the estimated number of workers and ONUs for these systems, assuming one system per establishment, based on the average number of worker and ONU per site from the BLS data analysis.

Table 2-23. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP for ConveyORIZED Vapor Degreasers

Exposed Workers ^a	Exposed Occupational non-users ^a	Total Exposed ^a	Estimated Number of Establishments	Workers per Site	Occupational non-users per Site
5,200	2,300	7,500	800	6	3

Note: Number of workers and occupational non-users per site are calculated by dividing the exposed number of workers or occupational non-users by the number of establishments. Values are rounded to the nearest integer.

a – Values rounded to 2 significant digits.

Assessment of Inhalation Exposure

There are no monitoring data specific to conveyORIZED degreasers that use 1-BP. Additionally, there is not sufficient data to model exposure to 1-BP from these degreasers.

The 2014 NEI contains emission data for dichloromethane (DCM), perchloroethylene (PERC), and trichloroethylene (TCE). Based on comparison of NEI data for OTVD and conveyORIZED vapor degreasers, emissions from conveyORIZED vapor degreasers are generally similar to that from OTVDs. As such, EPA assumed the associated 1-BP worker exposure for conveyORIZED degreasers may be similar to the exposure levels presented in Section 2.3.1.11 Batch Vapor Degreaser (Open-Top).

2.3.1.14 Cold Cleaner

Process Descriptions

Cold cleaners are non-boiling solvent degreasing units. Cold cleaning operations include spraying, brushing, flushing, and immersion. Figure 2-4 shows the design of a typical batch-loaded, maintenance cold cleaner, where dirty parts are cleaned manually by spraying and then soaking in the tank. After cleaning, the parts are either suspended over the tank to drain or are placed on an external rack that routes the drained solvent back into the cleaner. Batch manufacturing cold cleaners could vary widely, but have two basic equipment designs: the simple spray sink and the dip tank. The dip tank design typically provides better cleaning through immersion, and often involves an immersion tank equipped with agitation ([U.S. EPA, 1981](#)). Emissions from batch cold cleaning machines typically result from (1) evaporation of the solvent from the solvent-to-air interface, (2) “carry out” of excess solvent on cleaned parts, and (3) evaporative losses of the solvent during filling and draining of the machine ([U.S. EPA, 2006a](#)). Emissions from cold in-line (conveyORIZED) cleaning machines result from the same mechanisms, but with emission points only at the parts entry and exit ports ([U.S. EPA, 2006a](#)).

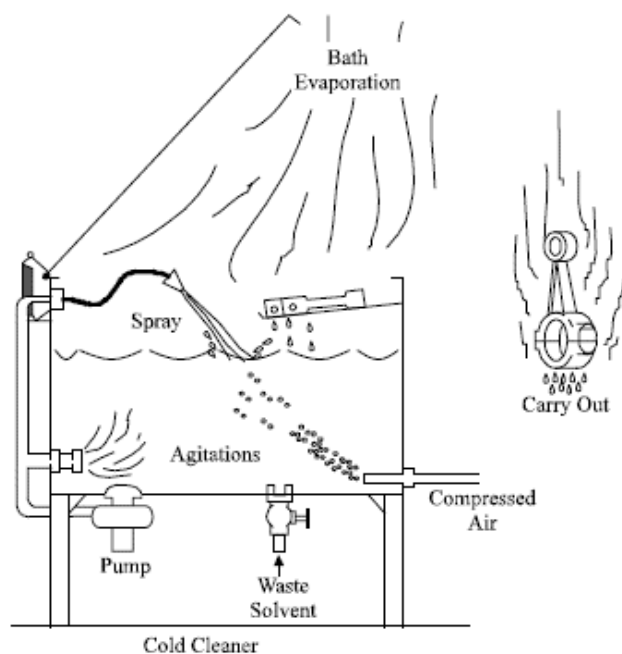


Figure 2-4. Typical Batch-Loaded, Maintenance Cold Cleaner ([U.S. EPA, 1981](#))

Number of Sites and Potentially Exposed Workers

There is no information to determine the number of workers and occupational non-users potentially exposed to 1-BP during cold cleaning. Based on literature search to date, EPA does not know how many facilities current use 1-BP in cold cleaning. It is possible that some of the degreasing facilities presented in Section 2.3.1.11 also use 1-BP as a cold cleaning solvent.

Assessment of Inhalation Exposure Based on Monitoring Data

The general worker activities for cold cleaning include placing the parts that require cleaning into a vessel. The vessel is usually something that will hold the parts but not the liquid solvent (i.e., a wire basket). The vessel is then lowered into the machine, where the parts could be sprayed, and then completely immersed in the solvent. After a short time, the vessel is removed from the solvent and allowed to drip or air dry. Depending on the industry and/or company, these operations may be performed manually (i.e., by hand) or mechanically. Sometimes parts require more extensive cleaning; in these cases, additional cleaning is performed including directly spraying, agitation, wiping or brushing ([Reh and Nemhauser, 2001](#); [U.S. EPA, 1997](#)).

Table 2-24 presents OSHA CEHD for two facilities. The first facility uses 1-BP to clean parts in an immersion process in an area with general ventilation. The second facility uses 1-BP in a degreasing tank equipped with a spray nozzle. The degreasing operation is conducted in an area with local exhaust ventilation. Based on the available process description, EPA assumes these facilities operate a cold cleaner, even though the equipment is not described in detail in the OSHA CEHD. For workers, only five data points are available – the median and maximum exposures are 4.30 ppm and 7.40 ppm 8-hr TWA, respectively, from the available dataset. For occupational non-users, the exposure value is based on a single data point for a Chemical Safety and Health Officer (CSHO), who is an official from OSHA or a state plan occupational safety and health program. The exposure for this individual measured 2.60 ppm 8-hr TWA. EPA presents this data point as the potential exposure level for an occupational non-user; however, the exposure level may not be representative because the CSHO is not regularly present

in the production area. It should be further noted that CEHD are obtained from OSHA inspections, and not intended to be representative of typical worker exposure. Due to uncertainty in the data quality and the low number of available data points, the assessed exposure may not be representative of the full range of cold cleaning exposure scenarios.

Table 2-24. Summary of 1-BP Inhalation Exposure Monitoring Data for Cold Cleaner

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Data Points	Confidence Rating of Air Concentration Data
	Central tendency	High-end (Max)	Central tendency	High-end (Max)		
Worker	4.30	7.40	1.71	3.79	5	High
ONU	2.60		1.03	1.33	1	

Source: ([OSHA, 2013b, c](#)).

Assessment of Inhalation Exposure Based on Modeling

The Cold Cleaning model, including all model input parameters, was previously peer reviewed as part of the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#). A more detailed description of the modeling approach is provided in the *Supplemental Information on Occupational Exposure Assessment (EPA, 2019g)*. The [EPA AP-42, Compilation of Air Emissions Factors](#) contains emission factors and process information developed and compiled from source test data, material balance studies, and engineering estimates ([U.S. EPA, 1981](#)). AP-42 Chapter 4.6 provides generic, non-methane VOC emission factors for several solvent cleaning operations, including cold cleaning and vapor degreasing. These emission factors suggest that cold cleaning emissions range from 3.2 to 57.1 percent of the emissions from a traditional open-top vapor degreaser ([U.S. EPA, 1981](#)). It is not known whether the emission factors derived using VOC data would be representative of 1-BP emissions, or whether the emission reduction when switching from vapor degreasing to cold cleaning would be similar across different chemicals. To model exposures during 1-BP cold cleaning, an exposure reduction factor, RF, with uniform distribution from 0.032 to 0.571 is applied to the vapor generation rate in the vapor degreasing model.

Figure 2-5 presents the model approach for cold cleaning. Except for the exposure reduction factor, the model approach and input parameters for cold cleaning are identical to those previously presented for batch vapor degreasing. EPA performed a *Monte Carlo* simulation with 100,000 iterations and the Latin Hypercube sampling method in [@Risk](#) to estimate 8-hr TWA near-field and far-field exposures, acute exposures, ADCs, and LADCs. Note the cold cleaning model approach and the underlying data used (i.e. EPA AP-42) do not differentiate between a spray versus immersion cold cleaner.

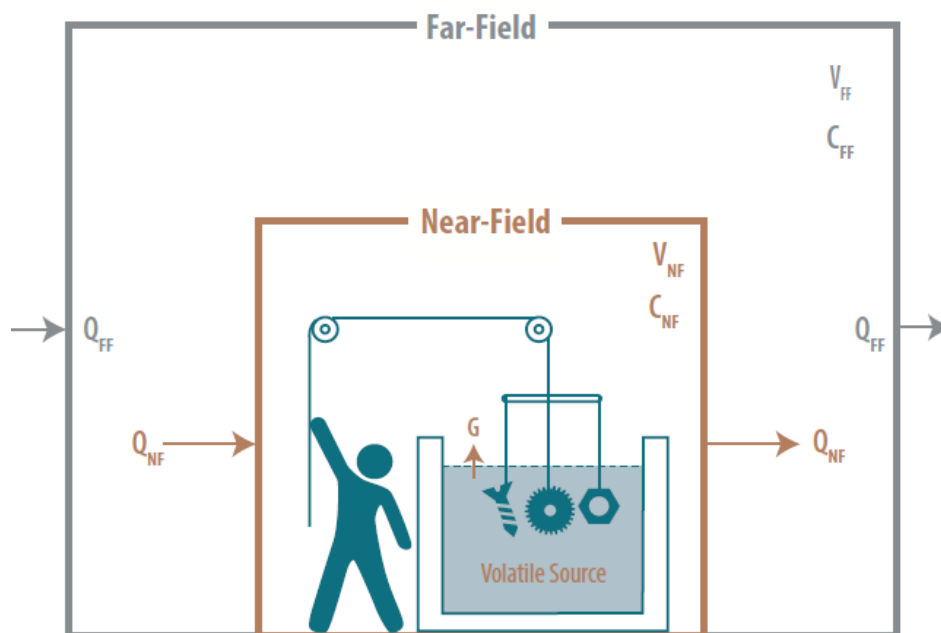


Figure 2-5. The Near-Field/Far-field Model for Cold Cleaning Scenario

Table 2-25 presents a statistical summary of the inhalation exposure modeling results. For workers, the 50th and 95th percentile exposures are 0.55 ppm and 11.91 ppm 8-hr TWA. For occupational non-users, the 50th and 95th percentile exposures are 0.29 ppm and 6.83 ppm 8-hr TWA. The model exposure levels are in good agreement with monitoring data.

Table 2-25. Summary of 1-BP 8-hr TWA Inhalation Exposures (AC, ADC and LADC) for Cold Cleaner Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	0.55	11.91	0.21	4.59	N/A – Modeled Data
ONU	0.29	6.83	0.11	2.63	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data from OSHA CEHD, and the data were determined to have a high confidence rating through EPA's systematic review process. However, CEHD data are obtained from OSHA inspections and are not intended to represent typical exposure levels at the workplace. In addition, monitoring data for a CSHO may not be representative of the exposure level for the typical occupational non-users.

The exposure monitoring data is supplemented with near-field/far-field exposure modeling using a *Monte Carlo* approach. The exposure model was peer reviewed as part of the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#). The model references EPA AP-42 emission factors for generic, non-methane VOC. These emission factors may not be representative of emissions for 1-BP, and could result in either an over- or underestimate. Despite these uncertainties, the model results are in good agreement

with the exposure monitoring data. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure.

2.3.1.15 Aerosol Spray Degreaser/Cleaner

Process Descriptions

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. Based on identified safety data sheets (SDS), 1-BP-based formulations typically use carbon dioxide, liquified petroleum gas (LPG) (i.e., propane and butane), 1,1,1,2-tetrafluoroethane, 1,1-difluoroethane, and pentafluorobutane as the carrier gas ([U.S. EPA, 2017c](#)). The aerosol droplets bead up on the fabricated part and then drip off, carrying away any contaminants and leaving behind a clean surface.

Figure 2-6 illustrates the typical process of using aerosol degreasing to clean components in commercial settings. One example of a commercial setting with aerosol degreasing operations is repair shops, where service items are cleaned to remove any contaminants that would otherwise compromise the service item's operation. Internal components may be cleaned in place or removed from the service item, cleaned, and then re-installed once dry ([U.S. EPA, 2014a](#)). Example uses of aerosol products containing 1-BP include general purpose degreasing, engine degreasing, brake cleaning, and metal product cleaning applications.

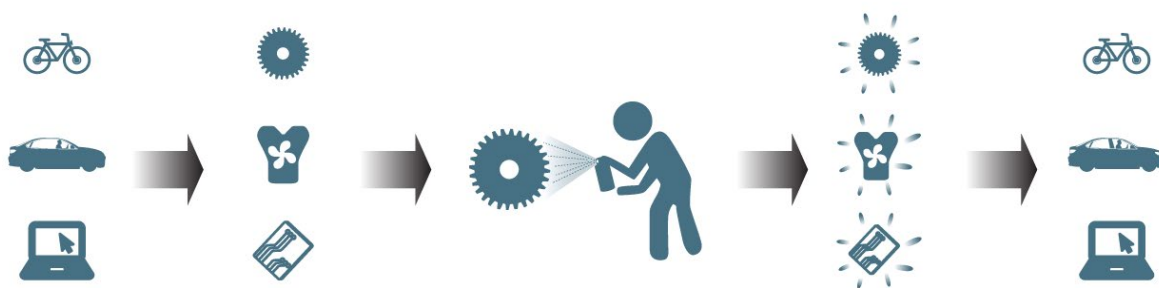


Figure 2-6. Overview of Aerosol degreasing

Number of Sites and Potentially Exposed Workers

NAICS industry sectors relevant to aerosol degreasing and BLS occupation codes where workers are potentially exposed to degreasing solvents are detailed in the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)). EPA assumed the types of occupation with potential solvent exposure are similar between vapor degreasing and aerosol degreasing.

EPA market report on 1-BP estimated that “1,000 to 5,000 businesses used 1-BP-based aerosol solvents in 2002 ([U.S. EPA, 2007c](#)), as cited in ([U.S. EPA, 2013c](#))”. This translates to a market penetration of approximately 0.4 percent to 2.2 percent. Based on these estimates, approximately 2,465 to 12,329 workers and occupational non-users are potentially exposed to 1-BP as an aerosol degreasing solvent (see Table 2-26). It is unclear whether the number of establishments using 1-BP-based aerosol solvents has changed substantially since 2002.

Table 2-26. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP in Aerosol Spray Degreaser/Cleaner

Exposed Workers ^a	Exposed Occupational non-users ^a	Total Exposed ^a	Estimated Number of Establishments	Workers per Site	Occupational non-users per Site
Low-end					
2,200	240	2,500	1,000	2	0.2
High-end					
11,000	1,200	12,000	5,000	2	0.2

Note: Number of workers and occupational non-users per site are calculated by dividing the exposed number of workers or occupational non-users by the number of establishments. The number of workers per site is rounded to the nearest integer. The number of occupational non-users per site is shown as 0.2, as it rounds down to zero.

a – Values rounded to 2 significant digits.

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-27 summarizes 8-hr TWA PBZ monitoring data for aerosol degreasing obtained from ([Stewart, 1998](#)) and ([Tech Spray, 2003](#)). The Stewart ([1998](#)) study measured 1-BP worker PBZ during an aerosol spray can application on a test substrate consisting of a small electric motor; the scenario was intended to simulate workers performing typical repair and maintenance work. The Tech Spray ([2003](#)) study measured worker exposure in a test scenario that simulated cleaning of printed circuit boards for the repair of computers and electrical systems. Among the two test studies, the 50th and 95th percentile worker exposures were 16.1 ppm and 31.6 ppm, respectively.

The Tech Spray study tested an exposure scenario where the 1-BP aerosol degreasing occurred inside a non-vented booth. Subsequently, the company tested the same scenario in a vented booth. With a non-vented booth, worker exposure ranged from 13 to 32 ppm 8-hr TWA. With the vented booth, worker exposure was reduced to 5.50 ppm 8-hr TWA based on a single data point. The representativeness of this single data point as a post-EC scenario is unknown. The vented booth scenario has a constant draw of 0.9 cubic meters per second during the 8-hour test. The data suggest the significance of ventilation and its impact on worker exposure.

Table 2-27. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Aerosol Spray Degreaser/Cleaner Based on Monitoring Data

Category ^a	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker, Pre EC	16.1	31.6	6.38	16.2	6	Medium
Worker, Post EC ^b	5.50		2.19	2.82	1	

Source: Stewart ([1998](#)); Tech Spray ([2003](#)), as cited in ([U.S. EPA, 2006b](#)). The vented booth scenario from Tech Spray is used as the post-EC scenario, and the remaining data points are used as the pre-EC scenario.

^a Worker includes operators, technicians, mechanics, and maintenance supervisor. Data are not available for occupational non-users.

^b The 8-hr TWA exposure estimate is combined with 50th and 95th percentile value on the number of working years to calculate LADC. See Appendix B.

In addition to the data summarized above, the Tech Spray study included a test scenario that measured short-term worker exposure that simulated an automotive repair shop. In this test, 1-BP was sprayed

continuously over a 15-minute period. In reality, workers are only expected to spray 1-BP for a few minutes at a time; as such, the test was intended to simulate a “worst-case” scenario with heavy 1-BP usage. The 15-min short term exposure for operators ranged from 190 to 1,100 ppm. Further, the 15-minute short term exposure for a worker in an adjacent room measured 11 ppm (([Tech Spray, 2003](#)), as cited in ([U.S. EPA, 2006b](#))). The presence of 1-BP in the adjacent room suggests the infiltration of contaminated air into other work areas.

Assessment of Inhalation Exposure Based on Modeling

Aerosol degreasing formulations containing 1-BP can be used at a variety of workplaces. For the purpose of modeling, EPA modeled worker exposure to 1-BP during brake servicing as a representative exposure scenario. EPA chose to model this scenario because the process of brake servicing is well understood and there is sufficient data to construct such a model. EPA believes brake servicing and engine degreasing at automotive maintenance and repair shops is a common application for products containing 1-BP, and the process is a representative aerosol degreasing scenario.

Figure 2-7 illustrates the *Brake Servicing Near-Field/Far-Field Inhalation Exposure Model*. The general model framework was previously included in the 2016 draft 1-BP Risk Assessment; however, specific model parameters have been updated with data from a recent CARB study. As the figure shows, 1-BP in aerosolized droplets immediately volatilizes into the near-field, resulting in worker exposures at a concentration C_{NF} . The concentration is directly proportional to the amount of aerosol degreaser applied by the worker, who is standing in the near-field-zone (i.e., the working zone). The volume of this zone is denoted by V_{NF} . The ventilation rate for the near-field zone (Q_{NF}) determines how quickly 1-BP dissipates into the far-field (i.e., the facility space surrounding the near-field), resulting in occupational non-user exposures to 1-BP at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the 1-BP dissipates out of the near-field. The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly 1-BP dissipates out of the surrounding space and into the outside air.

In this scenario, 1-BP vapors enter the near-field in non-steady “bursts,” where each burst results in a sudden rise in the near-field concentration, followed by a more gradual rise in the far-field concentration. The near-field and far-field concentrations then decay with time until the next burst causes a new rise in near-field concentration. The product application rate is based on a 2000 CARB report for brake servicing, which estimates that each facility performs on average 936 brake jobs per year, and that each brake job requires approximately 14.4 ounces of product. For each model iteration, EPA determined the concentration of 1-BP by assuming the formulation could be one of 25 possible aerosol degreasing products identified in the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane* ([U.S. EPA, 2017c](#)). Detailed model parameters and assumptions are presented in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)). EPA did not model a “post-EC” scenario because there is not sufficient information to determine the type and effectiveness of engineering control at automotive and other commercial degreasing facilities.

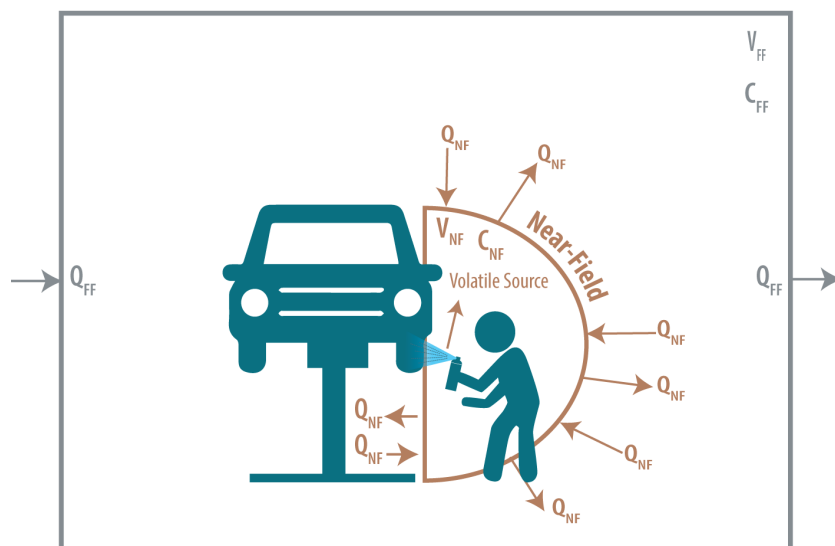


Figure 2-7. Schematic of the Near-Field/Far-Field Model for Aerosol degreasing

EPA performed a *Monte Carlo* simulation with 100,000 iterations and the Latin hypercube sampling method to model near-field and far-field exposure concentrations in the aerosol degreasing scenario. Table 2-28 presents a statistical summary of the exposure modeling results. The 50th and 95th percentile exposures are 6.37 ppm and 22.53 ppm 8-hr TWA for workers, and 0.11 ppm and 0.93 ppm 8-hr TWA for occupational non-users.

Table 2-28. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Aerosol Spray Degreaser/Cleaner Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	6.37	22.53	2.38	9.05	N/A – Modeled Data
ONU	0.11	0.93	0.04	0.36	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data specific to aerosol degreasing. The data come from two studies with “medium” confidence rating.

The exposure monitoring data are supplemented with the Brake Servicing Near-Field/Far-Field Inhalation Exposure Model, which provides exposure estimates for a brake cleaning scenario. The model uses a *Monte Carlo* approach to incorporate variability. Although the model scenario is specific to brake cleaning and may not encompass the full range of aerosol degreasing scenarios, the model results are in good agreement with monitoring data. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure.

2.3.1.16 Dry Cleaning

Process Descriptions

1-BP is a solvent used in dry cleaning machines. There are two known 1-BP based dry cleaning formulations, DrySolv® and Fabrisolv™ XL, which were introduced beginning in 2006. These formulations are often marketed as “drop-in” replacements for perchloroethylene (PERC), which indicates they can be used in third generation or higher PERC equipment ([TURI, 2012](#)). Third generation equipment, introduced in the late 1970s and early 1980s, are non-vented, dry-to-dry machines with refrigerated condensers. These machines are essentially closed systems and are only open to the atmosphere when the machine door is opened. In third generation machines, heated drying air is recirculated back to the drying drum through a vapor recovery system ([CDC, 1997](#)).

Fourth generation dry cleaning equipment are essentially third-generation machines with added secondary vapor control. These machines “rely on both a refrigerated condenser and carbon adsorbent to reduce the PERC concentration at the cylinder outlet below 300 ppm at the end of the dry cycle”, and are more effective at recovering solvent vapors. Fifth generation equipment have the same features as fourth generation machines, but also have a monitor inside the machine drum and an interlocking system to ensure that the concentration is below approximately 300 ppm before the loading door can be opened ([CDC, 1997](#)).

Dry cleaners who opt to use 1-BP can either convert existing PERC machines or purchase a new dry cleaning machine specifically designed for 1-BP. To convert existing PERC machines to use 1-BP, machine settings and components must be changed to prevent machine overheating and solvent leaks ([Blando et al., 2010](#)). 1-BP is known to damage rubber gaskets and seals. It can also degrade cast aluminum, which is sometimes used on equipment doors and other dry cleaning machine components. In addition, 1-BP is not compatible with polyurethane and silicone ([TURI, 2012](#)).

While conversion of a PERC machine to 1-BP is no longer recommended by the manufacturer, 1-BP remains the only drop-in replacement that does not require buying a new machine. In some cases, the shop owners may elect to do the conversion themselves to avoid the high cost of paying for a professional company for the conversion ([U.S. EPA, 2016b](#)).

Figure 2-8 provides an overview of the dry cleaning process. Worker exposure monitoring studies for 1-BP at dry cleaning facilities suggest workers are exposed when 1) adding make-up solvent, typically by manually dumping it through the front hatch, 2) opening the machine door during the wash cycle, and 3) removing loads from the machines ([Blando et al., 2010](#)).

Engineering controls such as local exhaust ventilation (LEV) located at or near the machine door can reduce worker exposure during machine loading, machine unloading, and maintenance activities ([NCDOL, 2013](#)). However, there are currently no regulatory requirements for installing such controls to reduce 1-BP emissions and associated worker exposures at dry cleaning facilities. In addition, engineering controls may not be economically feasible for dry cleaning shops.

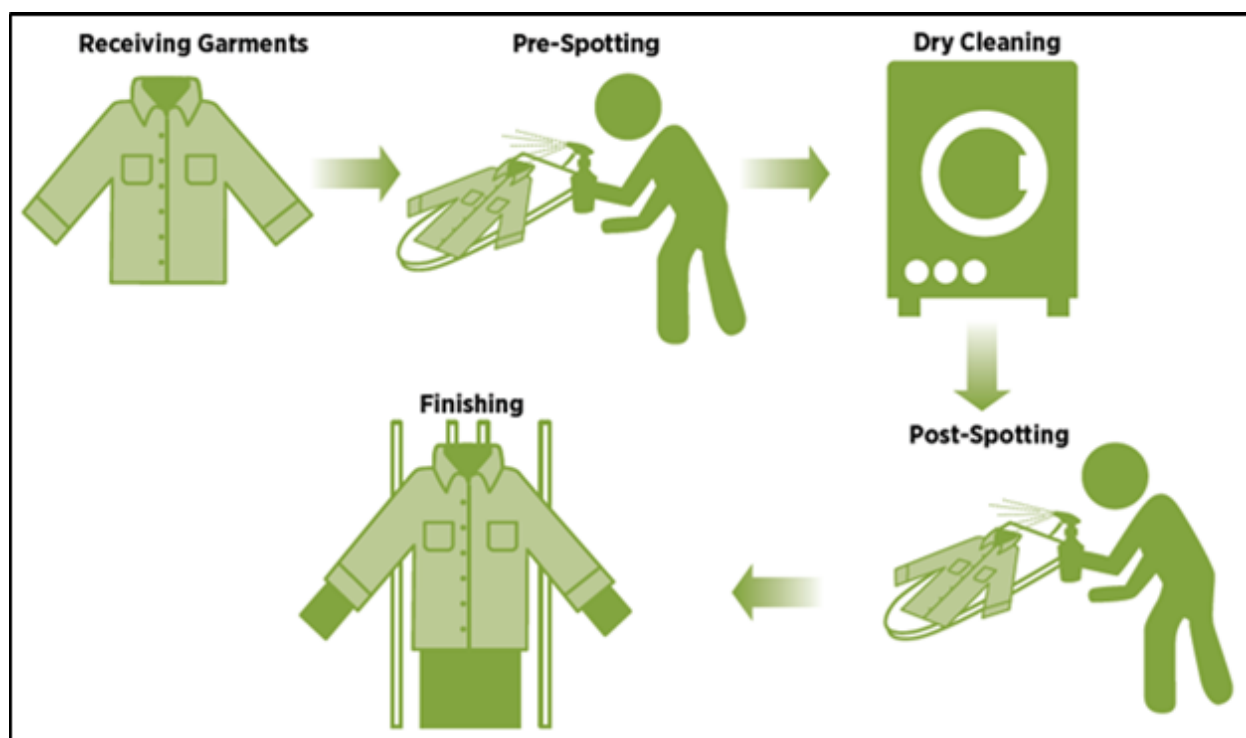


Figure 2-8. Overview of Dry Cleaning

Number of Sites and Potentially Exposed Workers

EPA estimated the number of workers and occupational non-users potentially exposed to 1-BP at dry cleaners using Bureau of Labor Statistics' OES data ([2016](#)) and the U.S. Census' SUSB ([2015](#)). The method for estimating number of workers is detailed in *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)). These estimates were derived using industry- and occupation-specific employment data from the BLS and U.S. Census. EPA anticipates that dry cleaners are categorized under NAICS 812320, "Drycleaning and Laundry Services (except Coin-Operated)".

According to a public comment submitted by Enviro Tech International, Inc. (Enviro Tech), a major 1-BP supplier, approximately 28 machines (nine converted PERC machines and 19 DrySolv machines) were known to be in service in 2016. The number of machines was reduced to 23 in 2017, after Enviro Tech ceased selling DrySolv to users of converted PERC machines ([Enviro Tech International, 2017](#)). More recent communication with Enviro Tech indicates only eight dry cleaning establishments are using 1-BP in 2019 ([Enviro Tech, 2019](#)). Assuming one machine per facility, EPA estimates a total of 32 workers and occupational non-users are exposed to 1-BP (Table 2-29).

Table 2-29. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP in Dry Cleaning Shops

Exposed Workers	Exposed Occupational non-users	Total Exposed	Estimated Number of Establishments	Workers per Site	Occupational non-users per Site
24	8	32	8	3	1

Source: ([U.S. BLS, 2016](#)) ([Bureau, 2015](#)) ([Enviro Tech, 2019](#))

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-30 presents an analysis of the 8-hr TWA Personal Breathing Zone (PBZ) monitoring data from literature. The data were obtained from two literature studies covering the same four dry cleaning shops in New Jersey. The studies noted that work load and work practices varied greatly among the shops, resulting in variability in 1-BP exposure across these shops. In addition, there can be significant variability in 1-BP exposure across different job titles, and in some cases on different days when the exposure monitoring was conducted. The exposure data were also impacted by the willingness of individual shops to participate in exposure monitoring. Note one study ([Eisenberg and Ramsey, 2010](#)) contains additional partial-shift exposure data that are not summarized here. For those data, an 8-hr TWA value was not obtained because owners of the shop requested that NIOSH remove the sampling equipment once they had finished running the dry cleaning machines ([Eisenberg and Ramsey, 2010](#)).

All four shops included in the studies used converted 3rd generation machines ([Blando et al., 2010](#)). The shops dry cleaned one to 14 loads of garments per day. Some shops that converted the machines themselves “cooked” the solvent, a practice that had been performed widely for PERC but is no longer recommended by the manufacturers for 1-BP operation ([Eisenberg and Ramsey, 2010](#)). Only one shop added make-up solvent on Sample Day 1 and Sample Day 2 by manually dumping a 5-gallon can of solvent product through the front hatch of the machine ([Blando et al., 2010](#)). The facilities had general building ventilation, ceiling-mounted or wall-mounted fans, but lacked controls specifically designed to reduce exposure to the dry cleaning solvent.

EPA defined workers as dry cleaning machine operators. For workers, the 50th and 95th percentile exposures are 29.4 ppm and 50.2 ppm 8-hr TWA, respectively. The exposure level is impacted by the number of loads cleaned, the number of solvent cooking cycles used, and whether any make-up solvent was added in that particular shop and on that particular day when the monitoring was conducted ([Blando et al., 2010](#)). The highest 1-BP concentration in air was found when a facility with a converted PERC machine cooked the solvent ([Eisenberg and Ramsey, 2010](#)).

EPA defined occupational non-users as employees who work in the dry cleaning shops but do not operate the machine. For occupational non-users, the 50th and 95th percentile exposures are 12.1 ppm and 20.6 ppm 8-hr TWA, respectively. The data suggest that 1-BP exposure for cashiers, clerks, and other employees at the shop can still be significant. In addition to occupational non-users, children may also be present at some small, family-owned dry cleaning shops, and thereby be exposed to 1-BP. The monitoring studies do not contain information on exposure to children.

Table 2-30. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Dry Cleaning Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker ^a	29.4	50.2	11.7	25.7	8	High
ONU ^b	12.1	20.6	4.80	10.6	6	

Source: ([Blando et al., 2010](#); [Eisenberg and Ramsey, 2010](#); [NIOSH, 2010](#))

^a Worker refers to dry cleaning machine operators.

^b Occupational non-user refers to cashiers and clerks.

Assessment of Inhalation Exposure Based on Modeling

Because there are multiple activities with potential 1-BP exposure at a dry cleaner, a multi-zone modeling approach is used to account for 1-BP vapor generation from multiple sources. This model framework was peer reviewed as part of the 2016 draft 1-BP Risk Assessment. The model has been updated to address public and peer review comments. The model also reflects additional information that became available since 2016; specifically, several model input parameters have been refined. Figure 2-9 illustrates this multi-zone approach, which considers the following three worker activities:

- **Spot cleaning of stains on both dirty and clean garments:** On receiving a garment, dry cleaners inspect for stains or spots they can remove as much of as possible before cleaning the garment in a dry cleaning machine. Spot cleaning may also occur after dry cleaning if the stains or spots were not adequately removed. Spot cleaning occurs on a spotting board and can involve the use of a spotting agent containing various solvents, such as 1-BP. Workers are exposed to 1-BP when applying it via squeeze bottles, hand-held spray bottles, or even from spray guns connected to pressurized tanks. Once applied, the worker may come into further contact with the 1-BP if using a brush, spatula, pressurized air or steam, or their fingers to scrape or flush away the stain ([Young, 2012](#); [NIOSH, 1997](#)). For modeling, EPA assumed the near-field is a rectangular volume covering the body of a worker.
- **Unloading garments from dry cleaning machines:** At the end of each dry cleaning cycle, workers manually open the machine door to retrieve cleaned garments. During this activity, workers are exposed to 1-BP vapors remaining in the dry cleaning machine cylinder. For modeling, EPA assumed that the near-field consists of a hemispherical area surrounding the machine door, and that the entire cylinder volume of air containing 1-BP exchanges with the workplace air, resulting in a “spike” in 1-BP concentration in the near-field, C_D , during each unloading event. This concentration is directly proportional to the amount of residual 1-BP in the cylinder when the door is opened. The near-field concentration then decays with time until the next unloading event occurs.
- **Finishing and pressing:** The cleaned garments taken out of the cylinder after each dry clean cycle contain residual solvents and are not completely dried ([Von Grote et al., 2003](#)). The residual solvents are continuously emitted into the workplace during pressing and finishing, where workers manually place the cleaned garments on the pressing machine to be steamed and ironed. EPA assumed any residual solvent is entirely evaporated during pressing, resulting in an increase in the near-field 1-BP concentration during this activity. Workers are exposed to 1-BP vapors while standing in vicinity of the press machine. For modeling, EPA assumed the near-field is a rectangular volume covering the body of a worker.

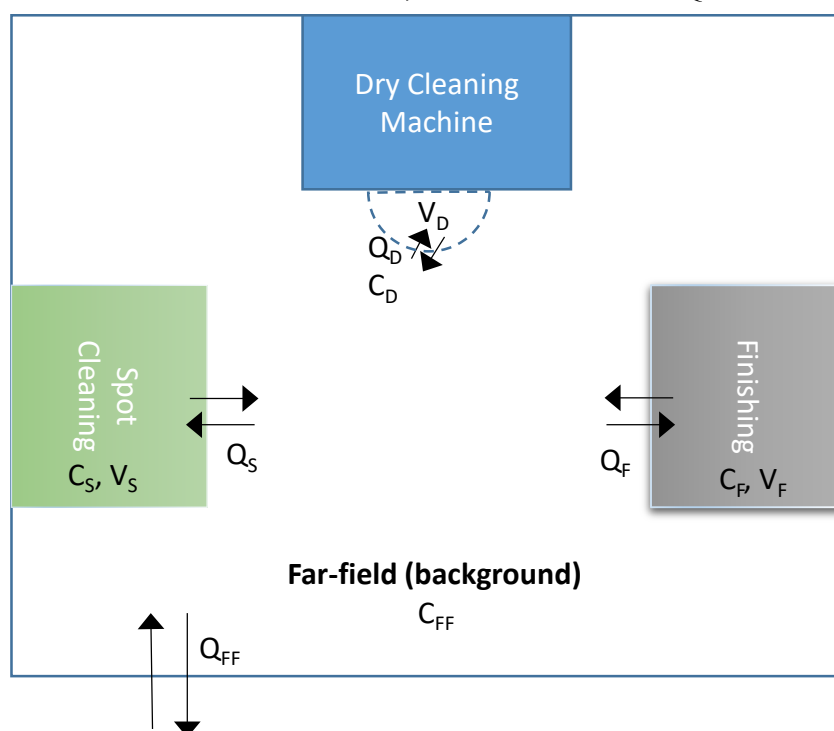


Figure 2-9. Illustration of the Multi-Zone Model

As the figure shows, 1-BP vapor is generated in each of the three near-fields, resulting in worker exposures at concentrations C_S , C_D , and C_F . The volume of each zone is denoted by V_S , V_D , and V_F . The ventilation rate for the near-field zone (Q_S , Q_D , Q_F) determines how quickly 1-BP dissipates into the far-field (i.e., the facility space surrounding the near-fields), resulting in occupational non-user exposures to 1-BP at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the 1-BP dissipates out of the near-field. The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly 1-BP dissipates out of the surrounding space and into the outside air. The *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)) summarizes the parameters and equations for the multi-zone model. The far-field volume, air exchange rate, and near-field indoor wind speed are identical to those used in the 1-BP Spot Cleaning Model (see Section 2.3.1.17). These values were selected using engineering judgment and literature data that EPA believed to be representative of a typical dry cleaner.

The dry cleaning industry is characterized by a large number of small businesses, many are family-owned and operated. EPA assumed small dry cleaners operate up to 12 hours a day and up to 6 days a week. In addition, EPA assumed each facility has a single machine. The assumption of a single machine per facility is supported by a recent industry study conducted in King County, Washington, where 96 percent of 151 respondents reported having only one machine at their facility. Four reported having two machines, and two reported having three machines ([Whittaker and Johanson, 2011](#)). Based on the survey results, this assumption is presumably representative of the majority of small dry cleaning shops.

EPA modeled the baseline scenario assuming the facility operates a converted third generation machine, the machine type observed at all three New Jersey dry cleaners in the Blando et al. ([2010](#)) study. For the engineering control scenario, EPA modeled a facility with a fourth generation machine. EPA believes facilities using 1-BP are unlikely to own fifth generation machines ([ERG, 2005](#)).

EPA assessed three types of workers within the modeled dry cleaning facility: 1) a worker who performs spot cleaning; 2) a worker who unloads the dry cleaning machine and finishes and presses the garments; and 3) an occupational non-user. Each worker type is described in further detail below. EPA assumed each worker activity is performed over the full 12-hour operating day.

- EPA assumed spot cleaning occurs for a duration varying from two to five hours in the middle of the twelve-hour day. The worker is exposed at the spot cleaning near-field concentration during this time, and at the far-field concentration for the remainder of the day. Spot cleaning can be performed for both dry cleaned loads and for laundered loads.
- EPA assumed a separate worker unloads the dry cleaning machine, and finishes and presses the garments. After each load, EPA assumed this worker spends five minutes unloading the machine, during which he or she is exposed at the machine near-field concentration. After unloading, the worker spends five minutes in the finishing near-field to prepare the garments. Then, the worker spends another 20 minutes finishing and pressing the cleaned garments. During this 20-minute period of finishing and pressing, the residual 1-BP solvent is off-gassed into the finishing near-field. The amount of residual 1-BP solvent is estimated using measured data presented in ([Von Grote et al., 2003](#)). These unloading and finishing activities are assumed to occur at regular intervals throughout the twelve-hour day. The frequency of unloading and finishing depends on the number of loads dry cleaned each day, which varies from one to 14, where 14 was the maximum number of loads observed in the studies ([Blando et al., 2010](#); [Eisenberg and Ramsey, 2010](#)). When this worker is not unloading the dry cleaning machine or finishing and pressing garments, the worker is exposed at the far-field concentration.
- EPA assumed one occupational non-user is exposed at the far-field concentration for twelve hours a day. The occupational non-user could be the cashier, tailor, or launderer, who works at the facility but does not perform dry cleaning activities.

Table 2-31 presents the *Monte Carlo* results with the Latin hypercube sampling method and 10,000 iterations. Statistics of the 12-hr TWA exposures (95th and 50th percentiles) are calculated at the end of the simulation after all iterations have completed. The AC, ADC, and LADC calculations are integrated into the *Monte Carlo* simulation, such that the exposure frequency matches the model input values for each iteration. As shown in the table, the worker who performs unloading and finishing activities have the highest exposure; this exposure can be reduced if the facility switches from a third generation to a fourth generation machine. However, the machine type does not significantly impact exposure level for other persons present at the facility, including the spot cleaner and the occupational non-user. The model values cover a wider distribution of exposure levels when compared to the monitoring data. This is likely due to the wide range of model input parameter values covering a higher number of possible exposure scenarios. However, the modeled occupational non-user exposures are lower than actual monitoring results. The model assumes the occupational non-user spends their time entirely in the far-field. In reality, it is reasonably foreseeable that these employees will occasionally perform activities in the near-field, thereby having a higher level of exposure.

Table 2-32 presents the exposure for children who may be present at the dry cleaning facility. Because many dry cleaners are family owned and operated, EPA assumed children may be present for a four-hour period (3 – 7pm) after school, during which they may be exposed at similar levels as occupational non-users. The table provides the 4-hr TWA exposure concentration and the 24-hr TWA AC. EPA could not calculate exposure for chronic scenarios (ADC and LADC) due to uncertainty in the exposure

frequency and number of years with exposure for children. EPA believes these exposures are unlikely to be chronic in nature.¹⁹

Table 2-31. Summary of 1-BP Dry Cleaning Exposures for Workers and Occupational Non-users Based on Modeling

Machine Type	12-hr TWA Exposures (ppm)		Acute, Non-Cancer Exposures (ppm)		Chronic, Non-Cancer Exposures (ppm)		Chronic, Cancer Exposures (ppm)	
	C _{1-BP} , 12-hr TWA		AC _{1-BP} , 24-hr TWA		ADC _{1-BP} , 24-hr TWA		LADC _{1-BP} , 24-hr TWA	
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile
Workers: Machine Unloading and Finishing (Near-Field)								
3 rd Gen.	14.1	60.5	7.06	30.3	4.98	21.70	1.89	8.57
4 th Gen.	2.38	6.36	1.19	3.18	0.84	2.30	0.31	0.94
Workers: Spot Cleaning (Near-Field)								
3 rd Gen.	2.93	7.93	1.47	3.97	1.03	2.83	0.39	1.14
4 th Gen.	2.40	5.65	1.20	2.83	0.85	2.02	0.32	0.82
Occupational non-users (Far-Field)								
3 rd Gen.	1.82	6.65	0.91	3.33	0.64	2.37	0.24	0.95
4 th Gen.	1.31	4.21	0.65	2.11	0.46	1.49	0.17	0.60

Confidence rating of air concentration data: N/A – modeled data.

Table 2-32. Summary of 1-BP Dry Cleaning Exposures for Children Based on Modeling

Machine Type	4-hr TWA Exposures (ppm)		Acute, Non-Cancer Exposures (ppm)		Chronic, Non-Cancer Exposures (ppm)		Chronic, Cancer Exposures (ppm)	
	C _{1-BP} , 4-hr TWA		AC _{1-BP} , 24-hr TWA		ADC _{1-BP} , 24-hr TWA		LADC _{1-BP} , 24-hr TWA	
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile
Children (Far-Field)								
3 rd Gen.	0.54	4.03	0.09	0.67	N/A	N/A	N/A	N/A
4 th Gen.	0.09	1.02	0.01	0.17	N/A	N/A	N/A	N/A

N/A – Not applicable

Confidence rating of air concentration data: N/A – modeled data.

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

For this condition of use, exposure is assessed using 1-BP personal breathing zone monitoring data from three different studies, all of which have a high confidence rating as determined through EPA's systematic review process. The monitoring data, which were collected from facilities using converted third generation machines, are in good agreement with model results for the same machine type.

The multi-zone Dry Cleaning model was previously peer reviewed as part of the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#). Since then, the model has been updated to address peer review comments and to incorporate additional available data. The model uses a *Monte Carlo* approach to incorporate variability in the environmental conditions, worker activity patterns, use rate, and other model input parameters. The model assumes each dry cleaner operates a single machine, and does not

¹⁹ EPA did not calculate acute risk for children at dry cleaners because the acute health domains (developmental effects) are not applicable to children. Further, EPA did not calculate chronic and cancer risks for children at dry cleaners because EPA believes exposure to children at workplaces are unlikely to be chronic in nature.

represent exposures for larger facilities that may have multiple machines. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure for these machine types.

2.3.1.17 Spot Cleaner, Stain Remover

Process Descriptions

EPA assessed a separate spot cleaning scenario at dry cleaners. This scenario represents dry cleaners or other shops that use 1-BP-based spot cleaning formulations but do not otherwise use 1-BP in a dry cleaning machine. The extent of such uses is likely limited, as Enviro Tech claimed that while DrySolv spotting products were advertised to the dry cleaning industry, most were never commercialized ([Enviro Tech International, 2017](#)).

On receiving a garment, dry cleaners inspect for stains or spots and remove as much of them as possible before cleaning the garment in a machine. As Figure 2-10 shows, spot cleaning occurs on a spotting board and can involve the use of a spotting agent containing various solvents, such as 1-BP. The spotting agent can be applied from squeeze bottles, hand-held spray bottles, or even from spray guns connected to pressurized tanks. Once applied, the dry cleaner may come into further contact with the 1-BP if using a brush, spatula, pressurized air or steam, or their fingers to scrape or flush away the stain ([Young, 2012](#); [NIOSH, 1997](#)).



Figure 2-10. Overview of Use of Spot Cleaning at Dry Cleaners

Number of Sites and Potentially Exposed Workers

See Section 2.3.1.16 for the estimated number of workers and occupational non-users at dry cleaning shops. Workers at these shops often perform multiple activities; as such, a single worker who spot treats the garments using 1-BP may also load and unload the dry cleaning machines.

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-33 presents 8-hr TWA PBZ monitoring data from OSHA CEHD for three facilities where spot cleaning is performed. At one facility, workers spray-applied solvent formulation to stained portions of dresses and did not wear any personal protective equipment. It is unclear if there were any engineering controls at the facility to mitigate worker exposure.

The 50th and 95th percentile exposure level for workers were 0.90 ppm and 4.73 ppm 8-hr TWA. No exposure monitoring data are available for occupational non-users.

Table 2-33. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Spot Cleaner Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker	0.90	4.73	0.36	2.42	6	High

Source: ([Osha, 2019](#), [2013b](#))

Assessment of Inhalation Exposure Based on Modeling

Figure 2-11 illustrates the near-field/far-field modeling approach that EPA applied to spot cleaning facilities. The model, including all input parameters, are described in more detail in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)). The model framework has been peer reviewed as part of the 2016 draft 1-BP Risk Assessment. Since 2016, the model has been updated to address public and peer review comments and to incorporate additional information that became available.

As the figure shows, chemical vapors evaporate into the near-field (at evaporation rate G), resulting in near-field exposures to workers at a concentration C_{NF} . The concentration is directly proportional to the amount of spot cleaner applied by the worker, who is standing in the near-field-zone (i.e., the working zone). The volume of this zone is denoted by V_{NF} . The ventilation rate for the near-field zone (Q_{NF}) determines how quickly the chemical of interest dissipates into the far-field (i.e., the facility space surrounding the near-field), resulting in occupational non-user exposures at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the chemical of interest dissipates out of the near-field. The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly the chemical dissipates out of the surrounding space and into the outdoor air.

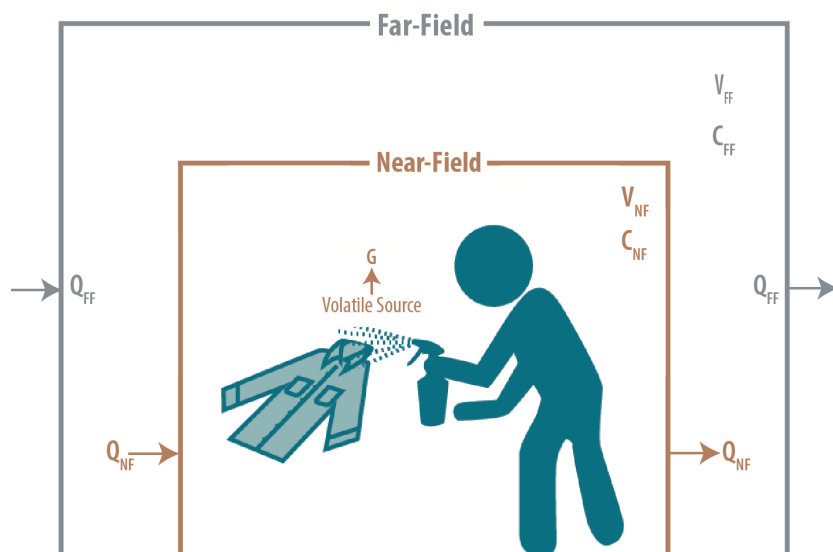


Figure 2-11. Schematic of the Near-Field/Far-Field Model for Spot Cleaning

To determine the 1-BP use rate, EPA conducted a targeted literature search to identify information on the typical amount of spotting agents used at dry cleaners. The Massachusetts Department of Environmental Protection (MassDEP) provided a comparative analysis of several dry cleaner case

studies using various PERC alternatives. This document estimates a dry cleaner using 1-BP spends \$60 per month on spotting agents. This particular facility dry cleans 100 pieces of garments per day. MassDEP noted that the facility size can vary greatly among individual dry cleaners ([MassDEP, 2013](#)). Blando et al. (2009) estimated that 1-BP solvent products cost \$45 per gallon. Based on this information, EPA calculated a spot cleaner use rate of 1.33 gallons per month, or 16 gallons per year. The Safety Data Sheet for DrySolv, a common 1-BP formulation, indicates the product contains greater than 87 percent 1-BP by weight ([Enviro Tech International, 2013](#)).

EPA performed *Monte Carlo* simulations, applying 100,000 iterations and the Latin hypercube sampling method. Table 2-34 presents a statistical summary of the exposure modeling results. The 50th and 95th percentile exposure for workers (near-field) are 3.24 ppm and 7.03 ppm 8-hr TWA, respectively. These results are generally comparable to the monitoring data. For occupational non-users (far-field), the 50th and 95th percentile exposure levels are 1.63 ppm and 4.68 ppm 8-hr TWA, respectively. The table also presents the AC, ADC, and LADC values, which are integrated into the *Monte Carlo*. EPA assumes no engineering controls (e.g. exhaust hoods) are present at spot cleaning facilities, because controls may not be financially feasible for small shops.

Table 2-34. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Use of Spot Cleaner Based on Modeling

Category	Acute, Non-Cancer Exposures (8-Hour TWAs in ppm)		Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm)		Chronic, Cancer Exposures (ppm)		Confidence Rating of Air Concentration Data
	AC _{1-BP, 8-hr TWA}		ADC _{1-BP, 8-hr TWA}		LADC _{1-BP, 8-hr TWA}		
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	3.24	7.03	0.76	1.66	0.29	0.68	N/A – Modeled Data
ONU	1.63	4.68	0.38	1.10	0.15	0.45	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

For this condition of use, the 1-BP personal breathing zone monitoring data have a high confidence rating as determined through EPA's systematic review process. It should be noted that, however, the data come from OSHA CEHD, which are not intended to represent typical workplace exposure level.

The monitoring data are supplemented with the near-field/far-field Spot Cleaning exposure model. The model incorporates a *Monte Carlo* simulation to address variability, and the model has been previously peer reviewed as part of the [2016 Draft Risk Assessment](#) (U.S. EPA, 2016d). Although there is uncertainty in the representativeness of the spot cleaner use rate from the MassDEP case study used in modeling, the model results are in good agreement with the monitoring data. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure.

2.3.1.18 Adhesive Chemicals (Spray Adhesives)

Process Descriptions

1-BP is used in spray adhesives for foam cushion manufacturing and fabrication (e.g., the furniture industry). Figure 2-12 illustrates a typical process of using spray adhesives. During foam cushion manufacturing and fabrication, foam is cut into pieces and then bonded together to achieve the

appropriate shape. Spray guns are used to spray-apply an adhesive onto flexible foam surfaces for bonding. Adhesive spraying typically occurs either on an open top workbench with side panels that may have some local ventilation, or in an open workspace with general room ventilation. After the adhesive is applied, workers assemble the cushions by hand-pressing together pieces of cut flexible foam ([NIOSH, 2003b](#), [2002b](#)).

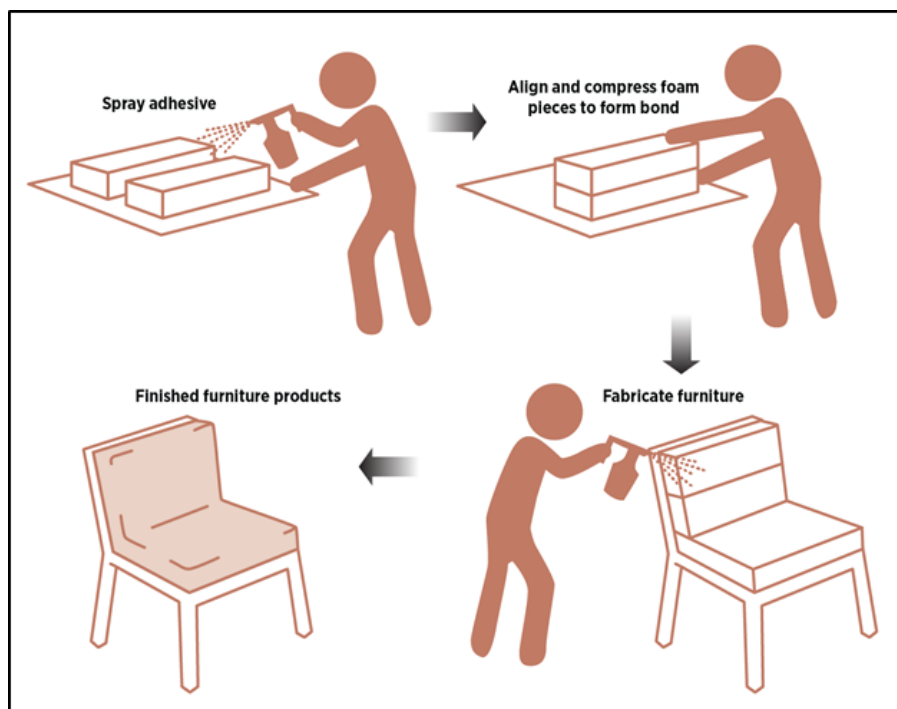


Figure 2-12. Overview of Use of Spray Adhesive in the Furniture Industry

Number of Sites and Potentially Exposed Workers

EPA estimated the number of workers potentially exposed to 1-BP in spray adhesives using Bureau of Labor Statistics' OES data ([2015](#)) and U.S. Census' SUSB ([2012](#)). The method for estimating number of workers is detailed in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)). The worker estimates were derived using industry- and occupation-specific employment data from these sources. The industry sectors and occupations that EPA determined to be relevant to spray adhesive use are presented in the 2016 draft 1-BP Risk Assessment.

The number of businesses in this use sector of 1-BP is estimated to be between 100 and 280 ([CDC, 2016](#); [U.S. EPA, 2007c](#)). Table 2-35 presents the estimated number of workers and occupational non-users using these estimates. The total number of potentially exposed workers and occupational non-users ranges from 1,503 to 4,209. Recent discussion with industry suggests the 1-BP market has since declined due to worker health issues associated with this use. In its 2017 public comment, Enviro Tech stated that it was aware of only two end users who currently use 1-BP as a carrier for an adhesive ([Enviro Tech International, 2017](#)). It is unclear whether the Enviro Tech estimate is comprehensive of the current spray adhesive market.

Table 2-35. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP in Spray Adhesive Use in Foam Cushion Manufacturing

Exposed Workers ^a	Exposed Occupational Non-Users ^a	Total Exposed ^a	Estimated Number of Establishments	Workers per Site	Occupational Non-Users per Site
Low-end					
550	950	1,500	100	6	10
High-end					
1,500	2,700	4,200	280	6	10

Note: Number of workers and occupational non-users per site are calculated by dividing the exposed number of workers or occupational non-users by the number of establishments. Values are rounded to the nearest integer.

a – Values rounded to 2 significant digits.

Assessment of Inhalation Exposure Based on Monitoring Data

1-BP exposure monitoring data were identified in several sources, including journal articles, NIOSH HHEs, and OSHA CEHD database. NIOSH HHEs are conducted at the request of employees, employers, or union officials and help inform on potential hazards present at the workplace. HHEs can also be conducted in response to a technical assistance request from other government agencies. OSHA CEHD are workplace monitoring data from OSHA inspections. These inspections can be random or targeted, or can be the result of a worker complaint.

Among these sources, three NIOSH studies provide the most comprehensive information on worker exposure to 1-BP from spray adhesives in foam cushion manufacturing. Two of the three HHEs also compare exposure pre- and post-engineering controls (EC). A summary of these HHEs follows:

- From March 1998 to April 2001, NIOSH investigated a facility in Mooresville, North Carolina to assess 1-BP exposures during manufacturing of foam seat cushions ([Reh et al., 2002](#)). The company had four departments: Saw, Assembly, Sew, and Covers. Workers in Assembly and Covers departments worked directly with the adhesive; however, workers in all four departments were exposed. The spray adhesive used at this facility contained between 60 and 80 percent 1-BP. NIOSH conducted an initial exposure assessment in 1998 and observed that the ventilation exhaust filters were clogged with adhesive. In 2001, NIOSH conducted a follow-up exposure assessment after the facility made improvements to its ventilation system.
- From November 2000 to August 2001, NIOSH investigated workplace exposures to 1-BP during manufacturing of foam seat cushions at another cushion company in North Carolina ([NIOSH, 2002b](#)). This facility uses a spray adhesive containing 55 percent 1-BP. NIOSH conducted an initial exposure assessment in 2000, and recommended that the facility reduce worker exposure by enclosing the spray stations to create “spray booths”. Subsequently, in 2001, NIOSH conducted a follow-up assessment after spray station enclosures were installed.
- From April 1999 to May 2001, NIOSH investigated another cushion company in North Carolina ([NIOSH, 2003b](#)). In this study, NIOSH conducted two separate exposure assessments. In the initial assessment, NIOSH measured 1-BP inhalation exposures to workers in and near the adhesive spray operation areas. In the second assessment, NIOSH measured additional 1-BP inhalation exposures at the facility. There were no changes to the facility’s local exhaust ventilation system between the first and second assessment.

Table 2-36 summarizes available 1-BP exposure data from the NIOSH and OSHA sources. The data set includes exposures in pre-EC and post-EC scenarios for each worker job category. EPA defined three job categories for 1-BP spray adhesive use:

- Sprayers: Workers who perform manual spraying of 1-BP adhesive as a regular part of his or her job;
- Non-sprayers: Workers who are not “sprayers”, but either handle the 1-BP adhesive or spend the majority of their shift working in an area where spraying occurs. For example, the NIOSH (2002) study indicated spraying occurs in the Assembly and Covers departments. EPA assumes workers in these departments who do not perform spraying still work in the vicinity of spraying operations and may be regularly exposed to 1-BP; and
- Occupational non-users: Workers who do not regularly perform work in an area of the facility where spraying occurs. For example, EPA assumes workers in the Saw and Sew departments of the 2002 NIOSH study (2002) are “occupational non-users”.

For each worker job category (sprayer, non-sprayer or occupational non-user) and exposure scenario (pre-EC or post-EC), EPA calculated the 50th and 95th percentile exposure levels from the observed data set. Pre-EC exposure scenarios suggest that all workers at foam cushion manufacturing facilities that use 1-BP spray adhesives have substantial exposure to 1-BP. Sprayers have the highest levels of exposure because they work directly with the 1-BP adhesive. However, non-sprayers and occupational non-users may also be exposed.

In general, exposure levels for job categories vary widely depending on the worker’s specific work activity pattern, individual facility configuration, and proximity to the 1-BP adhesive. For example, workers in the Saw and Sew departments in the NIOSH (2002) study classified as “occupational non-users” are exposed at levels above 100 ppm 8-hr TWA. The high exposure levels are caused by their proximity to spraying operations in other departments, even though no adhesive is used in the Saw and Sew departments (Reh et al., 2002). Additionally, some workers may not have a single assigned role; as such, their exposure level will vary depending on the specific tasks performed.

Post-EC exposure scenarios suggest that engineering controls such as ventilation and spray booth enclosure, if well designed, maintained, and operated, can reduce worker exposures by an order of magnitude. However, engineering controls alone do not reduce exposures for sprayers and non-sprayers to levels below 0.1 ppm, the time-weighted average threshold limit value (TLV) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH).

Additional 1-BP worker exposure monitoring data have been identified in other literature studies such as Hanley et al. (2009; 2006a), Ichihara et al. (2002), and Majersik et al. (2007). However, these studies are not used in EPA’s analysis because they either do not provide individual data points or lack specific information on worker job descriptions to adequately categorize the exposure results.

Table 2-36. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Spray Adhesive on Monitoring Data

Category ^a	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Sprayer, Pre EC	132.8	253.6	52.8	130.04	83	High
Sprayer, Post EC	17.8	41.9	7.08	21.5	49	
Non-Sprayer ^b , Pre EC	127.2	210.9	50.6	108.1	31	
Non-Sprayer ^b , Post EC	18.0	28.8	7.15	14.8	9	
ONU ^c , Pre EC	3.0	128.7	1.19	66.0	39	
ONU ^c , Post EC	2.0	5.48	0.79	2.81	17	

Sources: ([OSHA, 2013b](#); [NIOSH, 2003b, 2002b](#); [Reh et al., 2002](#))

^a EC = Engineering Controls. Pre-EC = Initial NIOSH visit; Post EC = Follow-up NIOSH visit engineering controls implemented: Enclosing spray tables to create “spray booths” and/or improve ventilation.

^b Non-Sprayer refers to those employees who are not sprayers, but either handle the adhesive or spend the majority of their shift working in an area where spraying occurs.

^c Occupational non-user refers to those employees who do not regularly work in a department/area where spraying occurs (e.g., employees in saw and sew departments).

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

This condition of use assesses exposure using 1-BP personal breathing zone monitoring data from several studies. All data have a high confidence rating as determined through EPA’s systematic review process. The individual data points in these studies are further characterized into either pre- or post-EC scenarios, based on reasonably available information on engineering control. EPA has a high level of confidence in the assessed exposure based on the confidence rating of the underlying monitoring data.

2.3.1.19 Other Uses

Process Descriptions

Based on products identified in EPA’s preliminary data gathering and information received in public comments, a variety of other aerosol and non-aerosol uses may exist for 1-BP [see Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane, [EPA-HQ-OPPT-2016-0741-0003](#) ([U.S. EPA, 2017c](#))]. Examples of these uses include, but are not limited to ([AIA, 2017](#); [CRC Industries Inc., 2017](#); [Enviro Tech International, 2017](#); [OSHA; NIOSH, 2013](#)):

- Aerosol mold cleaning and release: 1-BP is a carrier solvent in aerosol mold cleaning and release products. These products are used to coat the molds for injection molding, compression molding, blow molding and extrusion applications. The product use rate varies depending on mold size and frequency of re-application. This use is likely limited because 1-BP is not compatible with some mold release applications.
- Asphalt extraction: 1-BP is used for asphalt extraction in centrifuge extractors, vacuum extractors, and reflux extractors. In this process, 1-BP is used to separate asphalt from the aggregate and filler material to allow for determination of asphalt content. This condition of use is expected to make up one percent of the total domestic 1-BP use volume.

- Coin and scissor cleaner: 1-BP is used in product formulations designed to clean collectible coins and scissors.
- General purpose degreaser: General purpose degreasing products containing 1-BP (both aerosol and non-aerosol) are used in industrial settings, with usage varying widely by facility. Refineries and utilities are known to be the largest volume users, with usage being cyclical as 1-BP is used to clean and maintain equipment primarily during plant shutdowns. 1-BP is also used for heavy duty transportation maintenance, e.g., maintaining buses, trains, trucks, etc.
- High voltage cable cleaner: 1-BP is contained in both aerosol and non-aerosol cleaning products, which are used to clean the semi-conductive cores of high voltage cables when splicing and terminating cables. A few ounces of product are used to clean each splice.
- Refrigerant flush: 1-BP is used to flush oxygen lines in hospitals and in the aerospace industry. 1-BP is also used to clean refrigeration lines in various industries. This condition of use is expected to make up one percent of the total domestic 1-BP use volume.
- Temperature indicator: 1-BP is used in temperature indicating fluids and coatings. These coatings can be applied to fabrics, rubber, plastics, glass, and/or polished metal. When the substrate is heated, the coating will melt at the designated temperature, leaving a mark on the surface. This condition of use is expected to make up less than 0.5 percent of the total domestic 1-BP use volume.
- Other uses: 1-BP has a number of other uses, such as adhesive accelerant, as coating component for pipes and fixtures, and as laboratory chemical for research and development.

EPA expects the majority of these conditions of use to be niche uses.

Number of Sites and Potentially Exposed Workers

EPA has not identified information on the number of sites and potentially exposed workers associated with these uses. The use of 1-BP for these conditions of use is expected to be minimal. It is possible that some of the aerosol degreasing facilities presented in Section 2.3.1.15 also use 1-BP as a general-purpose cleaner/degreaser.

Assessment of Inhalation Exposure Based on Monitoring Data

EPA has not identified exposure data associated with these conditions of use. The worker activity, use pattern, and associated exposure will vary for each condition of use. For conditions of use where 1-BP is used in an aerosol application, the exposure levels may be as high as those presented in Section 2.3.1.15. Actual exposure levels for each condition of use will likely vary depending on the use volume, engineering control, and PPE.

2.3.1.20 Disposal, Recycling

Process Descriptions

Each of the conditions of use of 1-BP may generate waste streams that are collected and transported to third-party sites for disposal, treatment, or recycling. Industrial sites that treat or dispose onsite wastes that they themselves generate are assessed in each condition of use assessment in Sections 2.3.1.5 through 2.3.1.19. Wastes containing 1-BP that are generated during a condition of use and sent to a third-party site for treatment, disposal, or recycling may include wastewater, solid wastes, and other wastes.

Solid wastes are defined under RCRA as any material that is discarded by being: abandoned; inherently waste-like; a discarded military munition; or recycled in certain ways (certain instances of the generation and legitimate reclamation of secondary materials are exempted as solid wastes under RCRA). Solid wastes may subsequently meet RCRA's definition of hazardous waste by either being listed as a waste at 40 CFR §§ 261.30 to 261.35 or by meeting waste-like characteristics as defined at 40 CFR §§ 261.20 to 261.24. Solid wastes that are hazardous wastes are regulated under the more stringent requirements of Subtitle C of RCRA, whereas non-hazardous solid wastes are regulated under the less stringent requirements of Subtitle D of RCRA. Solid wastes containing 1-BP may be regulated as a hazardous waste under RCRA waste code D001 for ignitable liquids (40 CFR 261.21). 1-BP may also be co-mingled with solvent mixtures that are RCRA regulated substances. These wastes would be either incinerated in a hazardous waste incinerator or disposed to a hazardous waste landfill. Some amount of 1-BP may be improperly disposed as municipal wastes, although they are likely to be a small fraction of the overall waste stream. As stated in the Problem Formulation, releases to RCRA Subtitle C and Subtitle D landfills are not included in this risk evaluation.

Number of Sites and Potentially Exposed Workers

Table 2-37 presents the industry sectors likely involved in waste treatment and disposal, and the average number of workers and ONUs per site within these sectors based on EPA's analysis of BLS data. EPA calculated the total number of workers and ONUs potentially exposed to 1-BP by multiplying these estimates by the number of waste treatment and disposal facilities that reported releases to the TRI (i.e. facilities that reported one of the NAICS codes in Table 2-37 as their primary NAICS code in TRI). For reporting year 2016, three hazardous waste treatment and disposal facilities and one cement plant reported releases of 1-BP to the TRI. It is possible that additional hazardous waste treatment facilities treat and dispose 1-BP but do not meet the TRI reporting threshold for reporting year 2016. In addition, it is possible that some consumer products containing 1-BP may be improperly disposed as municipal solid wastes, and that some amount of 1-BP is present in non-hazardous waste streams.

Table 2-37. Estimated Number of Workers and Occupational Non-Users Potentially Exposed to 1-BP During Waste Handling

Exposed Workers	Exposed Occupational Non-Users	Total Exposed	Estimated Number of Establishments	Workers per Site	Occupational Non-Users per Site
NAICS 562211 Hazardous Waste Treatment and Disposal					
27	15	42	3	9	5
NAICS 562212 Solid Waste Landfill					
			unknown	3	2
NAICS 562213 Solid Waste Combustors and Incinerators					
			unknown	13	8
NAICS 562219 Other Nonhazardous Waste Treatment and Disposal					
			unknown	3	2
NAICS 327310 Cement Manufacturing					
22	3	25	1	22	3

Source: (U.S. BLS, 2016) (Bureau, 2015)

Note: Number of workers and occupational non-users per site are calculated by dividing the exposed number of workers or occupational non-users by the number of establishments. Values are rounded to the nearest integer.

Assessment of Inhalation Exposure Based on Modeling

EPA did not identify exposure monitoring data related to waste treatment and disposal sites. To assess worker exposure, EPA assumed wastes containing 1-BP are transported and handled as bulk liquid shipments and modeled exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* (previously described in Section 2.3.1.6).

Table 2-38 summarizes the model exposures from waste handling activities. The model assumes liquid wastes contain 100 percent 1-BP, and estimates central tendency and high-end exposure concentrations for waste unloading scenario at industrial facilities. The model exposure may not be representative of the full distribution of possible exposure levels at waste disposal facilities.

Table 2-38. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Disposal Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	1.14E-2	6.01E-2	4.55E-3	3.08E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure.

In addition, the model makes a simplifying assumption that 1-BP is present at 100 percent concentration in the waste. In reality, the waste material is likely a mixture of different solvents and impurities, containing only a fraction of 1-BP. EPA does not know the typical concentration of 1-BP in the waste stream.

Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.21 Summary of Inhalation Exposure Assessment

Table 2-39 summarizes the inhalation exposure estimates for all occupational exposure scenarios. Where statistics can be calculated, the central tendency estimate represents the 50th percentile exposure level of the available data set, and the high-end estimate represents the 95th percentile exposure level. For most conditions of use, the central tendency and high-end TWA exposures for both workers and ONUs are significantly above the ACGIH TLV of 0.1 ppm. The TWA exposures are 8-hr TWA, except for the dry cleaning condition of use, where exposures are modeled as 12-hr TWA.

For conditions of use where both monitoring and model data are available, the results were found to be in good agreement with each other (with difference less than one order of magnitude).

Table 2-39. Summary of Occupational Inhalation Exposure Results

Condition of Use	Exposure Scenario	Category	TWA Exposures		Chronic, Cancer Exposures		Statistical Value for Central Tendency and High-end	Data Type
			C1-BP, 8-hr or 12-hr TWA (ppm)		LADC1-BP, 8-hr or 24-hr TWA (ppm)			
			Central Tendency	High-end	Central Tendency	High-end		
Manufacture	-	Worker	9.00E-02	2.70E-01	3.58E-02	1.38E-01	Median, Maximum	Monitoring Data
Import, Processing as a Reactant, Processing – Incorporation into Articles, Repackaging	-	Worker	1.14E-02	6.01E-02	4.55E-03	3.08E-02	N/A – CT and HE ^b	Model (Deterministic)
Processing - Incorporation into Formulation	-	Worker	3.79E+00	1.89E+01	1.51E+00	9.69E+00	Geometric mean, Maximum	Monitoring Data
	-	ONU	3.25E-01	1.59E+00	1.29E-01	8.15E-01		
Batch Vapor Degreaser (Open-Top)	-	Worker	6.70E+00	4.94E+01	2.66E+00	2.53E+01	50 th and 95 th Percentile	Monitoring Data
	-	ONU	2.00E-02	2.15E+00	7.95E-03	1.10E+00		
	Pre-EC	Worker	1.89E+00	2.39E+01	7.04E-01	9.19E+00	50 th and 95 th Percentile	Model (Probabilistic)
	Post-EC	Worker	1.89E-01	2.39E+00	7.04E-02	9.19E-01		
	Pre-EC	ONU	9.93E-01	1.35E+01	3.71E-01	5.23E+00		
	Post-EC	ONU	9.93E-02	1.35E+00	3.71E-02	5.23E-01		
Batch Vapor Degreaser (Closed-loop)	-	Worker	3.78E-02	4.78E-01	1.41E-02	1.84E-01	50 th and 95 th Percentile	Model (Probabilistic)
	-	ONU	1.99E-02	2.70E-01	7.43E-03	1.05E-01		
Cold Cleaner	-	Worker	4.30E+00	7.40E+00	1.71E+00	3.79E+00	Median, Maximum	Monitoring Data
	-	ONU	2.60E+00		1.03E+00	1.33E+00	N/A (1 data point)	
	-	Worker	5.49E-01	1.19E+01	2.06E-01	4.59E+00	50 th and 95 th Percentile	Model (Probabilistic)
	-	ONU	2.89E-01	6.83E+00	1.08E-01	2.63E+00		
Aerosol Spray Degreaser/Cleaner	Pre-EC	Worker	1.61E+01	3.16E+01	6.38E+00	1.62E+01	50 th and 95 th Percentile	Monitoring Data
	Post-EC	Worker	5.50E+00		2.19E+00	2.82E+00	N/A (1 data point)	
	-	Worker	6.37E+00	2.25E+01	2.38E+00	9.05E+00	50 th and 95 th Percentile	Model (Probabilistic)
	-	ONU	1.10E-01	9.30E-01	4.00E-02	3.60E-01		
Adhesive Chemicals (Spray Adhesive)	Pre-EC	Sprayer	1.33E+02	2.54E+02	5.28E+01	1.30E+02	50 th and 95 th Percentile	Monitoring Data
	Post-EC	Sprayer	1.78E+01	4.19E+01	7.08E+00	2.15E+01		
	Pre-EC	Non-Sprayer	1.27E+02	2.11E+02	5.06E+01	1.08E+02		
	Post-EC	Non-Sprayer	1.80E+01	2.88E+01	7.15E+00	1.48E+01		
	Pre-EC	ONU	3.00E+00	1.29E+02	1.19E+00	6.60E+01		

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Condition of Use	Exposure Scenario	Category	TWA Exposures		Chronic, Cancer Exposures		Statistical Value for Central Tendency and High-end	Data Type
			C ₁ -BP, 8-hr or 12-hr TWA (ppm)		LADC ₁ -BP, 8-hr or 24-hr TWA (ppm)			
			Central Tendency	High-end	Central Tendency	High-end		
	Post-EC	ONU	2.00E+00	5.48E+00	7.95E-01	2.81E+00		
Dry Cleaning	-	Worker	2.94E+01	5.02E+01	1.17E+01	2.57E+01	50 th and 95 th Percentile	Monitoring Data
	-	ONU	1.21E+01	2.06E+01	4.80E+00	1.06E+01		
	3rd Gen	Spot Cleaner	2.93E+00	7.93E+00	3.94E-01	1.14E+00	50 th and 95 th Percentile	Model ^a (Probabilistic)
	3rd Gen	Machine & Finish	1.41E+01	6.05E+01	1.89E+00	8.57E+00		
	3rd Gen	ONU	1.82E+00	6.65E+00	2.43E-01	9.49E-01		
	3rd Gen	Child	5.41E-01	4.03E+00	N/A	N/A		
	4th Gen	Spot Cleaner	2.40E+00	5.65E+00	3.20E-01	8.22E-01		
	4th Gen	Machine & Finish	2.38E+00	6.36E+00	3.15E-01	9.35E-01		
	4th Gen	ONU	1.31E+00	4.21E+00	1.73E-01	5.96E-01		
	4th Gen	Child	8.96E-02	1.02E+00	N/A	N/A		
Spot Cleaner, Stain Remover	-	Worker	9.00E-01	4.73E+00	3.58E-01	2.42E+00	50 th and 95 th Percentile	Monitoring Data
	-	Worker	3.24E+00	7.03E+00	2.89E-01	6.82E-01		Model (Probabilistic)
	-	ONU	1.63E+00	4.68E+00	1.45E-01	4.45E-01		
Disposal, Recycling	-	Worker	1.14E-02	6.01E-02	4.55E-03	3.08E-02	N/A – CT and HE ^b	Model (Deterministic)

a – For this condition of use, the acute concentration (AC) and chronic, non-cancer exposure (ADC) differ from the TWA exposure. See previous subsections for AC and ADC values.

b – Based on distinct model scenarios that are likely representative of central tendency (CT) and high-end (HE) exposures.

2.3.1.22 Dermal Exposure Assessment

Dermal absorption of 1-BP depends on the type and duration of exposure. Where exposure is non-occluded, only a fraction of 1-BP that comes into contact with the skin will be absorbed as the chemical readily evaporates from the skin. However, dermal exposure may be significant in cases of occluded exposure, repeated contacts, or dermal immersion. For example, work activities with a high degree of splash potential may result in 1-BP liquids trapped inside the gloves, inhibiting the evaporation of 1-BP and increasing the exposure duration.

To assess exposure, EPA used the *Dermal Exposure to Volatile Liquids Model* (see following equation) to calculate the dermal retained dose. The equation modifies EPA/OPPT 2-Hand *Dermal Exposure to Liquids Model* (peer reviewed) by incorporating a “fraction absorbed (f_{abs})” parameter to account for the evaporation of volatile chemicals and a “protection factor (PF)” to account for glove use:

Equation 2-2. Equation for Calculating Occupational Dermal Exposure

$$D_{exp} = \frac{S \times (Q_u \times f_{abs}) \times Y_{derm} \times FT}{PF \times BW}$$

Where:

- D_{exp} is the dermal retained dose (mg/kg-day)
- S is the surface area of contact (cm²)
- Q_u is the quantity remaining on the skin after an exposure event (mg/cm²-event)
- Y_{derm} is the weight fraction of the chemical of interest in the liquid ($0 \leq Y_{derm} \leq 1$)
- FT is the frequency of events (integer number per day)
- f_{abs} is the fraction of applied mass that is absorbed (Default for 1-BP: 0.0016)
- PF is the glove protection factor (Default: see Table 2-40)
- BW is the body weight (Default: 80 kg)

The steady-state f_{abs} for 1-BP is estimated to be 0.16 percent in a non-occluded, finite dose scenario from a 2011 *in vitro* dermal penetration study of 1-BP conducted by Frasch et al. (2011). The author noted a large standard deviation in the experimental measurement, which is indicative of the difficulty in spreading a small, rapidly evaporating dose of 1-BP evenly over the skin surface.

Default glove PF values, which vary depending on the type of glove used and the presence of employee training program, are shown in Table 2-40. Note 1-BP easily travels through most glove materials. Recommended glove materials for protection against 1-BP are supported polyvinyl alcohol or multiple-layer laminates (OSHA, 2013d).

Table 2-40. Glove Protection Factors for Different Dermal Protection Strategies

Dermal Protection Characteristics	Setting	Protection Factor, PF
a. No gloves used, or any glove / gauntlet without permeation data and without employee training	Industrial and Commercial Uses	1
b. Gloves with available permeation data indicating that the material of construction offers good protection for the substance		5
c. Chemically resistant gloves (i.e., as <i>b</i> above) with “basic” employee training		10
d. Chemically resistant gloves in combination with specific activity training (e.g., procedure for glove removal and disposal) for tasks where dermal exposure can be expected to occur	Industrial Uses Only	20

Source: ([Marquart et al., 2017](#))

Table 2-41 presents the estimated dermal retained dose for *workers* in various exposure scenarios, including what-if scenarios for glove use. The exposure estimates assume one exposure event (applied dose) per work day and that 0.16 percent of the applied dose is absorbed through the skin. The exposure estimates are provided for each condition of use, where the conditions of uses are “binned” based on the maximum possible exposure concentration (Y_{derm}) and the likely level of exposure. The exposure concentration is determined based EPA’s review of currently available products and formulations containing 1-BP. For example, EPA found that 1-BP concentration in degreasing formulations such as Solvon PB can be as high as 97 percent:

- **Bin 1:** Bin 1 covers industrial uses that generally occur in closed systems. For these uses, dermal exposure is likely limited to chemical loading/unloading activities (e.g., connecting hoses) and taking quality control samples.
- **Bin 2:** Bin 2 covers industrial degreasing uses, which are not closed systems. For these uses, there is greater opportunity for dermal exposure during activities such as charging and draining degreasing equipment, drumming waste solvent, and removing waste sludge.
- **Bin 3:** Bin 3 covers the use of 1-BP in spray adhesives in foam cushion product manufacturing, which is a unique condition of use. Workers (sprayers) can be dermally exposed when mixing adhesive, charging adhesive to spray equipment, and cleaning adhesive spray equipment. Other workers (non-sprayers) may also have incidental contact with the applied adhesive during subsequent fabrication steps.
- **Bin 4:** Bin 4 covers commercial activities of similar maximum concentration. Most of these uses are uses at dry cleaners, and/or uses expected to have direct dermal contact with bulk liquids. At dry cleaning shops, workers may be exposed to bulk liquids while charging and draining solvent to/from machines, removing and disposing sludge, and maintaining equipment. Workers can also be exposed to 1-BP used in spot cleaning products at the same shop.
- **Bin 5:** Bin 5 covers aerosol uses, where workers are likely to have direct dermal contact with film applied to substrate and incidental deposition of aerosol to skin. This bin also covers miscellaneous non-aerosol applications that are typically niche uses of 1-BP.

As shown in the table, the calculated retained dose is low for all non-occluded scenarios as 1-BP evaporates quickly after exposure. Dermal exposure to liquid is not expected for occupational non-users, as they do not directly handle 1-BP.

EPA also considered potential dermal exposure in cases where exposure is occluded. See further discussion on occlusion in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)).

Strength, Limitation, and Uncertainty of the Dermal Exposure Assessment

Dermal exposures are assessed using the *Dermal Exposure to Volatile Liquids Model*, which relies on the Frasch et al. ([2011](#)) study to determine fractional absorption in accounting for chemical volatilization. Although the study presents 1-BP specific measurement, the study also noted a large standard deviation in the measured value. In addition, the underlying EPA dermal model assumes one exposure event per day, which likely underestimates exposure as workers often come into repeat contact with the chemical throughout their work day. Based on the uncertainties described above, EPA has a medium level of confidence in the assessed baseline exposure.

Glove protection factors are presented as what-if scenarios to show the potential effect of glove use on exposure levels. EPA does not know the actual frequency, type, and effectiveness of glove use in specific workplaces with 1-BP conditions of use.

Table 2-41. Estimated Dermal Retained Dose for Workers in All Conditions of Use

Condition of Use	Bin	Max Y _{derm}	Dermal Exposure (mg/kg-day)			
			No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (Industrial uses, PF = 20)
Manufacture	Bin 1	1.0	4.5E-02	9.0E-03	4.5E-03	2.2E-03
Import, Repackaging						
Processing - Incorporating into formulation						
Processing as a reactant						
Processing - Incorporating into articles						
Recycling						
Disposal						
Use - Batch Vapor Degreaser	Bin 2	0.97	4.4E-02	8.7E-03	4.4E-03	2.2E-03
Use – In-line Vapor Degreaser						
Use - Cold Cleaner						
Use – Adhesive Chemicals (Spray Adhesives)	Bin 3	0.8	3.6E-02	7.2E-03	3.6E-03	N/A
Use - Dry Cleaning	Bin 4	0.94	4.2E-02	8.4E-03	4.2E-03	N/A
Use - Spot Cleaner, Stain Remover						
Use - Other non-aerosol uses	Bin 5	1.0	4.5E-02	9.0E-03	4.5E-03	N/A
Use – Aerosol Spray Degreaser/Cleaner, Other aerosol uses						

2.3.2 Consumer Exposures

Consumer products containing 1-BP are readily available at retail stores and via the internet for purchase and use. Use of these products can result in exposures of the consumer user and bystanders to 1-BP during and after product use. Based on the availability and use of consumer products containing 1-BP, this assessment evaluates consumer exposures for the user and bystander of such products within a residence.

2.3.2.1 Consumer Exposures Approach and Methodology

Consumer products containing 1-BP were identified through review and searches of a variety of sources, including the National Institutes of Health (NIH) Household Products Database, various government and trade association sources for products containing 1-BP, company websites for Safety Data Sheets (SDS), Kirk-Othmer Encyclopedia of Chemical Technology, and the internet in general. These consumer products are summarized in a public use dossier and market profile report ([U.S. EPA, 2017c](#)) put together by EPA and included in the docket for this evaluation. The public use dossier and market profile report may not be a complete list of all consumer products available at the time of the searches because not all SDS display a complete list of chemical ingredients, therefore some products may contain 1-BP but cannot be confirmed by EPA. The public use dossier and market profile report are representative of information found at the time of the searches and are considered reasonably available information; but do not take into consideration company-initiated formulation changes, product discontinuation, or other business or market based factors that occurred after the documents were compiled.

For this evaluation, identified consumer products were categorized into groups based on consumer uses considering (1) consumer use patterns, (2) information reported in SDS, (3) product availability to the public, and (4) potential risk to consumers. Nine product groups known to contain 1-BP were identified and are summarized in Table 2-42.

Table 2-42. Consumer Uses and Routes of Exposure Assessed

Consumer Uses	Routes of Exposure
1. Adhesive Accelerant (Liquid Pump Spray) 2. General Purpose Spray Cleaner (Liquid Spray/Aerosol) 3. Spot Cleaner and Stain Remover (Liquid Spray/Aerosol) 4. Mold Cleaning and Release Product (Liquid Spray/Aerosol) 5. General Cleaners and Degreasers (Liquid Spray/Aerosol) 6. Electronics Degreasers (Liquid Spray/Aerosol)	Inhalation and Dermal
7. Coin and Scissors Cleaner (Liquid Bath) 8. Automobile AC Flush (Liquid)	Inhalation and Dermal
9. Insulation (Off-gassing)	Inhalation

2.3.2.2 Exposure Routes Evaluated

Table 2-42 also identifies the exposure routes evaluated for the nine product groups. Reasonably available information on the toxicity profile and physicochemical properties of 1-BP support inhalation as an expected route of exposure for human health concerns associated with consumer product uses. Dermal exposures are also reasonably foreseeable; however, limited toxicological data are available for this route of exposure, and no toxicokinetic information is available to

develop physiologically-based pharmacokinetic models. Therefore, this consumer exposure assessment considers dermal exposures but limits the presented results to certain scenarios described below.

Inhalation

Consumer and bystander inhalation exposure to 1-BP containing products primarily include direct inhalation of vapors, mists, and aerosols (e.g., aerosols from spray applications) and indirect inhalation exposures after application (e.g., as products dry and evaporate from surfaces to which it is applied or a pool of product during use). The magnitude of inhalation exposure depends on a variety of factors including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.

Dermal

Consumer dermal exposure to 1-BP resulting from product use occurs via vapor or mist deposition onto the skin or direct contact with material during product use or after application (e.g., from a surface prior to the surface fully drying). The magnitude of dermal exposure and permeation depends on several factors including skin surface area, product volume, concentration of 1-BP in products used, and dermal exposure duration. The potential for dermal permeation of 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and expected quick volatilization of product from surfaces.

2.3.2.3 Modeling Approach

EPA utilized a modeling approach to assess consumer exposure because emissions and chemical specific personal monitoring data associated with consumer use of products containing 1-BP were not identified during data gathering and literature searches performed as part of Systematic Review. Three models were used to evaluate consumer exposures, EPA's Consumer Exposure Model (CEM), EPA's Multi-Chamber Concentration and Exposure Model (MCCEM), and EPA's Indoor Environment Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model. A general overview and some details about each of these models are provided in the respective sections below. Readers can learn more about equations within the models, detailed input and output parameters, pre-defined scenarios, default values used, and supporting documentation by reviewing the CEM user guide ([U.S. EPA, 2019a](#)), CEM user guide appendices ([U.S. EPA, 2019b](#)), MCCEM user guide ([U.S. EPA, 2019d](#)), and IECCU user guide ([U.S. EPA, 2019c](#)).

The first six consumer uses identified in Table 2-42 were assessed for inhalation and dermal exposure using CEM because available, pre-defined scenarios within CEM aligned well with these consumer uses. Consumer uses 7 and 8 identified in Table 2-42 were assessed for inhalation exposure using MCCEM because the pre-defined scenario within MCCEM (exposure from a pool of liquid) aligns well with these two consumer uses. However, since MCCEM does not have a representative dermal model for these two consumer uses, CEM was used to evaluate dermal exposure. The final consumer use identified in Table 2-42 (Insulation, off-gassing) was evaluated for inhalation exposure using IECCU because it is a simulation program designed to model emissions from indoor sources like insulation over an extended period of time. This model can also

incorporate seasonal fluctuations as well as modeled emission rates over an extended period of time.

EPA evaluated acute inhalation and dermal exposure of consumers to 1-BP in this consumer exposure assessment. Acute inhalation exposure was evaluated for all nine consumer uses. Acute dermal exposure of consumers was evaluated for three of the nine consumer uses (General Cleaners and Degreasers, Coin and Scissors Cleaner, and Automobile AC Flush) due to the possibility of a continuous supply of product against the skin with limited or prohibited evaporation potential due to a barrier or direct immersion into a product. EPA does not expect exposure under any of the nine consumer uses evaluated to be chronic in nature because product use activities tend to be infrequent with relatively short durations of use. EPA therefore presents the acute consumer exposure results in this consumer exposure evaluation.

Consumer exposure was assessed for users and non-users (bystanders). EPA assumes, for this evaluation, consumer users are male or female adults (between 16 and 21 years of age and greater than 21 years of age), including woman of reproductive age. Non-users could be any age group ranging from infants to adults.

2.3.2.3.1 Overview of Models Used (CEM, MCCEM, and IECCU)

CEM

CEM is a deterministic model which utilizes user provided input parameters and various assumptions (or defaults) to generate exposure estimates. In addition to pre-defined scenarios, which align well with the first six consumer uses identified in Table 2-42, CEM is peer reviewed, provides flexibility to the user allowing modification of certain default parameters when chemical-specific information is available and does not require chemical-specific emissions data (which may be required to run more complex indoor/consumer models). The various assumptions (or defaults) are a combination of high-end and mean/central tendency values derived from literature and other studies therefore providing a diverse spectrum of parameters across which modeling occurs.

CEM predicts indoor air concentrations from consumer product use through a deterministic, mass-balance calculation derived from emission calculation profiles within the model. There are six emission calculation profiles with CEM (E1-E6) which are summarized in the CEM user guide ([U.S. EPA, 2019a](#)) and associated user guide appendices ([U.S. EPA, 2019b](#)). If selected, CEM is capable of providing a time series air concentration profile for each run. These are intermediate values produced prior to applying pre-defined activity patterns.

CEM uses a two-zone representation of the building of use when predicting indoor air concentrations. Zone 1 represents the room where the consumer product is used. Zone 2 represents the remainder of the building. Each zone is considered well mixed. CEM allows further division of Zone 1 into a near field and far field to accommodate situations where a higher concentration of product is expected very near the product user when the product is used. Zone 1-near field represents the breathing zone of the user at the location of the product use while Zone 1 far field represents the remainder of the Zone 1 room.

Inhalation exposure is estimated in CEM based on zones and pre-defined activity patterns. The simulation run by CEM places the product user within Zone 1 for the duration of product use while the bystander is placed in Zone 2 for the duration of product use. Following the duration of product use, the user and bystander follow one of three pre-defined activity patterns established within CEM, based on modeler selection. The selected activity pattern takes the user and bystander in and out of Zone 1 and Zone 2 for the period of the simulation. The user and bystander inhale airborne concentrations within those zones, which will vary over time, resulting in the overall estimated exposure to the user and bystander.

CEM contains two methodologies for estimating dermal exposure to chemicals in products, the permeability method (P-DER1) and the fraction absorbed method (A-DER1). Each of these methodologies further has two model types, one designed for dermal exposure from use of a product (P-DER1a and A-DER1a), the other designed for dermal exposure from use of an article (P-DER1b and A-DER1b). Each methodology has associated assumptions, uncertainties and data input needs within the CEM model. Both methodologies factor in the dermal surface area to body weight ratio and weight fraction of chemical in a consumer product.

The permeability model is based on the ability of a chemical to penetrate the skin layer once contact occurs. The permeability model assumes a constant supply of chemical, directly in contact with the skin, throughout the exposure duration. The ability to use the permeability method can be beneficial when chemical-specific skin permeability coefficients are available in the scientific literature. However, the permeability model within CEM does not consider evaporative losses when it estimates dermal exposure. The permeability model within CEM is therefore more representative of a dermal exposure condition where evaporation is limited or prohibited due to direct immersion of skin into a product or use of a product soaked rag or other barrier that is in direct contact with the skin during product use.

The fraction absorbed method is based on the absorbed dose of a chemical. This method essentially measures two competing processes, evaporation of the chemical from the skin and penetration of the chemical deeper into the skin. This methodology assumes the application of the chemical of concern occurs once to an input thickness and then absorption occurs over an estimated absorption time. The fraction absorbed method can be beneficial when chemical specific fractional absorption measurements are available in the scientific literature. The fraction absorbed model within CEM considers evaporative losses making this model more representative of a dermal exposure condition where there is not a constant supply of product against the skin and evaporation is not limited or prohibited.

MCCEM

Like CEM, MCCEM is peer reviewed and includes several distinct models appropriate for evaluating specific product and article types and use scenarios. Two of the distinct models (M32 and M33) can evaluate emission rates due to evaporation from a liquid in a container (a “solvent pool”). Model M32 applies to an evaporating solvent or solvent pool with a fixed surface area. At a given temperature, the emission rate in this model is determined by (1) the gas-phase mass transfer coefficient, (2) the vapor pressure, and (3) the back-pressure effect.

Model M33 was developed for sublimation of p-dichlorobenzene from moth cakes. However, because sublimation and evaporation of pure compounds share similar mechanisms, M33 can also be applied to emissions from solvent pools. At a given temperature, the emission rate in this model is dependent on the gas-phase mass transfer coefficient, the saturation concentration for a pure compound, and the prevailing indoor air concentration.

For both M32 and M33 models, the emission rate is governed by the source area and is not dependent on chemical mass, provided the duration of use is less than the time it takes for all of the chemical of concern to evaporate. Therefore, the emission rate determined using either model is assumed to be constant and in-effect until all available mass of the chemical of concern is evaporated.

MCCEM uses a two-zone representation of the building of use when predicting indoor air concentrations similar to CEM. MCCEM also is capable of further division of Zone 1 into near field and far field. Zone 1-near field represents the breathing zone of the user at the location of the product use while Zone 1 far field represents the remainder of the Zone 1 room. Inhalation exposure is estimated in MCCEM based on zones and pre-defined activity patterns again, similar to CEM.

IECCU

IECCU is a peer reviewed simulation program which can be used as (1) a general-purpose indoor exposure model in buildings with multiple zones, multiple chemicals and multiple sources and sinks or (2) as a special-purpose concentration model for simulating the effects of sources in unconditioned zones on the indoor environmental concentrations in conditioned zones. IECCU was developed by combining existing code and algorithms implemented in other EPA indoor exposure models and by adding new components and methods.

IECCU uses a general mass balance equation for a chemical of interest to calculate the time series of indoor concentrations. The equation combines all processes governing source emissions, convective transfer by bulk air, sorption, and re-emission by indoor sinks, interactions with airborne particles and settled dust and gas-phase chemical reactions.

Unlike CEM, IECCU does not yet provide default values for input parameters. As a result, model inputs are derived from empirical data or modeled estimates. It is the user's responsibility to choose appropriate modeling inputs for the chemical and exposure scenario of interest. Recent updates to the IECCU model enable it to handle pollutant sources with irregular emission rates as well as accept 10 minute, hourly or 12 hour averages.

2.3.2.3.2 Model Specific Approaches and Inputs

CEM Modeling Approach

The first six consumer uses identified in Table 2-42 were assessed for inhalation and dermal exposure using CEM. All six consumer uses utilized the E3 emissions model and profile for inhalation exposure. This model and profile assume a percentage of a consumer product used is aerosolized (e.g. overspray) and therefore immediately available for uptake by inhalation. The

associated inhalation model used for these six consumer uses was P-INH2. EPA also evaluated all six of these consumer uses utilizing the near-field and far-field option within CEM for inhalation exposure.

In an effort to characterize a potential range of consumer inhalation exposures, EPA varied three key parameters within the CEM model while keeping all other input parameters constant. The key parameters varied were duration of use per event (minutes/use), amount of chemical in the product (weight fraction), and mass of product used per event (gram(s)/use). These key parameters were varied because they provide representative consumer behavior patterns for product use. Additionally, CEM is highly sensitive to two of these three parameters (duration of use and weight fraction). Finally, all three parameters had a range of documented values within literature identified as part of Systematic Review allowing EPA to evaluate inhalation exposures across a spectrum of use conditions.

All six consumer uses utilized the permeability methodology and model (P-DER1b) for dermal exposure. This model considers a constant supply of the product on the skin throughout the exposure duration and does not consider evaporative loss. Because of these factors, dermal exposure results for this consumer exposure evaluation are only presented for three consumer uses with the possibility of a constant supply of product on the skin (general cleaners and degreasers, coin and scissors cleaner, and automobile AC flush).

To characterize a potential range of consumer dermal exposures, EPA varied two key parameters within CEM while keeping all other input parameters constant. The key parameters varied for dermal exposure evaluation were weight fraction and duration of use per event. The mass of product used is not a factor in the dermal exposure equations within CEM and therefore was not varied.

Once the data was gathered for the parameters to be varied, modeling was performed to cover all possible combinations of these three parameters. This approach results in a maximum of 27 different iterations for each consumer use. A table summarizing these 27 different iterations is included in Appendix E. Certain uses, however, only had a single value for one or more of the parameters varied which reduces the total number of iterations.

Post-processing to determine personal concentration exposures for the user and bystander was conducted outside of CEM using Microsoft Excel. EPA utilized the intermediate time series option within CEM to get the personal exposure time series for each iteration modeled. EPA then independently assigned the Zone 1, Zone 2, and outside (zero) concentration to the user and bystander based on the pre-defined activity pattern (stay at home) within CEM. Time-weighted average concentration exposures were then calculated from the personal exposure time series for each iteration modeled and the activity pattern within each consumer use category. Time weighted averages (TWA) were determined for 1 hour, 3 hours, 8 hours, and 24 hours, although for this consumer exposure evaluation the 24 hour TWA concentration was utilized based on health endpoints used to calculate risks.

CEM Inputs

Numerous input parameters are required to generate exposure estimates within CEM. These parameters include physical-chemical properties of the chemical of concern, product information (product density, water solubility, vapor pressure, etc.), model selection and scenario inputs (pathways, CEM emission model(s), emission rate, activity pattern, product user, background concentration, etc.), product or article property inputs (frequency of use, aerosol fraction, etc.), environmental inputs (building volume, room of use, near-field volume in room of use, air exchange rates, etc.), and receptor exposure factor inputs (body weight, averaging time, exposure duration inhalation rate, etc.). Several of these input parameters have default values within CEM based on the pre-defined use scenario selected. Default parameters within CEM are a combination of high-end and mean or median values found within the literature or based on data taken from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). Details on those parameters can be found within the CEM user guide ([U.S. EPA, 2019a](#)) and associated users guide appendices ([U.S. EPA, 2019b](#)), or can be cross referenced to U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). As discussed earlier, while default values are initially set in pre-defined use scenarios, CEM has flexibility which allows users to change certain pre-set default parameters and input several other parameters.

Key input parameters for the first six consumer uses identified in Table 2-42 evaluated with CEM are discussed below. Detailed tables of key input parameters used for each consumer use evaluated with CEM are provided in Appendix E. Detailed tables of all input parameters for each use evaluated with CEM are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment ([EPA, 2019f](#)).

Physical-chemical properties of 1-BP were kept constant across all consumer uses and iterations evaluated. The saturation concentration in air (one of the factors considered for scaling purposes) was estimated by CEM as 9.66E+05 milligrams per cubic meter. A chemical-specific skin permeability coefficient of 9.05E-03 centimeters per hour was found in literature ([DHHS, 2017](#)) and utilized for all scenarios modeled for dermal exposure.

Model selection is discussed in the previous section (CEM modeling approaches). Scenario inputs were also kept constant across all consumer uses and iterations. Emission rate was estimated using CEM. The activity pattern selected within CEM was stay-at-home. The start time for product use was 9:00 AM and the product user was an adult (>21 years of age) and a youth (16 through 20 years of age). The background concentration of 1-BP for this evaluation was considered negligible and therefore set at zero milligrams per cubic meter.

Frequency of use for acute exposure calculations was held constant at one event per day. The aerosol fraction (amount of overspray immediately available for uptake via inhalation) selected within CEM for all consumer uses evaluated was six percent. Building volume used for all consumer uses was the default value for a residence within CEM (492 cubic meters). The near-field volume selected for all consumer uses was one cubic meter. Averaging time for acute exposure was held constant at one day.

Certain model input parameters were varied across consumer use scenarios, but kept constant for all model iterations run for that particular consumer use. These input parameters include product

density, room of use, and pre-defined product scenarios within CEM. Product densities were extracted from product-specific SDS. Room of use was extracted from an EPA directed survey of consumer behavior patterns in the United States titled Household Solvent Products: A National Usage Survey ([U.S. EPA, 1987](#)) (Westat Survey), identified in the literature search as part of systematic review. The Westat survey is a nationwide survey which provides information on product usage habits for thirty-two different product categories. The information was collected via questionnaire or telephone from 4,920 respondents across the United States. The Westat Survey was rated as a high quality study during data evaluation within the systematic review process. The room of use selected for this evaluation is based on the room in which the Westat Survey results reported the highest percentage of respondents that last used a product within the room. When the Westat Survey identified the room of use where the highest percentage of respondents last used the product as “other inside room”, the utility room was selected within CEM for modeling. The pre-defined product scenarios within CEM were selected based on a cross-walk to similar product categories within the Westat Survey. Table 2-43 provides a crosswalk between the 1-BP Consumer Use Scenarios and the corresponding Westat product category selected to represent the exposure scenario.

Table 2-43. Crosswalk Between 1-BP Consumer Use Scenarios and Westat Product Category

1-BP Consumer Use Scenario	Representative Westat Product Category
1. Adhesive Accelerant	Contact Cement, Super Glues, And Spray Adhesives
2. General Spray Cleaner	Solvent Type Cleaning Fluids Or Degreasers
3. Spot Cleaner-Stain Remover	Spot Removers
4. Mold Cleaning-Release Product	Solvent Type Cleaning Fluids Or Degreasers
5. General Cleaner-Degreaser	Engine Degreasers
6. Degreasers-Electronic	Specialized Electronics Cleaners (TV, VCR, Razor, Etc.)
7. Coin Cleaner/Scissors	Not Applicable
8. Automobile Ac Flush	Not Applicable
9. Insulation	Not Applicable

Additional key model input parameters were varied across both consumer use scenario and model iterations. These key parameters were duration of use per event (minutes/use), amount of chemical in the product (weight fraction), and mass of product used per event (gram(s)/use). Duration of use and mass of product used per event values were both extracted from the Westat Survey ([U.S. EPA, 1987](#)). To allow evaluation across a spectrum of use conditions, EPA chose the Westat Survey results for these two parameters from the above cross-walked product categories representing the tenth, fiftieth (median), and ninety-fifth percentile data, as presented in the Westat Survey.

The amount of chemical in the product (weight fraction) was extracted from product specific SDS. This value was varied across the given range of products within the same category to obtain three values, when available. Unlike the Westat survey results which gave percentile data, however, product specific SDS across products did not have percentile data so the values chosen represented the lowest weight fraction, mean weight fraction (of the range available), and the highest weight fraction found. Even using this approach, some SDS were only available for a single product with a single weight fraction or very small range, or multiple products which only provided a single weight fraction or a very small range. For these product scenarios, only a single weight fraction was used in CEM for modeling. Table 2-44 summarizes the input parameter values used for these three parameters by consumer use.

Table 2-44. Model Input Parameters Varied by Consumer Use

Consumer Use	Duration of Use			Mass of Product Used			Amount of Chemical In Product		
	(minutes/use)			(gram(s)/use)			(weight fraction)		
	10 th	50 th	95 th	10 th	50 th	95 th	Low	Mean	High
Adhesive Accelerant	0.5	4.25	60	1.20	9.98	172.45		0.99 (single)	
General Spray Cleaner	2	15	120	21.86	126.86	1249.04		0.94 (single)	
Spot Cleaner/Stain Remover	0.5	5	30	9.76	51.91	434.43	0.276	0.58	0.922
Mold Cleaning/Release	0.5	2	30	3.84	21.14	192.21	0.32	0.6	0.915
General Cleaner-Degreaser	5	15	120	111.86	445.92	1845.17	0.109	0.505	0.9505
Degreaser-Electronic	0.5	2	30	1.56	19.52	292.74	0.496	0.72	0.972

MCCEM Modeling Approach

Consumer uses 7 and 8 identified in Table 2-42 (coin/scissors cleaner and automobile AC flush, respectively) were assessed for inhalation exposure using MCCEM. A general internet search and investigation into coin cleaning revealed an expected use pattern is to place the coin cleaner product into a small, open top dish or bowl. Coins to be cleaned are then placed within the pool of product, soaked, scrubbed/wiped, and then removed for drying. A similar search and investigation into automobile AC flush activities revealed an expected use pattern is to directly spray the flush product into the opened automobile AC system, which is then transferred via pressure through the system to the opposite end and flushed out into an open top bucket where it is collected.

Considering these expected use patterns, exposure to 1-BP within these products is assessed as evaporation from a liquid in a container. The M33 model was utilized to evaluate inhalation exposure for both consumer uses and applied by assuming a constant emission rate during the entire period when the source is active (product is used and remains open to the use environment). Use of the M33 model for these scenarios causes the emission rate to be governed by the source area and not chemical mass (weight fraction and mass of product used). Since the emission rate is not dependent on chemical mass for these two scenarios, only duration of use was varied for the multiple iterations run. This results in three exposure cases per consumer use, rather than the maximum of 27 exposure cases for consumer uses 1-6 modeled with CEM. Consistent with consumer uses 1-6, EPA evaluated both consumer uses 7 and 8 in Table 2-42 utilizing the near-field and far-field option for inhalation exposure.

Since MCCEM does not have a representative dermal model for these two consumer uses, CEM was used to evaluate dermal exposure. Like the first six consumer uses, EPA utilized the permeability methodology and model (P-DER1b) for dermal exposure. This model considers a constant supply of the product on the skin throughout the exposure duration and does not consider evaporative loss. Because of these factors and the anticipated use pattern for consumer uses 7 and 8 possibly being occluded in nature, dermal exposure for this evaluation is presented for both coin/scissors cleaner and automobile AC flush.

MCCEM Inputs

The inputs needed for MCCEM include: (1) the emission rate; (2) product amount and duration of use; (3) house and zone volumes; and (3) airflows to and from each zone. Like the CEM modeling approach, for MCCEM, the activity patterns are incorporated post-processing to determine inhalation exposure. Detailed tables of all input parameters for each use evaluated with MCCEM are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment ([EPA, 2019f](#)).

Emission Rate

The emission rate when using the M33 model and assuming zero for the prevailing indoor air concentration, as EPA did for these two scenarios, is the product of three quantities: (1) mass-transfer coefficient; (2) saturation concentration; and (3) exposed surface area. To estimate the mass-transfer coefficient, EPA used the program PARAMS (<https://www.epa.gov/air-research/parameters-params-program-versions n-1 1-indoor-emission-source-modeling>), which involves the following components:

- Air Density, calculated at 23 C and 50% RH;
- Viscosity of Air, calculated at 23 C;
- Velocity, the midpoint of the recommended range of 5-10 cm/s;
- Diffusivity in air, calculated using the Wilke Lee (WL) method (see input screen below); and
- Characteristic length – PARAMS describes this parameter as follows:
“Characteristic length is often approximated by the square root of the source area.”

The source area is used in estimating both the mass-transfer coefficient and the emission rate. For the coin cleaner, EPA chose a small bowl as the product reservoir with a 4-inch diameter, giving a source area of 81 cm², a characteristic length of 9 cm, and an estimated mass-transfer coefficient of 6.01 m/h (see input screen below). For the automobile AC flush, EPA chose a bucket as the flushed product reservoir with a 12-inch diameter, giving a source area of 730 cm², a characteristic length of 27.0 cm, and an estimated mass-transfer coefficient of 3.47 m/h. For the coin cleaner, multiplication by the mass-transfer rate (6.01 m/h) and the source area (81 cm² or 0.0081 m²) gives an emission rate of 47,026 mg/h (47 g/h). For the AC auto flush, multiplication by the mass-transfer rate (3.47 m/h) and the source area (730 cm² or 0.073 m²) gives an emission rate of 244,697 mg/h (244.7 g/h).

Product Amount and Duration of Use

As discussed above, the emission rate is governed by surface area of the solvent pool and not chemical mass for consumer uses 7 and 8 in Table 2-42. Therefore, only duration of use is varied for inhalation exposure. Based on the expected use conditions described above, and in an effort to characterize a potential range of consumer inhalation exposures, EPA chose three durations of use for the coin cleaner (15, 30, and 60 minutes) and three durations of use for the automobile AC flush (5, 15, and 30 minutes). While inhalation exposure for the coin cleaner consumer use is determined for 15, 30, and 60 minutes, EPA does not expect dermal contact will occur for the entire period of time the product is being used. Coin cleaning is expected to be a somewhat passive activity where coins may remain undisturbed within the pool for an extended period of time. As a

result, dermal exposure will occur for a shorter period of time when coins are placed into the product, potentially scrubbed/wiped within the product, and taken out for drying. Outside of these activities, dermal exposure is not expected to occur although the user will remain within the room inhaling the vapors expelled from the pool. For dermal exposure to coin cleaner product, EPA presents the exposure values representing the total exposure from use (cumulative which is beginning and end of use) for 2 minutes, 4 minutes, and 6 minutes of ongoing dermal exposure.

Unlike coin cleaning, automobile AC flushing is an active process where material is constantly sprayed into the system, flushed through, and exits the system. Inhalation exposure occurs for the entire period of time and since it is an active process, dermal exposure can also occur for the entire period of time. As a result, for dermal exposure automobile AC flush, EPA presents the exposure values representing 5, 15, and 30 minutes of ongoing dermal exposure.

Zone Definitions, Volumes, and Airflow Rates

The zone volumes and airflow rates for the coin cleaner consumer use are discussed below and summarized in a table in Appendix E. For this consumer use, EPA is assuming the zone of use to be the utility room, with a volume of 20 m³ that is further split into near-field and far-field zones for which the respective volumes (1 m³ and 19-m³) are consistent with CEM defaults. The assumed house volume is 446 m³, resulting in a volume of 426 m³ for the third zone, termed the “rest of house” or ROH.

The air exchange rate for the house (0.45) is the same as the CEM default. EPA used an interzonal airflow rate of 100 m³/h between the near field and far-field. EPA assumed that there was no air flow between the near field and outdoors (Zone 0). For the interzonal airflow rate between the utility room and ROH, the CEM default rate of 107.1 m³/h was used. For the auto AC flush scenario, EPA assumed the zone of use to be the garage with a volume of 118 m³. This volume is the average for 15 single-family homes with attached garages as reported by Batterman et al. ([Batterman et al., 2007](#)). The garage was further split into a 4-m³ near field and a 114-m³ far field. Zone 3 was defined as the entire house volume of 446 m³, which did not include the garage.

The air exchange rate for the house (0.45) matches that used for the coin cleaner consumer use. Relatively few measurements have been taken of garage air exchange rates. Emmerich et al. ([Emmerich et al., 2003](#)) used a blower door to measure the airtightness of garages under induced-pressurization conditions for a limited sample of homes but with a range of house ages, styles, and sizes. The average airtightness measured was 48 air changes per hour at 50 Pa (ACH50). This is consistent with values used by energy engineers and technicians who have performed such tests for many years, and corresponds to an air exchange rate of ~ 2.5/h (giving an airflow rate of 295 m³/h) under naturally occurring conditions. EPA also assumed an airflow rate of 107.1 m³/h between the garage and house as well as an airflow rate of zero between the near field and outdoors.

IECCU Approach and Inputs

The final consumer use identified in Table 2-42 (Insulation, off-gassing) was evaluated for inhalation exposure using IECCU. Modeling efforts estimated the air concentration of 1-BP by conducting a series of simulations for a “typical” residential building by using existing mass transfer models and simulation tools. Most parameters were either obtained from data in the

literature or estimated with empirical and QSAR models. The insulation source of 1-BP used was Polyiso insulation boards. Detailed tables of all input parameters for this use evaluated with IECCU are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment ([EPA, 2019f](#)).

A three-zone configuration described by Bevington et al. in Developing Consensus Standards for Measuring Chemical Emissions from Spray Polyurethane Foam (SPF) insulation ([Sebroski, 2017](#)) was used to represent a generic residential building, where the insulation is applied to both the attic and crawlspace. The baseline ventilation and interzonal air flows are shown in Figure 2-13. The ventilation rates for the three zones are shown in Table 2-45. EPA used the ventilation rates for the “vented” attic and crawlspace in this evaluation.

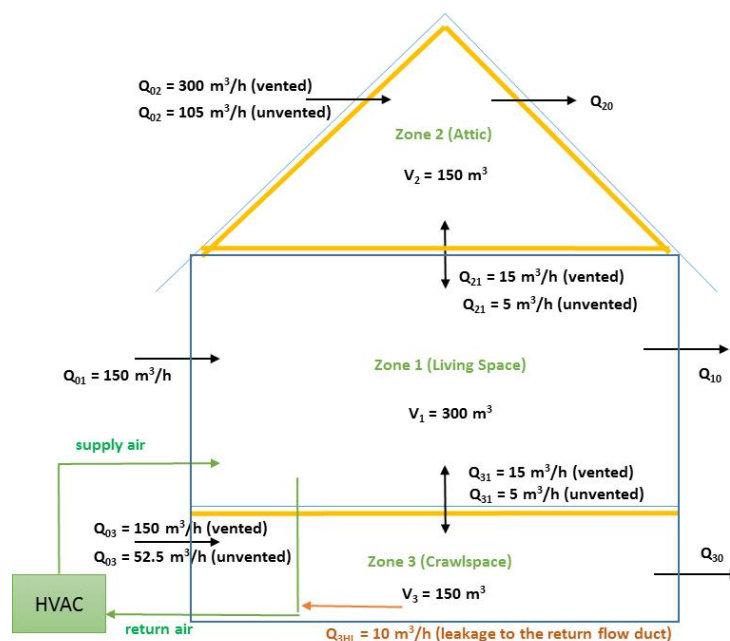


Figure 2-13. The three-zone configuration for a generic residential setting and baseline ventilation and interzonal air flows.

Table 2-45. Zone Names, Volumes, and Baseline Ventilation Rates

Zone name	Zone volume (m^3)	Ventilation rate (h^{-1})
Living space	300	0.5
Attic	150	2.0 (vented) 0.7 (unvented)
Crawlspace	150	1.0 (vented) 0.35 (unvented)

The general mass balance equation used by IECCU to determine the change in the concentration of a chemical of concern in air within a given zone is determined by six factors: (1) the emissions from the sources in the zone, (2) the rate of chemical removed from the zone by the ventilation and interzonal air flows, (3) the rate of chemical carried into the zone by the infiltration and interzonal air flows, (4) the rate of chemical sorption by interior surfaces, (5) the rate of chemical sorption by airborne particles, and (6) the rate of chemical sorption by settled dust. Given a set of initial

conditions, the general mass balance equation can be solved numerically. The physical-chemical properties of 1-BP make it a very volatile organic compound (VVOC). Thus, once emitted from the source, 1-BP tends to stay in the vapor phase. Since 1-BP is a VVOC, EPA excluded chemical sorption factors by interior surfaces, airborne particulate matter, and settled dust in the general mass balance equation for this consumer use. For this evaluation, EPA uses a source area of 180 m² in the attic and 120 m² in the crawlspace. Other parameters are summarized in Table 2-46.

Table 2-46. Parameters for the 1-BP Sources

Property	Value
Board thickness (cm)	10
1-BP content	0.50%
Density (g/cm ³)	0.03
Partition coef. (K) at 21 °C	3.8
K as a function of temp.	$a = 0.9$ $\Delta H_v = 8.14 \times 10^4$
Diffusion coef. (D) at 20 °C	1.76E-10
D as a function of temp.	$b = -8.323$ $\tau = 1676$

2.3.2.3.3 Consumer Modeling Results

Modeling results for inhalation and dermal exposures are summarized and discussed below. Results are broken down by consumer use scenario. A summary of all the results presented below is provided in Section 2.3.2.4 to allow comparison of results across scenarios. For purposes of presenting the results, three combinations are presented to provide results across a range of use patterns modeled. EPA uses the following descriptors for these three use patterns: high intensity use, moderate intensity use, and low intensity use. These descriptors are based on three key input parameters varied during the modeling (duration of use, weight fraction, and mass of product used) which are summarized in Table 2-44 but included here for ease of reference. High intensity use refers to the model iteration that utilized the 95th percentile duration of use and mass of product used (as presented in Westat) and the maximum weight fraction derived from product specific SDS, when available. Moderate intensity use refers to the model iteration that utilized the median (50th percentile) duration of use and mass of product used (as presented in Westat) and the mean weight fraction derived from product specific SDS, when available. Low intensity use refers to the model iteration that utilized the 10th percentile duration of use and mass of product used (as presented in Westat) and the lowest weight fraction derived from product specific SDS, when available. For certain situations, only a single value was identified for weight fraction in the product specific SDS. For those situations, that parameter is labeled single and the same value in all three use patterns in the summary tables below.

The coin cleaner and automobile AC flush consumer use results are still presented as high, moderate, and low intensity use patterns, but, as discussed earlier, the duration of use is based on expected durations of use from the use pattern investigations rather than specific Westat Survey durations of use. The insulation consumer use results are presented as single concentrations (24-hour maximum TWA concentration and annual average concentrations) for each of the three spaces evaluated (living space, attic, crawlspace) and therefore do not have a use pattern associated with them.

Table 2-47. Adhesive Accelerant-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24 hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	95 th (60)	Single (0.99)	95 th (172.45)	User	1.86E+01
				Bystander	4.52E+00
Moderate Intensity Use	50 th (4.25)	Single (0.99)	50 th (9.98)	User	1.17E+00
				Bystander	2.14E-01
Low Intensity Use	10 th (0.5)	Single (0.99)	10 th (1.20)	User	1.35E-01
				Bystander	2.54E-02

The adhesive accelerant consumer use was evaluated for inhalation exposure in the utility room. Table 2-47 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 1.35E-01 ppm to 1.86E+01 ppm. For the bystander, the 24-hour TWA air concentrations varied from 2.54E-02 ppm to 4.52E+00 ppm.

The range of concentrations modeled across all 9 combinations for the user has a maximum concentration of 2.01E+01 ppm and a minimum concentration of 1.29E-01 ppm. These values are different from the high and low intensity use pattern, respectively. The maximum concentration for this specific condition of use occurs when a high mass of product was used over a moderate duration. The minimum concentration for this specific condition of use occurs when a low mass of the product was used over a high (long) duration.

The range of concentrations modeled across all 9 combinations for the bystander has a maximum concentration of 4.52E+00 ppm and a minimum concentration of 2.54E-02 ppm. These values are the same as the high and low intensity use concentrations, respectively.

Table 2-48. General Spray Cleaners-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24 hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	95 th (120)	Single (0.94)	95 th (1249.04)	User	1.33E+02
				Bystander	3.28E+01
Moderate Intensity Use	50 th (15)	Single (0.94)	50 th (126.86)	User	1.42E+01
				Bystander	2.70E+00
Low Intensity Use	10 th (2)	Single (0.94)	10 th (21.86)	User	2.32E+00
				Bystander	4.44E-01

The general spray cleaner consumer use was evaluated for inhalation exposure in the utility room. Table 2-48 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 2.32E+00 ppm to 1.33E+02 ppm. For the bystander, the 24-hour TWA air concentrations varied from 4.44E-01 ppm to 3.28E+01 ppm.

The range of concentrations modeled across all 9 combinations for the user has a maximum concentration of 1.40E+02 ppm and a minimum concentration of 2.32E+00 ppm. The maximum

concentration for this specific condition of use is different than the high intensity use pattern and occurs when a high mass of product was used over a moderate duration.

The range of concentrations modeled across all 9 combinations for the bystander has a maximum concentration of 3.28E+01 ppm and a minimum concentration of 4.44E-01 ppm. These values are the same as the high and low intensity use concentrations, respectively.

Table 2-49. Spot Cleaners-Stain Remover-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	95 th (30)	Max (0.922)	95 th (434.43)	User	4.76E+01
				Bystander	9.61E+00
Moderate Intensity Use	50 th (5)	Mean (0.58)	50 th (51.91)	User	3.53E+00
				Bystander	6.57E-01
Low Intensity Use	10 th (0.5)	Min (0.276)	10 th (9.76)	User	2.71E-01
				Bystander	5.78E-02

The spot cleaners-stain remover consumer use was evaluated for inhalation exposure in the utility room. Table 2-49 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 2.71E-01 ppm to 4.76E+01 ppm. For the bystander, the 24-hour TWA air concentrations varied from 5.78E-02 ppm to 9.61E+00 ppm.

The range of concentrations modeled across all 27 combinations for the user has a maximum concentration of 4.76E+01 ppm and a minimum concentration of 2.71E-01 ppm. These values are the same as the high and low intensity use concentrations, respectively.

The range of concentrations modeled across all 27 combinations for the bystander has a maximum concentration of 9.61E+00 ppm and a minimum concentration of 5.78E-02 ppm. These values are the same as the high and low intensity use concentrations, respectively.

Table 2-50. Mold Cleaning-Release Product-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	95 th (30)	Max (0.915)	95 th (192.21)	User	2.09E+01
				Bystander	4.22E+00
Moderate Intensity Use	50 th (2)	Mean (0.6)	50 th (21.14)	User	1.43E+00
				Bystander	2.74E-01
Low Intensity Use	10 th (0.5)	Min (0.32)	10 th (3.84)	User	1.23E-01
				Bystander	2.64E-02

The mold cleaning-release product consumer use was evaluated for inhalation exposure in the utility room. Table 2-50 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 1.23E-01 ppm to 2.09E+01

ppm. For the bystander, the 24-hour TWA air concentrations varied from 2.64E-02 ppm to 4.22E+00 ppm.

The range of concentrations modeled across all 27 combinations for the user has a maximum concentration of 2.09E+01 ppm and a minimum concentration of 1.23E-01 ppm. These values are the same as the high and low intensity use concentrations, respectively.

The range of concentrations modeled across all 27 combinations for the bystander has a maximum concentration of 4.22E+00 ppm and a minimum concentration of 2.64E-02 ppm. These values are the same as the high and low intensity use concentrations, respectively.

Table 2-51. General Cleaner-Degreaser-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	95 th	Max	95 th	User	1.41E+02
	(120)	(0.9505)	(1845.17)	Bystander	4.09E+01
Moderate Intensity Use	50 th	Mean	50 th	User	1.90E+01
	(15)	(0.505)	(445.92)	Bystander	4.72E+00
Low Intensity Use	10 th	Min	10 th	User	1.04E+00
	(5)	(0.109)	(111.86)	Bystander	2.48E-01

The general cleaner-degreaser consumer use was evaluated for inhalation exposure in the garage. Table 2-51 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 1.04E+00 ppm to 1.41E+02 ppm. For the bystander, the 24-hour TWA air concentrations varied from 2.48E-01 ppm to 4.09E+01 ppm.

The range of concentrations modeled across all 27 combinations for the user has a maximum concentration of 1.50E+02 ppm and a minimum concentration of 9.81E-01 ppm. These values are different from the high and low intensity use pattern, respectively. The maximum concentration for this specific condition of use occurs when a high mass of product and a high weight fraction of 1-BP within the product was used over a low (short) duration of use. The minimum concentration for this specific condition of use occurs when a low mass of product and a low weight fraction of 1-BP within the product is used over a high (long) duration of use.

The range of concentrations modeled across all 9 combinations for the bystander has a maximum concentration of 4.52E+00 ppm and a minimum concentration of 2.54E-02 ppm. These values are the same as the high and low intensity use concentrations, respectively.

Table 2-52. General Cleaner-Degreaser-Dermal Exposure Dose

Scenario Description	Parameter Varied			Exposed Receptor	ADR (mg/kg-day)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	60	Single (0.80)	N/A	Adult	2.77E+01
				Youth A	2.59E+01
				Youth B	2.83E+01
Moderate Intensity Use	30	Single (0.80)	N/A	Adult	1.84E+00
				Youth A	1.72E+00
				Youth B	1.88E+00
Low Intensity Use	15	Single (0.80)	N/A	Adult	1.32E-01
				Youth A	1.24E-01
				Youth B	1.35E-01

The General Cleaner-Degreaser consumer use was evaluated for dermal exposure because of the possibility of a continuous supply of product to the skin during product use. Modeling used 10 percent of one hand as the area and body part impacted. Table 2-52 shows the acute dose rate (ADR) found across a range of use conditions for an adult (21 years of age and older), and two categories of youth, Youth A (16 through 20 years of age), and Youth B (11 through 15 years of age). Dermal exposure was only modeled for the user as a bystander is not expected to experience a dermal exposure.

The ADR for the Adult user varied from 1.32E-01 mg/kg-day to 2.77E+01 mg/kg-day. The ADR for the Youth A user varied from 1.24E-01 mg/kg-day to 2.83E+01 mg/kg-day. The ADR for the Youth B user varied from 1.35E-01 mg/kg-day to 2.83E+00 mg/kg-day.

Table 2-53. Degreasers-Electronic-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	95 th (30)	Max (0.972)	95 th (292.74)	User	3.02E+01
				Bystander	8.80E+00
Moderate Intensity Use	50 th (2)	Mean (0.72)	50 th (19.52)	User	1.40E+00
				Bystander	3.49E-01
Low Intensity Use	10 th (0.5)	Min (0.496)	10 th (1.56)	User	6.69E-02
				Bystander	1.90E-02

The degreaser-electronic consumer use was evaluated for inhalation exposure in the living room. Table 2-53 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 6.69E-02 ppm to 3.02E+01 ppm. For the bystander, the 24-hour TWA air concentrations varied from 1.90E-02 ppm to 8.80E+00 ppm.

The range of concentrations modeled across all 27 combinations for the user has a maximum concentration of 3.02E+01 ppm and a minimum concentration of 6.69E-02 ppm. These values are the same as the high and low intensity use concentrations, respectively.

The range of concentrations modeled across all 27 combinations for the bystander has a maximum concentration of 8.80E+00 ppm and a minimum concentration of 1.90E-02 ppm. These values are the same as the high and low intensity use concentrations, respectively.

Table 2-54. Coin Cleaners/Scissors-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	60	N/A	N/A	User	8.15E+00
				Bystander	1.37E+00
Moderate Intensity Use	30	N/A	N/A	User	3.66E+00
				Bystander	6.19E-01
Low Intensity Use	15	N/A	N/A	User	1.62E+00
				Bystander	2.92E-01

The coin/scissors cleaner consumer use was evaluated for inhalation exposure in the utility room. Table 2-54 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 1.62E+00 ppm to 8.15E+00 ppm. For the bystander, the 24-hour TWA air concentrations varied from 2.92E-02 ppm to 1.37E+00 ppm.

Table 2-55. Coin Cleaners/Scissors-Dermal Exposure Dose

Scenario Description	Parameter Varied			Exposed Receptor	ADR (mg/kg-day)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	60	Single (0.80)	N/A	Adult	1.48E+00
				Youth A	1.39E+00
				Youth B	1.52E+00
Moderate Intensity Use	30	Single (0.80)	N/A	Adult	7.41E-01
				Youth A	6.93E-01
				Youth B	7.59E-01
Low Intensity Use	15	Single (0.80)	N/A	Adult	2.47E-01
				Youth A	2.31E-01
				Youth B	2.53E-01

The coin/scissors cleaner consumer use was evaluated for dermal exposure because of the possibility of a continuous supply of product against the skin during product use. Modeling used 10 percent of one hand as the area and body part impacted. Table 2-55 shows the acute dose rate (ADR) found across a range of use conditions for an adult (21 years of age and older), and two categories of youth, Youth A (16 through 20 years of age), and Youth B (11 through 15 years of age). Dermal exposure was only modeled for the user as a bystander is not expected to experience a dermal exposure.

The ADR for the Adult user varied from 2.47E-01 mg/kg-day to 1.48E+00 mg/kg-day. The ADR for the Youth A user varied from 2.31E-01 mg/kg-day to 1.39E+00 mg/kg-day. The ADR for the Youth B user varied from 2.53E-01 mg/kg-day to 1.52E+00 mg/kg-day.

Table 2-56. Automobile AC Flush-Inhalation Exposure Concentrations

Scenario Description	Parameter Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	30	N/A	N/A	User	3.95E+00
				Bystander	6.67E-01
Moderate Intensity Use	15	N/A	N/A	User	1.70E+00
				Bystander	3.11E-01
Low Intensity Use	5	N/A	N/A	User	4.84E-01
				Bystander	9.88E-02

The automobile AC flush consumer use was evaluated for inhalation exposure in the garage. Table 2-55 shows the concentrations found across a range of use conditions. Indoor maximum 24-hour TWA air concentrations varied for the user from 4.84E-01 ppm to 3.95E+00 ppm. For the bystander, the 24-hour TWA air concentrations varied from 9.88E-02 ppm to 6.67E-01 ppm.

Table 2-57. Automobile AC Flush -Dermal Exposure Dose

Scenario Description	Parameter Varied			Exposed Receptor	ADR (mg/kg-day)
	Duration (min)	Weight Fraction (percent)	Mass used (grams)		
High Intensity Use	30	Single (0.90)	95 th	Adult	7.79E+01
				Youth A	7.34E+01
				Youth B	8.08E+01
Moderate Intensity Use	15	Single (0.90)	50 th	Adult	3.90E+01
				Youth A	3.67E+01
				Youth B	4.04E+01
Low Intensity Use	5	Single (0.90)	10 th	Adult	1.30E+01
				Youth A	1.22E+01
				Youth B	1.35E+01

The automobile AC flush consumer use was evaluated for dermal exposure because of the possibility of a continuous supply of product against the skin during product use. Modeling used the full area of face, hands, and arms as the area and body parts impacted. Table 2-57 shows the acute dose rate (ADR) found across a range of use conditions for an adult (21 years of age and older), and two categories of youth, Youth A (16 through 20 years of age), and Youth B (11 through 15 years of age). Dermal exposure was only modeled for the user as a bystander is not expected to experience a dermal exposure.

The ADR for the Adult user varied from 1.30E+01 mg/kg-day to 7.79E+01 mg/kg-day. The ADR for the Youth A user varied from 1.22E+01 mg/kg-day to 7.34E+01 mg/kg-day. The ADR for the Youth B user varied from 1.35E+01 mg/kg-day to 8.08E+01 mg/kg-day. The range of ADRs modeled across all 27 combinations for the Adult, Youth A, and Youth B users have maximums and minimums that are the same as the respective high and low intensity use patterns.

Table 2-58. Insulation-Inhalation Exposure Concentrations

Scenario Description	Exposed Receptor	24-hour TWA (ppm)	Annual Average (ppm)
Living Area	Bystander	3.34E-03	4.41E-04
Attic	Bystander	1.78E-02	2.39E-03
Crawlspace	Bystander	2.17E-02	2.88E-03

Although concentrations for the inhalation exposure are presented for all three areas within the residence, the attic and crawlspace concentrations are primarily included for comparison purposes. The attic and crawlspace are not expected to represent a livable area for human occupancy and therefore the primary focus for inhalation exposure purposes and associated risks is the “Living Area”. Table 2-58 shows the maximum 24-hour TWA indoor air concentration for the living area was 3.34E-03 ppm while the annual average indoor air concentration for the living area was 4.41E-04 ppm.

2.3.2.4 Summary of Consumer Exposure Assessment

Consumer exposure was evaluated for a total of nine consumer use groups summarized in Table 2-42 (adhesive accelerant, general spray cleaners, spot cleaner/stain remover, mold cleaning/release, general cleaner/degreasers, degreasers-electronics, coin/scissors cleaner, automobile AC flush, and insulation). All nine consumer uses were evaluated for inhalation exposure. Three of the nine consumer uses (general cleaner/degreasers, coin/scissors cleaner, and automobile AC flush) were evaluated for dermal exposure due to the possibility of these consumer uses being occluded in nature.

The results for all modeled consumer uses and exposure routes are summarized in Table 2-59 (Inhalation) and Table 2-60 (Dermal). Across all 9 consumer uses, the maximum inhalation concentration modeled for the user was 1.41E+02 ppm and the minimum inhalation concentration modeled for the user (excluding insulation) was 1.90E-02 ppm. Across all three consumer uses modeled for dermal exposure, the maximum ADR for the Adult user was 7.79E+01 mg/kg-day and the minimum was 1.32E-01 mg/kg-day. The maximum ADR for the Youth A user was 7.34E+01 mg/kg-day and the minimum was 1.24E-01 mg/kg-day. The maximum ADR for the Youth B user was 8.08E+01 mg/kg-day and the minimum was 1.35E-01 mg/kg-day.

Table 2-59. Inhalation Results Summary

Condition of Use	Scenario Description	24-hour TWA (ppm)		Model Used
		User	Bystander	
Adhesive Accelerant	High Intensity Use	1.86E+01	4.52E+00	CEM
	Moderate Intensity Use	1.17E+00	2.14E+00	
	Low Intensity Use	1.35E-01	2.54E-02	
General Spray Cleaners	High Intensity Use	1.33E+02	3.28E+01	CEM
	Moderate Intensity Use	1.42E+01	2.70E+00	
	Low Intensity Use	2.32E+00	4.44E-01	
Spot Cleaner/Stain Remover	High Intensity Use	4.76E+01	9.61E+00	CEM
	Moderate Intensity Use	3.53E+00	6.57E-01	
	Low Intensity Use	2.71E-01	5.78E-02	

Condition of Use	Scenario Description	24-hour TWA (ppm)		Model Used
		User	Bystander	
Mold Cleaning and Release	High Intensity Use	2.09E+01	4.22E+00	CEM
	Moderate Intensity Use	1.43E+00	2.74E-01	
	Low Intensity Use	1.23E-01	2.64E-02	
General Cleaners/Degreasers	High Intensity Use	1.41E+02	4.09E+01	CEM
	Moderate Intensity Use	1.90E+01	4.72E+00	
	Low Intensity Use	1.04E+00	2.48E-02	
Degreaser-Electronics	High Intensity Use	3.02E+01	8.80E+00	CEM
	Moderate Intensity Use	1.40E+00	3.49E-01	
	Low Intensity Use	6.69E-02	1.90E-02	
Coin/Scissors Cleaner	High Intensity Use	8.15E+00	1.37E+00	MCCEM
	Moderate Intensity Use	3.66E+00	6.19E-01	
	Low Intensity Use	1.62E+00	2.92E-01	
Automobile AC Flush	High Intensity Use	3.95E+00	6.67E-01	MCCEM
	Moderate Intensity Use	1.70E+00	3.11E-01	
	Low Intensity Use	4.84E-01	9.88E-02	

Table 2-60. Dermal Results Summary

Condition of Use	Scenario Description	Acute Dose Rate (mg/kg-day)			Model Used
		Adult	Youth A	Youth B	
General Cleaner/Degreaser	High Intensity Use	2.77E+01	2.59E+01	2.83E+01	CEM
	Moderate Intensity Use	1.84E+00	1.72E+00	1.88E+00	
	Low Intensity Use	1.32E-01	1.24E-01	1.35E-01	
Coin/Scissors Cleaner	High Intensity Use	1.48E+00	1.39E+00	1.52E+00	CEM
	Moderate Intensity Use	7.41E-01	6.93E-01	7.59E-01	
	Low Intensity Use	2.47E-01	2.31E-01	2.53E-01	
Automobile AC Flush	High Intensity Use	7.79E+01	7.34E+01	8.08E+01	CEM
	Moderate Intensity Use	3.90E+01	3.67E+01	4.04E+01	
	Low Intensity Use	1.30E+01	1.22E+01	1.35E+01	

Insulation Results

Figure 2-14 shows the predicted 1-BP concentration in the living area of a “typical residence”, as described earlier, over a one-year period after installation of Polyiso insulation in the residence attic and crawlspace. Unlike other 1-BP sources (e.g., liquid and aerosol sprays) summarized above, which cause short-term, high-level exposures (evaluated for acute exposure only), Polyiso insulation causes long-term, low-level exposure after the initial spike in concentration upon installation. To capture the risk resulting from the initial spike, EPA evaluated 1-BP for acute inhalation exposure using IECCU. It should be noted that Figure 2-14 displays 1-BP content in ($\mu\text{g}/\text{m}^3$) while Table 2-61 displays concentrations in ppm.

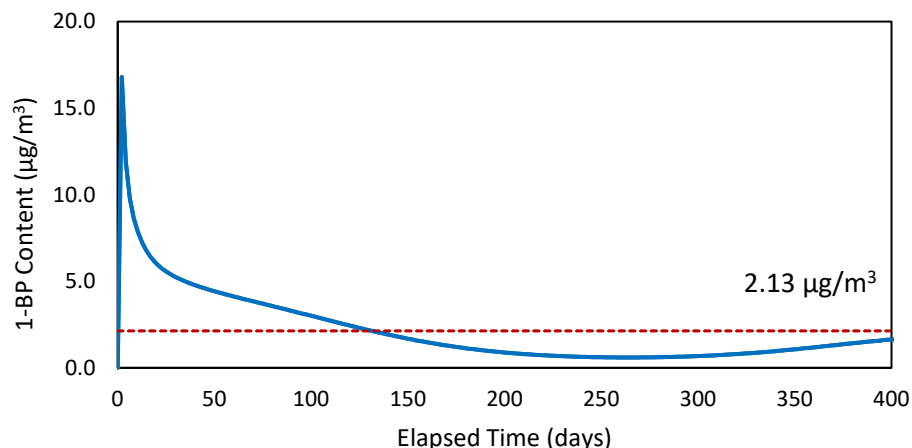


Figure 2-14. Predicted gas-phase 1-BP concentration in the living area. The dotted red line is the average concentration of 2.13 $\mu\text{g}/\text{m}^3$.

Table 2-61. Inhalation Results Summary-Insulation

Condition of Use	Scenario Description	Bystander Exposure Concentration (ppm)		Model Used
		24-hour maximum	Annual Average	
Insulation	Living Area	3.34E-03	4.41E-04	IECCU

2.3.2.5 Key Assumptions, Uncertainties, and Confidence

Modeling was used to evaluate consumer exposure concentrations for the conditions of use summarized in Table 2-42. Modeling for this evaluation required a variety of inputs where data were available or defaults were used, and certain assumptions were made in the absence of available data. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used. An overall review of these three factors can help develop a qualitative description of the confidence associated with these factors and results obtained.

Key Assumptions and Uncertainties

Consumer exposure for this evaluation is based on the assumption that the product used under the conditions of use summarized in Table 2-42 was only used once per day, except for insulation which evaluated exposure resulting from the initial spike in concentration as well as the annual average exposure. This assumption considers a single use event which may occur over a certain period of time and represents an expected consumer use pattern. There is a low uncertainty associated with this assumption.

Consumer exposure for this evaluation is also based on the assumption that a single product is used for a given day under a specific condition of use, except for insulation which evaluated exposure resulting from the initial spike in concentration as well as the annual average exposure. This assumption is primarily driven by the absence of information or data found during the systematic review process identifying multiple products, each containing the chemical of concern, were used by a consumer in a single day. There is a medium-low uncertainty associated with this assumption.

This evaluation assumes consumer exposure is not chronic in nature. This assumption is based on expected consumer use patterns and data found during systematic review that indicates frequency of use (days of use) of products containing the chemical of concern is not chronic in nature. This assumption also can be derived from the previous assumptions where a single product is used infrequently, once per day and therefore not chronic in nature. This assumption may result in underestimating the exposure of certain consumer users, in particular those consumers who may be do-it-yourselfers who may use products more frequently or may use more than one product within a single day, . There is a medium uncertainty associated with this assumption because of the possible of underestimating exposure of frequent use or multi-product users.

This evaluation assumes a background concentration of zero for the chemical of concern during evaluation of consumer exposure. This assumption is primarily driven by the physical-chemical properties of the chemical of concern which is the high vapor pressure and expected quick dissipation of the chemical of concern. There is a low uncertainty associated with this assumption.

Inputs and Uncertainties

Inputs for the modeling were a combination of physical-chemical properties of the chemical of concern, default values within the models used, values from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)), and Westat Survey ([U.S. EPA, 1987](#)) data found in the literature as part of the systematic review process. Physical-chemical properties of the chemical of concern are pre-defined and well-established in the literature. These properties do not change under standard conditions and therefore have very low uncertainty associated with them.

Default values within the models used are a combination of central tendency and high-end values derived from well-established calculations, modeling, literature, and from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). The models used have a wide variety of parameters with default values, although certain default values, but not all, can be changed (if information and data are available) prior to running the model. There is a medium-low uncertainty associated with these values due to the number of parameters where defaults are available.

Values from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)) are a combination of central tendency and high-end values which are well-established and commonly used for exposure evaluations and modeling. The values are derived from literature, modeling, calculations, and surveys. There is a low uncertainty associated with the values in U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)).

The Westat Survey ([U.S. EPA, 1987](#)) was previously described in this evaluation. It is an EPA directed national survey which received over 4,920 completed questionnaires from across the United States. The survey aimed to answer multiple questions related to the use of solvent-containing consumer products within thirty-two different common household product categories. Multiple aspects of the survey and survey results were utilized in this evaluation. Most of the consumer uses summarized in Table 2-42 aligned well with one of the thirty-two product categories within the Westat Survey. There is a medium-low uncertainty associated with the cross-walking of consumer uses with the Westat product categories.

The representativeness of the consumer use patterns (duration of use, amount used, room of use, etc.) described in the Westat Survey ([U.S. EPA, 1987](#)) is believed to remain strong when compared to present day consumer use patterns even though some aspects of the use may have changed (electronics cleaners were applied to VCRs in 1987, but now are applied to computer motherboards or DVD players). However, ease of access to products on-line or in big box stores (like home improvement stores), readily accessible how-to videos, and a consumer movement toward more do-it-yourself projects with products containing the chemical of concern could impact the representativeness of the consumer use patterns described within the Westat Survey and may lead to an underestimate of overall consumer exposure. There is a medium uncertainty associated with the representativeness of the consumer use patterns described within the Westat Survey and present day consumer use patterns.

Other Uncertainties

There are several other factors to which some level of uncertainty may apply. These include, but are not limited to, product use/availability, model specific factors, building characteristics, and use of personal protective equipment or natural/engineered controls.

As described in Section 2.3.2.1, the consumer use dossier and market profile were developed in 2016-2017 and are based on information available at that time. These do not take into consideration company-initiated formulation changes, product discontinuation, or other business or market based factors that occurred after the documents were compiled. However, unless these factors were in process while the dossier and market profile were being developed, it is unlikely any significant changes occurred since such changes often require considerable time to research, develop, and implement. Even with discontinuation of products, while they may readily be removed from shelves, product already purchased or picked up to be sold online shortly before discontinuation will take some time to work out of availability and consumer use. There is a medium-low uncertainty associated with the product use/availability of product containing the chemical of concern.

There are multiple model specific factors to which a level of uncertainty may apply including user groups (age groups), building characteristics, and inherent model parameters. Three user groups were modeled as users for dermal exposure for this evaluation (Adult, Youth A, and Youth B) which are defined in Section 2.3.2.3.3. There is a medium level of uncertainty associated with the appropriateness of Youth B (11-15 years of age) being a user for certain products like general cleaners/degreasers or AC Autoflush. The Youth B group is not expected to be a user of such products, unless it is in an elective class at school (like autoshop), or learning from parents about such cleaning or car maintenance activities. With more at-home do-it-yourself projects occurring, it is possible Youth B users of such products would be more common. There is a low uncertainty associated with Adults or Youth A groups being a user of such products.

There are multiple building characteristics considered when modeling consumer exposure including, but not limited to, room size, ventilation rate, and building size. For this evaluation, EPA relied on default values within the models for these parameters. These default values were primarily obtained from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). There is a medium low uncertainty associated with these parameters.

Room size varied for this evaluation based on room of use obtained from the Westat Survey ([U.S. EPA, 1987](#)) data. Room size relates to the volume of the room and is a sensitive parameter within the models. However, the room size of a standard bedroom, living room, kitchen, utility room, one or two car garage, etc. should be relatively consistent across building types (small or large residential homes, apartments, condominiums, or townhomes). Therefore, any uncertainty associated with room size is derived more from the room of use selected, rather than and wide variety of sizes of a particular room of use. Since the rooms of use selected for this evaluation are based on data collected by the Westat Survey, there is a low uncertainty associated with room sizes used for this evaluation.

Ventilation rate is another sensitive parameter within the models. Similar to the room of use, however, ventilation rates should be relatively consistent across building types where ventilation systems are properly maintained and balanced. Centralized ventilation systems are designed to deliver ventilation rates or air exchange rates which meet the American Society of Heating, Refrigeration, and Air Conditioning Engineers Standard Recommendations which are established for rooms, house types, commercial buildings, and others. Centralized ventilation systems may be larger for larger homes, but the ventilation rates delivered to the specific room of use should be relatively consistent across building types. Therefore, any uncertainty associated with ventilation rates is derived more from the proper design, balancing, and maintenance of ventilation systems. Ventilation rates for a particular room of use could be impacted by use of fans or opening windows within the room of use, however, most respondents to the Westat Survey indicated they did not have an exhaust fan on when using the products. Most respondents kept the door to the room of use open, but did not open doors or windows leading to the outside when using the products. There is a medium low uncertainty associated with the ventilation rates used for this evaluation.

Building size is another sensitive parameter within the models, however, the sensitivity derives from more mixing and dissipation outside of the room of use. There will be more variability in building size across building types so there is a medium low uncertainty associated with building size.

The use of personal protective equipment or natural/engineered controls by a consumer during product use is uncertain at best. It is not expected that consumers will utilize personal protective equipment like full face respirators, self-contained breathing apparatus, or engineering controls like hoods, baghouses, or incinerators when using consumer products in a residence or building to reduce inhalation risks. While it may be slightly more likely consumers may wear gloves or eye protection when using certain products, neither of these address inhalation exposure. Use of gloves by a consumer could decrease dermal exposure, assuming the gloves are high quality and chemical resistant. Latex gloves are a readily available glove, however, such gloves tear easily, and may not be resistant to breakdown by certain products used. Although the use of gloves could reduce dermal exposure, if used improperly (for example fully immersing hands into a product) could allow for leakage into the glove leading to an occluded scenario that is not otherwise expected.

Confidence

There is an overall high to high-medium confidence in all the results found for the consumer scenarios identified in Table 2-42 and evaluated in this evaluation. This confidence derives from a

review of the factors discussed above as well as previous discussions about the strength of the models and data used, sensitivity of the models, and approaches taken for this evaluation.

All three models used for this evaluation are peer reviewed models. The models themselves were used for this evaluation as they were developed and designed to be used. The equations within the models are derived, justified and substantiated by peer reviewed literature as described in the respective user guides and associated user guide appendices. The default values utilized in the models (and retained for this evaluation) are a combination of central tendency and high-end estimates from both peer reviewed literature and U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)) providing a representative spectrum of modeling results. Even though some values have high-end values (like building size or ventilation rates), it should be recognized that the sensitivity of these parameters are actually negative and the "higher" building sizes or higher ventilation rates actually would be expected to result in more mixing and dissipation leading to a lower exposure concentrations.

The data used in lieu of default values within the model are a combination of low, central tendency, and high-end values from the Westat Survey ([U.S. EPA, 1987](#)) which was rated as a high quality study as part of the systematic review process. The nine use scenarios evaluated for this evaluation aligned well with specific scenarios within the Westat Survey, pre-defined model scenarios, and other approaches taken. The deterministic approach taken for consumer exposure in this evaluation involved varying three parameters which were either highly sensitive or representative of consumer use patterns or both. The three parameters varied also provided a broad spectrum of consumer use patterns covering low, moderate, and high intensity uses and therefore are not limited to a high-end, worst-case type situation or an upper bounding estimate. Other aspects of the deterministic approach taken (like a single product used once per day) or consideration of only possible occluded scenarios are not upper bounding and in fact may result in an underestimate of actual consumer exposure.

2.4 Potentially Exposed or Susceptible Subpopulations

TSCA § 6(b)(4)(A) requires that a risk evaluation "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly."

For occupational exposures, EPA assessed exposures to workers and ONUs from all 1-BP conditions of use. Table 2-62 presents the percentage of employed workers and ONUs whom may be susceptible subpopulations within select industry sectors relevant to 1-BP conditions of use. The percentages were calculated using Current Population Survey (CPS) data for 2017. CPS is a monthly survey of households conducted by the Bureau of Census for the Bureau of Labor Statistics and provides a comprehensive body of data on the labor force characteristics. Statistics for the following subpopulations of workers and ONUs are provided: adolescents, men and women

of reproductive age,²⁰ and the elderly. For the purpose of this assessment, EPA considers “reproductive age” as age 16 to 54. As shown in Table 2-62, men make up the majority of the workforce in manufacturing sectors. In other sectors, women (including those of reproductive age and elderly women) make up nearly half of the workforce.

Adolescents, or persons between 16 and 19 years in age, are generally a small part of the total workforce. Table 2-63 presents further breakdown on the percentage of employed adolescents by industry subsectors. As shown in the table, they comprise less than two percent of the workforce, with the exception of repair and maintenance subsector where 1-BP may be used in aerosol degreasing, and the dry cleaning subsector where 1-BP may be used for dry cleaning and spot cleaning.

Table 2-62. Percentage of Employed Persons by Age, Sex, and Industry Sector

Age group	Sex	Manufacturing	Wholesale and retail trade	Professional and business services	Other services
Adolescent (16-19 years)	Male	0.8%	3.0%	0.7%	1.4%
	Female	0.4%	3.2%	0.5%	1.7%
Reproductive age (16-54 years)	Male	52.9%	42.8%	44.4%	35.2%
	Female	22.2%	35.4%	32.8%	38.4%
Elderly (55+)	Male	17.5%	12.3%	13.4%	13.1%
	Female	7.3%	9.6%	9.4%	13.3%

Source: ([U.S. BLS, 2017](#)). Percentage calculated using CPS table 14, “Employed persons in nonagricultural industries by age, sex, race, and Hispanic or Latino ethnicity.”

Table 2-63. Percentage of Employed Adolescents by Detailed Industry Sector

Sector	Subsector	Adolescents (16-19 years)
Manufacturing	All	1.2%
Wholesale and retail trade	Wholesale trade	1.4%
Professional and business services	Waste management and remediation services	0.9%
Other services	Repair and maintenance	3.1%
	Drycleaning and laundry services	3.7%

Source: ([U.S. BLS, 2017](#)). Percentage of adolescents calculated using CPS table 18b, “Employed persons by detailed industry and age.”

The CPS uses 2012 Census industry classification, which was derived from the 2012 NAICS. The Census classification uses the same basic structure as NAICS but is generally less detailed. 1-BP conditions of use fall under the following Census industry sectors:

- **Manufacturing** – The Manufacturing sector comprises establishments engaged in the mechanical, physical, or chemical transformation of materials, substances, or components

²⁰ While statistics on pregnant women are not available, CPS provides data on the number of employed female workers by age group, which allows for determination of the number of employed women of reproductive age.

into new products. Establishments in the sector are often described as plants, factories, or mills. For 1-BP, this sector covers most conditions of use that occur in an industrial setting, including: Manufacturing, Processing as a reactant, Processing – Incorporation into formulation, mixture, or reaction product, Incorporation into Articles, Spray adhesives, and the vast majority of facilities likely engaged in Vapor Degreasing (all degreaser types) and Cold Cleaning. This sector also covers cement manufacturing facilities that may burn waste containing 1-BP for energy recovery.

- **Wholesale and retail trade** – The wholesale trade sector comprises establishments engaged in wholesaling merchandise, generally without transformation, and rendering services incidental to the sale of merchandise. Wholesalers normally operate from a warehouse or office. This sector likely covers facilities that are engaged in the importation of 1-BP or products and formulations containing 1-BP. The retail trade sector comprises establishments engaged in retailing merchandise and rendering services incidental to the sale of merchandise.
- **Professional and business services** – This sector comprises establishments that specialize in a wide range of services. This sector covers waste management and remediation services, which includes establishments that may handle, dispose, treat, and recycle wastes containing 1-BP.
- **Other services** – This sector comprises establishments engaged in providing services not specifically provided for elsewhere in the classification system. For 1-BP, this sector covers the vast majority of commercial repair and maintenance facilities that are likely to use 1-BP for aerosol degreasing. The sector also covers the use of 1-BP in dry cleaning and spot cleaning.

For consumer exposures, EPA assessed exposures to users and non-users (bystanders). EPA assumes, for this evaluation, consumer users are male or female adults (between 16 and 21 years of age and greater than 21 years of age), including woman of reproductive age. Non-users could be any age group ranging from infants to adults (Section 2.3.2.3).

3 HAZARDS (Effects)

3.1 Environmental Hazards

3.1.1 Approach and Methodology

EPA identified environmental hazard data through a literature search for 1-BP as outlined in *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0047](#). As described below as well as in Appendix F, a total of one on-topic environmental hazard study (acute fish study; ([Geiger et al., 1988](#))) was identified and reviewed according to the systematic review criteria described in *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)) and *Strategy for Assessing Data Quality in TSCA Risk Evaluations* ([U.S. EPA, 2017e](#)). This study was determined to be high quality following data quality evaluation, and the full study quality evaluation is presented in the systematic review data evaluation document for ecological hazard studies (([EPA, 2019l](#))).

In addition to this study, five robust data summaries were identified in the European Chemicals Agency (ECHA) Database and were used to characterize the environmental hazards of 1-BP to aquatic receptors ([ECHA, 2017](#)). These data summaries characterized the environmental hazards of 1-BP to fish, aquatic invertebrates, algae and microorganisms (sludge). In addition to the summaries available in the ECHA database, copies of these study summaries are available in the docket ([EPA-HQ-OPPT-2016-0741-0047](#)), and the results are presented and discussed below ([EPA, 2019d](#)).

In the Problem Formulation ([U.S. EPA, 2018c](#)), it was preliminarily determined as a result of a screening-level comparison of available environmental hazard data with exposure concentrations that no further hazard analyses was necessary. Additionally, although terrestrial exposure pathways are included in the scope of the problem formulation, no further analyses of hazards to terrestrial receptors is necessary as a result of a consideration of the conditions of use, and physical chemical properties of 1-BP ([U.S. EPA, 2018c](#)). Consistent with the analysis plan of the Problem Formulation ([U.S. EPA, 2018c](#)), no further analysis of hazards to aquatic or terrestrial receptors was carried out as part of this evaluation under the conditions of use of this assessment.

3.1.2 Hazard Identification- Toxicity to Aquatic Organisms

No additional environmental hazard data were received following the publication of the problem formulation, however, two notable updates to the analysis of environmental hazard were made to the environmental hazard conclusions of this document. First, EPA evaluated (where possible) reasonably available environmental hazard data for 1-BP ([EPA, 2019l](#)). EPA was unable to obtain the full study reports for the data summaries identified in the ECHA Database so these data were not evaluated according to the systematic review criteria; however, EPA did consider the summaries in this analysis. Secondly, one additional study with green algae (*Pseudokirchneriella subcapitata*) was identified in the ECHA database which was not presented in the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)). These updates do not affect the preliminary conclusions of the screening-level analysis presented in the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)), so the preliminary conclusions that additional analysis of environmental hazards remains unchanged.

Acute Hazard

To assess aquatic toxicity from acute exposures, data for four taxonomic groups were available: to fish, aquatic invertebrates, algae and activated sludge. The results of these studies are discussed below and presented in Table_Apx F-2.

Two studies characterized the acute toxicity of 1-BP to fish. Following 96-hour exposure to fathead minnows (*Pimephales promelas*), a LC₅₀ value of 67.3 mg/L was reported ([Geiger et al., 1988](#)). This endpoint was also based on mortality observed in the test organisms and was calculated based on measured test concentrations. The study authors reported sublethal effects that included a loss of schooling behavior, hypoactivity, underreactive to external stimuli, increased respiration, dark coloration and loss of equilibrium prior to death. This study was evaluated by EPA for study quality and determined to be high confidence ([EPA, 2019l](#)). A second study, summarized in the ECHA database, reported an LC₅₀ of 24.3 mg/L ([ECHA, 2017](#)) ([EPA, 2019d](#)). This endpoint was based on mortality reported for rainbow trout (*Oncorhynchus mykiss*) following 96 hours of exposure and was calculated based on the mean-measured exposure concentrations. The study authors reported sublethal effects including lethargy (fish at base of test vessel), darkened pigmentation (body and/or eye orbits), loss of orientation (nose upwards), surface swimming, overturned individuals at base of test vessel, hyperventilation and pale faces with excessive mucus. EPA was unable to obtain the full study report for this summary; as a result, it was not evaluated by EPA for study quality. One study, reported in the ECHA database, characterized the environmental hazards of 1-BP to the aquatic invertebrate species *Daphnia magna*. The acute aquatic invertebrate EC₅₀ for 1-BP following 48 hours of exposure is 99.3 mg/L, based on measured test concentrations ([ECHA, 2017](#)) ([EPA, 2019d](#)). This endpoint is based on immobility of the test organisms. Only one sublethal effect, lethargy, was reported in the study. EPA was unable to obtain the full study report for this summary; as a result, it was not evaluated by EPA for study quality.

Two algae studies were summarized in the ECHA database. The first test, conducted in 2008 on the freshwater algae species *Pseudokirchneriella subcapitata*, reported an EC₅₀ following 96 hours of exposure of 52.4 mg/L (based on reductions in biomass) and 72.3 mg/L (based on a reduction in growth rate). These endpoints were based on measured test concentrations. The NOEC for this algae toxicity test based on reductions in biomass is 12.4 mg/L ([ECHA, 2017](#)) ([EPA, 2019d](#)). A second algae study, conducted in 1998, also on *P. subcapitata*, reported an EC_{50s} of 17 mg/L (based on a reduction in biomass) and > 54.98 mg/L (based on a reduction in growth rate). The study summary reported a NOAEC value of 0.93 mg/L for both reduction in biomass and growth rate. EPA was unable to obtain the full study reports for these summaries; as a result, they were not evaluated by EPA for study quality. The EC₅₀ and NOEC for micro-organisms toxicity study for a 5-minute time period was 270 mg/L and 100 mg/L ([ECHA, 2017](#)) ([EPA, 2019d](#)), respectively.

Chronic Hazard

The vapor pressure of 1-BP is 146.26 mmHg (19.5 kPa) at 20°C and the Henry's law constant is calculated to be over 700 Pa.M³/mol. These physical-chemical properties indicate that 1-BP is likely to volatilize quickly from water and that long-term presence in the aquatic compartment and resulting chronic exposure is only a likely scenario for environments near direct release sites. As

no data were available to characterize the hazards of chronic exposure to aquatic species, EPA estimated hazards from chronic exposure using an acute-to-chronic ratio (ACR). The most sensitive species following acute exposure, which in this case were freshwater fish, with a 96-hr LC_{50} of 67.3 mg/L (the value ([Geiger et al., 1988](#)) and 24.3 mg/L ([ECHA, 2017](#)) ([EPA, 2019d](#)) were divided by an ACR of 10 to estimate chronic values (ChV) for fish. This results in a fish chronic value (ChV) of $67.3 \text{ mg/L} / 10 = 6.73$ and $24.3 \text{ mg/L} / 10 = 2.43 \text{ mg/L}$, respectively. This approach was also used for aquatic invertebrates, where the 48-hr LC_{50} of 99.3 mg/L is divided by an acute-to-chronic ratio (ACR) of 10 to obtain a chronic value (ChV) for aquatic invertebrates. This results in a ChV of $99.3 \text{ mg/L} / 10 = 9.93 \text{ mg/L}$. Algae data were not used to calculate the hazard aquatic organisms from chronic exposure, because durations normally considered acute for other species (e.g. 48, 72 hours) can encompass several generations of algae. The reasonably available environmental hazard data for 1-BP are presented in greater detail in Appendix F.

3.1.3 Hazard Identification- Toxicity to Terrestrial Organisms

1-BP is expected to be present at limited concentrations in terrestrial ecosystems. As a result of high volatility (Vapor Pressure= 146.26 mmHg; Henry's Law constant of $7.3 \times 10^{-3} \text{ atm}\cdot\text{m}^3/\text{mole}$; see Table 1-1), high water solubility (2.4 g/L), low log K_{oc} (1.6), and conditions of use of the chemical, it is expected that that 1-BP will only be present in terrestrial environmental compartments as a transient vapor. No specific conditions of use (i.e. systematic application to land) were identified that resulted in systematic, significant airborne exposures that overlap with terrestrial habitats, so this is not a relevant route of exposure for 1-BP under the conditions of use of this risk evaluation. Additionally, 1-BP is not expected to bioaccumulate (BAF=12; BCF=11, see Table 2-1) and high volatility from water (Vapor Pressure= 146.26 mmHg; Henry's law constant= $7.3 \times 10^{-3} \text{ atm}\cdot\text{m}^3/\text{mole}$; see Table 1-1) means that exposures to terrestrial species through oral routes is limited. This preliminary conclusion is confirmed in this risk evaluation; no further analysis of hazards to terrestrial receptors was carried out as part of this evaluation, as exposure to terrestrial species is not a relevant route of exposure under the conditions of use of this assessment.

3.1.4 Weight of the Scientific Evidence

During the data integration stage of EPA's systematic review, EPA analyzed, synthesized, and integrated reasonably available data/information. This involved weighing scientific evidence for quality and relevance, using a Weight of the Scientific Evidence (WoE) approach ([U.S. EPA, 2018a](#)). The ecological risk assessor decided if data/information were relevant based on whether it has biological, physical-chemical, and environmental relevance ([U.S. EPA, 1998a](#)):

- Biological relevance: correspondence among the taxa, life stages, and processes measured or observed and the assessment endpoint.
- Physical-chemical relevance: correspondence between the chemical or physical agent tested and the chemical or physical agent constituting the stressor of concern.
- Environmental relevance: correspondence between test conditions and conditions in the region of concern. ([U.S. EPA, 1998a](#))

A total of one acute fish toxicity study as well as five toxicity studies summarized in ECHA were used to conduct a screening-level characterization of the environmental hazards of 1-BP. EPA was unable to obtain the full studies that were summarized in the ECHA database. The studies were in French and Japanese (with no U.S.A. sponsor); therefore, EPA decided not to make further attempts to obtain the full study reports for these endpoints. These study summaries as presented in the ECHA database are available in the docket ([EPA-HQ-OPPT-2016-0741-0047](#)) ([EPA, 2019d](#)).

As a result, only a single acute fish toxicity study identified during the literature search process (([Geiger et al., 1988](#))) has been evaluated according to the systematic review criteria in *The Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)). Although full studies summarized in ECHA have not been evaluated for data quality, according to the systematic review criteria in *The Application of Systematic Review in TSCA Risk Evaluations*, a qualitative consideration of the results of these summaries indicates that the hazard conclusions of these summaries are consistent with the results of the fish study that was reviewed for data quality. All studies indicate that 1-BP presents a low or moderate hazard to aquatic environmental receptors. As a result, the environmental hazards are primarily described using the acute fish study, which was rated as high confidence ([Geiger et al., 1988](#)) ([EPA, 2019i](#)). This study constitutes the best available data to assess the environmental hazards of 1-BP. In an effort to utilize all available data characterizing the environmental hazards of 1-BP, the data presented in the ECHA study summaries were considered to contextualize and characterize the potential hazards and risks of 1-BP to aquatic receptors.

3.1.5 Hazard Summary

1-BP presents a moderate hazard (according to the concern levels outlined in U.S. EPA ([2012e](#))²¹) to aquatic species based on acute exposure to fish, which were determined to be the most sensitive species based on available data, with an LC₅₀ of 24.3-67.3 mg/L ([Geiger et al., 1988](#)) ([ECHA, 2017](#)) ([EPA, 2019d](#)). Based on an estimate of hazard to fish from chronic exposure to 1-BP, a ChV of 9.93 mg/L was calculated.

This conclusion of moderate environmental hazard is supported by the environmental hazard study summaries presented in ECHA, where low or moderate hazard was reported for all aquatic taxa following acute exposure. This is similar to the predicted hazard from chronic exposure, where based on the application of an acute to chronic ratio to acute toxicity endpoints, moderate hazard is expected.

As discussed in Appendix F, hazard thresholds, known as Concentrations of Concern (COCs) were calculated to provide a conservative estimate for a screening level comparison with estimated surface water concentrations to identify potential concerns to aquatic species. The analysis of the environmental COCs are based on EPA methods ([U.S. EPA, 2012e](#)). To calculate acute COCs, the acute 96-hour fish toxicity values were divided by an assessment factor of 5 for acute and 10 for chronic. Therefore, the acute COCs for 1-BP ranged from 13,640-4,860 ppb (LC₅₀ (24.3 mg/L) / AF of 5 = 4.86 mg/L or 4,860 µg/L or ppb; LC₅₀ (67.3 mg/L) / AF of 5 = 13,640 µg/L or ppb). Based on estimated chronic hazard endpoints for fish, chronic COCs of 673-243 ppb were calculated (fish 96-hr LC₅₀ (67.3 mg/L) / 10 (ACR) / AF of 10 = 673 µg/L or ppb; fish 96-hr LC₅₀ (24.3 mg/L) / 10 (ACR) / AF of 10 = 0.243 mg/L or 243 µg/L or ppb). 1-BP is expected to be present at low concentrations in the terrestrial ecosystems and the sediment compartment of aquatic ecosystems so no further analysis of hazards to these environmental receptors is necessary.

²¹ Hazard concern levels for acute exposure: Low >100mg/L; Moderate >1.0 mg/L and <100 mg/L; High <1.0. Hazard concern levels for chronic exposure: Low >10 mg/L; Moderate >0.1 mg/L and <10 mg/L; High <0.1 ([U.S. EPA, 2012e](#)).

3.2 Human Health Hazard

3.2.1 Background on the Process of Systematic Review

EPA characterized gathered and evaluated information on the human health hazards associated with 1-BP exposure according to the process described in the *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)). EPA identified hazard data for 1-BP through an extensive literature search, as described in EPA's *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). Published and non-published data sources, including key and supporting studies identified in previous assessments, were evaluated during this process. EPA also relied heavily on the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)) to inform hazard characterization. EPA has high confidence in the toxicological studies used to support risk estimation.

Although EPA conducted a comprehensive search and screening process as described in section 1.5, EPA generally used previous chemical assessments, such as the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)), to identify key and supporting information that would be influential in the risk evaluation, including information supporting key analyses, arguments, and/or conclusions in the risk evaluation. Where applicable, EPA also considered newer information not considered in the previous chemical assessments. Using this pragmatic approach, EPA evaluated the confidence of the key and supporting data sources as well as newer information instead of evaluating all the underlying evidence published on the human health hazards of 1-BP exposure. This allowed EPA to maximize the scientific and analytical efforts of other regulatory and non-regulatory agencies by accepting for the most part, the scientific knowledge gathered and analyzed by others. The influential information sources used to support quantitative analyses represents a smaller pool of studies that were ultimately subjected to the TSCA systematic review process to ensure that the risk evaluation uses the best available science in the overall weight of evidence.

EPA assessed the quality of the key and supporting studies identified in the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)) based on the data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)); these key and supporting studies were determined to be of high quality (i.e., high confidence). The comprehensive results of the study evaluations can be found in the *Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies*. EPA-HQ-OPPT-2019-0235 ([EPA, 2019p](#)). Section 3.2 and Appendix I may also cite other data sources as part of the reasonably available information on the human health hazards of 1-BP. EPA did not subject these other data sources to the later phases of the systematic review process (i.e., data evaluation and integration). Only the key and supporting studies carried forward for dose-response analysis in the [2016 Draft Risk Assessment for 1-BP](#) ([U.S. EPA, 2016d](#)), and any new studies published since that time, were subjected to the TSCA systematic review process.

3.2.2 Approach and Methodology

Development of the 1-BP hazard and dose-response assessment considered principles set forth in various risk assessment guidance, and guidelines issued by the National Research Council and EPA. Figure 3-1 depicts the process EPA used to evaluate, extract and integrate 1-BP's human health hazard and dose-response information.

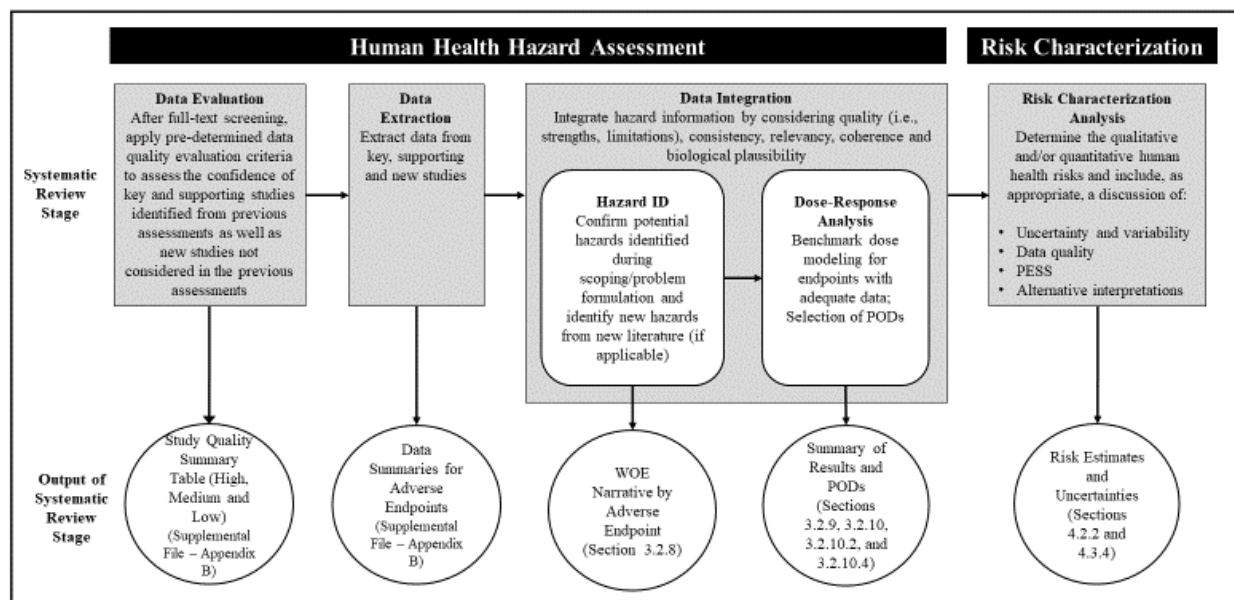


Figure 3-1. EPA Approach to Hazard Identification, Data Integration, and Dose-Response Analysis for 1-BP

1-BP does not have an existing EPA Integrated Risk Information System (IRIS) Toxicological Review; however, 1-BP has been the subject of numerous health hazard reviews including the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile (2017), and the National Institute for Occupational Safety and Health (NIOSH) Draft Criteria Document (2016), in addition to the 2016 Draft Risk Assessment (U.S. EPA, 2016d). During the analysis phase of the risk evaluation, EPA conducted a systematic review of the available literature, using these existing assessments as a starting point. Only the references identified as "on topic" and any new literature published since these existing assessments were considered relevant data/information sources in this draft risk evaluation, as described in EPA's *Strategy for Conducting Literature Searches for 1-BP (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0741-0047). These studies were screened against inclusion criteria in the PECO statement and the studies deemed suitable for dose-response analysis were further evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

EPA evaluated the quality of the key and supporting information that would be influential in the risk evaluation using the data evaluation criteria for human, animal, and in vitro studies described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). A summary of the relevant endpoints carried forward for dose-response assessment can be found in Table 3-1, including the no-observed- or lowest-observed-adverse-effect levels (NOAEL and LOAEL) for health endpoints by target organ/system, the corresponding benchmark concentration/dose lower confidence limits (BMCLs/BMDLs), when available, and the corresponding human equivalent concentrations/doses (HECs/HEDs), and uncertainty factors (Ufs). EPA has not developed data quality criteria for all types of hazard information such as toxicokinetics and mechanistic data.

EPA used these data to support the risk evaluation, but not for quantitative risk analysis. For example, supplemental studies were considered while investigating the 1-BP mode of action (MOA). These findings were considered in synthesizing the evidence and integrated as appropriate, into the relevant health effect sections in Section 3.2.7.

EPA's literature search results for 1-BP human health hazards yielded 813 studies (Section 1.5.1). This included 14 key and supporting studies that were identified from previous EPA assessments. Of the 799 new studies screened for relevance, 784 were excluded based on PECO (off topic). The remaining 15 new studies and 14 key and supporting studies were put through data evaluation; 24 studies were carried forward to data extraction/data integration. Toxicological information was extracted from studies deemed relevant and suitable for dose response analysis.

For this risk evaluation, all of the known human health hazards of 1-BP were described and reviewed. Based on this review, EPA narrowed the focus of the 1-BP hazard characterization to liver toxicity, kidney toxicity, reproductive/developmental toxicity, neurotoxicity, and cancer (brief summaries are presented for each hazard endpoint in Section 3.2.7); detailed summaries are presented in Appendix I. EPA identified or calculated points of departure (PODs). EPA defines a POD as the dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on the dose for an estimated incidence, or a change in response level from a dose-response model (e.g., benchmark dose or BMD), a NOAEL value, or a lowest observed adverse effect level (LOAEL) for an observed incidence, or a change in the level (i.e., severity) of a given response ([U.S. EPA, 2002](#)). PODs were adjusted as appropriate to conform to the specific exposure scenarios evaluated (e.g., to account for differences in the duration of inhalation exposure between humans and laboratory animals). Section 3.2.10 provides the dose-response assessment including the selection of PODs for cancer and non-cancer endpoints and the benchmark dose analysis used in the draft risk evaluation.

The inhalation and dermal routes of exposure were evaluated in this assessment. Insufficient toxicological data is available via the oral route. In accordance with EPA guidance, the exposure concentrations used in animal studies were adjusted according to the ratio of the blood:air partition coefficients, where a default ratio of 1 is applied when the partition coefficient for rats is greater than that of humans ([U.S. EPA, 2002, 1994](#)). For HEC/dermal HED calculations, these exposure concentrations were further adjusted from the exposure durations used in animal studies to durations deemed relevant for human exposure scenarios (e.g., 8-hours/day and 5 days/week for occupational exposures). The majority of exposures occur via inhalation, which is considered the primary route of exposure; however, the CSAC Peer Review of the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#) recommended that dermal exposures might be an important contributor to overall exposure and recommended that an estimate for dermal exposure also be included in the evaluation, with gaps/limitations clearly stated to address another potential workplace exposure pathway. Since there is limited toxicological data available by the oral and dermal route, physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have not been identified, and there are no relevant kinetic or metabolic information for 1-BP that would facilitate development of dosimetric comparisons, EPA chose to derive dermal HEDs by extrapolating from the inhalation PODs. The limitations of this approach are discussed Section 3.2.10.5 and Section 4.3.

EPA followed the recommendations in EPA's [Guidelines for Developmental Toxicity Risk Assessment](#) when making the decision to use developmental toxicity studies to evaluate risks that may be associated with acute exposure to 1-BP during occupational or consumer use of spray adhesive, dry cleaning or degreasing products that contain 1-BP. This decision is based on EPA's assumption that a single exposure during a critical window of fetal development may be sufficient to produce adverse developmental effects ([Guidelines for Developmental Toxicity Risk Assessment](#)).

3.2.3 Toxicokinetics

This section describes the available information on absorption, distribution, metabolism and excretion (ADME). For additional details, see Appendix H.

As discussed above in Section 3.2.2, EPA has not published systematic review criteria applicable to toxicokinetic studies, however all relevant toxicokinetic information was either obtained from previous regulatory and non-regulatory chemical assessments and/or was informally evaluated for overall data quality and relevance. Studies in humans and laboratory animals show that 1-BP may be absorbed following oral, inhalation or dermal exposure; however, dermal and inhalation pathways are expected to be more relevant for occupational exposures ([Frasch et al., 2011](#); [Hanley et al., 2009](#); [NIOSH, 2007](#); [Garner et al., 2006](#); [Jones and Walsh, 1979](#)). The extent of absorption via the inhalation route depends on the rate of transfer from pulmonary capillaries to blood (i.e., blood/air partition coefficient), and the rate of metabolism in various tissue compartments.

The blood:air partition coefficients calculated for 1-BP in rats (11.7) and humans (7.08) indicate that it is readily absorbed ([Meulenberg and Vijverberg, 2000](#)). Upon uptake, 1-BP distribution via the systemic circulation follows the individual tissue/blood partition coefficients for respective tissue compartments. The fat:blood partition coefficient (calculated as the ratio of fat:air and blood:air partition coefficients) for 1-BP in rats (20) and humans (18) suggests that it may partition to fat ([Meulenberg and Vijverberg, 2000](#)). Higher partitioning to muscle, liver and fat has been predicted for 1-BP in female versus male rats ([ECHA, 2012](#)).

Metabolism studies in rats and mice have shown that 1-BP can directly conjugate with glutathione forming N-acetyl-S-propyl cysteine, or be oxidized via cytochrome P450 enzymes (primarily CYP2E1) to reactive metabolites that can be further oxidized and/or conjugated with glutathione ([Jones and Walsh, 1979](#); [Barnsley et al., 1966](#)) (Figure 3-2). Glutathione conjugates formed via the glutathione-S-transferase catalyzed pathway are eventually excreted as mercapturic acid derivatives in urine. Although both pathways remain operative, the CYP2E1 pathway generally predominates at lower exposure concentrations ([Garner et al., 2006](#)).

1-BP may also be converted to either of two epoxide metabolites, glycidol and propylene oxide (see Appendix H and Figure 4.1 of IARC ([2018](#)))

Further evidence for the specific contribution of CYP2E1 to 1-BP metabolism is provided by studies with Cyp2e1^{-/-} knockout mice ([Garner et al., 2007](#)) which show the elimination half-life in these animals to be more than twice that seen in wild type mice (3.2 vs. 1.3 hours, respectively) following 1-BP inhalation exposure. The ratio of glutathione conjugation to 2-hydroxylation reactions increased 5-fold in Cyp2e1^{-/-} versus wild-type mice. Earlier work from this laboratory has shown that administration of 1-aminobenzotriazole (a general suicide inhibitor of P450) caused

nearly complete elimination of 1-BP oxidative metabolism, and a compensatory shift toward GSH conjugation in rats ([Garner et al., 2006](#)).

In humans and laboratory animals, 1-BP is rapidly eliminated from the body primarily via exhalation, with lesser amounts excreted in urine and feces ([Garner and Yu, 2014](#); [Garner et al., 2006](#); [Ishida et al., 2002](#)). In gas uptake studies with male and female rats, the elimination half-times calculated for 1-BP decreased with increasing air concentrations ([Garner and Yu, 2014](#)). Terminal elimination half-times in male and female mice following 1-BP inhalation exposure at $\leq$ 800 ppm ranged from 0.5 to 2 hrs ([Garner and Yu, 2014](#); [Garner et al., 2006](#)). ([Garner et al., 2006](#)) investigated the metabolism of 1-BP in male F344 rats and B6C3F1 mice following inhalation or tail vein injection and determined that the proportion of 1-BP metabolized via CYP2E1 oxidation versus glutathione conjugation was inversely proportional to dose in rats, but independent of dose in mice.

Occupational exposure studies have consistently identified significant correlations between 1-BP concentrations in ambient air and the levels of 1-BP or its metabolites in urine ([Ichihara et al., 2004b](#); [Kawai et al., 2001](#)). N-acetyl-S-(n-propyl)-L-cysteine (AcPrCys), produced via direct glutathione conjugation of 1-BP, was the primary urinary metabolite detected in exposed workers ([Hanley et al., 2010, 2009](#); [NIOSH, 2007](#); [Valentine et al., 2007](#); [Hanley et al., 2006a](#)).

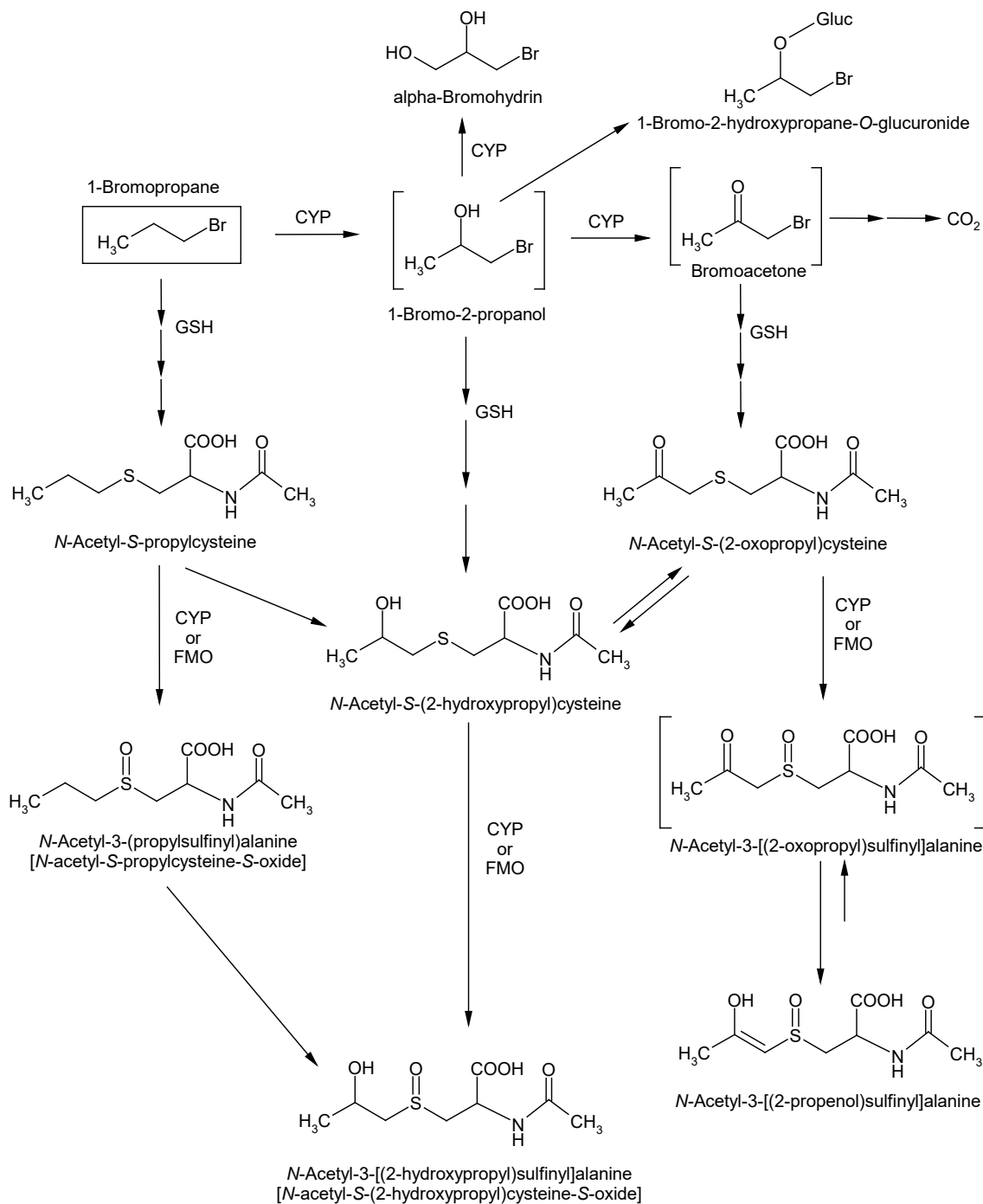


Figure 3-2. Metabolism of 1-Bromopropane in Male F-344 Rats and B6C3F1 Mice Following Inhalation Exposure or Tail Vein Injection*

*Structures in brackets are proposed intermediates and were not isolated in urine.

CYP = cytochrome P450 monooxygenase; FMO = flavin-containing monooxygenase; GSH = glutathione

Sources: Adapted from ([NTP, 2013a](#); [Garner et al., 2007](#); [Garner et al., 2006](#))

3.2.4 Biomarkers of Exposure

Several human and laboratory animal studies have investigated the utility of urinary biomarkers of 1-BP exposure ([Mathias et al., 2012](#); [Hanley et al., 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006a](#); [B Hymer and Cheever, 2005](#); [Ichihara et al., 2004a](#); [Kawai et al., 2001](#)). Bromide ion and N-acetyl-S-(n-Propyl)-L-Cysteine (AcPrCys) have shown the most promise as biomarkers of exposure to occupationally-relevant concentrations.

1-BP is metabolized rapidly, via glutathione conjugation and cytochrome P-450 mediated oxidation, producing many metabolites which are subsequently excreted in urine. Glutathione conjugation leads to bromide ion release and formation of mercapturic acid derivatives. Bromide ion levels have been used as an internal biomarker of 1-BP exposure. They are slowly excreted from the body; the elimination half-life of bromide ions in blood generally ranges from 10.5 to 14 days ([Mathias et al., 2012](#); [Hanley et al., 2006a](#)). N-acetyl-S-(n-propyl)-L-cysteine (AcPrCys) is the primary urinary metabolite found in 1-BP exposed workers (see below); it also is considered to be a valid biomarker for 1-BP exposure ([Mathias et al., 2012](#); [Valentine et al., 2007](#)).

Both Kawai ([2001](#)) and Ichihara ([2004a](#)) have shown a correlation between urinary 1-BP levels and 1-BP occupational exposure; however, the degree of correlation varied between studies. Kawai et al. ([2001](#)) reported a correlation coefficient of 0.9 for 1-BP concentrations in air and urine; the highest 1-BP concentration in air was 27.8 ppm (geometric mean = 1.42 ppm). Ichihara et al. ([2004a](#)) also reported a statistically significant correlation between 1-BP air concentrations and urinary levels measured on the same day ($r^2 = 0.39$; $p < 0.05$). NIOSH has suggested that urinary 1-BP levels may be a more suitable biomarker than urinary bromide concentrations; however, to ensure accuracy, samples must be tested immediately after collection using gas chromatography-mass spectrometry, which may be unfeasible or cost prohibitive ([NIOSH, 2003a](#)).

Both urine and serum bromide ion levels have been used as biomarkers of 1-BP exposure in workers. Toraason et al. ([2006](#)) found a high correlation ($p < 0.0001$) between 1-BP exposure and bromide ion concentrations in serum ($r^2 = 0.7$ to 0.8), and urine ($r^2 = 0.6$ to 0.9) when evaluating personal breathing zone samples from approximately 50 workers. Workplace exposures ranged from 0.2 to 270 ppm (TWA), and the correlation coefficient for 1-BP air levels and urinary bromide levels was 0.5. Using gas chromatography with electron capture detection to evaluate samples taken from Japanese workers ($n=33$) following 1-BP exposure during an 8-hour shift of cleaning and painting, ([Kawai et al., 2001](#)) reported a good correlation ($r^2 = 0.5$) between bromide levels in urine and 1-BP levels in air; however, control subjects exhibited high background levels of urinary bromide, which were subsequently linked to dietary exposure ([Zhang et al., 2001](#)). Hanley et al. ([2006a](#)) in 30 workers who were exposed to 1-BP spray adhesives to make polyurethane foam seat cushions. Personal breathing zone samples indicated a geometric mean exposure of 92 ppm (range = 45-200 ppm) for sprayers and 11 ppm for workers in other parts of the plant. The composite (48-hour) urinary bromide concentrations for sprayers ($n=12$) ranged from 119 to 250 mg/g creatinine and for non-sprayers ($n=17$) ranged from 5.5 to 149 mg/g creatinine. The composite bromide concentration in unexposed control subjects ($n=7$) ranged from 2.6 to 5.9 mg/g creatinine. Daily bromide excretion was approximately four times greater for sprayers than non-sprayers. Based on these results, urinary bromide concentration appears to be a useful index of 1-BP exposure.

Given the confounding factors identified ([Kawai et al., 2001](#)), a search for biomarkers of 1-BP exposure that are not influenced by dietary (or other non-occupational exposures) was initiated. Valentine et al. ([2007](#)), Mathias et al. ([2012](#)) and Hanley et al. ([2009](#)) demonstrated that the mercapturic acid derivative, AcPrCys, could be used as a urinary biomarker of 1-BP exposure. Both the availability of sensitive methods with an acceptable limit of detection (LOD) for this metabolite, and its demonstrated persistence in urine suggest that it may serve as a reliable biomarker of exposure. In addition, 1-BP volatility and rapid elimination in exhaled breath suggests that the measurement of mercapturic acid derivatives in urine may be preferable to 1-BP measurements. Valentine et al. ([2007](#)) sampled blood and urine from women in a 1-BP production facility in China ([Ichihara et al., 2004b](#)). A significant increase in AcPrCys adducts on human globin was demonstrated using LC/MS/MS to evaluate samples taken from 26 1-BP exposed workers and 32 non-exposed controls. Worker exposures ranged from 0.34 ppm to 49.2 ppm, and urinary AcPrCys levels analyzed using GC/MS, increased with increasing 1-BP exposure (n=47) ([Toraason et al., 2006](#)). Hanley et al. ([2009](#)) used aliquots from the urine specimens from those same workers who were exposed to 1-BP spray adhesives ([Hanley et al., 2006b](#)) who applied spray adhesives to foam cushions as described above, to determine the utility of AcPrCys as a biomarker for 1-BP exposure. Higher levels of urinary AcPrCys were observed in sprayers than non-sprayers (geometric mean was approximately four times higher in sprayers). AcPrCys and bromide levels were highly correlated ($p < 0.0001$) in the same urine samples, and both showed statistically significant Spearman's correlation coefficients based on 1-BP TWA exposure concentrations. Mathias et al. ([2012](#)) evaluated the same cohort of workers, reporting the results of Hanley et al. ([2009](#)) and 3-bromopropionic acid (3-BPA), which was evaluated for its potential to induce mutagenic effects and tumor formation in toxicological studies. When urine samples were analyzed for 3-BPA, it was not detected in 50 samples (LOD = 0.01 µg/mL). In a study of workers exposed to 1-BP based vapor degreasing solvent, Hanley et al. ([2010](#)) found AcPrCys in urine analyses were sensitive enough to measure exposure from these workers with much lower air exposures and AcPrCys was statistically associated with 1-BP TWAs.

At the time of the CSAC Peer Review for the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)), NHANES data was released on selected urinary metabolites of VOCs, primarily associated with tobacco smoking. Although it is not associated with smoking, AcPrCys (or BPMA) was included in the list of 28 VOC metabolites based on its similarity in chemistry to the other tobacco metabolites. NHANES data indicated that BPMA was detected in urine samples of children and adults from NHANES 2005-2006, 2011-2012, and 2013-2014 at approximately 3-4 µg/L (geometric mean) ([CDC, 2019](#)). Several papers describing the summary statistics of the exposures were published at this time, with one reporting a 99% detection of BPMA in 488 pregnant women in the National Childrens Study (2.6 ng/mL, 50th percentile) (([Boyle et al., 2016](#); [Jain, 2015](#); [Alwis et al., 2012](#))). These data were discussed during the Peer Review and the reviewers stated that "...the measurement of BPMA levels by Boyle et al. (2016) suggests the possibility of low level, but very widespread, non-occupational exposures to 1-BP; however, the Committee recognizes that there are some questions regarding the specificity of the biomarker used." The literature does not contain any additional information on the specificity of this biomarker since the last peer review. In addition, CDC has no further information on this biomarker. Therefore, it can still be assumed that the specificity of N-acetyl-S-(n-propyl)-L-cysteine as a biomarker for the U.S. population is questionable ([ATSDR, 2017](#)) and not informative for use in dose-response analysis.

3.2.5 Possible Mode of Action for 1-BP Toxicity

Although a mode of action has not been clearly established for 1-BP, various chemicals known to produce neuropathies in humans can be classified as hard or soft electrophiles according to the Hard and Soft Acid Base theory ([Pearson, 1990](#)). Based on this classification scheme, 1-BP is expected to induce adduct formation in vivo.

The primary metabolic pathways identified for 1-BP involve cytochrome P450 mediated oxidation (CYP2E1) and glutathione conjugation reactions which can produce numerous reactive intermediates (see Figure 3-3). Over 20 metabolites have been identified in rodent studies, including the four metabolites detected in urine samples taken from workers exposed to 1-BP ([Hanley et al., 2009](#)). These metabolites can react with critical cysteine, histidine and lysine residues, and thereby impact the structural and functional integrity of the cell ([Lopachin et al., 2009](#)).

Various reactive metabolites (e.g., glycidol, α -bromohydrin, bromoacetone) and potential targets for cellular binding interactions (e.g., DNA, mitochondria) have been identified for 1-BP ([NTP, 2013a](#)). Some 1-BP metabolites may exhibit alkylating activity. For example, further metabolism of bromoacetone in a manner analogous to acetone ([Casazza et al., 1984](#)), would result in formation of 1-hydroxy-1-bromoacetone, which yields pyruvate and CO₂, or 3-bromo-1-hydroxypropanone (BOP). BOP has been shown to inhibit sperm energetics and motility via its conversion to bromolactaldehyde and bromopyruvaldehyde, ultimately yielding 3-bromopyruvate ([Garner et al., 2007](#); [Porter and Jones, 1995](#)).

3-Bromopyruvate (3-BP) has been shown to produce many untoward effects, including lowered cell viability via production of reactive oxygen species ([Qin et al., 2010](#)) mitochondrial depolarization ([Macchioni et al., 2011](#)) and activation of mitochondrial apoptosis ([Ko et al., 2004](#)). It is a strong alkylating agent, and a known inhibitor of numerous enzymes, including glutamate decarboxylase ([Fonda, 1976](#)), glutamate dehydrogenase ([Baker and Rabin, 1969](#)), the mitochondrial pyruvate transporter ([Thomas and Halestrap, 1981](#)) and the pyruvate dehydrogenase complex ([Apfel et al., 1984](#); [Lowe and Perham, 1984](#)). 3-BP induced alkylation and inhibition of glyceraldehyde-3-phosphate dehydrogenase can impair energy production via glycolysis ([Da Silva et al., 2009](#); [Ganapathy-Kanniappan et al., 2009](#)) and induce apoptosis or necrosis as a result of ATP depletion due to impaired mitochondrial function ([Kim et al., 2008](#)).

The precise mechanism of action of 1-BP toxicity is not clearly understood, but likely relates to structural or functional modification of key signaling proteins as a result of cellular binding interactions induced by 1-BP or its metabolites. More research is needed to identify specific molecular targets and precursor events (e.g., organ-specific DNA adduct formation, oxidative stress responses) that precede toxicity. Since 1-BP can induce adverse effects in multiple organs acting directly as an alkylating agent, or indirectly via formation of reactive metabolites, different mechanisms may be operative in different organ systems. At least four possible mechanisms (e.g., genotoxicity, oxidative stress, immunosuppression, and cell proliferation) have been proposed ([NTP, 2013a](#)).

Several pathological conditions (e.g., alcoholism, diabetes), as well as chronic drug administration can induce CYP2E1 activity, and numerous cellular targets exist for 1-BP metabolites generated via CYP2E1 mediated oxidative metabolism. Interindividual variability in the expression and

function of CYP2E1 has been observed ([Neafsey et al., 2009](#)) and genetic polymorphisms in CYP2E1 expression have been linked to altered disease susceptibility ([Trafalis et al., 2010](#)). Though inconsistencies exist in the available data, it is suggested that chronic exposure to CYP2E1 inducers such as solvents (e.g., ethanol) and pharmaceuticals (e.g., isoniazid), may increase the probability of developing malignancy, especially for carriers of certain CYP2E1 alleles ([Trafalis et al., 2010](#)).

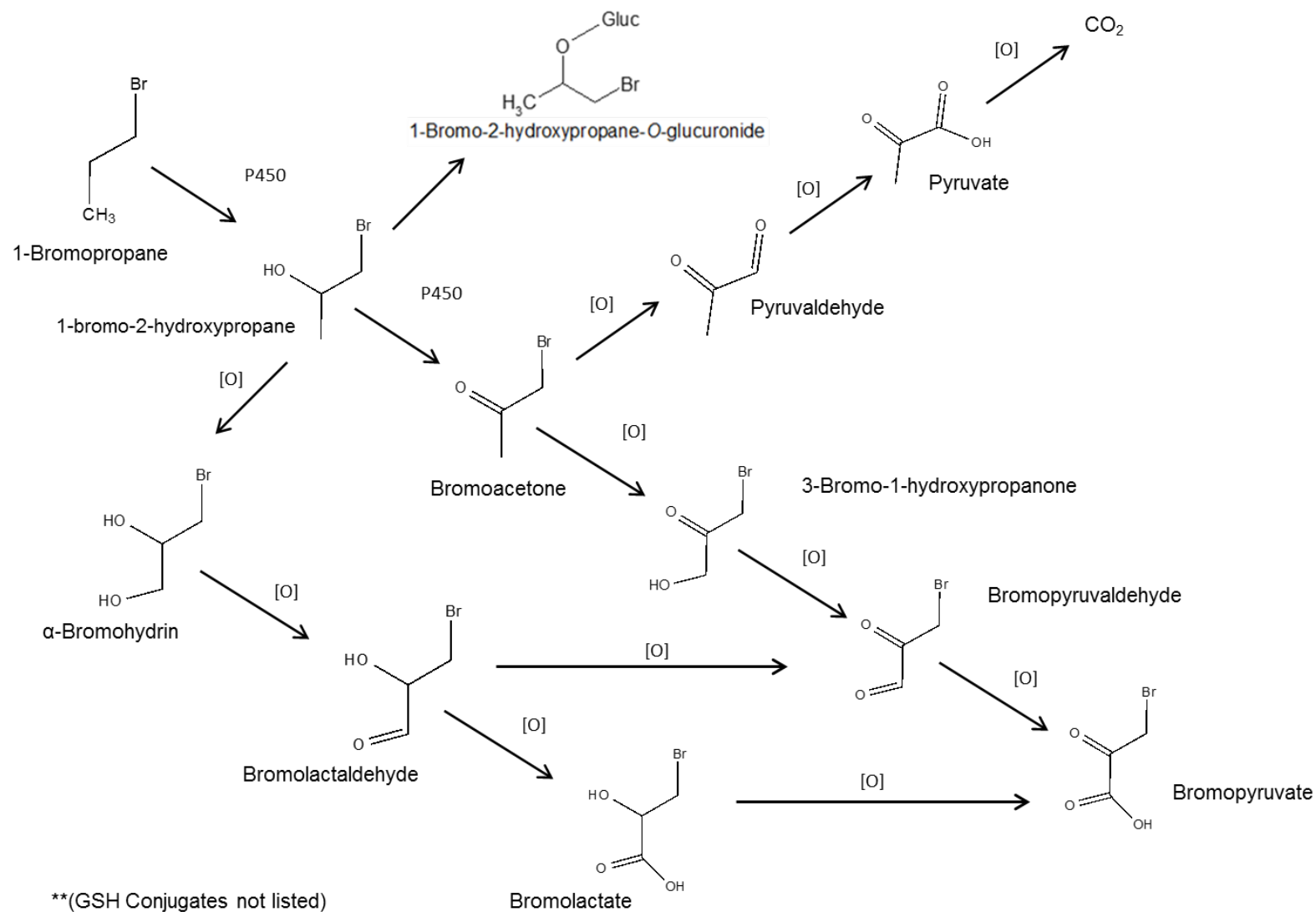


Figure 3-3. Proposed Intermediary Metabolism for 1-BP

Source:([Garner et al., 2007](#); [Garner et al., 2006](#))

3.2.6 PBPK Models

A PBPK model for 1-BP in rats was developed by ([Garner et al., 2015](#)). The model simulates 1-BP exposures via inhalation wherein distribution of 1-BP to tissues is assumed to be flow-limited. Metabolism of 1-BP was simulated with Michaelis-Menten kinetics for oxidative metabolism by cytochrome P450 and first order kinetics for GSH conjugation; parameters were fit to the time course data of chamber concentrations for 1-BP used in rat inhalation studies. Additional metabolic parameters were fit to time course data of chamber concentrations of 1-BP for rat inhalation studies when female rats were pretreated with either the cytochrome P450 inhibitor 1-aminobenzotriazole (ABT) or the GSH synthesis inhibitor D,L-buthionine (S,R)-sulfoximine (BSO). These results show the relative contributions of oxidative metabolism via cytochrome P450 and conjugation with GSH in female rats. Confidence in the PBPK model predictions for 1-BP concentrations in blood and tissues are limited by the lack of comparison of model predictions with measured data. The PBPK model was further extended to simulate human exposures by scaling the physiological parameters to humans, assuming the partition coefficients are the same in rats and humans and scaling metabolic parameters by $BW^{3/4}$. Cross species and route to route extrapolations with the Garner et al. ([2015](#)) model are precluded by the lack of data to inform a model of a species other than rat and a route other than inhalation.

3.2.7 Hazard Identification

This section summarizes the available cancer and non-cancer hazard information for 1-BP. A comprehensive summary table which includes all endpoints considered for this assessment is located in Appendix H. EPA reviewed the available data and key and supporting studies were evaluated for consistency and relevance to humans, according to the *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)). The results of the data quality evaluation for the non-cancer studies (key and supporting studies and new studies) are described in Section 3.2.7.1 and included in the data extraction summary tables in the supplementary files accompanying this document. As a result, EPA narrowed the focus of this assessment to six adverse health effect domains: (1) liver toxicity, (2) kidney toxicity, (3) reproductive toxicity, (4) developmental toxicity, (5) neurotoxicity, and (6) carcinogenicity. For non-cancer endpoints, emphasis was placed on acute/short term inhalation, and repeated-dose inhalation studies identified as most appropriate for hazard characterization and dose-response analysis. As discussed in Section 3.2.2, dermal HEDs for dermal exposures were derived by extrapolating from the inhalation PODs.

3.2.7.1 Non-Cancer Hazard Identification

Toxicity Following Acute Exposure

In animals, deaths from acute inhalation exposure to 1-BP occurred only at high exposure concentrations. LC_{50} values in rats ranged from 7,000 to 14,374 ppm for 4-hour inhalation exposure ([Kim et al., 1999a](#); [Elf Atochem, 1997](#)). Deaths were associated with an acute inflammatory response and alveolar edema ([Elf Atochem, 1997](#)). Similarly, for oral exposure, the LD_{50} was $>2,000$ mg/kg ([Elf Atochem, 1993a](#)). No information on 1-BP toxicity following acute exposure in humans was located.

Liver Toxicity

Data from animal studies suggest the liver is a target for 1-BP. Reported effects include liver histopathology (e.g., hepatocellular vacuolation, swelling, degeneration and necrosis), increased liver weight, and clinical chemistry changes indicative of hepatotoxicity ([Wang et al., 2012](#); [NTP, 2011a](#); [Liu et al., 2009](#); [Lee et al., 2007](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Kim et al., 1999a](#); [Kim et al., 1999b](#); [ClinTrials, 1997a, b](#)). Hepatic endpoints selected for dose-response analysis include datasets for histopathology (e.g., hepatocellular vacuolation) from subchronic duration inhalation studies in rats ([WIL Research, 2001](#); [ClinTrials, 1997a, b](#)).

Hepatotoxicity was not directly evaluated in any of the human studies identified in the literature; however, one study evaluated liver function indirectly in a cohort of 86 Chinese workers exposed to 1-BP (median exposure levels up to 22.6 ppm) for an average of approximately 40 months ([Li et al., 2010](#)) and no statistically significant clinical chemistry changes indicative of liver damage were observed.

Kidney Toxicity

Laboratory animal studies have provided evidence of renal toxicity following 1-BP exposure. Reported kidney effects include increased organ weight, histopathology (pelvic mineralization, tubular casts) and associated clinical chemistry changes (e.g., increased blood urea nitrogen) ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Kim et al., 1999a](#); [ClinTrials, 1997a, b](#)). Renal endpoints selected for dose-response analysis were for increased incidence of pelvic mineralization in male and female rats from a subchronic duration inhalation study by ([Yamada et al., 2003](#); [WIL Research, 2001](#)).

No studies that directly evaluated 1-BP induced renal effects in humans were identified in the published literature; however, no significant clinical chemistry changes indicative of kidney damage were observed in a cohort of 86 Chinese workers exposed to 1-BP (median exposure levels up to 22.58 ppm) for an average of approximately 40 months ([Li et al., 2010](#)) or in 45 workers exposed to a geometric mean concentration of 81.2 ppm for an average of 29 months ([NIOSH, 2003a](#)).

Immunotoxicity

There is limited evidence for immune effects of 1-BP in animal studies. Two independent studies of immune function showed that 1-BP can suppress immune responses in rodents ([Anderson et al., 2013](#); [Lee et al., 2007](#)). Anderson et al. (2010) reported a decreased IgM plaque-forming response to immunization with sheep red blood cells (sRBC) in splenocytes harvested from female rats and mice following subchronic inhalation exposure to 1-BP (NOAEL = 500 ppm in rats; LOAEL [no NOAEL identified] = 125 ppm in mice). Associated effects in both species included decreases in T cells and increases in natural killer cells in the spleen; other effects reported in mice include reduced splenic cellularity and decreased absolute spleen weight. ([Lee et al., 2007](#)) also reported a decreased antibody response to sRBC and reduced splenic cellularity in female mice after a single oral dose of 1-BP (LOAEL [no NOAEL identified] = 200 mg/kg). Investigation of immune endpoints in other studies (limited to organ weights and histopathology of spleen, thymus, and other lymphoreticular tissues) showed no effects at concentrations as high as 1000 ppm in rats and 500 ppm in mice following subchronic inhalation exposure, and 500 ppm in rats and 250 ppm in

mice following chronic inhalation exposure ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#); [Kim et al., 1999b](#); [ClinTrials, 1997a, b](#)). No information regarding 1-BP immunotoxicity in humans was located.

Reproductive Toxicity

Animal studies suggest that the reproductive system is a target of concern for 1-BP exposure. A two-generation reproduction inhalation (via whole-body exposure) study in rats reported adverse effects on male and female reproductive parameters ([WIL Research, 2001](#)). The majority of these effects exhibited a dose-response beginning at 250 ppm, with statistical significance observed at 500 ppm. Significant increases in the number of ‘former’ or ‘unaccounted’ implantation sites (i.e., the difference between the total number of implantation sites counted and the number of pups born) were reported by ([WIL Research, 2001](#)). EPA considers this finding to be indicative of post-implantation loss (pre-implantation loss could not be determined because of a lack of data on the number of primordial follicles at 100, 250 and 500 ppm). F₀ females experienced a 48% reduction in fertility at 500 ppm and complete infertility at 750 ppm. Other effects reported in this study include dose-related decreases in mating indices, increased estrous cycle length, and a significant trend of increasing numbers of F₀ females with evidence of mating without delivery (a Cochran Armitage trend test conducted by EPA calculated a *p*-value <0.0001).

Statistically significant changes in reproductive endpoints in F₀ males include decreased absolute prostate and epididymal weights at exposures $\geq$ 250 and 500 ppm respectively, as well as decreased sperm motility, and decreased mating (500 ppm) and fertility indices (750 ppm) ([WIL Research, 2001](#)). The findings described above are supported by similar reports of reproductive toxicity from independent laboratory studies with rats and mice, including spermatogenic effects (decreased sperm count, altered sperm morphology and decreased sperm motility) and organ weight changes in males (decreased epididymis, prostate and seminal vesicle weights) as well as estrous cycle alterations and decreased numbers of antral follicles in females ([NTP, 2011a](#); [Qin et al., 2010](#); [Liu et al., 2009](#); [Yu et al., 2008](#); [Banu et al., 2007](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000b](#)).

Developmental Toxicity

The developmental effects of 1-BP exposure have been evaluated on the basis of standard prenatal developmental toxicity studies, and a two-generation reproductive toxicity study in rats exposed via whole-body inhalation. Evidence for 1-BP induced developmental toxicity include dose related adverse effects on live litter size ([WIL Research, 2001](#)), postnatal survival ([Furuhashi et al., 2006](#)), pup body weight, brain weight and skeletal development ([Huntingdon Life Sciences, 1999](#)), ([Huntingdon Life Sciences, 2001](#)); ([WIL Research, 2001](#)). Further information on these endpoints can be found in Appendix H. No data were located on the developmental effects of 1-BP exposure in humans.

Neurotoxicity

Data from studies in humans and animals demonstrate that the nervous system is a sensitive target of 1-BP exposure. Both the central and peripheral nervous systems are affected. In animal inhalation studies, the degree or severity of neurotoxicity produced by 1-BP depends on the

concentration as well as duration of exposure, with lower concentrations being effective at longer exposures. Most inhalation studies using concentrations of ≥ 1000 ppm reported ataxia progressing to severely altered gait, hindlimb weakness to loss of hindlimb control, convulsions, and death (e.g., ([Banu et al., 2007](#); [Ishida et al., 2002](#); [Yu et al., 2001](#); [Fueta et al., 2000](#); [Ichihara et al., 2000a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). Concentrations of 400-1000 ppm produced neuropathological changes including peripheral nerve degeneration, myelin sheath abnormalities, and spinal cord axonal swelling ([Wang et al., 2002](#); [Yu et al., 2001](#); [Ichihara et al., 2000a](#)). Brain pathology has also been reported in several studies, including white and gray matter vacuolization, degeneration of Purkinje cells in the cerebellum and decreased noradrenergic but not serotonergic axonal density in frontal cortex and amygdala at exposures ≥ 400 ppm ([Mohideen et al., 2013](#); [Mohideen et al., 2011](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). Decreased brain weight has been reported in adult and developmental studies ([Subramanian et al., 2012](#); [Wang et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#); [Kim et al., 1999a](#); [ClinTrials, 1997b](#)). In a two-generation study ([WIL Research, 2001](#)), the NOAEL for decreased brain weight in F1-generation males was 100 ppm (BMD modeling did not produce an acceptable fit); this value is brought forward for risk assessment representing neuropathological changes.

Physiological, behavioral, and biochemical measures have been used to characterize and develop dose-response data for neurological effects. Motor nerve conduction velocity and latency measured in the rat tail nerve were altered at concentrations ≥ 800 ppm with progressive changes from 4 to 12 weeks of exposure ([Yu et al., 2001](#); [Ichihara et al., 2000a](#)). In the brain, electrophysiological changes in hippocampal slices were seen at concentrations of 400 ppm and above ([Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Fueta et al., 2000](#)); [Fueta et al., 2004](#); [Fueta et al., 2007](#); [Ueno et al., 2007](#)). Behavioral tests such as hindlimb grip strength, landing foot splay, traction (hang) time, gait assessment, motor activity, and water maze performance provide dose-response data and tend to be more sensitive than neuropathology or physiological changes, with effects at concentrations as low as 50-200 ppm ([Banu et al., 2007](#); [Honma et al., 2003](#); [Ichihara et al., 2000a](#)). Exposures to concentrations ≥ 50 ppm produce changes in neurotransmitters, biomarkers, and proteome expressions suggesting alterations in the function and maintenance of neural and astrocytic cell populations ([Huang et al., 2015](#); [Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Yoshida et al., 2007](#); [Wang et al., 2003](#); [Wang et al., 2002](#)). Although less extensively tested, oral or subcutaneous dosing of 1-BP resulted in similar findings as for inhalation exposure, with effects at ≥ 200 mg/kg-day ([Guo et al., 2015](#); [Zhong et al., 2013](#); [Wang et al., 2012](#); [Zhao et al., 1999](#)). Neurological endpoints selected for dose-response analysis were datasets for decreased time hanging from a suspended bar (traction time) in rats in a 3 -week inhalation study ([Honma et al., 2003](#)) and decreased hind limb grip strength in rats in a 12 -week inhalation study ([Ichihara et al., 2000a](#)). These functional measures are relevant to peripheral neurotoxicity reported in human studies.

Human studies (case-control studies, industrial surveys, and case reports) corroborate that the nervous system is a sensitive target of 1-BP exposure in humans. Clinical signs of neurotoxicity (including headache, dizziness, weakness, numbness in lower extremities, ataxia, paresthesias, and changes in mood) and motor and sensory impairments were noted in the case reports of workers occupationally exposed to 1-BP for 2 weeks to 3 years at estimated concentrations exceeding averages of 100 ppm ([Samukawa et al., 2012](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)), and in industrial surveys with average exposures greater than 81

ppm (ranging from 2 weeks to 9 years) ([NIOSH, 2003a, 2002a, c](#)). Cross-sectional studies of Chinese workers reported increased distal latency and decreased sural nerve conduction velocity in female workers. Statistically significant decreased vibration sense in toes was observed across all exposure groups (0.07-106.4 ppm) compared to controls ([EPA, 2019f](#); [Li et al., 2010](#); [Ichihara et al., 2004b](#)). There were several methodological limitations in these studies, discussed in depth in Appendix I.4; however, these studies provide evidence of neurotoxicity in workers exposed to 1-BP.

3.2.7.2 Genotoxicity and Cancer Hazards

Genetic Toxicity

Two bacterial reverse mutation studies of 1-BP are available Barber ([1981](#)) and BioReliance ([2015](#)). Both studies used test systems characterized as ‘closed’, but yielded different results for mutagenicity. In the study by Barber ([1981](#)), a positive mutagenicity result was observed for 1-BP in *Salmonella typhimurium* strains TA 1535 and TA 100 (but not TA 1537, TA 1538, or TA 98) in the presence and absence of metabolic activation. In contrast, the study by BioReliance ([2015](#)) found no evidence of mutagenicity in *S. typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537 or *Escherichia coli* strain WP2 uvrA (a DNA repair-deficient strain) in the presence or absence of metabolic activation. The major differences in experimental design between the two studies are the method of test substance application (vapor exposure of plated bacteria versus aqueous preincubation exposure) and the methods used to achieve a ‘closed’ system to account for the inherent volatility of 1-BP (fully enclosed test chamber versus preparation of solutions in screw-capped tubes). It is therefore likely the varied mutagenicity results from the two studies (i.e., positive results in the Barber ([1981](#)) study and negative results in the BioReliance ([2015](#)) study) are due to differences in the methods used for exposure and to compensate for the volatility of 1-BP in the bacterial reverse mutation assay. This assumption is supported by the fact that in the BioReliance ([2015](#)) study, analytical concentrations of 1-BP in preincubation tubes during the confirmatory assays were far below target, with 4-37% of target concentrations at the beginning of the preincubation period and 2-5% of target concentrations by the end of the preincubation period (see Appendix I for more details). Other tests for mutagenicity in bacteria were negative, but may not have been conducted in closed systems ([NTP, 2011](#); [Kim et al., 1998](#)).

In mammalian cells tested in vitro, increased mutation frequency was observed in mouse lymphoma cells exposed to 1-BP with or without activation ([Elf Atochem, 1996a](#)). Limited evidence of DNA damage was found in leukocytes in 1-BP-exposed workers (([Toraason et al., 2006](#)) and Appendix I.4). However, tests conducted in vivo were mostly negative, including assays for dominant lethal mutations and micronuclei induction in rats and mice ([NTP, 2011a](#); [Yu et al., 2008](#); [Kim et al., 1998](#); [Elf Atochem, 1995](#); [Saito-Suzuki et al., 1982](#)). Negative results were found for mutagenicity in inhalation studies in the Big Blue® mouse model ([Weinberg, 2016](#); [Young, 2016](#)), but these studies do not provide clear evidence against mutagenicity of 1-BP based on several conceptual, methodological, and study comprehensiveness uncertainties (see Appendix I.5.6).

Positive results have been observed in several genotoxicity tests using known or postulated metabolites of 1-BP (including glycidol, propylene oxide, α -bromohydrin, 3-bromo-1-propanol, and 1-bromo-2-propanol) ([NTP, 2014](#); [IARC, 2000, 1994](#)). Epoxide intermediates such as

propylene oxide and glycidol are expected to have more mutagenic activity than 1-BP ([IARC, 2018](#), [2000](#), [1994](#)).

Carcinogenicity

Evidence from chronic cancer bioassays in rats and mice suggests that 1-BP may pose a carcinogenic hazard to humans. Significant increases in the incidence of skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, rare large intestine adenomas in female F344 rats, and alveolar/bronchiolar adenomas or carcinomas (combined) in female B6C3F1 mice were observed following exposure to 1-BP via inhalation for two years ([NTP, 2011a](#)). NTP concluded that these data show some evidence for carcinogenicity in male rats, clear evidence for carcinogenicity in female rats, no evidence for carcinogenicity in male mice, and clear evidence for carcinogenicity in female mice. No other laboratory animal data, or human data were located on the carcinogenicity of 1-BP. IARC ([2018](#)) concluded that 1-BP “is *possibly carcinogenic to humans (Group 2B)*” based on the following characteristics: (a) strong evidence that 1-BP is electrophilic or can be metabolically activated to reactive intermediates; (b) strong evidence that 1-BP induces oxidative stress, induces chronic inflammation, and is immunosuppressive; (c) moderate evidence that 1-BP modulates receptor-mediated effects and is genotoxic; and (d) sufficient evidence in experimental animals for the carcinogenicity of 1-BP. By the criteria presented in EPA’s *Guidelines for Carcinogen Risk Assessment* ([U.S. EPA, 2005a](#)), 1-BP may be considered “*Likely to be Carcinogenic in Humans*” based on the positive findings for carcinogenicity in more than one test species together with positive findings for the direct reactivity of 1-BP with DNA and evidence that both 1-BP and its metabolites are positive in mutagenicity studies and other types of studies that assess genetic toxicity.

As noted above, 1-BP has been shown to be a multi-site carcinogen in rats and mice. The MOA for 1-BP carcinogenesis has not been established; however, there is data supporting a mutagenic MOA:

- a. Ames test: 1-BP was mutagenic with and without metabolic activation in the Ames *Salmonella* assay when testing was conducted in closed systems designed for testing volatile chemicals.
- b. Mammalian cells and tissues: 1-BP caused mutations in cultured mammalian cells with or without metabolic activation and DNA damage in cultured human cells without metabolic activation. Evidence of DNA damage in human leukocytes has also been demonstrated in 1-BP-exposed workers.
- c. Metabolic activation to mutagenic intermediates: Rodent metabolic studies have indicated that 1-BP can be activated by CYP2E1 to at least five different mutagenic intermediates ([NTP, 2014](#); [IARC, 2000](#), [1994](#)), including two clearly mutagenic and carcinogenic chemicals (glycidol and propylene oxide) IARC ([2018](#)), which are listed in the NTP Report on Carcinogens as “reasonably anticipated to be human carcinogens” ([2013a](#)). The role of epoxides as proximate carcinogens should be explored with regard to the mode of 1-BP carcinogenicity. Glycidol has been shown to induce tumors in the intestines ([NTP, 1990](#)), one of the carcinogenic targets of 1-BP. Propylene oxide inhalation has been shown to induce tumors at multiple sites including the thyroid, adrenal gland, and mammary gland ([IARC, 1994](#)). The available evidence suggests similar metabolic pathways for 1-BP in humans and rodents.

- d. Structure-Activity Relationship (SAR) consideration: SAR may be used as a criteria for consideration in EPA's Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#)). From the SAR point of view, 1-BP is a low molecular weight alkyl bromide that is electrophilic ([IARC, 2018](#); [NTP, 2013a](#)) and generally known to possess alkylating potential (1-BP has been shown to bind to DNA *in vitro*). Bromoethane and 1-bromobutane, two analogs of 1-BP, both produced positive results in the Ames assay when tested in closed systems. Bromoethane is a known carcinogen via the inhalation route of exposure ([NTP, 1989a](#)), whereas 1-bromobutane has not been tested for carcinogenic activity.

Other lines of evidence do not provide clear support for a mutagenic MOA) for 1-BP carcinogenicity including:

- a. Mixed results have been reported for 1-BP in the Ames assay. Some of these studies were complicated by the high volatility of 1-BP; those that failed to use a closed system may be considered invalid.
- b. Two *in vivo* micronucleus assays in bone marrow and circulating erythrocytes were negative; however, *in vivo* micronucleus assays are prone to false negatives Benigni ([2012](#)).
- c. 1-BP did not induce mutations at the *cH* gene of female B6C3F1 transgenic Big Blue® mice following whole-body inhalation exposure to 1-BP vapor concentrations of 62.5, 125, or 250 ppm for 5 days/week ([Weinberg, 2016](#)) or 7 days/week over a 28-day period ([Young, 2016](#)); however, limitations in test design limit the utility of these studies, as discussed in Appendix I.5.8.
- d. Other possible MOAs: NTP ([2013a](#)) suggests that in addition to mutagenicity, at least three other mechanisms, including oxidative stress, immunosuppression, and cell proliferation can contribute to the multi-stage process of carcinogenesis. Although more research (e.g., organ-specific *in vivo* DNA adduct studies) is needed to ascertain mutagenicity as the key molecular event, there is no definitive evidence which suggests that these other mechanisms may play a more important role than mutagenicity.

Following EPA's *Guidelines for Carcinogen Risk Assessment* ([U.S. EPA, 2005a](#)), the overall weight of the scientific evidence supports a mutagenic MOA for 1-BP induced carcinogenicity, including: demonstrated alkylating activity; evidence of DNA damage in leukocytes taken from 1-BP exposed workers; demonstrated mutagenicity (with metabolic activation) in cultured mammalian cells, and in the Ames assay (when test conditions included use of a closed system designed for testing volatile chemicals); evidence indicating 1-BP may form DNA adducts *in vitro*; evidence suggesting 1-BP may be a direct-acting mutagen, including demonstrated mutagenic activity in bacteria and mammalian cells in the absence of metabolic activation, and evidence indicating 1-BP metabolites (e.g., glycidol and propylene oxide) are mutagenic in multiple test systems (e.g., bacteria, yeast, *Drosophila*, and mammalian cells). Given the lack of specific mechanistic or dose-response information, linear extrapolation from the point of departure is recommended per EPA's *Guidelines for Carcinogen Risk Assessment* ([U.S. EPA, 2005a](#)).

3.2.8 Evidence Integration and Evaluation of Human Health Hazards

This section on evidence integration and evaluation of human health hazards provides a narrative concluding with the recommended approach for dose-response analysis. The readily available information on 1-BP human health hazards was integrated using a weight of evidence strategy

wherein the strengths, limitations and relevance of the hazard data were analyzed and summarized across studies. The best available human health hazard information was selected for benchmark dose modeling based on an integration of the data quality evaluation results, MOA information and overall weight-of-the-scientific evidence. Based on this approach, liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity, and neurotoxicity are the primary (non-cancer) health effects associated with 1-BP exposure. Emphasis on acute/short term inhalation, and repeated-dose inhalation studies was considered most appropriate for hazard characterization and dose-response analysis. As discussed in Section 3.2.2, the HEDs for dermal exposures were derived via extrapolation from the inhalation PODs.

3.2.8.1 Weight of the Scientific Evidence for Reproductive and Developmental Toxicity

Reproductive and developmental toxicity were identified as critical targets for 1-BP exposure based on a constellation of effects reported across studies, including a two-generation reproduction study ([WIL Research, 2001](#)), which showed adverse effects on male and female reproductive parameters, and the developing conceptus. Some of these endpoints were considered sufficient to include as PODs (see Section 3.2.10), while others were used as qualitative supporting evidence. Additional details can be found in Appendix H.

Quantitative and qualitative evidence of 1-BP reproductive toxicity in F₀ males include decreases in sperm motility, changes in normal sperm morphology, decreases in mating and fertility indices ([WIL Research, 2001](#)), and decreases in epididymal, prostate, and seminal vesicle weights following 1-BP (whole-body) inhalation exposure ([NTP, 2011a](#); [WIL Research, 2001](#); [Ichihara et al., 2000b](#)). Evidence of reproductive toxicity in F₀ females include decreased numbers of corpora lutea, antral follicles, and implantation sites ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#)). Other reported reproductive effects in females include a significant upward trend in increased estrous cycle length, and evidence of mating without delivery ([WIL Research, 2001](#)). Reported impairments in male and female reproductive function resulted in a 48% reduction in fertility at 500 ppm and complete infertility at 750 ppm in F₀ mating pairs ([WIL Research, 2001](#)). Although the adverse reproductive effects of 1-BP exposure have not been directly evaluated in humans, the results from laboratory animal studies suggest that it may impair reproductive function.

Evidence supporting fetal development as a sensitive target of 1-BP exposure is provided by a number of laboratory animal studies. The current database consists of developmental toxicity testing that shows severe effects resulting from prenatal exposure during gestation and postnatal exposure studies showing adverse developmental effects that manifest at various stages of development, and span multiple generations ([WIL Research, 2001](#)). Overall, the general consistency of findings indicative of impaired development across species, as reported in multiple studies from independent laboratories is taken as evidence of a causative association between 1-BP exposure and developmental toxicity. Reported adverse developmental effects following 1-BP exposure include dose-related decreases in live litter size ([WIL Research, 2001](#)), postnatal survival ([Furuhashi et al., 2006](#)), and pup body weight, brain weight and skeletal development ([Huntingdon Life Sciences, 1999](#)), ([Huntingdon Life Sciences, 2001](#)); ([WIL Research, 2001](#)). ([WIL Research, 2001](#)) also reported decreases in the number of implantation sites, and increases in ‘unaccounted’ implants for corresponding ovulatory events, reported as the difference between the total number of implantation sites counted and the number of pups born. EPA interpreted this finding as an

indication of post-implantation loss (pre-implantation loss could not be determined due to insufficient data on the number of primordial follicles). Additional qualitative evidence of impaired development is provided by results from dominant lethal assays with 1-BP which show increased implantation loss (at week 8) in rats subjected to five days of oral 1-BP exposure at 400 mg/kg ([Saito-Suzuki et al., 1982](#)) and in mice (at week 5) following 1-BP exposure via gavage administration at 600 mg/kg for ten days prior to mating ([Yu et al., 2008](#)). These findings are supported by consistent reports of 1-BP induced adverse developmental effects from independent laboratory studies with rats and mice. No corresponding epidemiological studies have been identified; however, the concordance of reported results across species and test laboratories is taken as evidence of a causative association between 1-BP exposure and developmental toxicity.

3.2.8.2 Weight of the Scientific Evidence for Neurotoxicity

Neurotoxicity has been identified as a critical effect for 1-BP based on over 15 years of behavioral, 161imilar161hological, neurochemical, and neurophysiological studies in rodents as well as cross-sectional studies and case reports in humans (Appendices I.1, I.3, and I.4). Overall, there is considerable support for the finding of peripheral neurotoxicity, and consistency in reports of impaired peripheral nerve function (sensory and motor) and adverse neuromuscular impacts. The effects are progressive in terms of exposure duration and concentration, and range from subtle changes in nervous system function and neurochemistry progressing to physiological manifestations of neuron damage to structural evidence of neuronal pathology.

This spectrum of adverse manifestations of peripheral neurotoxicity is reproducible across almost all of the experimental studies, with a few notable exceptions. In addition, symptoms in humans, such as peripheral weakness, numbness, ataxia, and paraparesis, are concordant with the signs seen in many rodent studies. At high concentrations (≥ 1000 ppm), toxicological reports in rodents include observations such as hindlimb weakness, ataxia, altered gait, and other signs typical of peripheral neuropathy ([Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Banu et al., 2007](#); [Honma et al., 2003](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Ishidao et al., 2002](#); [Yu et al., 2001](#); [Fueta et al., 2000](#); [Ichihara et al., 2000a](#); [Kim et al., 1999a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). However, in a chronic bioassay ([NTP, 2011a](#)) these signs were reported at 2000 ppm but not 1000 ppm; differences in timing and specificity of observations as well as training and blinding of personnel to dose assignment could account for the relative insensitivity of those specific outcomes. A number of papers that did not report any information about the general appearance and health of the animals were mostly mechanistic studies focused only on ex vivo endpoints ([Huang et al., 2015](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Mohideen et al., 2011](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Fueta et al., 2007](#); [Ueno et al., 2007](#); [Yoshida et al., 2007](#); [Fueta et al., 2004](#); [Wang et al., 2003](#); [Wang et al., 2002](#)). In human reports, severe neurological effects in workers occurred at relatively high exposures (>100 ppm) over a period of time of exposure ranging from weeks to months ([Samukawa et al., 2012](#); [CDC, 2008](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)).

There is general agreement between the 1-BP neurotoxic effects observed across studies using measures of peripheral nerve integrity evaluated by electrophysiological and behavioral tests. Nerve conduction velocity and distal latency in motor neurons are decreased in animals ([Yu et al., 2001](#); [Ichihara et al., 2000a](#); [Zhao et al., 1999](#)) [subcutaneous exposure]). These experimental findings corroborate the studies of factory workers that describe decreased nerve conduction and/or peripheral sensory impairment ([Li et al., 2010](#); [Ichihara et al., 2004a](#)). The epidemiological studies

are, however, somewhat limited by poorly defined exposures as well as concerns about the sensitivity and implementation of the vibration sense test methods used to assess motor and sensory deficits. Using an objective measure of grip strength in rats, decreased function that worsens with continued exposure has been reported in several laboratories ([Wang et al., 2012](#); [Banu et al., 2007](#); [Ichihara et al., 2000a](#)), [oral exposure] except one ([ClinTrials, 1997a](#)).

A number of animal studies report histopathology of the nervous system (brain, spinal cord, and/or peripheral nerves) at concentrations as low as 400 ppm ([Mohideen et al., 2013](#); [Subramanian et al., 2012](#); [Mohideen et al., 2011](#); [Wang et al., 2002](#); [Yu et al., 2001](#); [Ichihara et al., 2000a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997b](#)), but not in other studies that used even at higher concentrations ([NTP, 2011a](#); [Fueta et al., 2004](#); [Sohn et al., 2002](#); [WIL Research, 2001](#); [Kim et al., 1999a](#)). There are a few conflicting reports from the same laboratory ([ClinTrials, 1997a, b](#)), [4 wk vs 13 wk studies]; ([Sohn et al., 2002](#); [Kim et al., 1999a](#)). Such differences may be attributable to a number of experimental factors, including tissue preparation, fixation, staining, and sampling, measurement methodology, and training and blinding of personnel to dose group assignment.

Additional experimental animal studies report changes in brain weight, which is considered indicative of neurotoxicity even in cases where other histopathological changes are not evident ([U.S. EPA, 1998b](#)); however, several studies do describe corresponding neuropathology ([Wang et al., 2002](#); [WIL Research, 2001](#); [Kim et al., 1999a](#)). Decreased brain weight was reported with subacute to subchronic exposures in adult rats ([Subramanian et al., 2012](#); [Wang et al., 2003](#); [Ichihara et al., 2000a](#); [Kim et al., 1999a](#); [ClinTrials, 1997b](#)), and in offspring from a multi-generational reproductive toxicity study with lifetime exposures ([WIL Research, 2001](#)). Only two studies have measured brain weight and reported no effects: 1) ([Wang et al., 2002](#)), in which the duration of exposure (7 days) may not have been sufficient, and 2) the 13-wk study of ([ClinTrials, 1997a](#)), even though the same laboratory reported decreased brain weight at the same concentration with only 4 weeks of exposure (ClinTrials did not provide explanations for this contradictory finding).

Several studies report alterations in central nervous system neuronal communication, neurotransmitter levels, proteins, and oxidative stress markers, all of which are markers of neurotoxicity ([U.S. EPA, 1998b](#)). It is notable that database consistency is partially a function of multiple studies from a few laboratories ([Huang et al., 2015](#); [Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Mohideen et al., 2011](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Fueta et al., 2007](#); [Ueno et al., 2007](#); [Fueta et al., 2004](#); [Wang et al., 2003](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Fueta et al., 2000](#)). Other studies have reported cognitive deficits following 1-BP inhalation exposure ([Guo et al., 2015](#); [Zhong et al., 2013](#); [Honma et al., 2003](#)).

Overall, the experimental studies, supported by the epidemiological studies, reporting clinical and neurohistological signs provide strong evidence for peripheral neuropathology. Where quantifiable endpoints that are sensitive to relatively low exposures have been measured, there is generally good consistency in outcomes across laboratories, with only a few notable exceptions. There is also agreement in findings of central nervous system dysfunction in laboratory rodents, but there are no corresponding studies available for comparison in humans.

3.2.8.3 Weight of the Scientific Evidence for Cancer

Evidence from chronic cancer bioassays in rats and mice suggests that 1-BP may pose a carcinogenic hazard to humans ([IARC, 2018](#)). Significant increases in the incidence of skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, rare large intestine adenomas in female F344 rats, and alveolar/bronchiolar adenomas or carcinomas (combined) in female B6C3F1 mice were observed following exposure to 1-BP via whole-body inhalation for two years ([NTP, 2011a](#)). The exact mechanism/mode of action of 1-BP carcinogenesis is not established; however, an abundance of data exists and may provide a basis for weight of evidence considerations, including: *in vitro* tests, similarity in metabolism across species, SAR and other potential mechanisms of action. Although the results from Ames and other genotoxicity tests for 1-BP have been mixed, 1-BP was mutagenic in closed-system testing in the presence or absence of metabolic activation, induced DNA damage and repair in human cells in culture in the presence of metabolic activation, and induced mutations in mammalian cells in culture in the presence or absence of metabolic activation. Negative results were found for mutagenicity in inhalation studies in the Big Blue® mouse model ([Weinberg, 2016](#); [Young, 2016](#)) but these studies do not provide clear evidence against a mutagenic mode of action of 1-BP carcinogenicity based on several conceptual, and methodological uncertainties (see Appendix I.5.6). Rodent metabolic studies have indicated 1-BP can be activated by CYP2E1 to at least five mutagenic metabolites/intermediates, including two (glycidol and propylene oxide, see Appendix I.5.6; [NTP \(2013a\)](#), [Jones and Walsh\(1979\)](#), and [IARC \(2018\)](#)) that are clearly mutagenic and carcinogenic ([IARC, 2000, 1994](#)). Since humans have CYP2E1 activity in the lung and exhibit similar metabolic pathways for 1-BP as compared to rodents, the evidence from multiple species (rats and mice) for multiple cancer types following 1-BP exposure supports a carcinogenic hazard to humans. From the SAR point of view, 1-BP is a low molecular weight alkyl bromide with alkylating activity and two of its closest analogs (bromoethane and 1-bromobutane) both have provided positive Ames results when tested in closed systems. Bromoethane is a known carcinogen via the inhalation route of exposure, whereas 1-bromobutane has not been tested for carcinogenic activity. In addition to mutagenicity as a mechanism for induction of carcinogenicity by 1-BP, at least three other mechanisms, oxidative stress, immunosuppression, and cell proliferation, can act synergistically with mutagenicity and may thereby contribute to the multi-stage process of carcinogenesis.

3.2.9 Summary of Hazard Studies Used to Evaluate Acute and Chronic Exposures

EPA considered adverse effects for 1-BP across organ systems and a comprehensive summary table is in Appendix I (Table_Apx I-2). The full list of effects was screened to those that are relevant, sensitive and found in multiple studies which include the following types of effects: liver toxicity, kidney toxicity, immunotoxicity, developmental/reproductive toxicity, neurotoxicity, and cancer as described above. In general, adverse effects were observed in all of these systems in rats exposed to 1-BP by inhalation in the range of 100 – 1000 ppm (LOAELs). Using principles of systematic review, EPA selected endpoints from the highest quality studies with the least limitations for both non-cancer and cancer that were amenable to quantitative analysis for dose-response assessment as discussed in more detail below in Section 3.2.10. In the following sections, EPA identifies the appropriate toxicological studies to be used for acute and chronic exposure scenarios.

3.2.10 Dose-Response Assessment

EPA evaluated data from studies described above (Section 3.2.7) to characterize the dose-response relationships of 1-BP and selected studies and endpoints to quantify risks for specific exposure

scenarios. One of the additional considerations was that the selected key studies had adequate information to perform dose-response analysis for the selected PODs. EPA defines a POD as the dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on the dose for an estimated incidence, or a change in response level from a dose-response model (*i.e.*, BMD), a NOAEL or a LOAEL for an observed incidence or change in the level of response.

3.2.10.1 Selection of Studies for Non-Cancer Dose-Response Assessment

The non-cancer dose-response analysis in this assessment commenced with the review and selection of high quality toxicity studies that went through systematic review that reported both adverse non-cancer health effects and quantitative dose-response data (Table 3-1). The inhalation PODs selected (identified in earlier steps) were considered the most sensitive and biologically relevant endpoints from among these high quality key and supporting studies. As a result, the non-cancer dose-response assessment was organized into five health effect domains: (1) liver; (2) kidney; (3) reproductive; (4) developmental and (5) nervous system. HEC values were calculated for the inhalation and PODs identified within each health effect domain; dermal HED values were extrapolated from inhalation PODs. Endpoint and study-specific Ufs were selected based on EPA guidance ([U.S. EPA, 2002](#)) and used as the benchmark MOEs for risk calculations. These Ufs were applied to the PODs to account for (1) variation in susceptibility among the human population (*i.e.*, inter-individual or intraspecies variability); (2) uncertainty in extrapolating animal data to humans (*i.e.*, interspecies uncertainty); (3) uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure (*i.e.*, extrapolating from subchronic to chronic exposure); and (4) uncertainty in extrapolating from a LOAEL rather than from a NOAEL, with default values of 10 applied for each ([U.S. EPA, 2002](#)).

Table 3-1 summarizes the hazard studies and health endpoints by target organ/system that EPA considered suitable for carrying forward for dose-response analysis for the risk evaluation of the exposure scenarios identified in this work plan risk assessment. These equally high quality key and supporting studies in Table 3-1 are briefly described in the Section 3.2.7. Table 3-7 lists the most sensitive and biologically relevant PODs (and corresponding HECs/dermal HEDs) from among these studies by study type and duration (*i.e.*, acute vs. chronic) that were selected to be carried forward for risk estimations.

Benchmark dose (BMD) modeling was applied to these endpoints in a manner consistent with EPA [Benchmark Dose Technical Guidance](#). When the models were adequate, the model results were used as PODs. For studies in which BMD modeling did not achieve an adequate fit to the data, the NOAEL or LOAEL value was used for the POD. Details regarding BMD modeling can be found in the *Supplemental File: Information on Human Health Benchmark Dose Modeling* ([EPA, 2019e](#)). The PODs applied a duration adjustment to convert the air concentrations in laboratory animals for the study duration to exposure durations for workers (*i.e.* 8 hours/day, 5 days/week) and exposures of 24 hours per day for consumer exposure scenarios. Following EPA's *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* ([U.S. EPA, 1994](#)), EPA converted the adjusted POD to a human equivalent concentration (HEC) by calculating a dosimetric adjustment factor (DAF) based on the ratio between the animal and human blood:air partition coefficients, as shown below. For 1 BP, the blood:air partition coefficient for rats is greater than that for humans, so a default ratio of 1 was applied ([U.S. EPA, 1994](#)). HECs/dermal HEDs were rounded to two significant figures.

BMRs were selected for each endpoint. In cases where biologically relevant BMRs were not available the BMR was 10% for dichotomous endpoints and 1 standard deviation for continuous endpoints consistent with EPA [Benchmark Dose Technical Guidance](#). The liver and kidney endpoints were dichotomous (i.e. incidence) and a BMR of 10% was used in absence of a biologically relevant BMR. The reproductive effects that were able to be BMD modeled (see Table 3-1) were continuous and a BMR of 1 standard deviation was used in absence of a biologically relevant BMR. For pup body weight changes a BMR of 5% relative deviation from control mean was applied under the assumption that it represents a minimal biologically significant response. In adults, a 10% decrease in body weight in animals is generally recognized as a biologically significant response associated with identifying a maximum tolerated dose; during development, however, identification of a smaller (5%) decrease in body weight is consistent with the assumptions that development represents a susceptible lifestage and that the developing animal is more adversely affected by a decrease in body weight than the adult. In humans, reduced birth weight is associated with numerous adverse health outcomes, including increased risk of infant mortality as well as heart disease and type II diabetes in adults ([Barker, 2007](#); [Reyes and Mañalich, 2005](#)). For these reasons, a BMR of 5% relative deviation was selected for decreased pup weight. For post-implantation loss a dichotomous endpoint a BMR of 1% relative deviation was used based on the relative severity of this endpoint considering it similar to fetal mortality. For decreased live litter size a BMR of 5% relative deviation was used considering this is possibly a combination of reproductive effects (BMR of 10% relative deviation) and developmental effects including post-implantation loss similar to mortality (BMR of 1% relative deviation) for an overall BMR of 5% relative deviation. For decreased brain weight a BMR of 1% relative deviation was used considering the severity of this effect. For developmental endpoints BMCLs for alternative BMRs are also shown in parentheses for comparison. Alternative BMRs were 1 standard deviation for continuous endpoints and a 10% relative deviation for dichotomous endpoints (except for post-implantation loss the alternative BMR was a 5 % relative deviation because of the severity of this endpoint). For functional nervous system effects the endpoints were continuous and a BMR of 1 standard deviation was used. When BMD modeling was successful, the PODs were the BMCLs determined for each endpoint. The PODs for endpoints selected following dose-response analysis were calculated either by benchmark dose (BMD) modeling (when the model fit was adequate) or a NOAEL/LOAEL approach based on the endpoint evaluated (see Section 3.2.10.1 and Table 3-1 for all of the PODs).

Given the different exposure scenarios considered (both acute and chronic for spray adhesives, dry cleaning, and degreasing activities for occupational exposure scenarios; and only acute for spot cleaners for consumer exposure scenarios), different endpoints were used based on the expected exposure durations. For non-cancer effects, and based on a weight of the scientific evidence analysis of toxicity studies from rats and humans, risks for developmental effects that may result from a single exposure were evaluated for acute (short-term) exposures, whereas risks for other adverse effects (e.g., toxicity to liver, kidney, reproduction, development and nervous system) were evaluated for repeated (chronic) exposures to 1-BP. The rationale for using the range of toxic effects for chronic scenarios is based on the fact that relatively low dose and short term/sub-chronic exposures can result in long-term adverse consequences.

PODs for Acute Exposure

Acute exposure was defined for occupational settings as exposure over the course of a single work shift 8 hours and for consumers as a single day. Developmental toxicity (i.e. reduced number of live pups per litter; ([WIL Research, 2001](#))) was the endpoint selected as most relevant for calculating risks associated with acute occupational or consumer exposure (ADD exposure scenario relevance). The WIL Research ([2001](#)) study scored a High in systematic review data quality criteria ranking. The POD (reduced number of live pups per litter) was considered the most sensitive and biologically relevant developmental toxicity endpoint and is considered to be representative of a robust dataset, representing a continuum of adverse developmental outcomes. EPA considers the general consistency of the effects reported across studies to be supportive of the robustness of the developmental endpoint which exists along a continuum of adverse treatment effects, including mortality.

The acute scenario covers exposures incurred during a single day, with varying time intervals assumed for worker (an 8 hour work shift), and consumer (a 24 hour day) exposure scenarios. Usually, the daily dose is not adjusted for duration of exposure because appropriate pharmacokinetic data are not available. In cases where such data are available, adjustments may be made to provide an estimate of equal average concentration at the site of action for the human exposure scenario of concern. However, the short half-life for 1-BP suggests there will not be increasing body burden over multiple exposure days, therefore, no duration adjustment is needed. Further support for using this endpoint for acute (short-term) exposures is the fact that the male and female reproductive effects (in the F₀ males and females) collectively contributing to the decreases in live litter size, all occurred within a short window of exposure between ovulation and implantation. In addition, decreased live litter size occurred at relatively low exposures, suggesting that this was a sensitive and relevant endpoint, suitable for use in the risk assessment. A BMR of 5% was used to address the severity of this endpoint ([U.S. EPA, 2012a](#)). This BMR choice is a combination of reproductive effects where a BMR 10% would be used and developmental effects of post implantation loss which is considered a severe effect like mortality where a BMR of 1% would be used. The POD for the decreased live litter size was a BMCL of 31 ppm.

EPA used the BMDS nested dichotomous model (NCTR) to account for litter effect. However, this model can only be applied to increases in effects and therefore, increased post-implantation loss was the endpoint selected as most relevant for calculating risks associated with developmental toxicity following acute exposures ([WIL Research, 2001](#)) using nested modeling. Significant increases in the number of ‘former’ or ‘unaccounted’ implantation sites (i.e., the difference between the total number of implantation sites counted and the number of pups born) were reported by ([WIL Research, 2001](#)). EPA considers this finding to be indicative of post-implantation loss (pre-implantation loss could not be determined because of a lack of data on the number of primordial follicles at 100, 250 and 500 ppm). F₀ females experienced a 48% reduction in fertility at 500 ppm and complete infertility at 750 ppm and therefore these exposures were not included in the post-implantation loss modeling. A BMR of 1% was used to address the severity of this endpoint which is considered a severe effect like mortality ([U.S. EPA, 2012a](#)). The POD for the increased post-implantation loss was a BMCL of 24 ppm.

PODs for Chronic Exposure

Chronic exposure was defined for occupational settings as exposure reflecting a 40-hour work week. Non-cancer endpoints selected as most relevant for calculating risks associated with chronic (repeated) occupational exposures to 1-BP included toxicity to the liver, kidney, reproductive system, developmental effects, and the nervous system.

Table 3-1 summarizes the hazard studies and health endpoints by target organ/system that EPA considered suitable for the risk evaluation of chronic exposure scenarios. The high quality key and supporting studies in Table 3-1 are briefly described in the Section 3.2.7, along with other toxicity and epidemiological studies. BMD modeling was performed for these endpoints in a manner consistent with EPA [Benchmark Dose Technical Guidance](#). BMRs were selected for each endpoint. Hepatic endpoints selected for dose-response analysis include datasets for histopathology (e.g., hepatocellular vacuolation) from subchronic inhalation studies in rats ([ClinTrials, 1997a, b](#)) and ([WIL Research, 2001](#)). Benchmark dose modeling determined BMCL values of 143, 226 and 322 ppm for the three datasets modeled from these studies.

Renal endpoints selected for dose-response analysis include an increased incidence of pelvic mineralization in male and female rats from a subchronic inhalation study ([WIL Research, 2001](#)). Benchmark dose modeling determined BMCL values of 428 and 135 ppm, respectively, for these datasets.

Decreased epididymal weight, decreased prostate weight, decreased seminal vesicle weight, altered sperm morphology and decreased sperm motility were the male reproductive endpoints selected for dose-response analysis ([WIL Research, 2001](#); [Ichihara et al., 2000b](#)). Increased estrous cycle length and decreased antral follicle count were the female reproductive endpoints selected for dose-response analysis ([Yamada et al., 2003](#); [WIL Research, 2001](#)). The PODs for endpoints selected following dose-response analysis were calculated either by benchmark dose (BMD) modeling (when the model fit was adequate) or when BMD modeling did not find an adequate model fit a NOAEL/LOAEL approach was used and this occurred for the reproductive endpoint evaluated (see Section 3.2.10.1 and Table 3-1 for all of the PODs). The PODs were 38, 227, 250, 313 and 338 ppm for decreased relative seminal vesicle weight (use of absolute seminal vesicle weight produced the same BMCL), decreased percent normal sperm, decreased percent motile sperm, and absolute left and right cauda epididymal weights respectively, in males. The PODs were 200 and 250 ppm for decreased antral follicle count and increased estrous cycle length respectively, in females.

Decreased live litter size (i.e. reduced number of live pups per litter) was the endpoint selected as most relevant for calculating risks associated with developmental toxicity following chronic, exposures ([WIL Research, 2001](#)). In addition, decreased live litter size occurred at relatively low exposures, suggesting that this was a sensitive and relevant endpoint, suitable for use in the risk assessment. A BMR of 5% was used to address the severity of this endpoint ([U.S. EPA, 2012a](#)). The POD for the decreased live litter size was a BMCL of 43 ppm.

EPA used the BMDS nested dichotomous model (NCTR) to account for litter effect. However, this model can only be applied to increases in effects and therefore, increased post-implantation loss was the endpoint selected as most relevant for calculating risks associated with developmental

toxicity following chronic exposures ([WIL Research, 2001](#)) using nested modeling. Significant increases in the number of 'former' or 'unaccounted' implantation sites (i.e., the difference between the total number of implantation sites counted and the number of pups born) were reported by ([WIL Research, 2001](#)). EPA considers this finding to be indicative of post-implantation loss (pre-implantation loss could not be determined because of a lack of data on the number of primordial follicles at 100, 250 and 500 ppm). F₀ females experienced a 48% reduction in fertility at 500 ppm and complete infertility at 750 ppm and therefore these exposures were not included in the post-implantation loss modeling. A BMR of 1% was used to address the severity of this endpoint ([U.S. EPA, 2012a](#)). The POD for the increased post-implantation loss was a BMCL of 24 ppm.

Neurological endpoints selected for dose-response analysis for chronic, repeated exposures were datasets for decreased time hanging from a suspended bar (traction time) in rats in a 3-week inhalation study ([Honma et al., 2003](#)) and decreased hind limb grip strength in rats in a 12-week inhalation study ([Ichihara et al., 2000a](#)). These functional measures are relevant to peripheral neurotoxicity reported in human studies. Benchmark dose modeling for these continuous endpoints used a BMR of 1 standard deviation and determined BMCL values of 18 and 214 ppm, respectively, for these datasets.

Table 3-1. Endpoints Selected for the Inhalation Non-Cancer Dose-Response Analysis of 1-BP

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Liver	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL ₁₀ = 143.5	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	150	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Liver	Rat (male) (n=15/group)	100 to 600	6 hours/day, 5 days/week for 13 weeks	BMCL ₁₀ = 226.1	Increased incidence of cytoplasmic vacuolization	170	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(ClinTrials, 1997a)	High (1.5)
Liver	Rat (female) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21) for F ₀	BMCL ₁₀ = 322.1	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	340	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Kidney	Rat (female) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21) for F ₀	BMCL ₁₀ = 135.0	Increased incidence of pelvic minerali- zation (F ₀)	140	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Kidney	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL ₁₀ = 428.3	Increased incidence of pelvic minerali- zation (F ₀)	450	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Reproductive System	Rat (male) (n=8-9/group)	200 to 800	8 hours/day, 7 days/week for 12 weeks	BMCL _{1SD} = 38	Decreased absolute/ relative seminal vesicle weight	53	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Ichihara et al., 2000b)	High (1.7)
Reproductive System	Rat (female) (n=22- 25/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 188	Decreased number of implantation sites	200	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (male) (n=15- 25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	NOAEL* = 250	Decreased percent motile sperm (F ₀)	260	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (female) (n=22- 25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21) for F ₀	NOAEL* = 250	Increase in estrous cycle length (F ₀)	260	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (female) (n=10/ group)	200 to 800	8 hours/day, 7 days/week for 7 or 12 weeks	LOAEL* = 200	Decreased number of antral follicles (F ₀)	280	UF _S =1; UF _A =10; UF _H =10; UF _L =10; Total UF=1000	(Yamada et al., 2003)	High (1.6)
Reproductive System	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 313	Decreased left cauda epididymis absolute weight (F ₀)	330	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (male) (n=24- 25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 327	Decreased percent normal sperm morphology (F ₀)	340	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Reproductive System	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 338	Decreased right cauda epididymis absolute weight (F ₀)	350	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL ₁₀ = 356	Decreased Male and Female Fertility Index (F ₀)	370	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects (BMDS nested dichotomous model, NCTR)	Rat (n=25/ group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₁ = 23 (BMCL ₅ =89)	Post- implantation loss in F ₀ females	Acute ⁶ : 17 Chronic ⁶ : 24	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects (BMD modeling)	Rat (n=25/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₅ = 41 (BMCL _{1SD} =158)	Decreased live litter size (F ₁) at PND 0	Acute ⁶ : 31 Chronic ⁶ : 43	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects	Rat (female) (n=15- 22/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	BMCL ₁ = 50 (BMCL _{1SD} =260)	Decreased brain weight in F ₂ females at PND 21	53	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects	Rat (female) (n=25/group)	100 to 500	6 hours/day during gestation plus ≥ 21 weeks after PND21	BMCL ₁ = 82 (BMCL _{1SD} =327)	Decreased brain weight in adult F ₁ females	86	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Developmental Effects	Rat (male) (n=15- 22/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	BMCL ₁ = 98 (BMCL _{1SD} =395)	Decreased brain weight in F ₂ males at PND 21	100	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects	Rat (male) (n=24- 25/group)	100 to 500	6 hours/day during gestation plus ≥ 21 weeks after PND21	LOAEL* = 100	Decreased brain weight in adult F ₁ males	110	UF _S =1; UF _A =10; UF _H =10; UF _L =10; Total UF=1000	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (male) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	BMCL ₅ = 116 (BMCL _{1SD} =249)	Decreased pup body weights on PND 21 (F ₂ males)	120	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (male) (n=10- 24/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₁	BMCL ₅ = 123 (BMCL _{1SD} =229)	Decreased pup body weights on PND 28 (F ₁ males)	130	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (female) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	NOAEL* = 250	Decreased pup body weights on PND 14 (F ₂ females)	260	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (male) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	BMCL ₅ = 136 (BMCL _{1SD} =290)	Decreased pup body weights on PND 14 (F ₂ males)	300	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Developmental Effects	Rat (female) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	BMCL ₅ = 148 (BMCL _{1SD} =300)	Decreased pup body weights on PND 21 (F ₂ females)	320	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Nervous System	Rat (male) (n=5/group)	10 to 1000	8 hours/day, 7 days/week for 3 weeks	BMCL _{1SD} = 18.2	Decreased time hanging from a suspended bar (traction time)	25	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Honma et al., 2003)	High (1.6)
Nervous System	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating, throughout mating, and until GD 20 (≥ 16 weeks)	NOAEL* = 100	Decreased brain weight in F ₀ males	110	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Nervous System	Rat (male) (n=8-9/group)	200 to 800	8 hours/day, 7 days/week for 12 weeks	BMCL _{1SD} = 213.8	Decreased hind limb grip strength	300	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Nervous System	Rat (female) (n=25/group)	100 to 750	6 hours/day during pre-mating, throughout mating, and until GD 20 (≥ 16 weeks)	BMCL _{1SD} = 509	Decreased brain weight in F ₀ females	530	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)

¹Control concentrations are not included in the table.

² Acute exposures defined as those occurring within a single day. Chronic exposures defined as 10% or more of a lifetime ([U.S. EPA, 2011](#)).

³POD type can be NOAEL, LOAEL, or BMCL. For BMCLs, the subscript indicates the associated BMR. The BMRs are a percentage relative deviation (e.g., 10% relative deviation BMCL₁₀) or 1 standard deviation change (BMCL_{1SD}) from the mean for continuous data. Post-implantation loss was modeled with nested modeling to account for intra-litter correlations and litter-specific covariates. The dam weight litter specific covariate and without intra-litter correlations for the NCTR model was the selected model based on lowest AICs and lowest BMCL.

⁴HECs are calculated by duration adjustment and a human equivalent DAF. The adjusted POD is the POD x duration adjustment. The HEC_{EXRESP} = adjusted POD × DAF where the DAF is the ratio of blood:gas partition coefficients (animal:human). For 1-BP, the blood:air partition coefficient for rats is greater than that for humans, so a default ratio of 1 is applied ([U.S. EPA, 1994](#)). The baseline used for the duration adjustment was an 8 hours/day exposure for occupational exposure scenarios and 24 hours/day exposure for consumer exposure scenarios. For acute exposure the duration adjustment was (hours per day exposed ÷ 8) and for chronic exposure

(occupational scenarios) was $(\text{hours per day exposed} \div 8) \times (\text{days per week exposed} \div 5)$ to reflect a 40-hour work week. All of the endpoints used the chronic exposure duration adjustment except for the decreased live litter size (F_1) at PND 0 and post implantation loss as described above in Section 3.2.10.1. HECs are rounded to two significant digits.

⁵UF_S = subchronic to chronic UF (default value = 10); UF_A = interspecies UF (default value of 10); UF_H = intraspecies UF (default value = 10); UF_L = LOAEL to NOAEL UF (default value = 10) ([U.S. EPA, 2002](#)).

⁶The HEC for decreased live litter size and post-implantation loss were adjusted for acute and chronic occupational exposures as described in footnote 4.

* BMD modeling did not adequately fit the variance in the data so the NOAEL or LOAEL is presented.

⁷ Data Quality Criteria Ranking: High ≥ 1 and < 1.7 ; Medium ≥ 1.7 and < 2.3 ; Low ≥ 2.3 and ≤ 3 ; The numbers in parentheses reflect the score associated with the ranking. Lower scores reflect higher quality studies. Higher scores, reflect lower quality studies.

3.2.10.2 Selection of Studies for Carcinogenic Dose-Response Assessment

No data were located on the carcinogenicity of 1-BP in humans. In animals, the carcinogenicity of 1-BP was evaluated in well-designed studies conducted in rodents ([NTP, 2011a](#)). Male and female rats and mice were exposed to 1-BP via whole-body inhalation 6 hours/day, 5 days/week for 2 years. Cancer findings included significant increases in the incidences of: 1) skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, 2) rare large intestine adenomas in female F344 rats, and 3) alveolar/bronchiolar adenomas and carcinomas (combined) in female B6C3F1 mice.

Dose-Response Modeling

Benchmark dose-response modeling of the ([NTP, 2011a](#)) cancer data was performed for all three statistically significantly increased tumor types from the NTP study (i.e., skin tumors in male rats, intestinal tumors in female rats, and lung tumors in female mice). A brief summary of the methodology is presented here and more details are available in the *Supplemental File: Information on Human Health Benchmark Dose Modeling* ([EPA, 2019e](#)). Three approaches were applied; multistage modeling, frequentist model-averaging and Bayesian model averaging. The three approaches include the approach under EPA's 2005 cancer guidelines (i.e. multistage modeling) and two model averaging methods. The model averaging methods allow for an assessment of model uncertainty as described further below. Two options for BMR (0.1% and 10%) and added or extra risk were both modeled for comparison with EPA's 2005 cancer guidelines and comparison with the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)) and the 2016 NIOSH draft criteria document.

In agreement with EPA's long-standing approach all three tumor types from the NTP study ([NTP, 2011a](#)) were dose-response modeled with multistage models using the typical constrained model coefficients ≥ 0 ([U.S. EPA, 2012a](#)). Under U.S. EPA's 2005 cancer guidelines ([U.S. EPA, 2005a](#)), quantitative risk estimates from cancer bioassay data were calculated by modeling the data in the observed range to estimate a BMCL for a BMR of 10% extra risk, which is generally near the low end of the observable range for standard cancer bioassay data. The BMCs and BMCLs are shown in Table 3-2 in the Multistage columns for each of the three cancer datasets. Also the results for a BMR of 0.1% added risk are presented for comparison.

In addition to the multistage modeling, model averaging methods were applied, frequentist ([Wheeler and Bailer, 2007](#)) and Bayesian (USEPA 2018 [BMDS](#) software) to assess the impact of model uncertainty. In the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)), all dichotomous models in the BMD software (gamma, logistic, log-logistic, multistage, probit, log-probit, quantal-linear, and Weibull in [BMDS](#) Version 2.6) were fit to the incidence data for each of the three tumor types. The benchmark response level (BMR) used was 0.1% added risk (corresponding to a 1-in-1,000 working lifetime added risk of cancer) consistent with the 2016 NIOSH draft criteria document. A model-averaging (MA) technique ([Wheeler and Bailer, 2007](#)) was applied using the multistage, log-probit and Weibull models based on the observation that those 3 models performed better in bias and coverage than other combinations of models ([Wheeler and Bailer, 2007](#)). The model averaging applied statistics (bootstrapping technique) to weigh, based on fit, the models providing acceptable fit to the experimental dataset (as evidenced by a chi-square goodness-of-fit value > 0.10). Model-averaging software was restricted to avoid supralinear models, which exhibit

properties at the low dose that are not considered biologically plausible. The resulting model-average benchmark concentrations (MA BMCs) associated with 0.1% added risk and their 95% lower confidence limits (MA BMCLs) are shown in Table 3-2 in the Frequentist Model-Average (BMDS 2.6) column for each of the three cancer datasets.

Since the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#), EPA has conducted additional modeling, using the BMDS (Version 3.0) and more details are available in the *Supplemental File: Information on Human Health Benchmark Dose Modeling (EPA, 2019e)*. All dichotomous frequentist and Bayesian²² models in the BMD software (BMDS Version 3.0), were fit to the incidence data for each of the three tumor types. The benchmark response (BMR) levels used were 0.1% and 10% added and extra risk. The BMR used in the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#) was 0.1% added risk. The BMR of 10% extra risk which is generally near the low end of the observable range for standard cancer bioassay data was used. The Bayesian models and Bayesian model averaging solve issues associated with strict frequentist parameter bounds by replacing them with “soft bounds” defined by mildly informative prior density for the individual parameters of the models included in the analysis. Thus, in the cases where there are limited data, the shapes of the models are limited to dose-response shapes that are frequently seen in practice. In addition, because parameters are restricted through their prior density, the U.S. EPA BMDS 3.0 Bayesian model averaging approach allows for consideration of a large suite of models across many different study designs without typical model “degeneracy” or “overparameterization” concerns of previous model averaging approaches ([BMDS 3.0 User Guide](#)). The resulting model-average benchmark concentrations (MA BMCs) associated with 0.1% added risk (AR) and 10% extra risk (ER) and their 95% lower confidence limits (BMCLs), are shown in Table 3-2 in the Bayesian Model-Average (BMDS 3.0) column for each of the three cancer datasets.

Table 3-2. MultiStage Model, Model-Average (BMDS Version 2.6), and Model-Average (BMDS Version 3.0) BMC and BMCL Estimates of 1-BP Inhalation Exposure Associated with a 0.1% Added Risk and 10% Extra Risk of Tumors in Rodents

Species; Tumor Type	BMR	Multistage Model		Frequentist Model-Average (BMDS 2.6)		Bayesian Model-Average (BMDS 3.0)	
		BMC (ppm) ¹	BMCL (ppm) ¹	BMC (ppm)	BMCL (ppm)	BMC (ppm)	BMCL (ppm)
Male F344 rats; keratoacanthoma/squamous cell carcinoma (combined)	0.1% AR	2.96	1.78	3.73	2.25	9.81	1.47
	10% ER	303.8	185.2	--	--	433.5	220.6
Female F344 rats; large intestine adenoma	0.1% AR	5.27	3.10	13.5	4.85	23.8	7.98
	10% ER	555.3	326.7	--	--	601.5	392.4
Female B6C3F1 mice; alveolar/bronchiolar adenoma or carcinoma (combined)	0.1% AR	0.77	0.52	0.85	0.64	1.51	0.085
	10% ER	78.6	54.1	--	--	104.6	39.4

¹ First degree Multistage model was selected for all tumor datasets.

²² The Bayesian dichotomous models used in BMDS 3.0 are identical to the frequentist parametric models but incorporate prior information (e.g., parameter distributions) that is used in the model fit (cite BMDS 3.0 User Guide for details; <https://www.epa.gov/bmds/benchmark-dose-software-bmds-version-30-user-guide-readme>).

Extrapolation to Humans

The human equivalent values shown in Table 3-3 and Table 3-4 are extrapolated from the BMC and BMCL results to generate the target response in rodents exposed 6 hours/day for 5 days/week. The BMC and BMCL values are extrapolated to BMC_{HEC} and BMCL_{HEC} are shown in Table 3-3 based on occupational inhalation exposure to 1-BP during a 40-hour work week (8 hours/day, 5 days/week) or continuous 24 hours/day and 7 days/week. The dermal BMD_{HED} and BMDL_{HED} from the BMC and BMCL values are shown in Table 3-4.

These data were extrapolated to humans based on occupational exposure to 1-BP during a 40-hour work week (8 hours/day, 5 days/week) using the following methodology:

1. Conversion of BMC/BMCLs (ppm) to benchmark dose values (BMD/BMDL in mg/kg-day) by adjusting for the animal breathing rate and experimental exposure duration 6 hours/day²³;
2. Conversion of BMD/BMDLs in rodents to human equivalent BMD/BMDLs on the basis of the mg/kg-day dose scaled by body weight to the 0.75 power²⁴ and assuming dermal absorption is equivalent to inhalation absorption the BMD is the dermal HED; and
3. Adjustment of the human equivalent BMD/BMDLs (mg/kg-day) to BMC/BMCLs (ppm) that reflect exposure for either an 8-hour work day or 24-hour continuous exposure²⁵.

The human equivalent BMC and BMCL (BMC_{HEC} and BMCL_{HEC}) estimates using all three modeling approaches are shown in Table 3-3. Three combinations of modeling inputs are shown the multistage BMR 10% extra risk (ER) i.e. the approach under EPA's 2005 cancer guidelines, frequentist model averaging BMR 0.1% added risk for comparison with the [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#) and the 2016 NIOSH draft criteria document and Bayesian Model averaging BMR 10% ER as the latest modeling approach in BMDS. Since these BMCLs are for different BMRs they are not directly comparable.

²³BMD/BMDL (mg/kg-day) = BMC/BMCL (ppm) x (6 hours/24 hours) x (5.031 mg/m³ per ppm) x default inhalation rate (m³/day) ÷ default body weight (kg); where the default inhalation rate and body weight values are 0.36 m³/day and 0.380 kg for male F344 rats, 0.24 m³/day and 0.229 kg for female F344 rats, and 0.06 m³/day and 0.0353 kg for female B6C3F1 mice in chronic studies ([U.S. EPA, 1988](#)).

²⁴Human equivalent BMD/BMDL (mg/kg-day) = BMC/BMCL (mg/kg-day) x default body weight in rats or mice [kg] x (default body weight in humans [kg] ÷ default body weight in rats or mice [kg])^{0.75} ÷ default body weight in humans [kg]; where default body weight values are 0.380 kg for male F344 rats, 0.229 kg for female F344 rats, 0.0353 kg for female B6C3F1 mice, and 70 kg for humans ([U.S. EPA, 1988](#); [ICRP, 1975](#)).

²⁵BMC/BMCL (ppm) = (1 ppm per 5.031 mg/m³) x (default body weight in humans [kg]/default minute volume for human occupational exposure based on an 8-hour shift [m³/day] or a continuous exposure for 24-hours); where default body weight and minute volume values are 70 kg and 9.6 m³/8-hr day or 15 m³/24-hr day ([U.S. EPA, 1994](#)).

Table 3-3. BMC_{HEC} and BMCL_{HEC} Estimates of 1-BP Inhalation Exposures in Humans Exposed 40 hours/week (8 hours/day, 5 days/week) (ppm) or 24 hrs/day 7 days/week (ppm)

		Multistage Model BMR 10% ER		Frequentist Model- Average (BMDS 2.6) BMR 0.1% AR		Bayesian Model- Average (BMDS 3.0) BMR 10% ER	
Species; Tumor Type	Exposure duration	BMC _{HEC} (ppm)	BMCL _{HEC} (ppm)	BMC _{HEC} (ppm)	BMCL _{HEC} (ppm)	BMC _{HEC} (ppm)	BMCL _{HEC} (ppm)
Male F344 rats; keratoacanthoma/squamous cell carcinoma (combined)	40 hrs/wk	141	86	1.73	1.04	200	102
	24 hrs/day	90	55	1.01	0.67	128	65
Female F344 rats; large intestine adenoma	40 hrs/wk	254	149	6.17	2.22	275	179
	24 hrs/day	162	96	3.95	1.42	176	115
Female B6C3F1 mice; alveolar/bronchiolar adenoma or carcinoma (combined)	40 hrs/wk	36	25	0.39	0.30	49	18
	24 hrs/day	23	16	0.25	0.19	31	12

Table 3-4. BMD_{HED} and BMDL_{HED} Estimates of 1-BP Dermal Exposures Extrapolated from BMC and BMCL (mg/kg-day)

		Multistage Model BMR 10% ER		Frequentist Model- Average (BMDS 2.6) BMR 0.1% AR		Bayesian Model- Average (BMDS 3.0) BMR 10% ER	
Species; Tumor Type		BMD _{HED} (mg/kg/d)	BMDL _{HED} (mg/kg/d)	BMD _{HED} (mg/kg/d)	BMDL _{HED} (mg/kg/d)	BMD _{HED} (mg/kg/d)	BMDL _{HED} (mg/kg/d)
Male F344 rats; keratoacanthoma/squamous cell carcinoma (combined)		97	59	1.19	0.72	138	70
Female F344 rats; large intestine adenoma		175	103	4.26	1.53	190	124
Female B6C3F1 mice; alveolar/bronchiolar adenoma or carcinoma (combined)		25	17	0.27	0.21	34	13

Derivation of Inhalation Unit Risk Applying Age-Dependent Adjustment Factors (ADAFs)

Using the mode of action framework, age-dependent adjustment factors (ADAFs) are applied when developing cancer risk estimates when early-life susceptibility is assumed (ages 0-15) and when there is evidence of a MMOA in animal studies (EPA's Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#))); Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens ([U.S. EPA, 2005b](#)). For 1-BP, the weight of the scientific evidence for mutagenicity indicates that 1-BP is carcinogenic by a MMOA (see Appendix J); and early-life chronic exposure scenarios are assumed only for the inhalation route, and only for occupational scenarios for worker populations. However, ADAFs will not be applied for any occupational scenarios in this draft risk evaluation because worker populations are considered to be 16 years of age and older, ages not covered by the ADAF application guidance ([U.S. EPA, 2005b](#)). ADAFs will also not be applied for younger aged children spending time in the workplace (e.g. family owned businesses) because it is unlikely their exposures are chronic in nature.

Derivation of Inhalation Unit Risk and Dermal Slope Factor

The data for lung tumors based on the combined incidence of alveolar/bronchiolar adenoma or carcinoma in female mice (as shown in Section 3.2.10.2) was selected for derivation of the inhalation unit risk (IUR) and for the dermal slope factor. This POD is considered protective for the other tumor types. The BMCL_{HEC} values for both a 40 hours/week (8 hours/day, 5 days/week; and 24 hours/day) using all three modeling approaches (Multistage modeling and both Model Averaging approaches Frequentist Version 2.6 and Bayesian Version 3.0) are depicted in Table 3-5. These BMCL_{HEC} values represent the 95% lower confidence limit estimate of the occupational exposure concentration expected to produce a 1-in-10 (i.e., 10% BMR) or 1-in-1,000 (i.e. 0.1% BMR) lifetime extra (ER) or added risk (AR) of lung cancer, due to the different BMR values they are not directly comparable. These values were selected as the POD for the inhalation unit risk (IUR) value and the dermal slope factor because they reflect the statistical variability of the data and are protective of more sensitive individuals in the population. Although data suggest a mutagenic mode of action (MOA), the exact MOA of 1-BP-induced tumorigenesis is not known. In the absence of more definitive knowledge regarding the MOA of 1-BP, the inhalation unit risk and dermal slope factor were calculated using the default linear approach i.e. $IUR = BMR \div BMCL$ and rounded to 1 significant figure. The IURs are shown in Table 3-5 and the dermal cancer slope factors are shown in Table 3-6. While the BMCLs are not directly comparable because of different BMRs the IUR incorporate the BMR and can be compared.

Table 3-5. Inhalation Unit Risk (IUR) for Humans Exposed via Inhalation Based on Combined Alveolar/Bronchiolar Adenomas or Carcinomas Observed in Female Mice

Modeling Approach	BMR	BMCL _{HEC} (ppm)	IUR (per ppm)	IUR (per µg/m ³)
Human Exposures 40 hours/week (8 hours/day, 5 days/week)				
Multistage Model, ER	10%	25	4 x 10 ⁻³	8 x 10 ⁻⁷
Frequentist Model-Averaging, Version 2.6, AR	0.1%	0.3	3 x 10 ⁻³	7 x 10 ⁻⁷
Bayesian Model-Averaging, Version 3.0, ER	10%	18	6 x 10 ⁻³	1 x 10 ⁻⁶
Human Exposures 24 hours/day				
Multistage Model, ER	10%	16	6 x 10 ⁻³	1 x 10 ⁻⁶
Frequentist Model-Averaging, Version 2.6, AR	0.1%	0.19	5 x 10 ⁻³	1 x 10 ⁻⁶
Bayesian Model-Averaging, Version 3.0, ER	10%	12	9 x 10 ⁻³	2 x 10 ⁻⁶

Table 3-6. Cancer Slope Factor for Humans Exposed via Dermal Contact Extrapolated from Combined Alveolar/Bronchiolar Adenomas or Carcinomas Observed in Female Mice

Modeling Approach	BMR	BMDL _{HED} (mg/kg-day)	Slope Factor (per mg/kg-day)
Multistage Model, ER	10%	17	6 x 10 ⁻³
Frequentist Model-Averaging, Version 2.6, AR	0.1%	0.21	5 x 10 ⁻³
Bayesian Model-Averaging, Version 3.0, ER	10%	13	8 x 10 ⁻³

Overall, the IURs and dermal slope factors calculated by all three modeling approaches (Multistage modeling and both Model Averaging approaches Frequentist Version 2.6 and Bayesian Version 3.0) are nearly the same. The model averaging approaches can be used to assess the impact of model uncertainty and the similar results suggest model uncertainty is not significantly impacting the IUR or the slope factor. Therefore the IURs and cancer slope factor using the multistage modeling are used in cancer risk estimate calculations below consistent with EPA guidance EPA's Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment))).

The IUR and dermal slope factor were used in EPA risk evaluation to estimate extra cancer risks for the inhalation and dermal occupational exposure scenarios. There is high confidence in the IUR and the dermal slope factor because they were based on high quality animal data. Moreover, the weight of the scientific evidence supports a mutagenic mode of action for 1-BP carcinogenesis. EPA did not use the IUR or dermal slope factor to calculate the theoretical cancer risk associated with a single (acute) inhalation/or dermal exposure to 1-BP. Published methodology for extrapolating cancer risks from chronic to short-term exposures to mutagenic carcinogens caveat that extrapolation of lifetime theoretical extra cancer risks to single exposures has great uncertainties ([NRC, 2001](#)).

As [NRC \(2001\)](#) explains, “There are no adopted state or federal regulatory methodologies for deriving short-term exposure standards for workplace or ambient air based on carcinogenic risk, because nearly all carcinogenicity studies in animals and retrospective epidemiologic studies have entailed high-dose, long-term exposures. As a result, there is uncertainty regarding the extrapolation from continuous lifetime studies in animals to the case of once-in-a-lifetime human exposures. This is particularly problematical, because the specific biologic mechanisms at the molecular, cellular, and tissue levels leading to cancer are often exceedingly diverse, complex, or not known. It is also possible that the mechanisms of injury of brief, high-dose exposures will often differ from those following long-term exposures. To date, U.S. federal regulatory agencies have not established regulatory standards based on, or applicable to, less than lifetime exposures to carcinogenic substances.”

Thus, EPA risk evaluation for 1-BP does not estimate extra cancer risks for acute exposures because the relationship between a single short-term exposure to 1-BP and the induction of cancer in humans has not been established in the current scientific literature.

3.2.10.3 Potentially Exposed or Susceptible Subpopulations

The PECO statement in the the problem formulation in June, 2018 ([U.S. EPA, 2018c](#)) includes “potentially exposed or susceptible subpopulations such as infants, children, pregnant women, lactating women, women of child bearing age” as “populations” for the 1-BP Risk Evaluation. These susceptible subpopulations were considered against the available 1-BP specific data. Women of reproductive age, pregnant women and their offspring (fetal and postnatal) were identified as susceptible subpopulations based on the non-cancer effects associated with 1-BP exposure in rodent studies ([WIL Research, 2001](#)). A prenatal developmental toxicity study and a two-generation reproductive toxicity study in rats exposed to 1-BP via the inhalation route reported decreased live litter size ([WIL Research, 2001](#)), postnatal survival ([Furuhashi et al., 2006](#)), pup body weight, brain weight and skeletal development ([Huntingdon Life Sciences, 1999](#)), ([Huntingdon Life Sciences, 2001](#)); ([WIL Research, 2001](#)). No epidemiological studies on the developmental effects of 1-BP exposure were identified in the literature. Since effects were observed in animals after gestational and postnatal exposure, pregnant women, and their offspring were identified as susceptible subpopulations; however, there is some uncertainty about the critical window for increased susceptibility to 1-BP exposure .

Other data on the noncancer effects of 1-BP exposure were reviewed to identify potential susceptible subpopulations. A two-generation reproduction study in rats reported adverse effects on male and female reproductive parameters ([WIL Research, 2001](#)) such as, significant increases in post-implantation loss (pre-implantation loss could not be determined because of a lack of data on

the number of primordial follicles), reduced fertility in F0 females, and decreased mating indices, and increased estrous cycle length and pregnancy loss. In F0 males, statistically significant changes in reproductive endpoints included decreased absolute prostate and epididymal weights, decreased sperm motility, and decreased mating and fertility indices ([WIL Research, 2001](#)). These findings are supported by other studies ([NTP, 2011b](#); [Qin et al., 2010](#); [Liu et al., 2009](#); [Yu et al., 2008](#); [Banu et al., 2007](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#)), suggesting that males of reproductive age represent another susceptible subpopulation for 1-BP exposure.

The primary metabolic pathways identified for 1-BP involve cytochrome P450 mediated oxidation (CYP2E1) and glutathione conjugation reactions. Genetic polymorphisms and interindividual variability in the expression and function of CYP2E1 have been linked to altered disease susceptibility ([Neafsey et al., 2009](#)) ([Trafalis et al., 2010](#)). Although there are uncertainties in the available data, chronic exposure to CYP2E1 inducers (e.g., ethanol, isoniazid), may increase the probability of developing malignancy, especially for carriers of certain CYP2E1 alleles ([Trafalis et al., 2010](#)). Pre-existing health conditions, including alcoholism and diabetes also induce CYP2E1 activity, thereby enhancing susceptibility to the adverse effects of 1-BP exposure.

3.2.10.4 Points of Departure for Human Health Hazard Endpoints

Table 3-1 summarizes the hazard studies, health endpoints (PODs) by target organ/system, HECs and UFs that are relevant for the risk evaluation of acute and chronic exposure scenarios. Table 3-7 lists the selected HECs/dermal HEDs by study type and duration category (acute vs. chronic) carried forward for risk estimation. Appendix H contains a comprehensive summary table of adverse effects.

Inhalation HECs were converted to dermal HEDs using the following equation:

$$\text{Dermal HED (mg/kg-day)} = \frac{\text{inhalation POD (ppm)} \times 5.031 \text{ mg/m}^3 / \text{ppm} \times \text{duration adjustment} \times \text{ventilation rate (m}^3) \div \text{body weight (kg)}}{1}$$

where the inhalation HEC used was for a 40 hr work week (8 hrs / day, 5 days / week), the duration adjustment was (6 hours / 8 hours $\times$ 7 days / 5 days) to account for differences between animal exposure durations and expected human exposure durations, ventilation rate was 10 m³ (i.e. 1.25 m³ per hour for 8 hours) and the body weight was 80 kg. Note that the dermal exposure estimates account for the fraction of 1-BP that is absorbed (see Section 2.3.1.22) therefore an absorption adjustment is not applied in the route-to-route extrapolation.

Table 3-7. HECs/Dermal HEDs Selected for Non-Cancer Effects for 1-BP

Exposure Duration for Risk Analysis	Target Organ/System	Species	Route of Exposure	Range of Doses or Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	HEC ⁵ continuous	Dermal HED (mg/kg-day) ⁶	Uncertainty Factors (UFs) for Benchmark MOE ⁷	Reference	Data Quality Ranking ⁸
CHRONIC OCCUPATIONAL & CONSUMER	Liver	Rat (male) (n=25/group)	Inhalation	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice	BMCL ₁₀ = 143.5	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	150	36	95	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Kidney	Rat (female) (n=25/group)	Inhalation	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	BMCL ₁₀ = 135.0	Increased incidence of pelvic mineralization (F ₀)	140	34	89	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Reproductive System	Rat (male) (n=8-9/group)	Inhalation	200 to 800	8 hours/day, 7 days/week for 12 weeks	BMCL _{1SD} = 38	Decreased absolute/relative seminal vesicle weight	53	13	25	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Ichihara et al., 2000b)	High (1.7)
	Developmental Effects (BMDS nested dichotomous model, NCTR)	Rat (n=25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₁ = 24	Post-implantation loss in F ₀ females	24	6	15	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Developmental Effects (BMD modeling)	Rat (n=25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₅ = 41	Decreased live litter size (F ₁) at PND 0	43	10	27	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Nervous System	Rat (male) (n=5/group)	Inhalation	10 to 1000	8 hours/day, 7 days/week for 3 weeks	BMCL _{1SD} = 18.2	Decreased time hanging from a suspended bar (traction time)	25	6	12	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Honma et al., 2003)	High (1.6)

ACUTE OCCUPATIONAL & CONSUMER	Developmental Effects (BMDS nested dichotomous model, NCTR)	Rat (male) (n=24-25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	BMCL ₁ =24	Post-implantation loss in F ₀ females	17	6	11	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Developmental Effects (BMD modeling)	Rat (male) (n=24-25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	BMCL ₅ =41	Decreased live litter size (F ₁)	31	10	19	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

¹Control concentrations are not included in the table.

²Acute exposures defined as those occurring within a single day. Chronic exposures defined as 10% or more of a lifetime (U.S. EPA, 2011).

³POD type can be NOAEL, LOAEL, or BMCL. For BMCLs, the subscript indicates the associated BMR. The BMRs are a percentage relative deviation (e.g. 10% relative deviation BMCL₁₀) or 1 standard deviation change (BMCL_{1SD}) from the mean for continuous data. Post-implantation loss was modeled using the NCTR model.

⁴HECs/dermal HEDs are adjusted from the study conditions by the equation $HEC_{EXRESP} = POD \times \text{duration adjustment} \times DAF$. The DAF is the ratio of blood:gas partition coefficients (animal:human). For 1-BP, the blood:air partition coefficient for rats is greater than that for humans, so a default ratio of 1 is applied (U.S. EPA, 1994). For acute exposure the duration adjustment was (hours per day exposed $\div$ 8 or 24) and for chronic exposure the duration adjustment was (hours per day exposed $\div$ 8) $\times$ (days per week exposed $\div$ 5) to reflect a 40-hour work week. The effects all used the chronic exposure duration adjustment except for the decreased live litter size (F₁) at PND 0 and post-implantation loss as described above in Section 3.2.10.1. The differences in the HECs between the occupational and consumer exposures are due to the baseline used for the duration adjustment of acute occupational and consumer exposures; occupational exposures was 8 hours/day, and consumer exposures was 24 hours/day. HECs/dermal HEDs are rounded to two significant digits.

⁵HEC for continuous exposures 24 hours per day, 7 days per week

⁶The dermal HEDs for dermal exposures were extrapolated from the inhalation PODs in mg/kg-day using a duration adjustment, human ventilation rate and human body weight.

⁷UF_S = subchronic to chronic UF (default value = 10); UF_A = interspecies UF (default value of 10); UF_H = intraspecies UF (default value = 10); UF_L = LOAEL to NOAEL UF (default value = 10) (U.S. EPA, 2002).

* BMD modeling did not adequately fit the variance in the data so the LOAEL is presented

⁸Data Quality Criteria Ranking: High > 1 and < 1.7 ; Medium ≥ 1.7 and < 2.3 ; Low ≥ 2.3 and ≤ 3 ; The numbers in parentheses reflect the score associated with the ranking. Lower scores reflect higher quality studies. Higher scores, reflect lower quality studies.

3.2.10.5 Strength, Limitation, and Uncertainty of the Hazard Identification and Selection of PODs for Dose-Response Assessment

Limited toxicological data is available by the oral route, and no repeated-dose toxicity studies by the dermal route were identified on 1-BP. Although the oral repeated-dose toxicity studies are insufficient for a quantitative dose-response assessment, data from these studies were used as qualitative support in the weight of the scientific evidence for nervous system effects (see Section 3.2.8.2 and Appendix I), suggesting that, at least for the nervous system endpoints, the delivery of 1-BP via the inhalation- (i.e., pulmonary/systemic circulation) and oral- (i.e., portal circulation) routes of exposure results in comparable toxic endpoints. EPA chose to derive dermal HEDs for dermal exposures by extrapolating from other routes for systemic endpoints (i.e. not point of contact effects) and none of the key endpoints for 1-BP (liver, kidney, reproductive, developmental and nervous system effects) were considered point of contact therefore all were used for route-to-route extrapolation. The route-to-route extrapolations enabled EPA to estimate applied dermal PODs. Since physiologically based pharmacokinetic/ pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have not been identified, there is no relevant kinetic or metabolic information for 1-BP that would facilitate development of dosimetric comparisons, and the studies by the oral route were insufficient for quantitative dose-response assessment, EPA chose to derive dermal HEDs for dermal exposures by extrapolating from the inhalation PODs. However, the inhalation studies were performed by whole body exposure, rather than nose only exposure, which may have led to additional dosing by the oral and dermal routes of exposure, due to deposition on fur and the grooming behavior of rodents, resulting in uncertainty of actual dose received. It should be noted that EPA was unable to conclude with certainty that comparable toxic endpoints would be associated with the dermal route of exposure, considering the expected quantitative ADME differences and the absence of an adequate PBPK model. Notwithstanding these uncertainties, EPA considered this approach appropriate considering the comparable toxic endpoints identified in the available repeated-dose oral/inhalation toxicity studies and the uncertainty with the putative toxicant (i.e., 1-BP or a metabolite(s)).

Overall there is high confidence in all endpoints selected as PODs for both acute and chronic exposure. Endpoints selected for PODs for both acute and chronic exposure scenarios were derived from three studies, ([WIL Research, 2001](#)), ([Ichihara et al., 2000b](#)), and ([Honma et al., 2003](#)). These studies were selected because they all scored High in data evaluation, followed OECD guidance and Good Laboratory Practice, and were of longer duration with effects observed more consistently than other high-quality studies that were evaluated. In addition, these endpoints were identified as the most important endpoints relevant to acute and chronic exposures and were also the lowest available PODs. BMD modeling was used on the PODs from these studies to derive corresponding HECs/dermal HEDs and uncertainty factors in order to obtain more precise values. BMD modeling results always contain some level of uncertainty, and various factors such as model fit and BMR selection may have a large effect on the final POD value. The PODs from all three studies could be fit into BMD modeling, thereby reducing the uncertainty factors (i.e. $UF_L = 1$) used in deriving the benchmark MOE. EPA believes that the selected PODs best represent the hazards associated with 1-BP for quantitative risk estimation.

EPA considers some developmental toxicity endpoints observed in a repeat dose developmental toxicity study applicable to acute exposures. While there is some uncertainty surrounding this consideration because the precise critical exposure window is unknown, multiple publications

suggest that some developmental effects (e.g., decreased live litter size and increased post-implantation loss) may result from a single exposure during a critical window of development. In this draft risk evaluation, effects following acute exposures to 1-BP included decreased live litter size and increased post implantation loss ([WIL Research, 2001](#)). These specific developmental effects were considered the most sensitive HEC/dermal HED identified for an acute exposure duration, and are considered to be biologically relevant to the potentially exposed or susceptible subpopulation (i.e., adults of reproductive age and their offspring). Further support for using this endpoint for acute (short-term) exposures is the fact that the male and female reproductive effects (in the F₀ males and females) collectively contributing to the decreases in live litter size, all occurred within a short window of exposure between ovulation and implantation. While exposures during other lifestages (such as in childhood) may cause similar or related effects, without specific information on the mechanism of action or developmental windows of sensitivity for these specific developmental effects, there are uncertainties in extrapolating these effects for other lifestages in order to refine dose estimates for these additional lifestages.

4 RISK CHARACTERIZATION

4.1 Environmental Risk

EPA integrated relevant pathways of environmental exposure with available environmental hazard data to estimate risk to environmental receptors. EPA used estimated exposure values calculated from E-FAST and monitored data from TRI, as well as aquatic hazard values based on reasonably available hazard data to perform a quantitative screening-level determination of risks to aquatic species from acute and chronic exposures to 1-BP using the RQ method. EPA's approach is expected to represent a high-end estimate of aquatic exposure.

As a result of high volatility (Henry's Law constant of 7.3×10^{-3} atm-m³/mole), high water solubility (2.4 g/L), and low log K_{oc} (1.6) it is expected that 1-BP will only be present in terrestrial environmental compartments as a vapor. No specific conditions of use (i.e. systematic application to land) were identified that resulted in systematic, significant airborne exposures that overlap with terrestrial habitats, so this is not a relevant route of exposure for 1-BP under the conditions of use of this risk evaluation. Additionally, 1-BP is not expected to bioaccumulate (BAF=12; BCF=11, see Table 2-1) and high volatility (Vapor Pressure= 146.26 mmHg; Henry's law constant= 7.3×10^{-3} atm-m³/mole; see Table 1-1) means that exposure to terrestrial species through oral routes is negligible. No further analysis of risks to terrestrial receptors was carried out as part of this evaluation. as risks from these exposure pathways are not expected.

4.1.1 Aquatic Pathways

The purpose of the environmental risk characterization is to discuss whether there are exceedances of the concentrations of concern for the aquatic environment from levels of 1-BP found in surface water taking into consideration fate properties, relatively high potential for release, and the availability of environmental monitoring data and hazard data. Based on a qualitative assessment of the physical-chemical properties and fate of 1-BP in the environment, and a quantitative comparison of hazards and exposures for aquatic organisms, EPA calculated risks to the aquatic environment for the conditions of use of this risk evaluation. The results of the analyses are presented below. The environmental risk of 1-bromopropane is characterized by calculating risk quotients or RQs ([U.S. EPA, 1998a](#)) ([Barnthouse et al., 2008](#)); the RQ is defined as:

$$\text{RQ} = \text{Environmental Concentration/Effect Level}$$

To determine the risk of 1-BP to aquatic species using risk quotients (RQs) method., the "environmental concentration" represents the modeled exposure value calculated by E-FAST as described below, while the "effect level" represents the aquatic concentrations of concern (COCs) presented in Table 4-1. An RQ equal to 1 indicates that the exposures are the same as the concentration that causes effects. If the RQ is above 1, the exposure is greater than the effect concentration. If the RQ is below 1, the exposure is less than the effect concentration.

As described in greater detail in Appendix F.3, the acute and chronic concentrations of concern (COCs) for aquatic species (shown in Table 4-1) were calculated based on the results of the high confidence study ([Geiger et al., 1988](#)) and environmental hazard data for 1-BP summarized in the in ECHA (European Chemicals Agency) Database ([ECHA, 2017](#)) ([EPA, 2019d](#)). For a particular environment (e.g., aquatic environment), the COCs are based on the most sensitive species or the

species with the lowest toxicity value reported in that environment. After selecting the lowest toxicity values, an assessment factor (AF) is applied according to EPA methods ([Suter, 2016](#)) ([U.S. EPA, 2012e](#)) ([U.S. EPA, 2013b](#))²⁶.

Table 4-1. Concentrations of Concern (COCs) for Environmental Toxicity

Environmental Toxicity	Endpoint	Data Source	Concentration of Concern (COC)
Acute Toxicity, aquatic organisms	96-hour Fish LC ₅₀	(Geiger et al., 1988)	13460 µg/L
		(ECHA, 2017) (EPA, 2019d)	4,860 µg/L
Chronic Toxicity, aquatic organisms	Fish Chronic Value*	(Geiger et al., 1988)	673 µg/L
		(ECHA, 2017) (EPA, 2019d)	243 µg/L

* = The fish chronic value is calculated by dividing the 96-hour fish LC₅₀ by an acute to chronic ratio (ACR) of 10; due to lack of chronic fish and chronic aquatic invertebrate test data.

As described in Appendix G, EPA used the reported releases to water from EPA's Toxics Release Inventory (TRI) to predict surface water concentrations near reported facilities for this Risk Evaluation. To examine whether near-facility surface water concentrations could approach 1-BP's aquatic concentrations of concern, EPA employed a first-tier screening-level approach, using readily-available modeling tools and data, as well as conservative assumptions. EPA's Exposure and Fate Assessment Screening Tool ([U.S. EPA, 2007b](#)) was used to estimate site-specific surface water concentrations based on estimated loadings of 1-BP into receiving water bodies as reported to TRI. E-FAST 2014 incorporates stream dilution using stream flow information contained within the model. E-FAST also incorporates wastewater treatment removal efficiencies. Wastewater treatment removal was assumed to be 0% for this exercise, as reported loadings/releases are assumed to account for any treatment. As days of release and operation are not reported, EPA assumed a range of possible release days (i.e., 1, 20, and 100 days/year). Refer to the E-FAST 2014 Documentation Manual for equations used in the model to estimate surface water concentrations ([U.S. EPA, 2007b](#)). These estimated exposure concentrations were compared with the reasonably available information for aquatic organisms to identify potential risks.

Table 4-2 summarizes the risk quotients (RQs) for the acute and chronic risk of 1-BP, using reasonably available information, as well as using the lowest available endpoint derived from the ECHA summaries. The RQ values for risks from acute and chronic exposure are <0.01 and 0.12, respectively based on the reasonably available information, and 0.02 and 0.32 based on the lowest-bound ECHA summary data, respectively. These values indicate that risks are not identified for aquatic receptors based on the conditions of use in this risk evaluation. As previously stated, an RQ below 1, indicates that the exposure concentrations of 1-BP is less than the concentrations that would cause an effect to organisms in the aquatic pathways.

²⁶ For fish and aquatic invertebrates (e.g., daphnia), the acute COC values are calculated by dividing the selected environmental hazard endpoint by an AF of 5. For chronic COCs, an AF of 10 is used.

Table 4-2. Calculated Risk Quotients (RQs) for 1-BP

	Data Source	Concentrations of Concern (CoC)	Maximum Concentration	RQ
Acute Risk Scenario	(Geiger et al., 1988)	13,460 µg/L	78 µg/L	<0.01
	(ECHA, 2017) (EPA, 2019d)	4,860 µg/L		0.02
Chronic Risk Scenario	(Geiger et al., 1988)	673 µg/L	78 µg/L	0.12
	(ECHA, 2017) (EPA, 2019d)	243 µg/L		0.32

For environmental release pathways, EPA quantitatively evaluated surface water exposure to fish, invertebrates and aquatic plants. As explained in Section 2.1, 1-BP is not expected to absorb strongly to sediment or soil. If present in biosolids, 1-BP would be expected to associate with the aqueous component and/or volatilize to air as biosolids are applied to soil and allowed to dry. 1-BP is expected to volatilize readily from dry soil and surfaces due to its vapor pressure (high volatility (vapor pressure= 146.26 mmHg; Henry's law constant of 7.3×10^{-3} atm-m³/mole, see Table 1-1). 1-BP has demonstrated moderate toxicity to aquatic organisms, and overall the exposures to surface water from biosolids are estimated to be below concentrations of concern for these taxa. Therefore, no analysis for risks to aquatic organisms from biosolids is necessary.

No sediment monitoring data for 1-BP is available, but physical-chemical characteristics such as a high vapor pressure= 146.26 mmHg and Henry's law constant of 7.3×10^{-3} atm-m³/mole (see Table 1-1) suggest that 1-BP is expected to quickly volatilize from water and resultingly be present in very limited amounts in aquatic environments. 1-BP in sediment is expected to be in the pore water rather than adsorbed to the sediment solids based on a high water solubility (2.4 g/L) and low log K_{oc} (1.6). Overall, because 1-BP is not expected to accumulate in sediments, sediment-dwelling organisms are not expected to be exposed to a greater concentration of 1-BP than aquatic organisms and sediment is not expected to be a source of 1-BP to overlying surface water.

4.2 Human Health Risk

1-BP exposure is associated with a variety of cancer and non-cancer effects deemed relevant to humans for risk estimations for the acute and chronic scenarios and populations addressed in this draft risk evaluation. Based on a weight of the scientific evidence analysis of the reasonably available toxicity studies from rats and humans, these effects include liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity and neurotoxicity. The rationale for using the range of toxic effects for chronic exposures is based on the fact that relatively low dose, short term/sub-chronic exposures can result in long-term adverse consequences. The adverse developmental effects are also deemed important for risk estimation for the acute exposure scenarios and populations addressed in this draft risk evaluation. The rationale for using 1-BP associated developmental effects for evaluating risks associated with acute exposures is based on the understanding that a single exposure during a critical window of vulnerability can adversely impact the conceptus.

1-BP is carcinogenic in animals. EPA derived an IUR and dermal slope factor based on lung tumors in female mice to evaluate cancer risk. The weight of the scientific evidence analysis for the cancer endpoint was sufficient to support a mutagenic mode of action for 1-BP carcinogenesis.

4.2.1 Risk Characterization Approach

Table 4-3, Table 4-4, and Table 4-5 show the use scenarios, populations of interest and toxicological endpoints used for acute and chronic exposures, respectively.

Table 4-3. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Occupational Risks Following Acute Exposures to 1-BP

Populations And Toxicological Approach	Occupational Use Scenarios of 1-BP
Population of Interest and Exposure Scenario	Workers: Adult male and female¹ (>16 years old) who directly handle 1-BP as part of their job function (typically 8-hr work day). Occupational Non-user: Adult male and female¹ (>16 years old) who do not directly handle 1-BP, but who are potentially exposed by being present in the surrounding work area of building (typically 8-hr work day).
Health Effects of Concern, Concentration and Time Duration	<u>Non-Cancer Health Effects:</u> Decreased live litter size (F₁) using BMD modeling; Post-implantation loss in F₀ females using NCTR modeling (WIL Research, 2001)² 1. Non-cancer hazard values or Point of Departures (PODs; BMD): 8-hr HEC: 31 ppm; 24-hr dermal HED: 19 mg/kg-day 2. Non-cancer hazard values or Point of Departures (PODs; NCTR): 8-hr HEC: 17 ppm; 24-hr dermal HED: 11 mg/kg-day <u>Cancer Health Effects:</u> Cancer risks following acute exposures were not estimated. Relationship is not known between a single short-term exposure to 1-BP and the induction of cancer in humans.
Uncertainty Factors (UF) used in Non-Cancer Margin of Exposure (MOE) calculations	$(UFS=1) \times (UFA=10) \times (UFH=10) \times (UFL=1)^3 = 100$ Total UF=Benchmark MOE=100
Notes: ¹ Includes pregnant women and adults of reproductive age. ² The risk assessment for acute exposures focused on developmental toxicity effects as the most sensitive health effect when compared to other potential acute effects (i.e., neurotoxicity). ³ UFS=subchronic to chronic UF; UFA=interspecies UF; UFH=intraspecies UF; UFL=LOAEL to NOAEL UF	

Table 4-4. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Consumer Risks Following Acute Exposures to 1-BP

Population and Toxicological Approach	Consumer Use Scenarios of 1-BP (9 Scenarios)
Population of Interest	Women and adults of reproductive age ¹ Users (Youth 11-15, Youth 16-20, Adult 21 years and greater) Bystander (Any age group (infant to elderly))
Exposure Scenario ² : Users, High-intensity use	95 th percentile duration of use 95 th percentile mass of product used High weight fraction (amount of chemical in product)
Exposure Scenario ² : Users, moderate intensity use	50 th percentile duration of use 50 th percentile mass of product used Mean/median weight fraction (amount of chemical in product)
Exposure Scenario ² : Users, low intensity use	10 th percentile duration of use 10 th percentile mass of product used Low weight fraction (amount of chemical in product)
Population of Interest and Exposure Scenario: Non-User	Women and adults of reproductive age non-users ⁴ and individuals of multiple age groups that are exposed to indirect 1-BP exposures by being in the rest of the house.
Health Effects of Concern, Concentration and Time Duration	<u>Non-Cancer Health Effects:</u> Decreased live litter size (F ₁) using BMD modeling; Post-implantation loss in F ₀ females using NCTR modeling (WIL Research, 2001) ⁵ 1. Non-cancer hazard values or Point of Departures (PODs; BMD): 24-hr HEC: 10 ppm; 24-hr HED: 19 mg/kg-day 2. Non-cancer hazard values or Point of Departures (PODs; NCTR): 24-hr HEC: 6 ppm; 24-hr HED: 11 mg/kg-day <u>Cancer Health Effects:</u> Cancer risks following acute exposures were not estimated. Relationship is not known between a single short-term exposure to 1-BP and the induction of cancer in humans.
Uncertainty Factors (UF) used in Non-Cancer Margin of Exposure (MOE) calculations	(UFS=1) x (UFA= 10) x (UFH=10) x (UFL=1) ⁶ = 100 Total UF=Benchmark MOE=100
Notes: ¹The risk assessment for acute exposures focused on the most sensitive life stage in humans, which is women and adults of reproductive age and fetus (i.e., pregnant user) due to concerns for developmental effects. ²E-FAST/CEM provided the 24-hr acute exposure estimate and the HECs were adjusted to 24-hrs. ³It is assumed no substantial buildup of 1-BP in the body between exposure events due to 1-BP's short biological half-life (<2 hours). ⁴EPA believes that the users of these products are generally adults or youth (11-20 yrs of age), but any age group may be a bystander living in the house where product was used. ⁵The risk assessment for acute exposures focused on developmental toxicity effects as the most sensitive health effect when compared to other potential acute effects (i.e., neurotoxicity). ⁶UFS=subchronic to chronic UF; UFA=interspecies UF; UFH=intraspecies UF; UFL=LOAEL to NOAEL UF	

Table 4-5. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Occupational Risks Following Chronic Exposures to 1-BP

Populations and Toxicological Approach	Occupational Use Scenarios of 1-BP
Population of Interest and Exposure Scenario	Workers: Adult male and female^{1,2} (>16 years old) who directly handle 1-BP as part of their job function (typically 260 days per year over lifetime working years, see the <i>1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment</i> (EPA, 2019g)). Occupational Non-user: Adult male and female^{1,2} (>16 years old) who do not directly handle 1-BP, but who are potentially exposed by being present in the surrounding work area of building (typically 260 days per year over lifetime working years, see the <i>1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment</i> (EPA, 2019g)).
Health Effects of Concern, Concentration and Time Duration	Non-Cancer Health Effects: 1. Non-cancer health effects for inhalation and dermal exposures: A range of possible chronic non-cancer adverse effects in liver, kidney, nervous system, reproductive system and developmental effects (including 2 modeling approaches for developmental effects) 2. Non-cancer hazard values or Point of Departures (PODs): The most sensitive POD (i.e., 8-hr and 24-hr HEC expressed in ppm; 24-hr dermal HED expressed as mg/kg-day) within each health endpoint domain. See Table 3-1. Cancer Health Effects: 1. Cancer health effects for inhalation and dermal exposures: Data for lung tumors (NTP, 2011a) in female mice was selected as the POD considered protective for the other tumor types. 2. Cancer Inhalation Unit Risk (IUR): See Table 3-5 and Table 3-6 for IUR values and dermal slope factors using model averaging and multistage modeling approaches; the IUR (40 hrs/wk and 24 hrs/day) and dermal cancer slope factor using the multistage modeling are used in the cancer risk estimate calculations.
Uncertainty Factors (UF) Used in Non-Cancer Margin of Exposure (MOE) calculations	Study- and endpoint-specific UFs. See Table 3-1.
Notes: ¹ Includes pregnant women and adults of reproductive age. ² The risk assessment for chronic exposures for developmental effects focused on the most sensitive life stage in humans, which are women and adults of reproductive age and fetus (i.e., pregnant worker). For other health effects (e.g., liver, kidney, etc.), healthy female or male workers were assumed to be the population of interest.	

EPA applied a composite UF of 100 for the acute and chronic inhalation benchmark MOE, based on the following considerations:

- An interspecies uncertainty/variability factor of 10 (UF_A) was applied for animal-to-human extrapolation. This uncertainty factor is comprised of two separate areas of uncertainty to account for differences in the toxicokinetics and toxicodynamics of animals and humans. In this assessment, a portion of the toxicokinetic uncertainty may be accounted for by the calculation of an HEC and application of a dosimetric adjustment factor as outlined in the

RfC methodology (U.S. EPA, 1994b); however, an UF_A of 10 is retained to account for additional toxicokinetic differences that remain unaccounted;

- 1-BP is irritating to the respiratory tract and rodents exhibit physiological responses (such as reflex bradypnea) that differ from humans and may alter uptake due to hyper- or hypoventilation, therefore, an UF_A of 10 is retained to account for pharmacokinetic differences (OECD 39);
- A default intraspecies uncertainty/variability factor (UF_H) of 10 was applied to account for variation in sensitivity within human populations due to limited information regarding the degree to which human variability (i.e., gender, age, health status, or genetic makeup) may impact the disposition of or response to, 1-BP;
- Interindividual variability in the expression and functional capacity of CYP2E1 has been observed (Neafsey et al., 2009) and genetic polymorphisms in CYP2E1 expression have been linked to altered disease susceptibility (Trafalis et al., 2010); and,
- A LOAEL-to-NOAEL uncertainty factor (UF_L) of 1 was applied because BMD modeling was used to derive the HEC.

A subchronic-to-chronic uncertainty factor (UF_s) was not applied because the key study used a chronic exposure protocol.

Although EPA's RfC guidance suggests that the 3-fold uncertainty factor for toxicokinetic differences may be eliminated based on higher partitioning in the rodent (i.e., blood/air partition coefficient of 11.7 in rats versus 7.1 in man), the available information is insufficient to determine whether critical metabolic pathways scale across species according to body weight. Because 1-BP is irritating to the respiratory tract and rodents exhibit physiological responses (such as reflex bradypnea) which may alter uptake due to hyper- or hypoventilation, the maximum uncertainty factor (i.e., UF_A of 10) was retained to account for pharmacokinetic differences between rodents and humans.

Acute and chronic MOEs (MOE_{acute} or $MOE_{chronic}$) were used in this evaluation to estimate non-cancer risks using Equation 4-1.

Equation 4-1. Equation to Calculate Non-Cancer Risks Following Acute or Chronic Exposures Using Margin of Exposures

$$MOE_{acute\ or\ chronic} = \frac{\text{Non – cancer Hazard value (POD)}}{\text{Human Exposure}}$$

Where:

MOE	= Margin of exposure (unitless)
Hazard value (POD)	= HEC (ppm)
Human Exposure	= Exposure estimate (in ppm) from occupational or consumer exposure assessment. ADCs were used for non-cancer chronic risks and acute concentrations were used for acute risks (see Section 2.3.1.18 through Section 2.3.1.18).

EPA used margin of exposures (MOEs)²⁷ to estimate acute or chronic risks for non-cancer based on the following:

- The highest quality HECs/dermal HEDs within each health effects domain reported in the literature;
- The endpoint/study-specific UFs applied to the HECs/dermal HEDs per EPA [Guidance \(U.S. EPA, 2002\)](#); and
- The exposure estimates calculated for 1-BP uses examined in this risk evaluation (see Section 2.3).

MOE estimates allow for the presentation of a range of risk estimates. The occupational exposure scenarios considered both acute and chronic inhalation and dermal exposures. All consumer uses considered only acute inhalation and dermal exposure scenarios. Different adverse endpoints were used based on the expected exposure durations. For non-cancer effects, risks for developmental effects were evaluated for acute (short-term) exposures, whereas risks for other adverse effects (toxicity to the liver, kidney, nervous system, developmental effects, and the reproductive system) were evaluated for repeated (chronic) exposures to 1-BP.

For occupational exposure calculations, the 8 hr TWA was used to calculate MOE estimates for acute and chronic exposures.

The total UF for each non-cancer POD was the benchmark MOE used to interpret the MOE risk estimates for each use scenario. The MOE estimate was interpreted as a potential human health concern if the MOE estimate was less than the benchmark MOE (i.e. the total UF). On the other hand, the MOE estimate indicated negligible concerns for adverse human health effects if the MOE estimate exceeded the benchmark MOE. Typically, the larger the MOE, the more unlikely it is that a non-cancer adverse effect would occur.

MOE estimates were calculated for all of the studies per health effects domain that EPA considered suitable for the risk evaluation of acute and chronic exposure scenarios in the work plan risk assessment for 1-BP.

Extra cancer risks for repeated exposures to 1-BP were estimated using Equation 2-1. Estimates of extra cancer risks should be interpreted as the incremental probability of an individual developing cancer over a lifetime as a result of exposure to the potential carcinogen (i.e., incremental or extra individual lifetime cancer risk).

Equation 4-2. Equation to Calculate Extra Cancer Risks

$$\text{Risk} = \text{Human Exposure} \times \text{IUR}$$

Where:

Risk	= Extra cancer risk (unitless)
Human exposure	= Exposure estimate (LADC in ppm) from occupational exposure assessment
IUR	= Inhalation unit risk (3×10^{-3} per ppm)

²⁷ Margin of Exposure (MOE) = (Non-cancer hazard value, POD) ÷ (Human Exposure). Equation 4-1. The benchmark MOE is used to interpret the MOEs and consists of the total UF shown in Table 3-1. See Section 3.2.10.1 for an explanation of the benchmark MOE.

4.2.2 Risk Characterization For Acute, Non-Cancer Inhalation Exposures

Non-cancer MOE estimates for acute inhalation and dermal exposures to 1-BP were derived for both occupational scenarios and consumer scenarios. Cancer risk estimates for acute inhalation exposures to 1-BP were not derived for occupational or consumer scenarios because the published methodology for extrapolating cancer risks from chronic to short-term exposures to mutagenic carcinogens caveat that extrapolation of lifetime theoretical extra cancer risks to single exposures has great uncertainty ([NRC, 2001](#)).

The risk assessment for acute inhalation and dermal exposures used developmental toxicity data to evaluate the risks following acute exposures with the TSCA condition of use scenarios identified for 1-BP under the scope of this evaluation. EPA based its acute risk assessment on developmental toxicity (i.e., decreased live litter size, and increases in post-implantation loss), the most sensitive HEC/dermal HED identified for an acute exposure duration ([WIL Research, 2001](#)), which is representative of potentially exposed or susceptible subpopulation (i.e., adults of reproductive age and their offspring). For acute exposure scenarios, EPA did not assess risks to children who may be present in the workplace (e.g., dry cleaners) due to the uncertainties in extrapolating these specific developmental effects for this lifestage. See Section 3.2.10.5 for additional discussion..

The risk assessment for acute exposures used the hazard value from the ([WIL Research, 2001](#)) two-generation reproductive toxicity study to evaluate risks for each occupational and consumer exposure scenario.

Non-cancer MOE estimates for acute occupational exposure scenarios are presented in Table 4-6 through Table 4-25. Non-cancer MOE estimates for acute consumer exposure scenarios are presented in Table 4-26. MOE estimates (HEC in ppm/exposure estimate in ppm; dermal HED exposure estimate in mg/kg-day) lower than the Benchmark MOE (Total UF) indicate potential health risks and are highlighted in red. Where the sample size of the underlying exposure data is sufficiently large to calculate statistics, the central tendency estimate is based on the 50th percentile exposure level of the dataset, while the high-end estimate is based on the 95th percentile exposure. See Section 2.3.1.2 for detailed descriptions of central tendency and high-end estimates.

For occupational scenarios, EPA evaluated the impact of potential respirator use based on respirator APF of 10, 25, and 50. The calculated MOE with respirator use is then compared to the benchmark MOE to determine the level of APF required to mitigate risk for all health domains. The MOE estimates for these respirator scenarios assume workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity where there is potential exposure to 1-BP. For some occupational conditions of use, respirators with an APF of 50 do not reduce worker exposure to levels where the calculated MOE is greater than the benchmark MOE. EPA does not evaluate respirator use for occupational non-users because they do not directly handle 1-BP and are unlikely to wear respirators. In addition, EPA believes small commercial facilities performing dry cleaning and spot cleaning are unlikely to have a respiratory protection program.

Non-cancer MOE estimates for acute consumer inhalation exposure scenarios are presented in Table 4-26. MOE estimates (HEC in ppm/exposure estimate in ppm; dermal HED exposure estimate in mg/kg-day) lower than the Benchmark MOE (Total UF) indicate potential health risks and are highlighted in red.

Use: Manufacturing, Import, Repackaging, Processing as a Reactant, and Processing – Incorporation into Articles and Formulation Based on Monitoring Data and Modeling

MOE estimates for manufacturing, import, repackaging, processing as a reactant, and processing and incorporation into articles for workers, for both monitoring data and modeling, and with and without the use of an APF, are presented in Table 4-6, Table 4-7, and Table 4-8. In some instances, data was either not available or not applicable for occupational non-users.

Table 4-6. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Manufacture Based on Monitoring Data (U.S.)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	344	N/A	3,444	100
		High-end	115	N/A	1,148	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	189	N/A	1,889	100
		High-end	63	N/A	630	

Note: Exposure monitoring was not performed for ONUs at this manufacturing facility. Based on the process and work activity description, exposure to ONU is expected to be negligible.

MOE estimates for manufacturing using monitoring data are presented in Table 4-6. MOE estimates were above the benchmark MOE by 1-2 orders of magnitude for all worker scenarios without an APF, with one exception. This exception included a scenario where the MOE estimate was below the benchmark MOE for workers for high-end exposure estimates when using the NCTR modeling approach. In contrast, when an APF was applied in worker scenarios, the MOE estimates were above the benchmark MOE by several orders of magnitude.

Table 4-7. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Import, Repackaging, Processing as a Reactant, and Processing – Incorporation into Articles Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	2,709	N/A	100
		High-end	515	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	1,486	N/A	100
		High-end	283	N/A	

N/A – Not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

MOE estimates for import, repackaging, or processing using modeling are presented in Table 4-7. APFs were not applied. MOE estimates were above the benchmark MOE by several orders of magnitude.

Table 4-8. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Processing – Incorporation into Formulation Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	8	95	409	100
		High-end	2	19	82	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	4	52	224	100
		High-end	1	11	45	

MOE estimates for incorporation into formulation based on monitoring data are presented in Table 4-8. MOE estimates for workers were below the benchmark MOE by 1-2 orders of magnitude without the use of an APF. In this same scenario, MOE estimates for occupational non-users were slightly increased but still under the benchmark MOE by 1-2 orders of magnitude for central tendency and high-end exposure levels. When an APF was applied, MOE estimates were above the benchmark MOE by several orders of magnitude in workers for central tendency exposure levels, but below the benchmark MOE by several orders of magnitude for high-end exposure levels.

Use: Batch Vapor Degreaser (Open-Top) Based on Monitoring Data and Modeling (Pre-EC)

MOE estimates for batch vapor degreaser (open top) based on monitoring data and modeling are presented in Table 4-9 and Table 4-10, respectively.

Table 4-9. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	5	1,550	231	100
		High-end	1	14	31	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	3	850	127	100
		High-end	0.3	8	17	

When monitoring data was used (Table 4-9), MOE estimates were below the benchmark MOE for workers (central tendency and high-end exposure levels) and occupational non-users (central tendency exposure levels) by 1-2 orders of magnitude without the use of an APF, with two exceptions. These exceptions include occupational non-users for central tendency exposure estimates. When an APF was applied, MOE estimates for workers were above the benchmark MOE by 1-2 orders of magnitude for central tendency exposure levels, but below the benchmark MOE by 1-2 orders of magnitude for high-end exposure levels.

Table 4-10. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Modeling (Pre-EC)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	16	31	820	100
		High-end	1	2	65	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	9	17	450	100
		High-end	1	1	36	

When modeling was used (Table 4-10), MOE estimates were below the benchmark MOE by several orders of magnitude for both workers and occupational non-users without the use of an APF. When an APF was applied, MOE estimates were above the benchmark MOE by several orders of magnitude for workers for central tendency exposure levels, but below the benchmark MOE by 1-2 orders of magnitude for high-end exposure levels.

Use: Batch Vapor Degreaser (Open-Top) Based on Modeling (Post-EC)

MOE estimates for batch vapor degreaser (open-top) based modeling (post-EC) are presented in Table 4-11.

Table 4-11. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Modeling (Post-EC)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=25	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	164	312	4,099	100
		High-end	13	23	324	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	90	171	2,248	100
		High-end	7	13	178	

When an APF was not applied, MOE estimates were below the benchmark MOE by 1-2 orders of magnitude for high-end exposure estimates (for workers and occupational non-users alike), and for the central tendency estimates for workers. In this same scenario, MOE estimates were above the benchmark MOE for workers and occupational non-users (central tendency exposure estimates), and for occupational non-users (central tendency exposure estimates; acute HEC derived using the NCTR modeling approach). When an APF was applied, MOE estimates were below the benchmark MOE by several orders of magnitude for workers.

Use: Batch Vapor Degreaser (Closed-Loop) Based on Modeling

MOE estimates for batch vapor degreaser (closed-loop) based on modeling are presented in Table 4-12.

Table 4-12. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Closed-Loop) Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	820	1,561	8,199	100
		High-end	65	115	648	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	450	856	4,496	100
		High-end	36	63	355	

MOE estimates were above the benchmark MOE by several orders of magnitude for both workers and occupational non-users for central tendency and high-end exposure estimates in all cases with or without the use of an APF, with few exceptions. These exceptions included scenarios in which an APF was not applied, and in scenarios for high-end exposure estimates only (acute HEC using the BMD modeling approach for workers: and acute HEC using the NCTR modeling approach for workers and occupational non-users).

Use: Cold Cleaner Based on Monitoring Data and Modeling

MOE estimates for cold cleaner based on monitoring data and monitoring are presented in Table 4-13 and Table 4-14, respectively.

Table 4-13. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	7	12	360	100
		High-end	4	12	209	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	4	7	198	100
		High-end	2	7	115	

MOE estimates for cold cleaner based on monitoring data are presented in Table 4-13. When an APF was not applied, MOE estimates were below the benchmark MOE by 1-2 orders of magnitude for both workers and occupational non-users for all exposure estimates. When an APF was applied, MOE estimates were above the benchmark MOE by several orders of magnitude for workers for all exposure estimates

Table 4-14. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	56	107	2,822	100
		High-end	3	5	130	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	31	59	1,548	100
		High-end	1	2	71	

MOE estimates for cold cleaner based on modeling are presented in Table 4-14. Similar findings were noted when compared to monitoring data. When an APF was not applied, MOE estimates were below the benchmark MOE by 1-2 orders of magnitude for both workers and occupational non-users for all exposure estimates, with one exception. This exception was for occupational non-users for central tendency exposure estimates for the HEC using the BMD modeling approach. When an APF was applied, MOE estimates were above the benchmark MOE by several orders of magnitude for workers for all exposure estimates, except for high-end exposure estimates for the HEC using the NCTR modeling approach where it was below the benchmark MOE by 1-2 orders of magnitude.

Use: Aerosol Spray Degreaser Based on Monitoring Data (Pre-, and Post-EC); and Modeling

MOE estimates for aerosol spray degreaser based on monitoring data (for pre-EC and post-EC) and modeling are presented in Table 4-15, Table 4-16, and Table 4-17. Data for occupational non-users were not available in some instances.

Table 4-15. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Monitoring Data (Pre-EC)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	2	No data	97	100
		High-end	1	No data	49	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	1	No data	53	100
		High-end	1	No data	27	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

MOE estimates for aerosol spray degreaser based on monitoring data for pre-EC scenarios is presented in Table 4-15. MOE estimates in workers were below the benchmark MOE by several orders of magnitude without the application of an APF. When an APF was applied, MOE estimates in workers were closer to, but still below the benchmark MOE.

Table 4-16. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Monitoring Data (Post-EC)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	N/A (Single data point)	6	No data	282	100
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17		3	No data	155	100

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

MOE estimates for aerosol spray degreaser based on monitoring data for post-EC scenarios is presented in Table 4-16. MOE estimates in workers were below the benchmark MOE by several orders of magnitude without the use of an APF. When an APF was applied, MOE estimates in workers were above the benchmark MOE by 1-2 orders of magnitude.

Table 4-17. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	5	282	243	100
		High-end	1	33	69	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	3	155	133	100
		High-end	1	18	38	

MOE estimates for aerosol spray degreaser based on modeling is presented in Table 4-17. As with monitoring data (pre-, and post-EC), similar findings were noted when modeling was used. MOE estimates were below the benchmark MOE by several orders of magnitude for workers and occupational non-users when an APF was not applied, with two exceptions. These exceptions included occupational non-users for central tendency exposure estimates where the MOE estimate was above the benchmark MOE by 1-2 orders of magnitude. When an APF was applied, MOE estimates in workers were above the benchmark MOE by 1-2 orders of magnitude for central tendency exposure levels, but below the benchmark MOE by 1-2 orders of magnitude for high-end exposure levels.

Use: Dry Cleaning Based on Monitoring Data and Modeling (3rd and 4th Generation Machines)

MOE estimates for dry cleaning based on monitoring data and modeling (3rd and 4th generation machines) are presented in Table 4-18, Table 4-19, and Table 4-20. An APF was not applied in any scenario.

Table 4-18. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	1	3	100
		High-end	1	2	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	1	1	100
		High-end	0.3	1	

Table 4-19. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (3rd Generation Machine)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	7	1	11	100
	High-end	3	0.3	3	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	Central tendency	4	1	6	100
	High-end	1	0.2	2	

Study: ([WIL Research, 2001](#))

Note: Based on acute HEC of 10 ppm and 5.7 ppm.

Table 4-20. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (4th Generation Machine)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	8	8	15	100
	High-end	4	3	5	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	Central tendency	5	5	9	100
	High-end	2	2	3	

Study: ([WIL Research, 2001](#))

Note: Based on acute HEC of 10 ppm and 5.7 ppm.

MOE estimates between monitoring data and modeling were similar. In all cases, the MOE estimates were below the benchmark MOE by several orders of magnitude for both central tendency and high-end exposures for workers and occupational non-users alike.

Use: Spot Cleaner Based on Monitoring Data and Modeling

MOE estimates using monitoring data and modeling for spot cleaner are presented in Table 4-21 and Table 4-22. Data for occupational non-users was not available for monitoring data. An APF was not applied in any scenario.

Table 4-21. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	34	No data	100
		High-end	7	No data	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	19	No data	100
		High-end	4	No data	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

Table 4-22. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	10	19	100
		High-end	4	7	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	5	10	100
		High-end	2	4	

MOE estimates between monitoring data and modeling for workers were similar. MOE estimates were below the benchmark MOE by several orders of magnitude for both central tendency and high-end exposure levels for workers based on monitoring data, and for workers and occupational non-users based on modeling.

Use: Adhesive Chemicals (Spray Adhesive) Based on Monitoring Data (Pre-, and Post-EC)

MOE estimates using pre-and post-EC monitoring data for adhesive chemicals (spray adhesive) are presented in Table 4-23 and Table 4-24. MOE estimates are presented for worker (sprayer and non-sprayer) and for occupational non-users.

Table 4-23. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesive) Based on Monitoring Data (Pre-EC)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	0.2	0.2	10	12	12	100
	High-end	0.1	0.1	0.2	6	7	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	Central tendency	0.1	0.1	6	6	7	100
	High-end	0.1	0.1	0.1	3	4	

Note: Based on acute HEC of 31 ppm and 17 ppm.

Table 4-24. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesive) Based on Monitoring Data (Post-EC)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	2	2	16	87	86	100
	High-end	1	1	6	37	54	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	Central tendency	1	1	9	48	47	100
	High-end	0.4	1	3	20	29	

Note: Based on acute HEC of 31 ppm and 17 ppm.

MOE estimates between pre- and post-EC monitoring data were similar. MOE estimates were below the benchmark MOE by several orders of magnitude in worker and occupational non-user scenarios when an APF was not applied. When an APF was applied, MOE estimates were below the benchmark MOE by several orders of magnitude for workers in pre-EC conditions, and below but closer to the benchmark MOE in post-EC conditions.

Use: Disposal Based on Modeling

MOE estimates using modeling for disposal are presented in Table 4-25. Occupational non-users were not applicable to this scenario. APFs were not applied.

Table 4-25. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Disposal Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	2,709	N/A	100
		High-end	515	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	17	Central tendency	1,486	N/A	100
		High-end	283	N/A	

N/A – not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

MOE estimates were above the benchmark MOE by several orders of magnitude for all worker exposure scenarios evaluated.

Consumer Conditions of Use Based on Modeling

MOE estimates for the consumer conditions of use based on modeling (high, moderate, and low intensity use scenarios) are presented in Table 4-26. A brief discussion of the approach and the risk calculations spreadsheet is provided in the 1-BP Supplemental File Consumer Exposure Risk Calculations ([EPA, 2019c](#)).

Table 4-26. Non-Cancer Risk Estimates for Acute 24-hr Inhalation Exposure Following Consumer Uses of 1-BP (Benchmark MOE = 100) Based on Modeling

Condition of Use	Scenario Description	Acute Non-Cancer MOE (24-Hour TWA)			
		Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)		Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001)	
		User	Bystander	User	Bystander
Adhesive Accelerant	High Intensity Use	0.5	2	0.3	1
	Moderate Intensity Use	9	47	5	28
	Low Intensity Use	74	393	45	236
General Spray Cleaner	High Intensity Use	0.1	0.3	0.1	0.2
	Moderate Intensity Use	0.7	4	0.4	2
	Low Intensity Use	4	23	3	14
Spot Cleaner/ Stain Remover	High Intensity Use	0.2	1	0.1	0.6
	Moderate Intensity Use	3	15	2	9
	Low Intensity Use	37	173	22	104
Mold Cleaning/ Release	High Intensity Use	0.5	2	0.3	2
	Moderate Intensity Use	7	37	4	22
	Low Intensity Use	81	379	49	228

Condition of Use	Scenario Description	Acute Non-Cancer MOE (24-Hour TWA)			
		Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)		Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001)	
		User	Bystander	User	Bystander
General Cleaner/ Degreaser	High Intensity Use	0.1	0.2	0.1	0.2
	Moderate Intensity Use	0.5	2	0.3	1
	Low Intensity Use	10	40	6	24
Degreaser- Electronics	High Intensity Use	0.4	1	0.2	0.7
	Moderate Intensity Use	7	29	4	17
	Low Intensity Use	150	526	90	315
Coin Cleaner	High Intensity Use	6	34	4	21
	Moderate Intensity Use	3	16	2	10
	Low Intensity Use	1	7	0.7	5
Automobile AC Flush	High Intensity Use	21	100	13	61
	Moderate Intensity Use	6	32	4	19
	Low Intensity Use	3	15	2	9
Insulation	Living Area	N/A	3000	N/A	1800
	Attic	N/A	562	N/A	337
	Crawlspace	N/A	462	N/A	277
Overall	Maximum	150	526	90	315
	Minimum	0.1	0.3	0.1	0.2

Note: Acute HEC = 6 ppm (decreased live litter size) and 10 ppm (post-implantation loss).

MOE estimates were below the benchmark MOE by 1-2 orders of magnitude for both the user and bystander for all consumer uses with a few exceptions. These exceptions included insulation conditions of use, and low intensity use for some conditions of use where, in those instances, the MOE estimate was above the benchmark MOE by several orders of magnitude.

MOE estimates for chronic exposures were not derived for consumer scenarios since these were not considered chronic in nature.

4.2.2.1 Non-Cancer MOEs for Chronic Occupational Exposure Scenarios

EPA estimated the non-cancer MOE estimates associated with chronic exposures following 1-BP conditions of use in the workplace. Since 1-BP exposure may be associated with a variety of non-cancer health effects, this assessment estimated MOEs for liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity and neurotoxicity following chronic inhalation exposures. EPA used the HEC specific to each health effect domain for calculating MOE estimates. Table 4-27 through Table 4-46 present the non-cancer risks for chronic occupational scenarios. MOE estimates for a range of health effects were calculated (See the Supplemental File: Occupational Risk Calculator ([EPA, 2019h](#))). Where the sample size of the underlying exposure data is sufficiently large to calculate statistics, the central tendency estimate is based on the 50th

percentile exposure level of the dataset, while the high-end estimate is based on the 95th percentile exposure. See Section 2.3.1.2 for detailed descriptions of central tendency and high-end estimates. These tables also evaluate the impact of potential respirator use and present the respirator that would be needed (based on respirator APF of 10, 25, and 50) to mitigate risk for all health domain. The MOE estimates for these respirator scenarios assume workers wear respirators for the entire duration of the work activity throughout their career (e.g. typically 260 days per year and over 31 years per lifetime for many occupational scenarios). Because respirators are uncomfortable, interfere with communication, limit vision, and make it hard to breathe, and the onus is on the worker to don and doff them correctly, the use of respirators on a continuous, long-term basis may not be practical. EPA does not evaluate respirator use for occupational non-users because they do not directly handle 1-BP and are unlikely to wear respirators. In addition, EPA believes small commercial facilities performing dry cleaning and spot cleaning are unlikely to have a respiratory protection program.

Use: Manufacturing, Import, Repackaging, Processing as a Reactant, and Processing – Incorporation into Articles and Formulation Based on Monitoring Data and Modeling

MOE estimates for chronic occupational exposure scenarios following the use of 1-BP in manufacturing, import, repackaging, processing as a reactant, and processing and incorporation into articles for workers, for both monitoring data and modeling, and with and without the use of an APF, are presented in Table 4-27, Table 4-28, and Table 4-29. Data for occupational non-users was either not available or not applicable in some scenarios.

Table 4-27. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Manufacture (U.S.) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	1,667	N/A	16,667	100
		High-end	556	N/A	5,556	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	1,556	N/A	15,556	100
		High-end	519	N/A	5,185	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	589	N/A	5,889	100
		High-end	196	N/A	1,963	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	478	N/A	4,778	100
		High-end	159	N/A	1,593	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	267	N/A	2,667	100
		High-end	89	N/A	889	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	278	N/A	2,778	100
		High-end	93	N/A	926	

Notes: ¹MOEs (HEC in ppm/exposure estimate in ppm) lower than the Benchmark MOE (Total UF) indicate potential health risks and are denoted in bold.

Exposure monitoring was not performed for ONUs at this manufacturing facility. Based on the process and work activity description, exposure to ONU is expected to be negligible.

MOE estimates for manufacturing based on monitoring data are presented in Table 4-27. MOE estimates in workers were above the benchmark MOE by several orders of magnitude in all cases, including with and without the application of an APF, with few exceptions. These exceptions included scenarios without the use of an APF for workers for high-end exposure estimates for either the developmental toxicity HEC using the NCTR modeling approach, or the nervous system HEC. In these scenarios, the MOE estimate was slightly below the benchmark MOE.

Table 4-28. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Import, Processing as a Reactant, and Processing – Incorporation into Articles Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	13,110	N/A	100
		High-end	2,494	N/A	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	12,236	N/A	100
		High-end	2,328	N/A	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	4,632	N/A	100
		High-end	881	N/A	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	3,758	N/A	100
		High-end	715	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	2,098	N/A	100
		High-end	399	N/A	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	2,185	N/A	100
		High-end	416	N/A	

N/A – Not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

MOE estimates in workers for import and processing based on modeling are presented in Table 4-28. MOE estimates were above the benchmark MOE by several orders of magnitude in all scenarios for both central tendency and high-end exposure levels.

Table 4-29. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Processing – Incorporation into Formulation Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	40	462	1,979	100
		High-end	8	94	397	

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	37	431	1,847	100
		High-end	7	88	370	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	14	163	699	100
		High-end	3	33	140	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	11	132	567	100
		High-end	2	27	114	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	6	74	317	100
		High-end	1	15	63	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	7	77	330	100
		High-end	1	16	66	

MOE estimates for incorporation into formulation based on monitoring data are presented in Table 4-29. MOE estimates were below the benchmark MOE by 1-2 orders of magnitude for both workers and occupational non-users without the use of an APF in most cases, with the exception of central tendency exposure levels for the occupational non-user for the liver, kidney, reproductive system, and developmental (using BMD modeling) health effect endpoints, where the MOE estimates were above the benchmark MOE by 1-2 orders of magnitude. When an APF was applied, MOE estimates in workers were above the benchmark MOE by several orders of magnitude in all worker scenarios, with the exception of high-end exposures estimates for the developmental (using the NCTR modeling approach) and nervous system health effect endpoints, where the MOE estimates were below the benchmark MOE by 1-2 orders of magnitude.

Use: Batch Vapor Degreaser (Open-Top) Based on Monitoring Data

MOE estimates for batch vapor degreasing (open-top) based on monitoring data are presented in Table 4-30.

Table 4-30. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	22	7,500	1,119	100
		High-end	3	70	152	

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	21	7,000	1,045	100
		High-end	3	65	142	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	8	2,650	396	100
		High-end	1	25	54	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	6	2,150	321	100
		High-end	1	20	44	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	4	1,200	179	100
		High-end	0.5	11	24	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	4	1,250	187	100
		High-end	1	12	25	

When an APF was not applied, MOE estimates for workers were below the benchmark MOE by several orders of magnitude in all cases; MOE estimates for occupational non-users were below the benchmark MOE by 1-2 orders of magnitude for high-end exposure estimates, but above the benchmark MOE by several orders of magnitude for central tendency exposure estimates. When an APF was applied, MOE estimates in workers were above the benchmark MOE by several orders of magnitude for both exposure levels for the liver and kidney health effect endpoints; for central tendency exposure levels for the reproductive system, developmental (both modeling approaches), and for the nervous system health effect endpoints. When an APF was applied, MOE estimates in workers were below the benchmark MOE for high-end exposure levels for the reproductive system, developmental (both modeling approaches), and nervous system health effect endpoints by 1-2 orders of magnitude.

Use: Batch Vapor Degreaser (Open-Top) Based on Modeling (Pre-, and Post-EC)

MOE estimates for batch vapor degreasing (open-top) based on modeling (pre-, and post-EC) are presented in Table 4-31 and Table 4-32.

Table 4-31. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) (Pre-EC) Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	79	151	3,967	100
		High-end	6	11	314	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	74	141	3,703	100
		High-end	6	10	293	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	28	53	1,402	100
		High-end	2	4	111	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	23	43	1,137	100
		High-end	2	3	90	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	13	24	635	100
		High-end	1	2	50	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	13	25	661	100
		High-end	1	2	52	

MOE estimates for batch vapor degreasing (open-top) based on modeling (pre-EC) are presented in Table 4-31. MOE estimates for both workers and occupational non-users were below the benchmark MOE by 1-2 orders of magnitude in workers and occupational non-users when an APF was not applied, with two exceptions. These exceptions included central tendency exposure estimates for occupational non-users for liver and kidney health effect endpoints, where the MOE estimates were slightly above the benchmark MOE. When an APF was applied, MOE estimates in workers were above the benchmark MOE by several orders of magnitude, in most cases, for central tendency and high-end exposure levels, with few exceptions. These exceptions included high-end exposure levels for developmental (both modeling approaches) and nervous system health effect endpoints where the MOE estimates were slightly or 1-2 orders of magnitude below the benchmark MOE.

Table 4-32. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) (Post-EC) Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	793	1,510	7,934	100
		High-end	63	111	627	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	741	1,410	7,405	100
		High-end	59	104	585	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	280	534	2,803	100
		High-end	22	39	222	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	227	433	2,274	100
		High-end	18	32	180	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	127	242	1,269	100
		High-end	10	18	100	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	132	252	1,322	100
		High-end	10	19	105	

MOE estimates for batch vapor degreasing (open-top) based on modeling (post-EC) are presented in Table 4-32. In contrast to MOE estimates based on pre-EC in workers and occupational non-users when an APF was not applied in Table 4-31 above, MOE estimates for post-EC were, in some cases, above the benchmark MOE by 1-2 orders of magnitude. This was seen in workers for central tendency (but not high-end) exposure levels for liver, kidney, and developmental (both modeling approaches) health effect endpoints. MOE estimates in workers without the use of an APF for high-end exposure levels were below the benchmark MOE by 1-2 orders of magnitude for all health effect endpoints. A similar pattern was noted for occupational non-users. When an APF was applied, MOE estimates in workers were above the benchmark MOE by several orders of magnitude in most cases, with the exception of high-end exposures for developmental (NCTR modeling approach) and nervous system health effect endpoints, where the MOE was at or slightly above the benchmark MOE.

Use: Batch Vapor Degreaser (Closed-Loop) Based on Modeling

MOE estimates for batch vapor degreaser (closed-loop) based on modeling are presented in Table 4-33.

Table 4-33. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Closed-Loop) Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	3,967	7,551	39,671	100
		High-end	314	555	3,135	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	3,703	7,048	37,026	100
		High-end	293	518	2,926	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	1,402	2,668	14,017	100
		High-end	111	196	1,108	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	1,137	2,165	11,372	100
		High-end	90	159	899	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	635	1,208	6,347	100
		High-end	50	89	502	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	661	1,259	6,612	100
		High-end	52	93	523	

MOE estimates were above the benchmark MOE by several orders of magnitude in workers and occupational non-users for both central tendency and high-end exposure estimates for all health effect endpoints whether or not an APF was applied, with few exceptions. These exceptions included high-end exposure estimates for workers (without the use of an APF) for the developmental (using both modeling approaches) and nervous system health effect endpoints. MOE estimates for occupational non-users in these excepted scenarios were also below the benchmark MOE for high-end exposure estimates for developmental (NCTR modeling approach) and nervous system health effect endpoints.

Use: Cold Cleaner Based on Monitoring Data and Modeling

MOE estimates for cold cleaner based on monitoring data and modeling are presented in Table 4-34 and Table 4-35.

Table 4-34. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	35	58	1,744	100
		High-end	20	58	1,014	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	33	54	1,628	100
		High-end	19	54	946	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	12	20	616	100
		High-end	7	20	358	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	10	17	500	100
		High-end	6	17	291	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	6	9	279	100
		High-end	3	9	162	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	6	10	291	100
		High-end	3	10	169	

MOE estimates for cold cleaner based on monitoring data are presented in Table 4-34. When an APF was not applied, MOE estimates were below the benchmark MOE by 1-2 orders of magnitude for all health effect endpoints in workers and occupational non-users for both central tendency and high-end exposure levels. When an APF was applied, MOE estimates for workers and occupational non-users were above the benchmark MOE by several orders of magnitude in most cases.

Table 4-35. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	273	519	13,657	100
		High-end	13	22	630	

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	255	484	12,746	100
		High-end	12	20	588	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	97	183	4,825	100
		High-end	4	8	223	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	78	149	3,915	100
		High-end	4	6	181	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	44	83	2,185	100
		High-end	2	4	101	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	46	86	2,276	100
		High-end	2	4	105	

MOE estimates for cold cleaner based on modeling are presented in Table 4-35. The pattern of MOE estimates were similar to those with monitoring data, with a few exceptions. These exceptions included central tendency MOE estimates that were above the benchmark MOE in workers for liver and kidney health effect endpoints; and in the occupational non-user for liver, kidney, reproductive and developmental health effect endpoints.

Use: Aerosol Spray Degreaser/Cleaner Based on Monitoring Data (Pre- and Post-EC)

MOE estimates for aerosol spray degreaser/cleaner based on monitoring data (pre- and post-EC) are presented in Table 4-36 and Table 4-37. Data for occupational non-users was not available. Exposure levels for post-EC monitoring data were based on a single data point.

Table 4-36. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner (Pre-EC) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	9	No data	467	100
		High-end	5	No data	238	

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	9	No data	436	100
		High-end	4	No data	222	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	3	No data	165	100
		High-end	2	No data	84	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	3	No data	134	100
		High-end	1	No data	68	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	1	No data	75	100
		High-end	1	No data	38	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	2	No data	78	100
		High-end	1	No data	40	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

MOE estimates for aerosol spray degreaser/cleaner based on pre-EC monitoring data are presented in Table 4-36. When an APF was not applied, MOE estimates for workers were below the benchmark MOE by 1-2 orders of magnitude for all health effect endpoints for all exposure levels (central tendency or high-end). When an APF was applied, MOE estimates for workers were above the benchmark MOE by 1-2 orders of magnitude for liver, kidney, reproductive (central tendency exposure levels only), and developmental (BMD modeling; central tendency exposure levels); and below the benchmark MOE by 1-2 orders of magnitude for developmental (BMD modeling; high-end exposure levels), and developmental (NCTR modeling approach) and nervous system health effect endpoints for both central tendency and high-end exposure levels.

Table 4-37. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner (Post-EC) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=25	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	N/A (single data point)	27	No data	682	100
				No data		
Kidney Increased pelvic mineralization (WIL Research, 2001)	140		25	No data	636	100
				No data		
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53		10	No data	241	100
				No data		
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43		8	No data	195	100
				No data		
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24		4	No data	109	100
				No data		
Nervous System Decreased traction time (Honma et al., 2003)	25		5	No data	114	100
				No data		

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

MOE estimates for aerosol spray degreaser/cleaner based on post-EC monitoring data are presented in Table 4-37. The pattern of MOE estimates for workers were similar to those based on pre-EC monitoring data. When an APF was not applied, MOE estimates for workers were below the benchmark MOE by 1-2 orders of magnitude for all health effect endpoints for the single data point exposure level. In contrast to Table 4-40 above when MOE estimates in workers were based on pre-EC monitoring data and when an APF was used, MOE estimates for workers based in post-EC monitoring data were above the benchmark MOE by 1-2 orders of magnitude for all health effect endpoints.

Use: Aerosol Spray Degreaser/Cleaner Based on Modeling

MOE estimates for aerosol spray degreaser/cleaner based on modeling are presented in Table 4-38.

Table 4-38. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	24	1,364	1,177	100
		High-end	7	161	333	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	22	1,273	1,099	100
		High-end	6	151	311	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	8	482	416	100
		High-end	2	57	118	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	7	391	338	100
		High-end	2	46	95	
Developmental Effects Post-Implantation Loss (F0) (WIL Research, 2001); NCTR Model	24	Central tendency	4	218	188	100
		High-end	1	26	53	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	4	227	196	100
		High-end	1	27	55	

When an APF was not applied, MOE estimates for workers were below the benchmark MOE for both central tendency and high-end exposure levels for all health effect endpoints by 1-2 orders of magnitude. MOE estimates for occupational non-users were above the benchmark MOE by several orders of magnitude for liver and kidney (central tendency and high-end exposure levels), and reproductive, developmental, and nervous system (central tendency exposure levels) health effect endpoints. When an APF was applied, MOE estimates for workers for both central tendency and high-end exposure levels were above the benchmark MOE by several orders of magnitude for liver, kidney, reproductive (central tendency and high-end exposure levels) health effect endpoints; and developmental (both modeling approaches; central tendency only), and nervous system (central tendency exposure levels only) health effect endpoints. MOE estimates in workers were below (in some instances close to) the benchmark MOE when an APF was applied for developmental (both modeling approaches; high-end exposure levels only) and nervous system (high-end exposure levels only) health effect endpoints.

Use: Adhesive Chemicals (Spray Adhesives) Based on Monitoring data (Pre- and Post-EC)

MOE estimates for adhesive chemicals (spray adhesives) based on monitoring data (pre- and post-EC) are presented in Table 4-39 and Table 4-40.

Table 4-39. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesives) (Pre-EC) Based on Monitoring Data

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	1	1	50	56	59	100
	High-end	0.6	0.7	1.2	30	36	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	1	1	47	53	55	100
	High-end	0.6	0.7	1	28	33	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	0.4	0.4	18	20	21	100
	High-end	0.2	0.3	0.4	10	13	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	0.3	0.3	14	16	17	100
	High-end	0.2	0.2	0.3	8	10	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NCTR Model	Central tendency	0.2	0.2	8	9	9	100
	High-end	0.1	0.1	0.2	5	6	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	0.2	0.2	8	9	10	100
	High-end	0.1	0.1	0.2	5	6	

Note: Based on HEC values of 150 ppm, 140 ppm, 53 ppm, 43 ppm, 24 ppm, and 25 ppm.

MOE estimates for adhesive chemicals (spray adhesives) based on pre-EC monitoring data are presented in Table 4-39. MOE estimates in workers and occupational non-users were below the benchmark MOE by 1-2, and sometimes several orders of magnitude, for all health effect endpoints, for both central tendency and high-end exposure levels, whether or not an APF was applied.

Table 4-40. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesives) (Post-EC) Based on Monitoring Data

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	8	8	75	421	417	100
	High-end	4	5	27	179	260	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	8	8	70	393	389	100
	High-end	3	5	26	167	243	
Reproductive System Decreased seminal vesicle	Central tendency	3	3	27	149	147	100

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
weight (Ichihara et al., 2000b)	High-end	1	2	10	63	92	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	2	2	22	121	119	100
	High-end	1	1	8	51	75	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NCTR Model	Central tendency	1	1	12	67	67	100
	High-end	1	1	4	29	42	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	1	1	13	70	69	100
	High-end	1	1	5	30	43	

Note: Based on HEC values of 150 ppm, 140 ppm, 53 ppm, 43 ppm, 24 ppm, and 25 ppm.

MOE estimates for adhesive chemicals (spray adhesives) based on post-EC monitoring data are presented in Table 4-40. When an APF was not applied, a similar pattern of MOE estimates was observed for workers (sprayer, non-sprayer, and occupational non-users alike) as with the pre-EC monitoring data scenario (Table 4-39). However, unlike in the pre-EC monitoring data scenario, when an APF was applied in the post-EC monitoring data scenario for the worker (sprayer and non-sprayer), some MOE estimates were increased above the benchmark for some health effect endpoints (liver and kidney for both central tendency and high-end exposure levels), reproductive system (central tendency exposure levels only), and developmental (BMD modeling; central tendency exposure levels only). Under these conditions and for all other scenarios, while the MOE estimates were higher than in the pre-EC scenario, they still remained below the benchmark MOE.

Use: Dry Cleaning Based on Monitoring Data

MOE estimates for dry cleaning based on monitoring data are presented in Table 4-41. APFs were not applied in this scenario.

Table 4-41. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	5	12	100
		High-end	3	7	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	5	12	100
		High-end	3	7	

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	2	4	100
		High-end	1	3	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	1	4	100
		High-end	1	2	
Developmental Effects Post-Implantation Loss (F0) (WIL Research, 2001); NCTR Model	24	Central tendency	1	2	100
		High-end	0.5	1	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	1	2	100
		High-end	0.5	1	

MOE estimates were below the benchmark MOE for the worker and occupational non-user for both central tendency and high-end exposure estimates by 1-2 orders of magnitude for all health effect endpoints.

Use: Dry Cleaning Based on Modeling (3rd and 4th Generation)

MOE estimates for dry cleaning based on modeling (3rd and 4th generation) are presented in Table 4-42 and Table 4-43. APFs were not applied.

Table 4-42. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (3rd Generation)

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	35	7	56	100
	High-end	13	2	15	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	33	7	53	100
	High-end	12	2	14	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	13	3	20	100
	High-end	5	1	5	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	10	2	16	100
	High-end	4	0.5	4	

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NCTR Model	Central tendency	5	1	9	100
	High-end	2	0.3	2	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	6	1	10	100
	High-end	2	0.3	3	

MOE estimates for dry cleaning based on modeling (3rd generation) for both the worker and occupational non-user were below the benchmark MOE by 1-2 orders of magnitude for both central tendency and high-end exposure levels for all health effect endpoints.

Table 4-43. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (4th Generation)

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	42	43	78	100
	High-end	18	16	24	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	40	41	74	100
	High-end	17	15	23	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	15	16	28	100
	High-end	6	6	9	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	12	12	22	100
	High-end	5	4.4	7	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NCTR Model	Central tendency	7	7	12	100
	High-end	3	3	4	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	7	7	13	100
	High-end	3	3	4	

MOE estimates for dry cleaning based on modeling (4th generation) showed the same pattern as with dry cleaning based on modeling (3rd generation). MOE estimates for both worker and occupational non-users were below the benchmark MOE by 1-2 orders of magnitude for both central tendency and high-end exposure levels for all health effect endpoints.

Use: Spot Cleaner Based on Monitoring Data and Modeling

MOE estimates for spot cleaner based on monitoring data and modeling are presented in Table 4-44 and Table 4-45. Monitoring data for the occupational non-user were not available. APFs were not applied.

Table 4-44. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	167	No data	100
		High-end	32	No data	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	156	No data	100
		High-end	30	No data	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	59	No data	100
		High-end	11	No data	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	48	No data	100
		High-end	9	No data	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	27	No data	100
		High-end	5	No data	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	28	No data	100
		High-end	5	No data	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

MOE estimates for spot cleaner for the worker based on monitoring data were below the benchmark MOE for both central tendency and high-end exposure estimates by 1-2 orders of magnitude for all health effect endpoints with two exceptions; central tendency exposure levels for liver and kidney health effect endpoints.

Table 4-45. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	197	390	100
		High-end	90	136	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	184	364	100
		High-end	84	127	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	70	138	100
		High-end	32	48	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	56	112	100
		High-end	26	39	
Developmental Effects Post-Implantation Loss (F0) (WIL Research, 2001); NCTR Model	24	Central tendency	31	62	100
		High-end	14	22	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	33	65	100
		High-end	15	23	

MOE estimates for spot cleaner for the worker based on modeling showed the same pattern as that for monitoring data – MOE estimates were below the benchmark MOE for both central tendency and high-end exposure estimates by 1-2 orders of magnitude for all health effect endpoints with two exceptions; central tendency exposure levels for liver and kidney health effect endpoints. MOE estimates for the occupational non-user based on modeling were available. In this scenario, MOE estimates were slightly above the benchmark MOE in most cases for the liver and kidney (both central tendency and high-end exposure levels), reproductive system (central tendency exposure level only), and developmental (BMD modeling; central tendency exposure level only) health effect endpoints. MOE estimates for occupational non-users were below the benchmark MOE by 1-2 orders of magnitude for all other health effect endpoints.

Use: Disposal Based on Modeling

MOE estimates for disposal based on modeling are presented in Table 4-46. Exposures for the occupational non-user are expected to be negligible in this scenario.

Table 4-46. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Disposal Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	13,110	N/A	100
		High-end	2,494	N/A	
Kidney Increased pelvic mineralization (WIL Research, 2001)	140	Central tendency	12,236	N/A	100
		High-end	2,328	N/A	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	4,632	N/A	100
		High-end	881	N/A	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	43	Central tendency	3,758	N/A	100
		High-end	715	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NCTR Model	24	Central tendency	2,098	N/A	100
		High-end	399	N/A	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	2,185	N/A	100
		High-end	416	N/A	

N/A – Not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

MOE estimates for the worker were above the benchmark MOE by several orders of magnitude for both central tendency and high-end exposure estimates for all health effect endpoints

4.2.2.2 Cancer Evaluation for Occupational Scenarios

EPA estimated the excess cancers associated with chronic inhalation and dermal exposures following 1-BP conditions of use in the workplace, based on monitoring data and modeling (probabilistic vs deterministic). The excess cancer estimation for 1-BP consisted of multiplying the occupational scenario-specific estimates (i.e., LADC) for both workers and occupational non-users by EPA's inhalation unit risk (IUR) to estimate the excess cancers. Excess cancer risks were expressed as number of cancer cases per million.

Table 4-47 presents the inhalation cancer risk estimates for all occupational 1-BP conditions of use. The table also presents the impact of potential respirator use based on respirator APF of 10, 25, and 50. Figure 4-1 and Figure 4-2 present the incremental individual lifetime cancer risks for the 50th and 95th percentile for exposures to 1-BP during these same occupational conditions of use.

The exposure frequency (*i.e.*, the amount of days per year for workers or occupational non-users exposed to 1-BP) was assumed to be 260 days per year for all conditions of use except for dry cleaning, where employees at small, family-owned businesses were assumed to work up to six days

per week over 52 weeks per year. The number of working years was assumed to be 31 years as central tendency, and 40 years as high-end over a 78-year lifespan.

EPA typically uses a benchmark cancer risk level of 1×10^{-4} for determining the acceptability of the cancer risk in a population. Since the benchmark cancer risk level will be determined during risk management, the occupational estimates for excess cancer risk were compared to the benchmark levels of 10^{-4} , 10^{-5} , and 10^{-6} incremental or extra individual lifetime risk. The benchmark levels were:

1. 1×10^{-6} : the probability of 1 chance in 1 million of an individual developing cancer
2. 1×10^{-5} : the probability of 1 chance in 100,000 of an individual developing cancer, which is equivalent to 10 cancer cases in 1 million
3. 1×10^{-4} : the probability of 1 chance in 10,000 of an individual developing cancer, which is equivalent to 100 cancer cases in 1 million

Table 4-47. Inhalation Cancer Risk Estimates for Occupational Use of 1-BP (Benchmark = 1×10^{-4})

Condition of Use	Category		IUR (ppm ⁻¹)	Cancer Risk		Respirator APF	Cancer Risk with Respirator		Exposure Data Type
				Central tendency	High-end		Central tendency	High-end	
Manufacturing (US)	-	Worker	0.004	1.43E-04	5.54E-04	10	1.E-05	5.54E-05	Monitoring Data
Import, Repackaging, Processing -- Incorporation into Article	-	Worker	0.004	1.82E-05	1.23E-04	10	2.E-06	1.23E-05	Model (Deterministic)
Processing - Incorporation into Formulation	-	Worker	0.004	6.03E-03	3.88E-02	50	1.E-04	7.75E-04	Monitoring Data
	-	ONU	0.004	5.17E-04	3.26E-03	N/A	N/A	N/A	
Vapor Degreasing, Open-Top	-	Worker	0.004	1.07E-02	1.01E-01	50	2.E-04	2.03E-03	Monitoring Data
	-	ONU	0.004	3.18E-05	4.40E-03	N/A	N/A	N/A	
	Pre-EC	Worker	0.004	2.82E-03	3.68E-02	50	6.E-05	7.35E-04	Model (Probabilistic)
	Post-EC	Worker	0.004	2.82E-04	3.68E-03	50	6.E-06	7.35E-05	
	Pre-EC	ONU	0.004	1.49E-03	2.09E-02	N/A	N/A	N/A	
	Post-EC	ONU	0.004	1.49E-04	2.09E-03				
Vapor Degreasing, closed-loop	-	Worker	0.004	5.63E-05	7.35E-04	10	6.E-06	7.35E-05	Model (Probabilistic)
	-	ONU	0.004	2.97E-05	4.19E-04	N/A	N/A	N/A	
Cold Cleaning	-	Worker	0.004	6.84E-03	1.52E-02	50	1.E-04	3.04E-04	Monitoring Data
	-	ONU	0.004	4.13E-03	5.33E-03	N/A	N/A	N/A	
	-	Worker	0.004	8.23E-04	1.84E-02	50	2.E-05	3.67E-04	Model (Probabilistic)
	-	ONU	0.004	4.33E-04	1.05E-02	N/A	N/A	N/A	
Aerosol Degreasing	Pre-EC	Worker	0.004	2.55E-02	6.47E-02	50	5.E-04	1.29E-03	Monitoring Data
	Post-EC	Worker	0.004	8.74E-03	1.13E-02	50	2.E-04	2.26E-04	
	-	Worker	0.004	9.52E-03	3.62E-02	50	2.E-04	7.24E-04	Model (Probabilistic)
	-	ONU	0.004	1.60E-04	1.44E-03	N/A	N/A	N/A	

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Condition of Use	Category		IUR (ppm ⁻¹)	Cancer Risk		Respirator APF	Cancer Risk with Respirator		Exposure Data Type
				Central tendency	High-end		Central tendency	High-end	
Spray Adhesive	Pre-EC	Sprayer	0.004	2.11E-01	5.20E-01	50	4.E-03	1.04E-02	Monitoring Data
	Post-EC	Sprayer	0.004	2.83E-02	8.59E-02	50	6.E-04	1.72E-03	
	Pre-EC	Non-Sprayer	0.004	2.02E-01	4.33E-01	50	4.E-03	8.65E-03	
	Post-EC	Non-Sprayer	0.004	2.86E-02	5.92E-02	50	6.E-04	1.18E-03	
	Pre-EC	ONU	0.004	4.77E-03	2.64E-01	N/A	N/A	N/A	
	Post-EC	ONU	0.004	3.18E-03	1.12E-02	N/A	N/A	N/A	
Dry Cleaning	-	Worker	0.004	4.67E-02	1.03E-01	N/A	N/A	N/A	Monitoring Data
	-	ONU	0.004	1.92E-02	4.23E-02				Model (Probabilistic)
	3rd Gen	Spot Cleaner	0.004	1.57E-03	4.58E-03				
	3rd Gen	Machine & Finish	0.004	7.54E-03	3.43E-02				
	3rd Gen	ONU	0.004	9.71E-04	3.80E-03				
	4th Gen	Spot Cleaner	0.004	1.28E-03	3.29E-03				
	4th Gen	Machine & Finish	0.004	1.26E-03	3.74E-03				
	4th Gen	ONU	0.004	6.94E-04	2.39E-03				
Spot Cleaning	-	Worker	0.004	1.43E-03	9.69E-03	N/A	N/A	N/A	Monitoring Data
	-	Worker	0.004	1.16E-03	2.73E-03				Model (Probabilistic)
	-	ONU	0.004	5.82E-04	1.78E-03				
Disposal, Recycling	-	Worker	0.004	1.82E-05	1.23E-04	10	2.E-06	1.23E-05	Model (Deterministic)

N/A – Not applicable. EPA believes respirator use is unlikely for workers at small commercial facilities (dry cleaners, spot cleaners) and for occupational non-users.

The range of extra cancer risks calculated for workers in each use category are described in Table 4-47 and Figure 4-1 and Figure 4-2. Risk estimates are based on occupational exposure values derived from monitoring and modeling data (with and without engineering controls). The benchmark cancer risk estimate of 1×10^{-4} was exceeded for all of the uses in workers and occupational non-users for both central tendency and high-end exposure estimates for both monitoring and modeling data with or without the use of an APF in most cases with few exceptions. These exceptions included cancer risk estimates when respirators were assumed to be used for: manufacturing, import, repacking, processing – incorporation into article for the worker; vapor degreasing open-top for the occupational non-user; vapor degreasing closed-loop for workplace exposures; and disposal, recycling for the worker. In most cases, benchmark cancer risk estimates were similar between monitoring and modeling within each use.

The high-end excess cancer risks calculated for workers and occupational non-users exceeded all identified cancer benchmarks (i.e., 1×10^{-4} (1 in 10,000), 1×10^{-5} (1 in 100,000) and 1×10^{-6} (1 in 1,000,000)) in most of the use scenarios evaluated under the scope of this evaluation. In most cases a 1,000-fold exceedance of the 1 in 1,000,000 cancer risk benchmark was observed (this corresponds to a cancer risk greater than 1×10^{-3} (or a probability of 1 in 1,000 that an exposed individual will develop cancer). It is important to note however, that this value reflects the excess lifetime cancer risk estimated for high-end (i.e., typically 95th percentile) exposures that occur over the assumed duration of an occupational life (i.e., for most occupational conditions of use, 8 hours/day, 260 days/yr for 40 years of a 78 year lifespan). Although most occupational exposure concentrations at the central tendency level are about an order of magnitude lower than those at the high-end level (shown in Section 2), the associated risk estimates at the central tendency level exceeded the 1 in 10,000 cancer benchmark for most uses (see Figure 4-1).

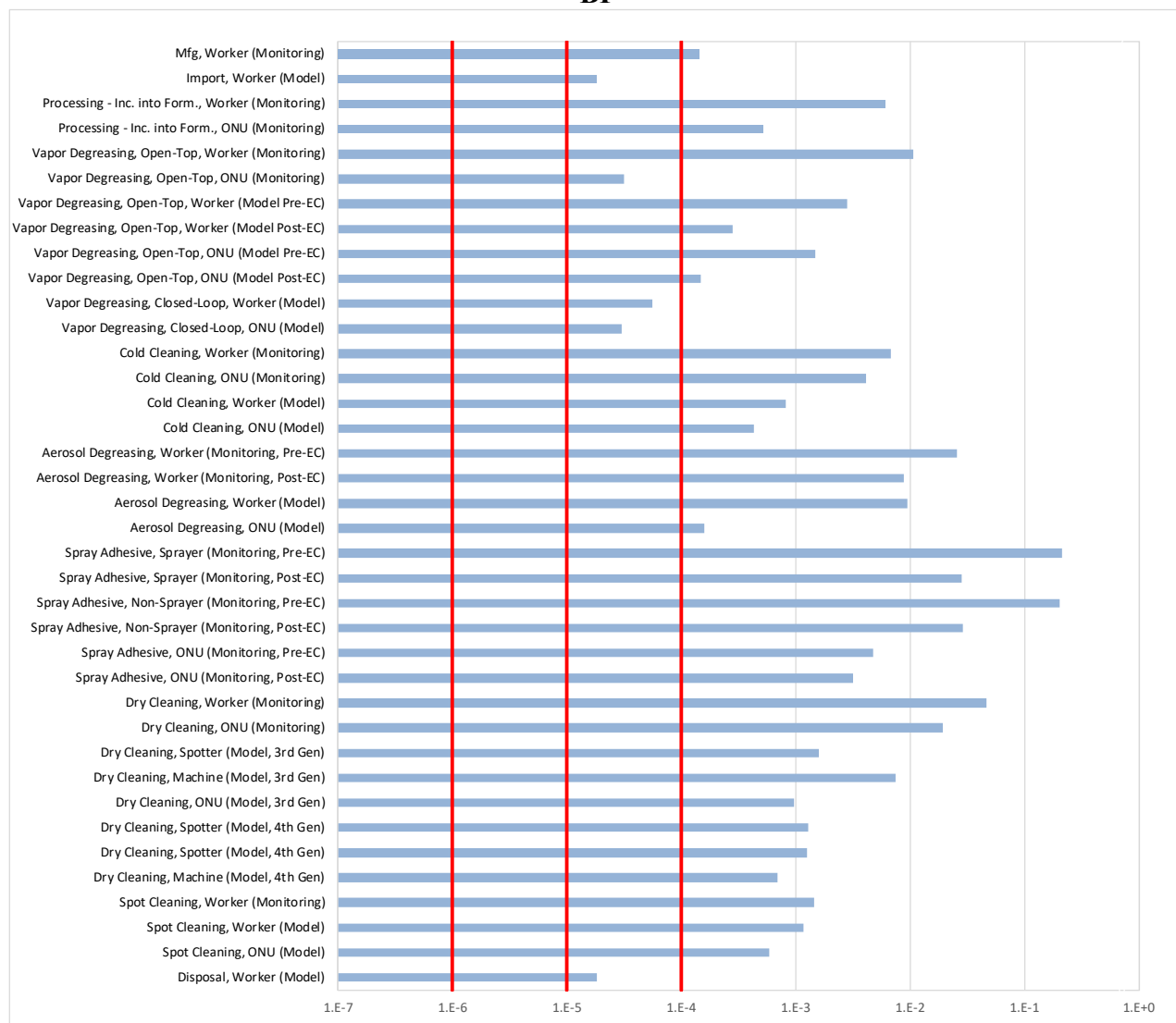
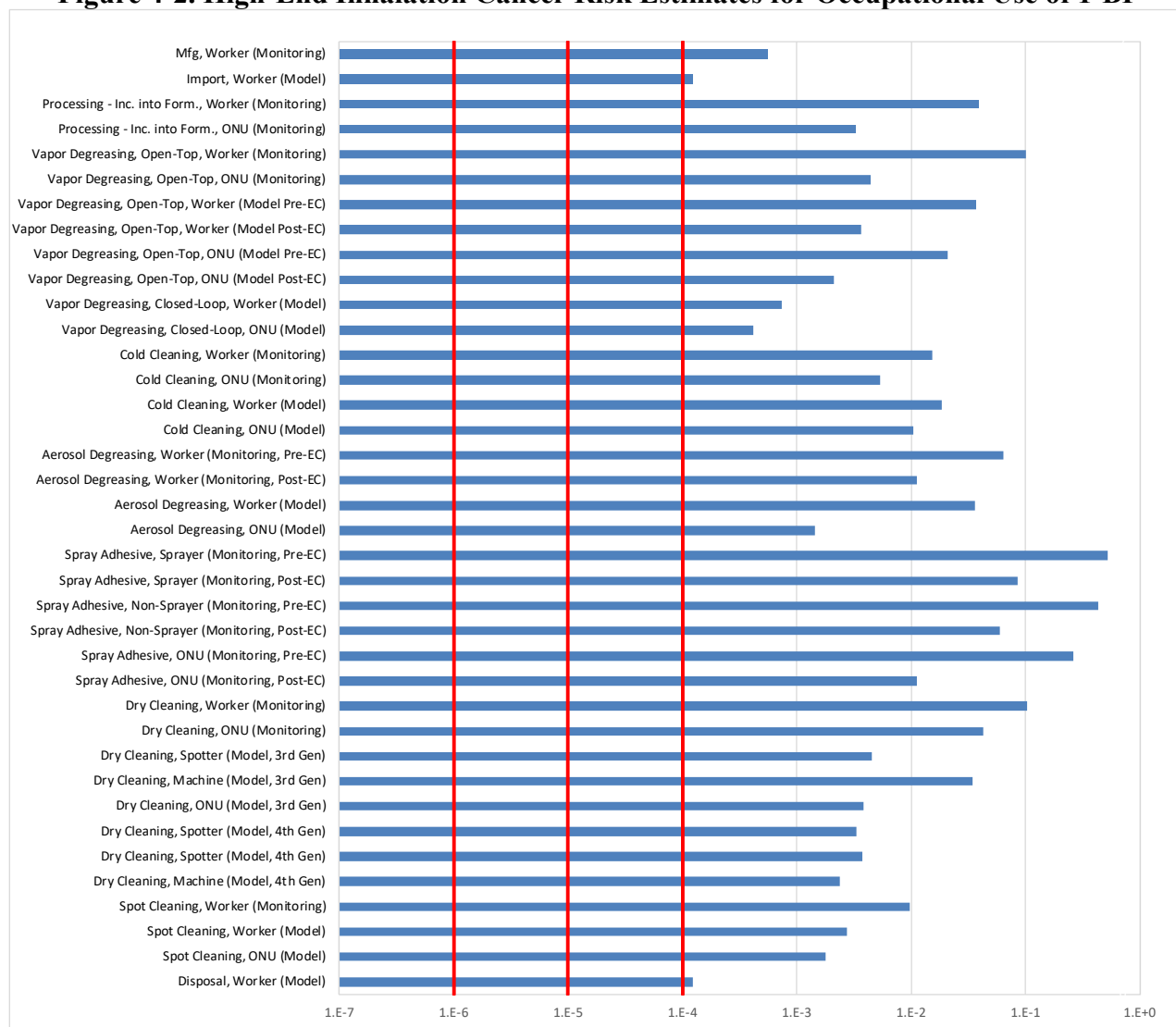
Figure 4-1. Central Tendency Inhalation Cancer Risk Estimates for Occupational Use of 1-BP

Figure 4-2. High-End Inhalation Cancer Risk Estimates for Occupational Use of 1-BP

4.2.3 Risk Characterization For Acute and Chronic, Non-Cancer and Cancer Dermal Occupational Exposures

For dermal exposure, conditions of use with similar exposure concentration, exposure level, and potential for occlusion are “binned” as described in Section 2.3.1.22. MOE estimates for occupational conditions of use (Bins 1-5) following acute and chronic dermal exposures based on modeling and what-if glove protection factors are presented in Table 4-48, Table 4-49, Table 4-50, Table 4-51 and Table 4-52. Cancer risk estimates for these same conditions of use following chronic dermal exposures are presented in Table 4-53.

Use: Manufacture, Import, Processing, and Disposal (Bin 1)

MOE estimates for manufacture, import, processing, and disposal activities for both acute and chronic dermal exposure scenarios are presented in Table 4-48.

Table 4-48. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Manufacture, Import, Processing, and Disposal (Bin 1)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Acute, Non-Cancer	Develop. (litter size)	19	423	2,114	4,228	8,456	100
	Develop. (post-impl. loss)	11	245	1,224	2,448	4,895	
Chronic, Non-Cancer	Liver	95	2,114	10,570	21,139	42,279	100
	Kidney	89	1,980	9,902	19,804	39,608	
	Reproductive System	25	556	2,781	5,563	11,126	
	Develop. (litter size)	27	601	3,004	6,008	12,016	
	Develop. (post-impl. loss)	15	334	1,669	3,338	6,676	
	Nervous System	12	267	1,335	2,670	5,340	100

MOE estimates for Manufacture, Import, Processing, and Disposal (Bin 1) were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to markedly increase by several orders of magnitude above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Vapor Degreaser and Cold Cleaner (Bin 2)

MOE estimates for vapor degreaser and cold cleaner conditions of use for both acute and chronic exposure scenarios are presented in Table 4-49.

Table 4-49. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Vapor Degreaser and Cold Cleaner (Bin 2)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Acute, Non-Cancer	Develop. (litter size)	19	436	2,179	4,359	8,717	100
	Develop. (post-impl. loss)	11	252	1,262	2,523	5,047	
Chronic, Non-Cancer	Liver	95	2,179	10,897	21,793	43,586	100
	Kidney	89	2,042	10,208	20,417	40,833	
	Reproductive System	25	574	2,868	5,735	11,470	
	Develop. (litter size)	27	619	3,097	6,194	12,388	
	Develop. (post-impl. loss)	15	344	1,721	3,441	6,882	
	Nervous System	12	275	1,376	2,753	5,506	100

MOE estimates for vapor degreaser and cold cleaner conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to markedly increase by several orders of magnitude above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Spray Adhesive (Bin 3)

MOE estimates for spray adhesive conditions of use for both acute and chronic exposure scenarios are presented in Table 4-50.

Table 4-50. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Spray Adhesive (Bin 3)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Acute, Non-Cancer	Develop. (litter size)	19	528	2,642	5,285	N/A	100
	Develop. (post-impl. loss)	11	306	1,530	3,060		
Chronic, Non-Cancer	Liver	95	2,642	13,212	26,424		100
	Kidney	89	2,476	12,378	24,755		
	Reproductive System	25	695	3,477	6,954		
	Develop. (litter size)	27	751	3,755	7,510		
	Develop. (post-impl. loss)	15	417	2,086	4,172		
	Nervous System	12	334	1,669	3,338		100

MOE estimates for spray adhesive conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to markedly increase by several orders of magnitude above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Dry Cleaning and Spot Cleaner (Bin 4)

MOE estimates for dry cleaning and spot cleaner conditions of use for both acute and chronic exposure scenarios are presented in Table 4-51.

Table 4-51. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Dry Cleaning and Spot Cleaner (Bin 4)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Acute, Non-Cancer	Develop. (litter size)	19	450	2,249	4,498	N/A	100
	Develop. (post-impl. loss)	11	260	1,302	2,604		
Chronic, Non-Cancer	Liver	95	2,249	11,244	22,489		100
	Kidney	89	2,107	10,534	21,068		
	Reproductive System	25	592	2,959	5,918		
	Develop. (litter size)	27	639	3,196	6,392		
	Develop. (post-impl. loss)	15	355	1,775	3,551		
	Nervous System	12	284	1,420	2,841		100

MOE estimates for dry cleaning and spot cleaner conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to markedly increase by several orders of magnitude above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Aerosol Spray Degreaser/Cleaner, Other Aerosol and Non-aerosol Uses (Bin 5)

MOE estimates for aerosol spray degreaser/cleaner, and other aerosol and non-aerosol conditions of use for both acute and chronic exposure scenarios are presented in Table 4-52.

Table 4-52. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner, Other Aerosol and Non-aerosol Uses (Bin 5)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Acute, Non-Cancer	Develop. (litter size)	19	423	2,114	4,228	N/A	100
	Develop. (post-impl. loss)	11	245	1,224	2,448		
Chronic, Non-Cancer	Liver	95	2,114	10,570	21,139		100
	Kidney	89	1,980	9,902	19,804		
	Reproductive System	25	556	2,781	5,563		
	Develop. (litter size)	27	601	3,004	6,008		
	Develop. (post-impl. loss)	15	334	1,669	3,338		
	Nervous System	12	267	1,335	2,670		100

MOE estimates aerosol spray degreaser/cleaner, and other aerosol and non-aerosol conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to markedly increase by several orders of magnitude above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Bins 1-5

Cancer risk estimates for occupational conditions of use (category Bins 1-5) are presented in Table 4-53.

Table 4-53. Cancer Risk Estimates for Dermal Exposure Following Occupational Use of 1-BP

Category	Dermal Slope Factor (mg/kg-day) ⁻¹	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Bin 1: Manufacture, Import, Processing, and Disposal	0.006	1.38E-04	2.77E-05	1.38E-05	6.91E-06	1E-04
Bin 2: Vapor Degreaser, Cold Cleaner		1.34E-04	2.68E-05	1.34E-05	6.71E-06	1E-04
Bin 3: Spray Adhesives		1.11E-04	2.21E-05	1.11E-05	N/A	1E-04
Bin 4: Dry Cleaning, Spot Cleaning		1.30E-04	2.60E-05	1.30E-05	N/A	1E-04
Bin 5: Aerosol Spray Degreaser/Cleaner, Other Aerosol and Non-aerosol Uses		1.38E-04	2.77E-05	1.38E-05	N/A	1E-04

The benchmark cancer risk estimate (1×10^{-4}) was exceeded for all conditions of use (Bins 1-5) when no gloves were used (PF=1); however, as the PF increased between 5 and 20, the benchmark cancer risk estimate (1×10^{-4}) was not exceeded.

Consumer Uses (General Cleaner/Degreaser, Coin Cleaner, Automobile AC Flush, Overall)

MOE estimates for consumer conditions of use (general cleaner/degreaser, coin cleaner, automobile AC Flush, and overall) are presented in Table 4-54. A brief discussion of the approach and the risk calculations spreadsheet is provided in the 1-BP Supplemental File Consumer Exposure Risk Calculations ([EPA, 2019c](#)).

Table 4-54. Non-Cancer Risk Estimates for Acute 24-hr Dermal Exposure Following Consumer Uses of 1-BP

Condition of Use	Scenario Description	Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001) HED = 19 mg/kg-day			Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001) HED = 11 mg/kg-day		
		Adult	Youth A	Youth B	Adult	Youth A	Youth B
General Cleaner/Degreaser	High Intensity Use	0.7	0.7	0.7	0.4	0.4	0.4
	Moderate Intensity Use	106	11	10	6	6	6
	Low Intensity Use	144	153	141	83	89	81
Coin Cleaner	High Intensity Use	13	14	13	7	8	7
	Moderate Intensity Use	16	27	25	15	16	14
	Low Intensity Use	77	82	75	45	48	43
Automobile AC Flush	High Intensity Use	0.2	0.3	0.2	0.1	0.2	0.1
	Moderate Intensity Use	0.5	0.5	0.5	0.3	0.3	0.3

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	Low Intensity Use	2	2	1	0.9	0.9	0.8
Overall	Maximum	144	153	141	83	89	81
	Minimum	0.2	0.3	0.2	0.1	0.2	0.1

MOE estimates were below the benchmark MOE for all conditions of use, all scenario descriptions, and all conditions of use in all users (Adult, Youth A, and Youth B), except for low intensity use of the general cleaner/degreaser for the developmental effects, decreased litter size.

4.3 Assumptions and Key Sources of Uncertainty

The characterization of variability and uncertainty is fundamental to any risk evaluation. Variability refers to “the true heterogeneity or diversity in characteristics among members of a population (i.e., inter-individual variability) or for one individual over time (intra-individual variability)” ([U.S. EPA, 2001](#)). The risk evaluation was designed to reflect critical sources of variability to the extent allowed by available methods and data and given the resources and time available.

On the other hand, uncertainty is “the lack of knowledge about specific variables, parameters, models, or other factors” ([U.S. EPA, 2001](#)) and can be described qualitatively or quantitatively. Uncertainties in the risk evaluation can raise or lower the confidence of the risk estimates. In this assessment, the uncertainty analysis also included a discussion of data gaps/limitations. The next sections describe the uncertainties and data gaps in the exposure, hazard/dose-response and risk characterization.

One key uncertainty is whether the human populations that are at greatest risk, based on the integration of information regarding highly exposed groups (or “potentially exposed”) and biologically susceptible subpopulations, have been adequately defined and characterized. Workers, and consumers (i.e., receptors who use a product directly) and bystanders (i.e., receptors who are non-product users that are incidentally exposed to the product or article) in residential settings, (includes industrial and commercial facilities manufacturing, processing or using 1-BP), and in co-located residences or businesses who are also biologically susceptible individuals would represent the most susceptible populations. For example, workers who are reproductive age men and women, pregnant women (and their fetus), and adolescent workers are both high exposure and biologically susceptible groups. Analyses have been performed to understand the risk for the identified potentially susceptible populations.

4.3.1 Uncertainties of the Occupational Exposure Assessment

EPA addressed variability in the exposure models by identifying key model parameters to apply a statistical distribution that mathematically defines the parameter’s variability. EPA defined statistical distributions for parameters using documented statistical variations where available. Where the statistical variation is not known, assumptions are made to estimate the parameter distribution using available literature data. See the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019g](#)) for statistical distribution for each model input parameter. The following sections discuss uncertainties in the occupational exposure assessment.

Number of Workers

There are a number of uncertainties surrounding the estimated number of workers potentially exposed to 1-BP, as outlined below. Most are unlikely to result in a systematic underestimate or overestimate, but could result in an inaccurate estimate.

CDR data are used to estimate the number of workers associated with the following conditions of use: Manufacturing, Import, Processing as a Reactant, and Incorporation into Formulation, Mixture, or Reaction Product. There are inherent limitations to the use of CDR data. First, manufacturers and importers are only required to report if they manufactured or imported 1-BP in

excess of 25,000 pounds at a single site during any calendar from 2012 to 2015; as such, CDR may not capture all sites and workers associated with any given chemical. Second, the estimate is based on information that is known or reasonably ascertainable to the submitter. CDR submitters (chemical manufacturers and importers) do not always have accurate information on the number of potentially exposed workers at downstream processing sites.

There are also uncertainties associated with BLS data, which are used to estimate the number of workers for the remaining conditions of use. First, BLS' OES employment data for each industry/occupation combination are only available at the 3-, 4-, or 5-digit NAICS level, rather than the full 6-digit NAICS level. This lack of granularity could result in an overestimate of the number of exposed workers if some 6-digit NAICS are included in the less granular BLS estimates but are not, in reality, likely to use 1-BP for the assessed condition of use. EPA addressed this issue by refining the OES estimates using total employment data from the U.S. Census' SUBS. However, this approach assumes that the distribution of occupation types (SOC codes) in each 6-digit NAICS is equal to the distribution of occupation types at the parent 5-digit NAICS level. If the distribution of workers in occupations with 1-BP exposure differs from the overall distribution of workers in each NAICS, then this approach will result in inaccuracy.

Second, EPA's judgments about which industries (represented by NAICS codes) and occupations (represented by SOC codes) are associated with the uses assessed in this report are based on EPA's understanding of how 1-BP is used in each industry. Designations of which industries and occupations have potential exposures is nevertheless subjective, and some industries/occupations with few exposures might erroneously be included, or some industries/occupations with exposures might erroneously be excluded. This would result in inaccuracy but would be unlikely to systematically either overestimate or underestimate the count of exposed workers.

Analysis of Occupational Exposure Monitoring Data

To analyze exposure monitoring data, EPA categorized individual PBZ data point as either "worker" or "occupational non-user". Exposures for occupational non-users can vary substantially. Most data sources do not sufficiently describe the proximity of these employees to the 1-BP exposure source. As such, exposure levels for the "occupational non-user" category will have high variability depending on the specific work activity performed. It is possible that some employees categorized as "occupational non-user" have exposures similar to those in the "worker" category depending on their specific work activity pattern.

Some data sources may provide exposure estimates that are higher than typical across the distribution of facilities for that condition of use. For example, NIOSH HHEs for the spray adhesive use were conducted to address concerns regarding adverse human health effects reported following 1-BP exposure with spray adhesive use in furniture manufacturing. Two HHEs were requested by the North Carolina Department of Labor; one was conducted in response to a confidential request submitted by the facility's employees.

There are limited exposure monitoring data in literature for certain conditions of use or job categories. For example, very few data points are available for cold cleaning and for spot-cleaning. Where few data are available, the assessed exposure levels are unlikely to be representative of worker exposure across the entire job category or industry. In addition, exposure data for

compliance safety and health officers may not be representative of typical exposure levels for occupational non-users.

For vapor degreasing and cold cleaning, several sources do not contain detailed information describing the type of degreaser or cleaner present at the facility. The lack of such information results in uncertainty in the assessed exposure levels associated with specific subcategories of such equipment. For example, the data presented for batch open-top vapor degreasers may actually include data associated with other types of degreaser.

Where the sample data set contains six or more data points, the 50th and 95th percentile exposure concentrations were calculated from the sample to represent central tendency and high-end exposure levels. The underlying distribution of the data, and the representativeness of the available data, are not known.

Near-Field / Far-Field Model Framework

The near-field / far-field approach is used as a framework to model inhalation exposure for many conditions of use. The following describe uncertainties and simplifying assumptions generally associated with this modeling approach:

- There is some degree of uncertainty associated with each model input parameter. In general, the model inputs were determined based on review of available literature. Where the distribution of the input parameter is known, a distribution is assigned to capture uncertainty in the *Monte Carlo* analysis. Where the distribution is unknown, a uniform distribution is often used. The use of a uniform distribution will capture the low-end and high-end values but may not accurately reflect actual distribution of the input parameters.
- The model assumes the near-field and far-field are each well mixed, such that each of these zones can be approximated by a single, average concentration.
- All of the emissions from the facility are assumed to enter the near-field zone. This assumption will overestimate exposures and risks in facilities where some of the emissions do not enter the airspaces relevant to the worker exposure modeling.
- The exposure models estimate airborne concentrations. Exposures are calculated by assuming workers spend the entire activity duration in their respective exposure zones (i.e., the worker in the near field and the occupational non-user in the far field). Since vapor degreasing and cold cleaning involve automated processes, a worker may actually walk away from the near-field during part of the process and return when it is time to unload the degreaser. As such, assuming the worker is exposed at the near-field concentration for the entire activity duration may overestimate exposure.
- For certain 1-BP applications (e.g. vapor degreasing and cold cleaning), 1-BP vapor is assumed to emit continuously while the equipment operates (i.e. constant vapor generation rate). Actual vapor generation rate may vary with time. However, small time variability in vapor generation is unlikely to have a large impact in the exposure estimates as exposures are calculated as a time-weighted average.
- The exposure models represent model workplace settings for each 1-BP condition of use. The models have not been regressed or fitted with monitoring data.
- The models represent a baseline scenario that do not have LEV. EPA does not have adequate data to construct LEV systems into the exposure models. Additionally, there is no data on the fraction of U.S. facilities that use LEV. Where available, “what-if” values on

engineering control effectiveness are applied to the model baseline to provide post-EC scenarios. These values were obtained by reviewing statements made in published literature regarding potential emission or exposure reductions after implementation of engineering control or equipment substitution.

Each subsequent section below discuss uncertainties associated with the individual models.

Vapor Degreasing and Cold Cleaning Model

The vapor degreasing and cold cleaning assessments use a near-field / far-field approach to model worker exposure. In addition to the uncertainties described above, the vapor degreasing and cold cleaning models have the following uncertainties:

- To estimate vapor generation rate for vapor degreasing, EPA references a 1-BP emission factor developed by CARB for the California Solvent Cleaning Emissions Inventories ([CARB, 2011](#)). The emission factor is an average emission for the “vapor degreasing” category for the California facilities surveyed by CARB. The category includes batch-loaded vapor degreaser, aerosol surface preparation process, and aerosol cleaning process. For the purpose of modeling, EPA assumes the 1-BP emission factor is entirely attributed to vapor degreasing applications. The representativeness of the emission factor for vapor degreasing emissions in other geographic locations within the U.S. is uncertain.
- The CARB emission factor covers batch degreasing units. However, CARB does not further specify whether these are open-top vapor degreasers, enclosed, or other types of batch degreasers. EPA assumes the emission factor is representative of open-top vapor degreaser, as it is the most common design for batch units using 1-BP. In addition, EPA assumes that the surveyed facilities likely switched to using 1-BP, an alternative, non-HAP solvent, as a way of complying with Federal and State regulations for HAP halogenated solvents (i.e., chemical substitution, rather than equipment changes).
- The CARB emission factor, in the unit of pound per employee-year, was developed for the purpose of estimating annual emissions. These types of emission factor typically reflect the amount of solvent lost / emitted, some of which may not be relevant to worker exposure. For example, 1-BP emitted and captured through a stack may not result in worker exposure. Therefore, assuming all of the 1-BP is emitted into the workplace air may result in overestimating of exposure. In addition, the use of an annual emission factor does not capture time variability of emissions. The approach assumes a constant emission rate over a set number of operating hours, while actual emissions and worker exposures will vary as a function of time and worker activity.
- EPA combines the CARB emission factor with nationwide Economic Census employment data across 78 NAICS industry sector codes. It should be noted that vapor degreasing is not an industry-specific operation. Only a subset of facilities within the 78 selected industry sectors are expected to operate vapor degreasers. Therefore, the industry-average employment data may not be representative of the actual number of employees at vapor degreasing facilities.
- To estimate worker exposure during cold cleaning, EPA applied an emission reduction factor to the vapor degreasing model by comparing the AP-42 emission factors for the two applications. The AP-42 emission factors are dated. Furthermore, the cold cleaning model results have not been validated with actual monitoring data.

- EPA assumes workers and occupational non-users remove themselves from the contaminated near- and far-field zones at the conclusion of the task, such that they are no longer exposed to any residual 1-BP in air.
- The model assumes an exposure reduction of 90 percent with engineering control. In reality, engineering controls and their effectiveness are site-specific. Additionally, the 90 percent reduction is a value based on TCE, and may not be applicable to a more volatile chemical such as 1-BP.

Aerosol Degreasing Model

The aerosol degreasing assessment also uses a near-field/far-field approach to model worker exposure. Specific uncertainties associated with the aerosol degreasing scenario are presented below:

- The model references a CARB ([2000](#)) study on brake servicing to estimate use rate and application frequency of the degreasing product. The brake servicing scenario may not be representative of the use rates for other aerosol degreasing applications involving 1-BP.
- The Use Dossier ([U.S. EPA, 2017c](#)) identifies 25 different aerosol degreasing formulations containing 1-BP. For each *Monte Carlo* iteration, the model determines the 1-BP concentration in product by selecting one of 25 possible formulations, assuming equal probability of each formulation being used. In reality, some formulations are likely more prevalent than others.

Dry Cleaning Model

The multi-zone dry cleaning model also uses a near-field/far-field approach. Specific uncertainties associated with the dry cleaning scenario are presented below:

- The model assumes each facility only has one dry cleaning machine, cleaning one to fourteen loads of garments per day. While the dry cleaning facilities in Blando et al. ([2010](#)) and NIOSH ([2010](#)) appear to only have one machine, the representativeness of these two studies is not known. Larger facilities are likely to have more machines, which could result in additional 1-BP exposures.
- The model conservatively uses a hemispherical volume based on the dry cleaning machine door diameter as the near-field for machine unloading. The small near-field volume results in a large spike in concentration when the machine door is opened, where any residual 1-BP solvent is assumed to be instantaneously released into the near-field. In reality, the residual solvent will likely be released continuously over a period of time. In addition, the worker may move around while unloading the garments, such that the worker's breathing zone will not always be next to the machine door throughout the duration of this activity. Therefore, these assumptions may result in an overestimate of worker exposure during machine unloading.
- Many of the model input parameters were obtained from ([Von Grote et al., 2003](#)), which is a German study. Aspects of the U.S. dry cleaning facilities may differ from German facilities. However, it is not known whether the use of German data will under- or over-estimate exposure.
- The model does not cover all potential worker activities at dry cleaners. For example, workers could be exposed to 1-BP emitted due to equipment leaks, when re-filling 1-BP solvent into dry cleaning machines, when interrupting a dry cleaning cycle, or when

performing maintenance activities (e.g., cleaning lint and button traps, raking out the still, changing solvent filter, and handling solvent waste) ([OSHA, 2005](#)). However, there is a lack of information on these activities in the literature, and the frequency of these activities is not well understood. The likelihood of equipment leaks is dependent on whether the machines are properly converted and maintained. The frequency of solvent re-filling depends on a specific dry cleaner's workload and solvent consumption rate, which is also affected by the presence of leaks. Based on observations reported by ([NIOSH, 2010](#)) and ([Blando et al., 2010](#)), solvent charging is not performed every day. EPA was unable to develop a modeling approach for these exposure activities due to the lack of available information.

Spot Cleaning Model

The spot cleaning assessment also uses a near-field/far-field approach to model worker exposure. The model estimates a use rate of 16 gallons per year spot cleaner. This value was derived using a MassDEP case study for one specific dry cleaner in Massachusetts, handling 100 pieces of garments per day. MassDEP noted that the size of each dry cleaner can vary substantially. As such, the spot cleaner use rate will also vary by the individual facility work load. The representativeness of the spot cleaner use rate from this case study is not known.

Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model

For Import/repackaging, Processing as a reactant, and Processing – Incorporation into articles, the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate the airborne concentration associated with generic chemical loading scenarios at industrial facilities. Specific uncertainties associated with this model are described below:

- After each loading event, the model assumes saturated air containing 1-BP that remains in the transfer hose and/or loading arm is released to air. The model calculates the quantity of saturated air using design dimensions of loading systems published in the OPW Engineered Systems catalog and engineering judgment. These dimensions may not be representative of the whole range of loading equipment used at industrial facilities handling 1-BP.
- The model estimates fugitive emissions from equipment leaks using total organic compound emission factors from EPA's Protocol for Equipment Leak Emission Estimates (1995), and engineering judgement on the likely equipment type used for transfer (e.g. number of valves, seals, lines, and connections). The applicability of these emission factors to 1-BP, and the accuracy of EPA's assumption on equipment type are not known.
- The model assumes the use a vapor balance system to minimize fugitive emissions. Although most industrial facilities are likely to use a vapor balance system when loading/unloading volatile chemicals, EPA does not know whether these systems are used by all facilities that potentially handle 1-BP.

Modeling Dermal Exposures

The *Dermal Exposure to Volatile Liquids Model* is used to estimate dermal exposure to 1-BP in occupational settings. The model assumes a fixed fractional absorption of the applied dose, however, fractional absorption may be dependent on skin loading conditions. The model also

assumes a single exposure event per day based on existing framework of the *EPA/OPPT 2-Hand Dermal Exposure to Liquids Model* and does not address variability in exposure duration and frequency.

4.3.2 Uncertainties of the Consumer Exposure Assessment

Modeling was used to evaluate consumer exposure concentrations resulting from the use of the following consumer products containing 1-BP: Adhesive Accelerants, General Spray Cleaner, Spot Cleaner/Stain Remover, Mold Cleaning/Release, General Cleaner-Degreaser, Degreaser-Electronic, Coin Cleaner, Automobile AC Flush, and Insulation. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used.

4.3.2.1 Consumer Use Information

The consumer use dossier and market profile documents ([U.S. EPA, 2017](#)) were developed in 2016 and 2017 based on information reasonably available at that time. These do not take into consideration company-initiated formulation changes, product discontinuation, or other business or market based factors occurring after the documents were compiled. While there may be some uncertainty associated with products identified in 2016 and 2017 remaining readily available, EPA believes the information utilized to identify the consumer uses is the best available information and therefore have a high confidence in this information.

EPA found national survey information related to use of household products containing solvents ([EPA, 1987](#)) that was compiled in 1987. While this survey is an older survey, many of the product categories within the survey align well with the consumer use scenarios identified above. Additionally the consumer use profiles and patterns evaluated by the survey remain strong when compared to present day consumer use patterns even though some aspects of the use may have changed. Regardless of these similarities and strengths, EPA realizes there is still some level of uncertainty associated with the survey data and its application to current day consumer use patterns, amount used, or duration of use. While some level of uncertainty remains, the approach taken for this evaluation to vary key inputs across the spectrum of use patterns captured by the survey should reduce the uncertainties.

4.3.2.2 Model Assumptions and Input Parameters

There is a high degree of confidence in the consumer product weight fractions identified for the consumer products evaluated in this assessment. Product weight fractions were obtained from product specific SDS and when a range of weight fractions exists across several products within a single condition of use evaluated, modeling was conducted across the range of weight fractions capturing a low, moderate, and high weight fraction value.

There is a high degree of confidence in certain modeling inputs to the various models used, including vapor pressure, molecular weight, room volumes, whole house volume, and air exchange rate. The physical-chemical properties of 1-BP are well documented and therefore have a high degree of confidence. The room and house volumes as well as air exchange rates are based on values from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)) and therefore also have a high degree of confidence.

4.3.3 Uncertainties in the Hazard and Dose-Response Assessments

4.3.3.1 Uncertainties and Assumptions in the Environmental Hazard Assessment

While EPA has determined that sufficient data are available to characterize the overall environmental hazards of 1-BP under the conditions of use of this evaluation, there are data gaps and uncertainties regarding the environmental hazards of 1-BP. There is uncertainty with using publicly available environmental hazard data from the ECHA database since full studies are not available for data quality evaluation. Regardless, the use of these hazard endpoints, which in the case of acute exposure to fish constitute the most sensitive endpoint, in a screening-level comparison with estimated surface water concentrations indicates that risks are not identified for 1-BP. As a result, obtaining these full study reports would not alter the risk determination for aquatic species.

No chronic toxicity studies identified that directly assess the chronic duration effects of 1-BP to the environment. As a result, hazard to aquatic species resulting from chronic exposure was estimated using an acute-to-chronic exposure to acute hazard data. This value represents an estimation of chronic hazard and there are uncertainties regarding the use of this value. Despite these uncertainties, the use of an acute to chronic ratio is a commonly utilized technique to estimate potential hazards to environmental receptors from chronic exposures and represents the best available data for 1-BP. Frequency and duration of exposure also affects potential for adverse effects in aquatic organisms, especially for chronic exposures. In the case of 1-BP, the number of days that a COC was exceeded was not calculated using E-FAST, but instead the maximum expected surface water concentration from an acute exposure, representing a high-end estimate of exposure interval or pulse exposure, was compared to the estimated chronic concentrations of concern. This conservative screening-level approach is expected to be protective of longer-term chronic exposures which are generally lower than acute-duration exposures.

A lack of sediment and terrestrial toxicity test data creates some uncertainty associated with this assessment. Regardless, the potential exposures to terrestrial and sediment-dwelling aquatic species are expected to be low based on the physical-chemical/fate properties (relatively high volatility (henry's law constant of 7.3×10^{-3} atm-m³/mole), high water solubility (2.4 g/l), and low logK_{oc} (1.6)) indicating that 1-BP present in water is likely to volatilize and does not have high sorption to sediment.

The lack of monitoring data to characterize the concentrations of 1-BP present in aquatic sediment represents an uncertainty regarding aquatic hazard. As discussed above, the physical chemical properties indicate that the potential for continuous exposure to terrestrial and sediment-dwelling organisms is unlikely under the conditions of use for 1-BP, so this uncertainty isn't expected to affect the risk determination for this pathway.

Assessment factors (AFs) were used to calculate the acute and chronic COCs for 1-BP. As described in Appendix F, AFs account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are routinely used within TSCA for assessing the hazard of new industrial chemicals (with very limited environmental test data). Some uncertainty may be associated with the use of the specific AFs used in the hazard assessment.

4.3.3.2 Uncertainties and Assumptions in the Non-Cancer/Cancer Hazard/Dose-Response Assessments

EPA's risk assessment relied on the hazard values (i.e., HECs/HEDs/ADAFs) derived in this evaluation. These hazard values were used to estimate acute and chronic risks to various health effects following 1-BP exposure related to specific 1-BP uses.

There are several uncertainties inherent to the data and the assumptions used to support the derivation of the acute and chronic non-cancer PODs for different health effects domains. Below is a summary of the major uncertainties affecting the non-cancer hazard/dose response approach used for this assessment.

The uncertainties in hazard and dose response assessment are predicated on the health protective assumptions of relevancy of cancer and non-cancer findings in rodents being relevant to humans.

Decreased live litter size was selected as an endpoint to evaluate risks associated with acute exposures to 1-BP. Although the developmental toxicity studies included repeated exposures, EPA considered evidence that a single exposure to a toxic substance can result in adverse developmental effects, described by ([Van Raaij et al., 2003](#)), as relevant to 1-BP. This is a very health protective assumption.

Although there is evidence of biological effects in both the fetus and neonate, there are uncertainties in extrapolating doses for these lifestages. It is not known if 1-BP or its metabolites are transferred to the pups via lactation. It is possible that the doses reaching the fetus and the neonate are similar and that these lifestages are equally sensitive; however, it is also possible that one lifestage is more sensitive than the other or that internal doses are different. Additional data would be needed to refine dose estimates for the fetus and pups in order to identify the specific windows of sensitivity. EPA assumes that a single exposure at any point during pregnancy can have a detrimental impact (leading to fetal mortality). This health protective approach will overestimate risks to the workers and consumers following acute exposures, especially for those lifestages below reproductive age.

Neurotoxicity produced by 1-BP are based on rodent and human literature, with considerable similarities in both qualitative and quantitative outcomes. In the human and rodent literature, the most consistent responses are symptoms of frank neurotoxicity occurring at high exposures, with effects that are progressive at repeated exposures to low concentrations. In humans, the reports of effects in factory workers with lower exposures are limited by questions regarding exposure characterization, measurement techniques, and sensitivity. For these reasons, the data are not sufficiently robust for quantitative dose-response analysis. On the other hand, the findings of decreased peripheral nerve function are supported by parallel measures in several rodent studies.

Protection of Different Lifestages and Subpopulations: EPA is interested in the impact of 1-BP on other lifestages and subpopulations. Consideration of other lifestages, such as male and non-pregnant female workers in the occupational environment, children in the home environment would require using an alternative POD based on systemic toxicity, instead of using the POD based on developmental toxicity. Other endpoints associated with systemic toxicity generally had higher human equivalent concentrations than those associated with developmental toxicity. Therefore

EPA assumed that margins of exposure for pregnant women would also be protective of other lifestages.

While it is anticipated that there may be differential 1-BP metabolism based on lifestage; currently there are no data available, therefore the impact of this cannot be quantified. Similarly, while it is known that there may be genetic differences that influence CYP2E1 metabolic capacity, there may also be other metabolizing enzymes that are functional and impact vulnerability. There is insufficient data to quantify these differences for risk assessment purposes.

Heterogeneity among humans is an uncertainty associated with extrapolating the derived PODs to a diverse human population. One component of human variability is toxicokinetic, such as variations in CYP2E1 and glutathione transferase activity in humans ([Arakawa et al., 2012](#); [Trafalis et al., 2010](#)) which are involved in 1-BP metabolism in humans. EPA did not have chemical-specific information on susceptible subpopulations, or the distribution of susceptibility in the general population that could be used to decrease or increase the default intraspecies UF_H for toxicodynamic variability of 3. As such, EPA used an intraspecies UF_H of 10 for the risk assessment.

Uncertainties in the acute and chronic hazard values stem from the following sources:

Non-cancer hazard values (e.g., NOAELs, LOAELs, BMD): PODs were identified from the animal studies that were suitable for dose-response analysis. The process of identifying PODs for various health effects domains involved the evaluation of the strengths and limitations of the data and the weight of evidence for a particular health effects domain before supporting an association between 1-BP exposure and various human health effects. The selected PODs values (e.g., NOAEL, LOAEL or BMD) depend on the current available data and could change as additional studies are published.

Also, when selecting a BMD as a POD, the selection of the benchmark dose response (BMR) (e.g., 1%, 5% or 10% level) directly affects the calculation of the BMD. There are uncertainties related to the BMRs since their selection depends on scientific judgments on the statistical and biological characteristics of the dataset and how the BMDs will be finally used.

In addition, there are uncertainties about the appropriate dose-response model used to generate the BMDs. However, these uncertainties should be minimal if the chosen model fits well the observable range of the data, as discussed in EPA [Benchmark Dose Technical Guidance](#).

1. **Duration adjustment to continuous exposure:** Most of the PODs used to derive HECs came from studies that did not expose animals or humans to 1-BP on a continuous basis. These PODs were then mathematically adjusted to reflect equivalent continuous exposures (daily doses) over the study exposure period under the assumption that the effects are related to concentration $\times$ time ($C \times t$), independent of the daily (or weekly) exposure regimen ([U.S. EPA, 2011](#)). However, the validity of this assumption is generally unknown, and, if there are dose-rate effects, the assumption of $C \times t$ equivalence would tend to bias the POD downwards ([U.S. EPA, 2011](#)). A single exposure to 1-BP at a critical window of fetal development was assumed to produce adverse developmental effects. This is a health

protective approach and no duration adjustment was performed for adverse developmental outcomes.

2. **Extrapolation of repeated dose developmental effects to acute scenarios:** EPA considers developmental toxicity endpoints to be applicable to acute exposures. While there is some uncertainty surrounding this consideration because the precise critical exposure window is unknown, multiple publications suggest that developmental effects (e.g., decreased live litter size and increased post-implantation loss) may result from a single exposure during a critical window of development. There are uncertainties related to whether developmental effects observed in developmental toxicity studies may result from a single exposure to 1-BP. In this evaluation, the acute risk assessment used the hazard value for decreases in litter size and increases in post-implantation loss from the ([WIL Research, 2001](#)) two-generation reproductive toxicity study. This is considered a health protective approach.

For cancer hazard assessment, the major uncertainty is whether the mechanism/mode of action of 1-BP carcinogenesis should be considered mutagenic or nongenotoxic. The uncertainty arose mainly because 1-BP is highly volatile, resulting in positive results for mutagenicity in Ames tests that were conducted using closed-system methods designed for testing volatile chemicals but negative Ames test results in studies that may not have used closed-system test methods. Despite focusing solely on tests using desiccators or closed systems for *in vitro* testing, the equivocality remains as both positive and negative data were reported. While a mutagenic mode of action may be assumed to be operative at least in part for the carcinogenicity of 1-BP the default linear extrapolation method for dose-response is used. For the cancer dose-response assessment uncertainties exist arising from the animal to human extrapolation in the derivation of the IUR. A source of uncertainty is the cancer model used to estimate the POD for the IUR derivation. The POD was based on a model averaging approach to fit the bioassay data for lung tumors. Although the model average fit the data alternate model selections can also fit the data. A sensitivity analysis comparing reasonable alternate model choices found similar PODs therefore the impact of selecting between alternative models results in similar IURs.

Data gaps exist regarding *in vitro* mutagenicity study results and the mutagenic properties of 1-BP and its metabolites, studies of mutation in workers exposed to 1-BP over time, studies of the human population with cyp2E1 polymorphisms and cancer, and studies to evaluate developmental life stage exposure and cancer in childhood and adulthood. Further research is required at the molecular level to demonstrate that the cellular events are operative, development of a set of key events to understand the adverse outcome pathway from chemical exposure to phenotypic changes that ultimately lead to cancer.

4.3.4 Uncertainties in the Risk Assessment

4.3.4.1 Environmental Risk

EPA did not quantitatively assess potential risks to terrestrial receptors and sediment-dwelling organisms. Instead, a consideration of the physical-chemical and environmental fate characteristics of the chemical led EPA to determine that the potential exposures to organisms in these compartments are expected to be low. As discussed above in Section 3.1, as well as in the Problem Formulation, this assumption was based on the high volatility (Henry's Law constant of 7.3×10^{-3} atm-m³/mole), high water solubility (2.4 g/L), and low log K_{oc} (1.6) which suggests that 1-BP will

only be present at low concentrations in the sediment and terrestrial environmental compartments. This assumption of low potential for exposure based on physical-chemical characteristics is uncertain as it is not verified with monitoring data or hazard data specifically related to these organism. However, this uncertainty is not expected to affect the risk conclusions as sufficient data are available to indicate that these exposures are not significant enough to be biologically relevant.

The reasonably available environmental toxicity information for 1-BP indicate that the hazard to aquatic organisms is moderate, but a comparison of these hazard values with estimated environmental releases did not identify risks to the environment. While EPA has determined that sufficient data are available to characterize the overall environmental hazards of 1-BP, there are limited environmental toxicity studies available for assessing the long-term effects of 1-BP to aquatic species that may create some uncertainty associated with this assessment.

As described in Appendix G and Section 4.1, this assessment presents a screening-level assessment of relevant routes of exposure, which in the case of 1-BP are the aquatic exposure pathways, to evaluate ecological exposures in the US that may be associated with releases of 1-BP to surface waters. The foundation of the ecological risk assessment process is the relationship between the amount of a substance a receptor is exposed to and the potential for adverse effects resulting from the exposure. This established dose-response relationship provides the ability to quantitatively evaluate the potential environmental impacts that may result from a given exposure scenario. Because of uncertainties inherent in deriving RQ's, values are protective so that the risk estimate can state with a high degree of confidence that RQ values < 1 are not an ecological risk and can be screen out from further analysis.

This assessment was intended as a first-tier, or screening-level, evaluation. Discharging or releasing facilities were chosen from EPA's TRI.

An environmental risk evaluation used reasonably available environmental hazard, exposure, fate, and chemistry data, but was still a screening-level evaluation due to the limited amount of hazard and exposure information. EPA characterized the environmental hazards of 1-BP using reasonably available data for the chemical. As EPA was unable to obtain the full studies reports of the environmental hazard summaries in the ECHA database, the studies that reported these endpoints were not evaluated using the systematic review process. As such, there is uncertainty regarding the study quality of the data behind these summaries. Regardless, as no additional data were identified following the publication of the problem formulation so, these studies were used to help characterize the environmental hazards and risks of 1-BP to aquatic receptors.

4.3.4.2 Human Health Characterization

The non-cancer acute or chronic evaluations were expressed in terms of MOEs. MOEs are obtained by comparing the hazard values (i.e., HEC) for various 1-BP-related health effects with the exposure concentrations for the specific use scenarios. Given that the MOE is the ratio of the hazard value divided by the exposure, the confidence in the MOEs is directly dependent on the uncertainties in the hazard/dose-response and exposure assessments that supported the hazard and exposure estimates used in the MOE calculations.

Overall uncertainties in the exposure estimates used in the MOE calculations include uncertainties in the exposure monitoring and modeling. In the occupational exposure monitoring data for

workers, the sites used to collect 1-BP were not selected randomly; therefore, the reported data may not be representative of all occupational exposure scenarios. The exposure modeling approaches used for both occupational and consumer scenarios employed knowledge-based assumptions that may not apply to all occupational- and consumer-use scenarios.

The benchmark MOE used to evaluate risks for each use scenario represents the product of all UFs used for each non-cancer POD. These UFs accounted for various uncertainties including:

1. **Animal-to-human extrapolation (UF_A):** The UF_A accounts for the uncertainties in extrapolating from rodents to humans. In the absence of data, the default UF_A of 10 is adopted which breaks down to a factor of 3 for toxicokinetic variability and a factor of 3 for pharmacodynamic variability. There is no PBPK model for 1-BP to account for the interspecies extrapolation using rodent pharmacokinetic data in order to estimate internal doses for a particular dose metric.
2. **Inter-individual variation (UF_H):** The UF_H accounts for the variation in sensitivity within the human population. In the absence of data, the default UF_H of 10 is adopted which breaks down to a factor of 3 for toxicokinetic variability and a factor of 3 for pharmacodynamic variability. Since there is no PBPK model for 1-BP to reduce the human toxicokinetic/toxicodynamic variability, the total UF_H of 10 was retained.
3. **Extrapolation from subchronic to chronic (UF_S):** The UF_S accounts for the uncertainty in extrapolating from a subchronic to a chronic POD. Typically, a UF_S of 10 is used to extrapolate a POD from a less-than-chronic study to a chronic exposure. The same is true for a developmental toxicity study because the developmental period is recognized as a susceptible life stage where exposure during certain time windows is more relevant to the induction of developmental effects than lifetime exposure ([2016](#)). Thus, a UF_S of 10 was retained for all of the HECs discussed in the OPPT's risk assessment.
4. **LOAEL-to-NOAEL extrapolation (UF_L):** The UF_L accounts for the uncertainty in extrapolating from a LOAEL to a NOAEL. A value of 10 is the standard default UF_L value, although lower values (e.g., 3) can be used if the effect is considered minimally adverse at the LOAEL or is an early marker for an adverse effect ([U.S. EPA, 2002](#)). Typically, UF_L ranging from 3 to 30 (i.e., 3, 10, or 30) are used in the HECs. For one of the reproductive PODs ([Yamada et al., 2003](#)), a UF_L value of 10 was used based on a minimally adverse effect, which resulted in a total UF of 1000.

The human populations considered in this draft risk evaluation include individuals of both sexes (≥ 16 and older, including pregnant females) for occupational and consumer settings. Although exposures to younger non-users may be possible, the margins of exposure calculated for women of reproductive age are expected to be protective of this sensitive subpopulation. Currently there are insufficient data regarding specific genetic and/or lifestage differences that could impact 1-BP metabolism and toxicity for further refinement of the risk assessment.

The chronic risks for the occupational scenarios assumed that the non-cancer human health effects are constant for a working lifetime based on the exposure assumptions used in the occupational exposure assessment. However, the risks could be under- or over-estimated depending on the variations to the exposure profile of the workers and occupational non-users using 1-BP-containing adhesives, dry cleaning and spot cleaners, vapor degreasing, cold cleaning, and aerosol degreasers.

Confidence in the PBPK model predictions for 1-BP concentrations in blood and tissues are limited by the lack of comparison of model predictions with measured data. The PBPK model was further extended to simulate human exposures by scaling the physiological parameters to humans, assuming the partition coefficients are the same in rats and humans and scaling metabolic parameters by $BW^{3/4}$. Cross species and route to route extrapolations with the Garner et al. (2015) model are precluded by the lack of data to inform a model of a species other than rat and a route other than inhalation.

Limited toxicological data is available by the oral route, and no repeated-dose toxicity studies by the dermal route were identified on 1-BP. However, although the toxicological data via the oral route is insufficient for quantitative dose-response assessment, data from these studies were used for qualitative support in the weight of the scientific evidence for nervous system effects (see Section 3.2.8.2 and Appendix I), suggesting that, at least for the nervous system endpoint, the delivery of 1-BP via the inhalation- (i.e., pulmonary/systemic circulation) and oral- (i.e., portal circulation) routes of exposure results in comparable toxic endpoints. EPA chose to derive dermal HEDs for dermal exposures by extrapolating from other routes for systemic endpoints (i.e. not point of contact effects) and none of the key endpoints for 1-BP (liver, kidney, reproductive, developmental and nervous system effects) were considered point of contact therefore all were used for route-to-route extrapolation. The route-to-route extrapolations enabled EPA to estimate applied dermal PODs. Since physiologically based pharmacokinetic/ pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have not been identified, there is no relevant kinetic or metabolic information for 1-BP that would facilitate development of dosimetric comparisons, and the studies by the oral route were insufficient for quantitative dose-response assessment, EPA chose to derive dermal HEDs for dermal exposures by extrapolating from the inhalation PODs. However, the inhalation studies were performed by whole body exposure, rather than nose only exposure, which may have led to additional dosing by the oral and dermal routes of exposure, due to deposition on fur and the grooming behavior of rodents, resulting in uncertainty of actual dose received. It should be noted that EPA was unable to conclude with certainty that comparable toxic endpoints would be associated with the dermal route of exposure, considering the expected quantitative ADME differences and the absence of an adequate PBPK model. Notwithstanding these uncertainties, EPA considered this approach appropriate considering the comparable toxic endpoints identified in the available repeated-dose oral/inhalation toxicity studies and the uncertainty with the putative toxicant (i.e., 1-BP or a metabolite(s)).

As discussed previously, the estimates for extra cancer risk were based on the assumption of linearity in the relationship between 1-BP exposure and probability of cancer. Uncertainties are introduced in the cancer risks when there is limited information justifying the linear cancer dose-response model when compared to other available models. In the case of 1-BP, the cancer IUR was based on reliable data supporting a mutagenic mode of action for at least 1-BP-induced lung tumors (NTP, 2011a).

4.4 Other Risk Related Considerations

4.4.1 Potentially Exposed or Susceptible Subpopulations

TSCA requires that a risk evaluation “determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a *potentially exposed or susceptible*

subpopulation (PESS) identified as relevant to the risk evaluation by the Administrator, under the conditions of use.” TSCA § 3(12) states that “the term ‘potentially exposed or susceptible subpopulation’ means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly.”

4.4.1.1 Exposure Considerations

In developing the exposure assessment for 1-BP, EPA analyzed reasonably available information to ascertain whether some human receptor groups may have greater exposure or susceptibility than the general population to the hazard posed by 1-BP. Exposures of 1-BP would be expected to be higher amongst groups with 1-BP containing products in their homes, and workers who use 1-BP as part of typical processes.

EPA identified potentially exposed or susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In Section 2.4, EPA addressed the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure in occupational settings. In Section 2.3.2, EPA addresses the potentially exposed or susceptible subpopulations for consumer users between the ages of 11-21 as well as adults. EPA also addresses potentially exposed or susceptible subpopulations for bystanders within residences where a consumer product containing 1-BP may be used. Bystanders, for purposes of this risk evaluation, can be any age group (infant to elderly).

Of the human receptors identified in the previous sections, EPA identifies the following as potentially exposed or susceptible subpopulations due to their *greater exposure* and considered them in the risk evaluation:

- Workers and occupational non-users. EPA assessed exposure to these subpopulations using a combination of personal exposure monitoring data (measured data) and modeling approaches. The exposure estimates were applicable to both male and female workers of reproductive age, including adolescents. Section 2.4 provides more details on these subpopulations across various industry sectors that are likely to use 1-BP.
- Consumer users and bystanders associated with consumer use. 1-BP has been identified as being used in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure. A description of the exposure assessment for consumers is available in Section 2.3.2.

There are some exposure scenarios where greater exposure from multiple sources may occur and individuals who may have greater potential for exposure to 1-BP. For example, some workers and occupational non-users may also use consumer products containing 1-BP, and have additional exposure outside of the workplace.

4.4.1.2 Aggregate and Sentinel Exposures

Section 2605(b)(4)(F)(ii) of TSCA requires EPA, as a part of the risk evaluation, to describe whether aggregate or sentinel exposures under the conditions of use were considered and the basis for their consideration. EPA has defined aggregate exposure as “the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways.”

As part of this risk evaluation, EPA considered aggregate exposures by evaluating exposure and risk from both the inhalation and dermal routes for workers and consumers in scenarios where such exposures are expected. EPA expects workers to be exposed via both inhalation of 1-BP vapor and dermal contact with liquid containing 1-BP. Similarly, EPA expects certain consumer users to be exposed via both the inhalation of 1-BP vapor and dermal contact with liquid containing 1-BP.

EPA defines sentinel exposure as “the exposure to a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures.” In terms of this risk evaluation, EPA considered sentinel exposures by considering exposures to populations who may have upper bound exposures – for example, workers who perform activities with higher exposure potential, or consumers who have higher exposure potential (e.g., those involved with do-it-yourself projects) or certain physical factors like body weight or skin surface area exposed. EPA characterized high-end exposures in evaluating exposure using both monitoring data and modeling approaches. Where statistical data are available, EPA typically uses the 95th percentile value of the available dataset to characterize high-end exposure for a given condition of use.

5 RISK DETERMINATION

5.1 Unreasonable Risk

5.1.1 Overview

In each risk evaluation under TSCA section 6(b), EPA determines whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use. The determination does not consider costs or other non-risk factors. In making this determination, EPA considers relevant risk-related factors, including, but not limited to: the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any potentially exposed or susceptible subpopulations); the severity of hazard (including the nature of the hazard, the irreversibility of the hazard); and uncertainties. EPA takes into consideration the Agency's confidence in the data used in the risk estimate. This includes an evaluation of the strengths, limitations and uncertainties associated with the information used to inform the risk estimate and the risk characterization. This approach is in keeping with the Agency's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726)²⁸.

Under TSCA, conditions of use are defined as the circumstances, as determined by the Administrator, under which the substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of. TSCA §3(4).

An unreasonable risk may be indicated when health risks under the conditions of use are identified by comparing the estimated risks with the risk benchmarks and where the risks affect the general population or certain potentially exposed or susceptible subpopulations (PESS), such as consumers. For other PESS, such as workers, an unreasonable risk may be indicated when risks are not adequately addressed through expected use of workplace practices and exposure controls, including engineering controls or use of personal protective equipment (PPE). An unreasonable risk may also be indicated when environmental risks under the conditions of use are greater than environmental risk benchmarks.

EPA uses the terms "indicates unreasonable risk relative to the Agency's risk benchmarks" to indicate EPA concern for potential unreasonable risk. For non-cancer endpoints, "less than MOE benchmark" is used to indicate potential unreasonable risk; this occurs if an MOE value is less than the benchmark MOE (e.g., MOE 0.3 < benchmark MOE 30). EPA uses the term "greater than risk benchmark" to indicate potential unreasonable risk for cancer endpoints, this occurs if the lifetime cancer risk value is greater than 1 in 10,000 (e.g., cancer risk value is 5×10^{-2} which is greater than the standard range of acceptable cancer risk benchmarks of 1×10^{-4} to 1×10^{-6}). For environmental endpoints, to indicate potential unreasonable risk EPA uses a risk quotient (RQ) value "greater than 1" (e.g. RQ >1). Conversely, this risk determination uses the term "does not indicate

²⁸ This risk determination is being issued under TSCA section 6(b) and the terms used, such as unreasonable risk, and the considerations discussed are specific to TSCA. Other statutes have different authorities and mandates and may involve risk considerations other than those discussed here.

unreasonable risk relative to risk benchmarks” to indicate no EPA concern for potential unreasonable risk. More details are described below.

The degree of uncertainty surrounding the MOEs, cancer risk or RQs are a factor in determining whether or not unreasonable risk is present. Where uncertainty is low, and EPA has high confidence in the hazard and exposure characterizations (for example, the basis for the characterizations is measured or monitoring data or a robust model and the hazards identified for risk estimation are relevant for conditions of use), the Agency has a higher degree of confidence in its risk determination. EPA may also consider other risk factors, such as severity of endpoint, reversibility of effect, or exposure-related considerations such as magnitude or number of exposures, in determining that the risks are unreasonable under the conditions of use. Where EPA has made assumptions in the scientific evaluation, whether or not those assumptions are protective, will also be a consideration. Additionally, EPA considers the central tendency and high-end scenarios when determining the unreasonable risk. High-end risk estimates (e.g. 95th percentile) are generally intended to cover individuals or sub-populations with greater exposure and central tendency risk estimates are generally estimates of average or typical exposure.

Conversely, EPA may make a no unreasonable risk determination for conditions of use where the substance’s hazard and exposure potential, or where the risk-related factors described previously, lead EPA to determine that the risks are not unreasonable.

5.1.2 Risks to Human Health

5.1.2.1 Determining Non-Cancer Risks

Margins of exposure (MOEs) are used in EPA’s risk evaluations as a starting point to estimate non-cancer risks for acute and chronic exposures. The non-cancer evaluation refers to potential adverse health effects associated with health endpoints other than cancer, including to the body’s organ systems, such as reproductive/developmental effects, cardiac and lung effects, and kidney and liver effects. The MOE is the point of departure (an approximation of the no-observed adverse effect level (NOAEL) or benchmark concentration / dose level (BMCL/BMDL)) for a specific health endpoint divided by the exposure concentration for the specific scenario of concern. The benchmark for the MOE that is used accounts for the total uncertainty in a point of departure, including, as appropriate: (1) the variation in sensitivity among the members of the human population (i.e., intrahuman/intraspecies variability); (2) the uncertainty in extrapolating animal data to humans (i.e., interspecies variability); (3) the uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure to lifetime exposure (i.e., extrapolating from subchronic to chronic exposure); and (4) the uncertainty in extrapolating from a lowest observed adverse effect level rather than from a NOAEL. MOEs can provide a non-cancer risk profile by presenting a range of estimates for different non-cancer health effects for different exposure scenarios and are a widely recognized point estimate method for evaluating a range of potential non-cancer health risks from exposure to a chemical.

A calculated MOE that is less than the benchmark MOE indicates the possibility of risk to human health. Whether EPA those risks are unreasonable will depend upon other risk-related factors, such as severity of endpoint, reversibility of effect, exposure-related considerations (e.g. duration, magnitude, frequency of exposure, population exposed), and the confidence in the information used to inform the hazard and exposure values. If the calculated MOE is greater than the benchmark MOE, generally it is less likely that there is risk.

Uncertainty factors also play an important role in the risk estimation approach and in determining unreasonable risk. A lower benchmark MOE (e.g. 30) indicates greater certainty in the data (because fewer of the default uncertainty factors are relevant to a given point of departure as described above were applied). A higher benchmark MOE (e.g. 1000) would indicate more uncertainty in risk estimation and extrapolation for the MOE for specific endpoints and scenarios. However, these are often not the only uncertainties in a risk evaluation.

5.1.2.2 Determining Cancer Risks

EPA estimates cancer risks by determining the incremental increase in probability of an individual in an exposed population developing cancer over a lifetime (excess lifetime cancer risk (ELCR)) following exposure to the chemical under specified use scenarios. Standard cancer benchmarks used by EPA and other regulatory agencies are an increased cancer risk above benchmarks ranging from 1 in 1,000,000 to 1 in 10,000 (i.e., 1×10^{-6} to 1×10^{-4}) depending on the subpopulation exposed. Generally, EPA considers 1×10^{-6} to 1×10^{-4} as the appropriate benchmark for the consumer users, and non-occupational potentially exposed or susceptible subpopulations (PESS).²⁹

For 1-BP, EPA, consistent with case law and 2017 NIOSH guidance³⁰, used 1×10^{-4} as the benchmark for the purposes of this risk determination for individuals in industrial and commercial work environments subject to Occupational Safety and Health Act (OSHA) requirements. It is important to note that 1×10^{-4} is not a bright line and EPA has discretion to make risk determinations based on other benchmarks as appropriate based on analysis. It is important to note that exposure related considerations (duration, magnitude, population exposed) can affect EPA's estimates of the ELCR.

5.1.3 Environmental Risk

To assess environmental risk, EPA identifies and evaluates environmental hazard data for aquatic, sediment-dwelling, and terrestrial organisms exposed under acute and chronic exposure conditions. The environmental risk includes any risks that exceed benchmarks to the aquatic environment from levels of the evaluated chemical found in the environment (e.g., surface water, sediment, soil, biota) based on the fate properties, relatively high potential for release, and the availability of environmental monitoring data and hazard data.

Environmental risks are estimated by calculating a risk quotient (RQ). The RQ is defined as:

²⁹ As an example, when EPA's Office of Water in 2017 updated the Human Health Benchmarks for Pesticides, the benchmark for a "theoretical upper-bound excess lifetime cancer risk" from pesticides in drinking water was identified as 1 in 1,000,000 to 1 in 10,000 over a lifetime of exposure (EPA. Human Health Benchmarks for Pesticides: Updated 2017 Technical Document. January 2017. <https://www.epa.gov/sites/production/files/2015-10/documents/hh-benchmarks-techdoc.pdf>). Similarly, EPA's approach under the Clean Air Act to evaluate residual risk and to develop standards is a two-step approach that includes a "limit on maximum individual lifetime [cancer] risk (MIR) of approximately 1 in 10 thousand" (54 FR 38045, September 14, 1989) and consideration of whether emissions standards provide an ample margin of safety to protect public health "in consideration of all health information, including the number of persons at risk levels higher than approximately 1 in 1 million, as well as other relevant factors" (54 FR 38045, September 14, 1989).

³⁰ NIOSH [2017]. Current intelligence bulletin 68: NIOSH chemical carcinogen policy, available at <https://www.cdc.gov/niosh/docs/2017-100/pdf/2017-100.pdf>.

$$RQ = \text{Environmental Concentration} / \text{Effect Level}$$

An RQ equal to 1 indicates that the exposures are the same as the concentration that causes effects. If the RQ exceeds 1, the exposure is greater than the effect concentration and there is potential for risk presumed. If the RQ does not exceed 1, the exposure is less than the effect concentration and there is no risk presumed. The Concentrations of Concern or hazard value for certain aquatic organisms, sediment-dwelling or terrestrial organisms are used to calculate RQs for acute and chronic exposures. For environmental risk, EPA is more likely to determine that there is unreasonable risk if the RQ exceeds 1 for the conditions of use being evaluated. Consistent with EPA's human health evaluations, the RQ is not always treated as a bright line and other risk-based factors may be considered (e.g., exposure scenario, uncertainty, severity of effect) for purposes of making a risk determination.

5.2 Risk Determination for 1-Bromopropane

EPA's determinations of unreasonable risk for the conditions of use of 1-BP listed below are based on health risks to: workers during occupational exposures; occupational non-users exposed to 1-BP indirectly by being in the same work area of the building; consumers users; bystanders or non-users exposed indirectly by being in the house where consumer or where commercial residential uses are carried out. As described below, EPA did not find unreasonable risks to the environment for the conditions of use of 1-BP listed below.

Environmental risks: EPA integrated relevant pathways of environmental exposure with available hazard data to estimate risk to environmental receptors. The high volatility, high water solubility and low Log K_{oc} of 1-BP suggest that 1-BP will only be present at low concentrations in the sediment and terrestrial environmental compartments, so these pathways were not further analyzed in this risk evaluation since risk from these exposure pathways are not expected.

In this risk evaluation, EPA calculated risk to the aquatic organisms. For all conditions of use, EPA did not identify any exceedances of benchmarks to aquatic organisms from exposures to 1-BP in surface waters. The RQ values for acute and chronic risks are <0.01 and 0.12, respectively based on the best available science, and 0.02 and 0.32 based on the lowest-bound ECHA summary data, respectively (Table 4-2). An RQ that does not exceed 1 indicates that the exposure concentrations of 1-BP are less than the concentrations that would cause an effect to organisms in the aquatic pathways. Because the RQ values do not exceed 1, and because EPA used a conservative screening level approach, these values indicate there are no unreasonable risks of 1-BP to the aquatic pathways. As a result, EPA does not find unreasonable risks to the environment from the conditions of use for 1-BP.

General population: As part of the problem formulation for 1-BP, EPA identified general population exposures via surface water, drinking water, and sediment as pathways for no further analysis in the risk evaluation. In addition, OCSPP understands from OAR that the Agency is finishing review of comments on this draft notice to add 1-BP to the list of HAPs under Section 112 of the Clean Air Act, 42 U.S.C. 7412 and intends to finalize an action before the end of 2019. OCSPP works closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes

and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should focus on those exposure pathways associated with TSCA uses that are not subject to the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of concern to EPA. Exposures to 1-BP receptors (i.e., general population) may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. As described above, no further analysis was needed for exposures via surface water, drinking water and sediment, or other environmental statutes administered by EPA would adequately assess and would effectively manage these exposures. Therefore, EPA did not evaluate hazards or exposures to the general population in this risk evaluation, and there is no risk determination for the general population.

In the Table 5-1 below, EPA identifies a single human health adverse effect as the “unreasonable risk driver” for a particular condition of use. This is the effect that is most sensitive, and it is expected that managing risks for this effect will address other identified risks. As described in Section 4, additional significant risks associated with more than one adverse effect (e.g. developmental, reproductive, liver, kidney, nervous system) were identified for many conditions of use.

Table 5-1. Unreasonable Risk Determination

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
Manufacturing	Domestic Manufacturing	Domestic Manufacturing	Section 6(b)(4)(A) unreasonable risk determination for domestic manufacture of 1-BP: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Exposure scenario with highest risk estimate: Worker: - Developmental adverse effects from acute inhalation exposure. - Cancer resulting from chronic inhalation exposure. Benchmark: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimate: Workers: - Developmental adverse effects: MOE = 63 for workers using no PPE (high-end estimate) (Table 4-6).Table 4-6). Note: There is no unreasonable risk when PPE (APF=10) is used. - Cancer: $5.54\text{E-}04$ for workers using no PPE (high-end estimate) (Table 4-47).Table 4-47). Note: There is no unreasonable risk when PPE (APF=10) is used. Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations</u>: For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-48).Table 4-48). And, while other risk estimates from other exposure scenarios from acute and chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			to those benchmarks when expected use of PPE was considered (Table 4-27 and Table 4-53). Table 4-27 and Table 4-53). Based on the process and work activity description, exposure to occupational non-users was expected to be negligible (Table 4-6 Table 4-6 and Table 4-27 Table 4-27). Estimated exposed population: 35 to 73 workers.
Manufacturing	Import	Import	Section 6(b)(4)(A) unreasonable risk determination for import of 1-BP: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate</u>: Workers: Cancer resulting from chronic dermal exposure. <u>Benchmark</u>: Cancer: 10^{-4}. <u>Risk estimate</u>: Workers: Cancer: Dermal: $1.38\text{E-}04$ for workers using no PPE (Table 4-53). Note: There is no unreasonable risk when PPE (gloves PF=5) are used. Systematic Review confidence rating (health hazard): High. <u>Systematic Review confidence rating (health dermal exposure)</u>: Medium. Risk estimates derived using the <i>EPA Dermal Exposure to Volatile Liquids</i> model. <u>Risk considerations</u>: For workers, non-cancer MOEs from acute and chronic inhalation and dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-7, Table 4-28 and Table 4-48). And, while cancer risk estimates from chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-47 and Table 4-53). For occupational non-users, exposures were expected to be negligible (Table 4-7 and Table 4-28). Estimated exposed population: 30 to 94 workers.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
Processing	Processing as a reactant	Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing	Section 6(b)(4)(A) unreasonable risk determination for processing of 1-BP as a reactant: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate</u>: Workers: Cancer resulting from chronic dermal exposure. <u>Benchmark</u>: Cancer: 10^{-4}. <u>Risk estimate</u>: Workers: Cancer: Dermal: $1.38\text{E-}04$ for workers using no PPE (Table 4-53). Note: There is no unreasonable risk when PPE (gloves PF=5) are used. Systematic Review confidence rating (health hazard): High. Systematic Review confidence rating (health dermal exposure): Medium. Risk estimates derived using the <i>EPA Dermal Exposure to Volatile Liquids</i> model. <u>Risk considerations</u>: For workers, non-cancer MOEs from acute and chronic inhalation and dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-7, Table 4-28 and Table 4-48). And, while cancer risk estimates from chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-47 and Table 4-53). For occupational non-users, exposures were expected to be negligible (Table 4-7 and Table 4-28). Estimated exposed population: 30 to 72 workers.

Processing	Processing – incorporating into formulation, mixture or reaction product	Solvents for cleaning or degreasing in manufacturing of: - all other chemical product and preparation - computer and electronic product - electrical equipment, appliance and component - soap, cleaning compound and toilet preparation - services	Section 6(b)(4)(A) unreasonable risk determination for processing of 1-BP into a formulation, mixture, or reaction product: - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver:</u> Workers and occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. <u>Benchmarks:</u> Workers and occupational non-users: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimates: Workers: - Developmental adverse effects: Acute inhalation MOEs 224 and 45 (central tendency and high-end) with respiratory protection (an APF=50) (Table 4-8). Chronic inhalation MOEs 317 and 63 (central tendency and high-end) with respiratory protection (an APF=50) (Table 4-29). - Cancer: Inhalation: $1.E-04$ and $7.75E-04$ (central tendency and high-end) with respiratory protection (an APF = 50) (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 52 and 11 (central tendency and high-end) (Table 4-8). Chronic inhalation MOEs 74 and 15 (central tendency and high-end (Table 4-29). - Cancer: Inhalation: $5.17E-04$ and $3.26E-03$ (central tendency and high-end) (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): Medium. High for the monitoring data. <u>Risk considerations:</u> The assessment of inhalation exposure from this type of processing is based on monitoring data, however, the data may not be representative of exposures across the range of facilities that formulate products containing 1-BP.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-48).Table 4-48). And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53).Table 4-53). <u>Estimated exposed population</u>: 220 to 1,046 including both workers and occupational non-users.
Processing	Processing - incorporating into articles	Solvents (which become part of product formulation or mixture) in construction	Section 6(b)(4)(A) unreasonable risk determination for processing of 1-BP for incorporation into articles: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate</u>: Workers: Cancer resulting from chronic dermal exposure. <u>Benchmark</u>: Cancer: 10^{-4}. <u>Risk estimate</u>: Workers: Cancer: Dermal: $1.38\text{E-}04$ for workers using no PPE (Table 4-53). Note: There is no unreasonable risk when PPE (gloves APF=5) are used. Systematic Review confidence rating (health hazard): High. Systematic Review confidence rating (health dermal exposure): Medium. Risk estimates derived using the <i>EPA Dermal Exposure to Volatile Liquids</i> model. <u>Risk considerations</u>: For workers, non-cancer MOEs from acute and chronic inhalation and dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-7, Table 4-28 and Table 4-48). And, while cancer risk estimates from chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			benchmarks when expected use of PPE was considered (Table 4-47 and Table 4-53). For occupational non-users, exposures were expected to be negligible (Table 4-7 and Table 4-28). Estimated exposed population: 15 workers.
Processing	Repackaging	Solvent for cleaning or degreasing in all other basic organic chemical manufacturing	Section 6(b)(4)(A) unreasonable risk determination for repackaging of 1-BP as a solvent for cleaning or degreasing in all other basic organic chemical manufacturing: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate:</u> Workers: Cancer resulting from chronic dermal exposure. <u>Benchmark:</u> Cancer: 10^{-4}. <u>Risk estimate:</u> Workers: Cancer: Dermal: $1.38\text{E-}04$ for workers using no PPE (Table 4-53). Note: There is no unreasonable risk when PPE (gloves PF=5) are used. Systematic Review confidence rating (health hazard): High. Systematic Review confidence rating (health dermal exposure): Medium. Risk estimates derived using the <i>EPA Dermal Exposure to Volatile Liquids</i> model. <u>Risk considerations:</u> For workers, non-cancer MOEs from acute and chronic inhalation and dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-7, Table 4-28 and Table 4-48). And, while cancer risk estimates from chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-47 and Table 4-53). For occupational non-users, exposures were expected to be negligible (Table 4-7 and Table 4-28).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Estimated exposed population: 30 to 94 workers.
Processing	Recycling	Recycling	Section 6(b)(4)(A) unreasonable risk determination for recycling of 1-BP: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate:</u> Workers: Cancer resulting from chronic dermal exposure. <u>Benchmark:</u> Cancer: 10^{-4}. <u>Risk estimate:</u> Cancer: Dermal: $1.38\text{E-}04$ for workers using no PPE (Table 4-53). Note: There is no unreasonable risk when PPE (gloves PF=5) are used. Systematic Review confidence rating (health hazard): High. Systematic Review confidence rating (health dermal exposure): Medium. Risk estimates derived using the <i>EPA Dermal Exposure to Volatile Liquids</i> model. <u>Risk considerations:</u> For workers, non-cancer MOEs from acute and chronic inhalation and dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-25Table 4-25, Table 4-46Table 4-46 and Table 4-48). And, while cancer risk estimates from chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-47 and Table 4-53). For occupational non-users, exposures were expected to be negligible (Table 4-25Table 4-25 and Table 4-46Table 4-46). <u>Estimated exposed population:</u> over 49 workers and 18 occupational non-users.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
Distribution in commerce	Distribution in commerce	Distribution in commerce	<u>Section 6(b)(4)(A) unreasonable risk determination for distribution in commerce of 1-BP:</u> Does not present an unreasonable risk of injury to health (workers, occupational non-users, consumers and bystanders) or to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Other risk considerations:</u> A quantitative evaluation of the distribution of 1-BP was not included in the risk evaluation because exposures and releases from distribution were considered within each condition of use.
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (e.g., open-top)	Section 6(b)(4)(A) unreasonable risk determinations for industrial and commercial use of 1-BP as a solvent for degreasing in batch vapor degreasers (open-top) and in-line vapor degreaser (e.g., conveyorized, web cleaner): - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver:</u> Workers and occupational non-users: - Developmental adverse effects resulting from acute inhalation exposure. - Cancer resulting from chronic inhalation exposure. <u>Benchmarks:</u> - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. <u>Risk estimates:</u> <u>Workers:</u> - Developmental adverse effects: Acute inhalation MOEs 127 and 17 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-9). Chronic inhalation MOEs 179 and 24 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-30Table 4-30). - Cancer: Chronic inhalation 2.E-04 and 2.03E-03 (central tendency and high-end, open-top) with respiratory protection (APF=50) (Table 4-47). <u>Occupational non-users:</u> - Developmental adverse effects: Acute inhalation MOEs 171 and 13 (central tendency and high-end) with expected workplace engineering controls (Table 4-11). Chronic inhalation MOEs 242 and 18 (central
		In-line vapor degreaser (e.g., conveyorized, web cleaner)	

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			tendency and high-end) with expected workplace engineering controls (Table 4-32). - Cancer: Chronic inhalation 1.49E-04 and 2.09E-03 (central tendency and high-end) with expected workplace engineering controls (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations:</u> EPA obtained monitoring data for workers and occupational non-users from several sources. In addition, EPA conducted a near-field/far-field model for vapor degreasing (to identify risks to the worker using the chemical and to the occupational non-user who may be nearby or in the same facility). Also, EPA was able to model open top degreasing operations using two scenarios: pre-engineering control (which was generally comparable to the exposures reported in literature) and post-engineering control. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-49). And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53). <u>Estimated exposed population:</u> 4,712 to 23,558 workers and occupational non-users. These estimates likely cover a range of degreasing operations and are not specific to batch vapor degreasers.

Industrial/ commercial use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (e.g., closed-loop)	Section 6(b)(4)(A) unreasonable risk determinations for industrial and commercial use of 1-BP as a solvent for degreasing in batch vapor degreasers (e.g., closed loop): - Presents an unreasonable risk of injury to health (occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver:</u> Occupational non-users: - Developmental adverse effects resulting from acute inhalation exposure. - Cancer resulting from inhalation exposure. <u>Benchmarks:</u> - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. <u>Risk estimates:</u> Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 856 and 63 (central tendency and high-end) (Table 4-12). Chronic inhalation MOEs 1,208 and 89 (central tendency and high-end) (Table 4-33). - Cancer: Chronic inhalation 2.97E-05 and 4.19E-04 (central tendency and high-end) (Table 4-47). Systematic Review confidence rating (health hazard): High. Systematic Review confidence rating (inhalation exposure): Medium. Modeled data. <u>Risk considerations:</u> There are no 1-BP monitoring data specific to closed-loop degreasers. A NEWMOA study states air emissions can be reduced by 98 percent or more when a closed-loop degreaser is used instead of an open-top vapor degreaser. This reduction factor was applied to the vapor degreasing model results of the open-top vapor degreasers to estimate exposure to batch closed-loop vapor degreasers. Occupational non-users unreasonable risk determination reflects potential severity of effect associated with exposures to 1-BP and the expected absence of PPE. While risk estimates for other pathways of occupational exposure for this condition of use (such as chronic inhalation and dermal exposures) indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these pathways do not indicate risk relative to those

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			benchmarks when expected use of PPE was considered (Table 4-12, Table 4-33, Table 4-47, Table 4-49 and Table 4-53). <u>Estimated exposed population</u>: 5,192 (workers) and 2,346 (occupational non-users).
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Cold cleaner	Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of 1-BP as a solvent for degreasing in cold cleaning: - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Workers: Cancer resulting from chronic inhalation exposure. Occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. <u>Benchmarks</u>: Workers and occupational non-users: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimates: Workers: - Cancer: Inhalation: 1.E-04 and 3.04E-04 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 7 (central tendency and high-end) (Table 4-13). Chronic inhalation MOEs 9 (central tendency and high-end) (Table 4-34). - Cancer: Inhalation: 4.13E-03 and 5.33E-03 (central tendency and high-end) (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			<u>Risk considerations:</u> EPA utilized OSHA data for two facilities. However, due to the low number of available data points, the assessed exposure may not be representative of the full range of cold cleaning exposure scenarios. Additionally, a cold cleaning model was used to confirm the risk estimates based on emission factors derived using VOC data; however, it is not known if such emission factors are representative of 1-BP emissions. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-49). While risk estimates for other pathways of occupational exposure for this condition of use (such as acute and chronic inhalation and chronic dermal exposures) indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these pathways do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-13, Table 4-334-34 and Table 4-53). <u>Estimated exposed population:</u> There is no information to determine the number of workers and occupational non-users potentially exposed to 1-BP during cold cleaning. Based on literature search to date, EPA does not know how many facilities currently use 1-BP in cold cleaning. It is possible that some degreasing facilities utilizing batch vapor degreasers also use 1-BP as a cold cleaning solvent.
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Aerosol spray degreaser/ cleaner	Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of 1-BP as a solvent for degreasing in the form of aerosol spray degreaser or cleaner: - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Workers: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. <u>Benchmarks</u>: Workers and occupational non-users: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimates: Workers: - Developmental adverse effects: Acute inhalation MOEs 133 and 38 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-17). Chronic inhalation MOEs 188 and 53 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-38). - Cancer: Inhalation: 2.E-04 and 7.24E-04 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 155 and 18 (central tendency and high-end) (Table 4-17). Chronic inhalation MOEs 218 and 26 (central tendency and high-end) (Table 4-38). - Cancer: Inhalation: 1.60E-04 and 1.44E-03 (central tendency and high-end) (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations</u>: EPA considered two studies with monitoring data. In addition, EPA modeled workers and occupational non-users exposures to 1-BP during brake servicing as a representative exposure scenario. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-52). Table 4-52). And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Estimated exposed population: 2,465 to 12,329 workers and occupational non-users. This is based on 2002 market data; it is unclear whether the number of establishments using 1-BP-based aerosol solvents has changed substantially since 2002.
Industrial/ commercial use	Adhesives and sealants	Adhesive chemicals – spray adhesive for foam cushion manufacturing and other uses	Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of 1-BP as an adhesive and sealant, including the spray adhesive for foam cushion manufacturing: - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Workers (for sprayer and non-sprayer): - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposure. Occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. <u>Benchmarks</u>: Workers and occupational non-users: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimates: Workers (for sprayer and non-sprayer): - Developmental adverse effects: Acute inhalation MOEs 48 and 20 (central tendency and high-end, for sprayer) and 47 and 29 (central tendency and high-end, for non-sprayer) with expected workplace engineering controls and respiratory protection (APF=50) (Table 4-24). Chronic inhalation MOEs 67 and 29 (central tendency and high-end, for sprayer) and 67 and 42 (central tendency and high-end, non-sprayer) with expected workplace engineering controls and respiratory protection (APF=50) (Table 4-40).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			- Cancer: Inhalation: 6.E-04 and 1.72E-03 (central tendency and high-end, for sprayer) and 6.E-04 and 1.18E-03 (central tendency and high-end, for non-sprayer), with expected workplace engineering controls and respiratory protection (APF=50) (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 9 and 3 (central tendency and high-end) with expected workplace engineering controls (Table 4-24). Chronic inhalation MOEs 12 and 4 (central tendency and high-end) with expected workplace engineering controls (Table 4-40). - Cancer: Inhalation: 3.18E-03 and 1.12E-02 (central tendency and high-end) with expected workplace engineering controls (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations:</u> Monitoring data for this condition of use were identified in several sources, including journal articles, NIOSH HHEs, and OSHA CEHD database. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-50).Table 4-50). And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53). <u>Estimated exposed population:</u> 551 to 1,543 workers, and 952 to 2,666 occupational non-users, for a total maximum of 4,209 individuals.

Industrial/ commercial use	Cleaning and furniture care products	Dry cleaning solvent	Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of 1-BP as a cleaning and furniture care product in the form of dry-cleaning solvent: - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Workers (for spot cleaner and machine and finish): - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. Occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. Benchmarks: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimates: Workers (for spot cleaner and machine and finish): - Developmental adverse effects: Acute inhalation MOEs 5 and 2 (central tendency and high-end, for spot cleaner and machine and finish,) when using 4th generation machines (Table 4-20). Chronic inhalation MOEs 7 and 3 (central tendency and high-end, for spot cleaner and machine and finish,) when using 4th generation machines (Table 4-43). - Cancer: Inhalation: 1.28E-03 and 3.29E-03 (central tendency and high-end, for spot cleaner) and 1.26E-03 and 3.74E-03 (central tendency and high-end, for machine and finish), when using 4th (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 9 and 3 (central tendency and high-end) when using 4th generation machines (Table 4-20).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Chronic inhalation MOEs 12 and 4 (central tendency and high-end) when using 4th generation machines (Table 4-43). - Cancer: Inhalation: 6.94E-04 and 2.39E-03 (central tendency and high-end) when using 4th generation machines (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations:</u> EPA considered two studies of dry-cleaning establishments in New Jersey. Modeling allowed EPA to estimate exposures for multiple workers within the dry-cleaning facility, including workers performing different tasks and to account for the use of 4th generation dry cleaning machines. Monitoring data for this condition of use were identified in several sources, including journal articles and NIOSH HHEs. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-51).Table 4-51). And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53). <u>Estimated exposed population:</u> 92 workers and occupational non-users.
Industrial/ commercial use	Cleaning and furniture care products	Spot cleaner, stain remover	Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of 1-BP as a cleaning and furniture care product in the form of spot cleaner and stain remover: - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Workers: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. <u>Benchmarks</u>: Workers and occupational non-users: - Developmental adverse effects: MOE 100. - Cancer: 10^{-4}. Risk estimates: Workers: - Developmental adverse effects: Acute inhalation MOEs 19 and 4 (central tendency and high-end) (Table 4-21). Chronic inhalation MOEs 27 and 5 (central tendency and high-end) (Table 4-44). - Cancer: Inhalation: $1.43\text{E-}03$ and $9.69\text{E-}03$ (central tendency and high-end) (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 10 and 4 (modeled central tendency and high-end) (Table 4-22). Chronic inhalation MOEs 62 and 22 (modeled central tendency and high-end) (Table 4-45). - Cancer: Inhalation: $5.82\text{E-}04$ and $1.78\text{E-}03$ (modeled central tendency and high-end) (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations</u>: EPA utilized monitoring data from OSHA for three facilities where spot cleaning is performed. EPA also developed a spot cleaning model. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-51). And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Estimated exposed population: 92 workers and occupational non-users are exposed to 1-BP in dry cleaning, which includes estimates of individuals exposed during spot cleaning and stain removing.
Industrial/ commercial use	Cleaning and furniture care products	Liquid cleaner (e.g., coin and scissor cleaner)	Section 6(b)(4)(A) unreasonable risk determinations for industrial and commercial use of 1-BP as a cleaning and furniture care product in the form of liquid cleaner (e.g., coin and scissor cleaner) and liquid spray or aerosol cleaner, as well as other industrial and commercial uses (arts, crafts and hobby materials – adhesive accelerant; automotive care products – engine degreaser, brake cleaner; anti-adhesive agents – mold cleaning and release product; building/construction materials not covered elsewhere – insulation; electronic and electronic products and metal products; functional fluids (closed systems)-refrigerant; functional fluids (open system) - cutting oils; asphalt extraction; laboratory chemicals; temperature indicator – coatings): - Presents an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Workers: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. Occupational non-users: - Developmental adverse effects resulting from acute and chronic inhalation exposures. - Cancer resulting from chronic inhalation exposures. <u>Benchmarks:</u> Workers and occupational non-users: - Developmental adverse effects: MOE 100. - Cancer: 10⁻⁴.
		Liquid spray/aerosol cleaner	
	Other uses	Arts, crafts and hobby materials - adhesive accelerant	
		Automotive care products – engine degreaser, brake cleaner	
		Anti-adhesive agents – mold cleaning and release product	
		Building/constr uction materials not covered elsewhere – insulation	

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
		Electronic and electronic products and metal products	Risk estimates: Workers: - Developmental adverse effects: Acute inhalation MOEs 133 and 38 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-17). Chronic inhalation MOEs 188 and 53 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-38). - Cancer: Inhalation: 2.E-04 and 7.24E-04 (central tendency and high-end) with respiratory protection (APF=50) (Table 4-47). Occupational non-users: - Developmental adverse effects: Acute inhalation MOEs 155 and 18 (central tendency and high-end) (Table 4-17). Chronic inhalation MOEs 218 and 26 (central tendency and high-end) (Table 4-38). - Cancer: Inhalation: 1.60E-04 and 1.44E-03 (central tendency and high-end) (Table 4-47). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (inhalation exposure): High. <u>Risk considerations:</u> Based on products identified in EPA's preliminary data gathering and information received in public comments, a variety of other aerosol and non-aerosol uses may exist for 1-BP. EPA expects the majority of these conditions of use to be niche uses. EPA has not identified exposure data associated with these conditions of use. The worker activity, use pattern, and associated exposure will vary for each condition of use. For conditions of use where 1-BP is used in an aerosol application, the exposure levels may be as high as those presented for aerosol spray degreaser and cleaner. Actual exposure levels for each condition of use will likely vary depending on the use volume, engineering control, and PPE. For aerosol spray degreaser and cleaner, EPA considered two studies with monitoring data. In addition, EPA modeled worker exposure to 1-BP during brake servicing as a representative exposure scenario to include occupational non-users. For workers, non-cancer MOEs from acute and chronic dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table
		Functional fluids (closed systems) – refrigerant	
		Functional fluids (open system) – cutting oils	
		Other – asphalt extraction	
		Other – laboratory chemicals	
		Temperature indicator – coatings	

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			4-52Table 4-52)Table 4-49. And, while cancer risk estimates from chronic dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-53). <u>Estimated exposed population</u> : EPA has not identified information on the number of potentially exposed workers associated with this condition of use.
Consumer use	Solvent (for cleaning or degreasing)	Aerosol spray degreaser/cleaner	Section 6(b)(4)(A) unreasonable risk determination for consumer use of 1-BP as a solvent (for cleaning or degreasing) in the form of aerosol spray degreaser or cleaner: - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Consumers: Developmental adverse effects resulting from acute inhalation and dermal exposures. Bystanders: Developmental adverse effects resulting from acute inhalation exposures <u>Benchmark</u>: Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimate: Consumers: Developmental adverse effects: Acute inhalation MOE 0.3 (moderate intensity use) (general cleaner/degreaser) (Table 4-26). Acute dermal MOE 3 (adult, moderate intensity use) (Table 4-54Table 4-54). Bystanders: Developmental adverse effects: Acute inhalation MOE 1 (moderate intensity use) (general cleaner/degreaser) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium. <u>Risk considerations</u>: Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population:</u> There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Cleaning and furniture care products	Spot cleaner, stain remover	Section 6(b)(4)(A) unreasonable risk determination for consumer use of 1-BP as a cleaning and furniture care product in the form of spot cleaner or stain remover: - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver:</u> Consumers and bystanders: Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark:</u> Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimates: Consumers: Developmental adverse effects: Acute inhalation MOE 2 (moderate intensity use) (Table 4-26). Bystanders: Developmental adverse effects: Acute inhalation MOE 9 (moderate intensity use) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium. <u>Risk considerations:</u> Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population:</u> There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Cleaning and furniture care products	Liquid cleaner (e.g., coin and scissor cleaner)	Section 6(b)(4)(A) unreasonable risk determinations for consumer use of 1-BP as a cleaning and furniture care product in the form of liquid cleaner (e.g., coin and scissor cleaner): - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Consumers: Developmental adverse effects resulting from acute inhalation and dermal exposures. Bystanders: Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark:</u> Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimate: Consumers: Developmental adverse effects: Acute inhalation MOE 2 (moderate intensity use) (Table 4-26). Acute dermal MOE 8 (adult, moderate intensity) (Table 4-54Table 4-54) Bystanders: Developmental adverse effects: Acute inhalation MOE 10 (moderate intensity use) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			<u>Risk considerations:</u> Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population:</u> There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Cleaning and furniture care products	Liquid spray/aerosol cleaner	Section 6(b)(4)(A) unreasonable risk determinations for consumer use of 1-BP as a cleaning and furniture care product in the form of liquid spray or aerosol cleaner: - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver:</u> Consumers and bystanders: Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark:</u> Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimates: Consumers: Developmental adverse effects: Acute inhalation MOE 0.4 (moderate intensity use) (general spray cleaner) (Table 4-26). Bystanders: Developmental adverse effects: Acute inhalation MOE 2 (moderate intensity use) (general spray cleaner) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			<u>Risk considerations:</u> Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population:</u> There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Other uses	Arts, crafts and hobby materials - adhesive accelerant	Section 6(b)(4)(A) unreasonable risk determination for consumer use of 1-BP as arts, crafts and hobby materials in the form of adhesive accelerant: - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver:</u> Consumers and bystanders : Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark:</u> Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimates: Consumers: Developmental adverse effects: Acute inhalation MOE 5 (moderate intensity use) (Table 4-26). Bystanders: Developmental adverse effects: Acute inhalation MOE 28.00 (moderate intensity use) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			<u>Risk considerations:</u> Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population:</u> There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Other uses	Automotive care products – refrigerant flush	Section 6(b)(4)(A) unreasonable risk determination for consumer use of 1-BP as automotive care products in the form of refrigerant flush: - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). Unreasonable risk driver: Consumers: Developmental adverse effects resulting from acute inhalation and dermal exposures. Bystanders: Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark:</u> Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimates: Consumers: Developmental adverse effects: Acute inhalation MOE 4 (moderate intensity use) (Table 4-26). Acute dermal MOE 0.1 (adult, moderate intensity use) (Table 4-54Table 4-54).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Bystanders: Developmental adverse effects: Acute inhalation MOE 19 (moderate intensity use) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium. <u>Risk considerations</u>: Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population</u>: There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Other uses	Anti-adhesive agents - mold cleaning and release product	Section 6(b)(4)(A) unreasonable risk determinations for consumer use of 1-BP as anti-adhesive agents in the form of mold cleaning and release product: - Presents an unreasonable risk of injury to health (consumers and bystanders). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Unreasonable risk driver</u>: Consumers and bystanders: Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark</u>: Consumers and bystanders: Developmental adverse effects MOE 100. Risk estimates: Consumers: Developmental adverse effects: Acute inhalation MOE 4 (moderate intensity use) (Table 4-26).

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			Bystanders: Developmental adverse effects: Acute inhalation MOE 22 (moderate intensity use) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium. <u>Risk considerations</u>: Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population</u>: There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Consumer use	Other uses	Building/construction materials not covered elsewhere - insulation	Section 6(b)(4)(A) unreasonable risk determination for consumer use of 1-BP as building/construction materials not covered elsewhere in the form of insulation: - Does not present an unreasonable risk of injury to health (consumers or bystanders) or to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate</u>: Consumers: Developmental adverse effects resulting from acute inhalation exposures. <u>Benchmark</u>: Developmental adverse effects MOE 100. <u>Risk estimate</u>: Developmental adverse effects: Acute inhalation MOE 277 (crawl space) (Table 4-26). Systematic Review confidence rating (hazard): High. Systematic Review confidence rating (exposure): High to high-medium.

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			<u>Risk considerations</u>: Modeling was used to evaluate consumer exposure resulting from the use of consumer products containing 1-BP. Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used, including: the consumer products identified in 2016 and 2017, the national survey information related to use of household products contained solvents compiled in 1987, the weight fractions identified for consumer products based on SDSs, the physical chemical properties of 1-BP used in the models, and the volumes and air exchange rates values used from U.S. EPA's Exposure Factors Handbook. <u>Estimated exposed population</u>: There is some general uncertainty regarding the nature and extent of the consumer use of 1-BP for the products within the scope of this evaluation.
Disposal	Disposal	Municipal waste incinerator	Section 6(b)(4)(A) unreasonable risk determination for the disposal of 1-BP: - Does not present an unreasonable risk of injury to health (workers and occupational non-users). - Does not present an unreasonable risk of injury to the environment (aquatic, sediment dwelling and terrestrial organisms). <u>Exposure scenario with highest risk estimate</u>: Workers: Cancer resulting from chronic dermal exposure. <u>Benchmark</u>: Cancer: 10^{-4}. <u>Risk estimate</u>: Workers: Cancer: Dermal: $1.38\text{E-}04$ for workers using no PPE (Table 4-53). Note: There is no unreasonable risk when PPE (gloves APF=5) are used. Systematic Review confidence rating (health hazard): High. <u>Systematic Review confidence rating (health dermal exposure)</u>: Medium. Risk estimates derived using the EPA Dermal Exposure to Volatile Liquids model. <u>Risk considerations</u>: non-cancer MOEs from acute and chronic inhalation and dermal exposures were greater than the MOE benchmark indicating no unreasonable risk (Table 4-25Table 4-25, Table 4-46Table 4-46, and Table
		Off-site waste transfer	

Condition of Use			Unreasonable Risk Determination ¹
Life Cycle Stage	Category	Sub-Category	
			4-48). And, while cancer risk estimates from chronic inhalation and dermal exposures indicate risk relative to the Agency's risk benchmarks in the absence of PPE, risk estimates for these scenarios do not indicate risk relative to those benchmarks when expected use of PPE was considered (Table 4-47 and Table 4-53). For occupational non-users, exposures were expected to be negligible (Table 4-25Table 4-25 and Table 4-46Table 4-46). <u>Estimated exposed population</u>: over 49 workers and 18 occupational non-users.

¹ EPA expects there is compliance with federal and state laws, such as worker protection standards, unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE consistent with the applicable SDSs in a manner adequate to protect them.

6 REFERENCES

- AIA. (2017). Re: Posting EPA-HQ-OPPT-2016-0723 1-Bromopropane (n-Propyl bromide) (CASRN 106-94-5). (EPA-HQ-OPPT-2016-0741-0014).
- AIHA. (2009). Mathematical models for estimating occupational exposure to chemicals. In CB Keil; CE Simmons; TR Anthony (Eds.), (2nd ed.). Fairfax, VA: AIHA Press.
- Alwis, KU; Blount, BC; Britt, AS; Patel, D; Ashley, DL. (2012). Simultaneous analysis of 28 urinary VOC metabolites using ultra high performance liquid chromatography coupled with electrospray ionization tandem mass spectrometry (UPLC-ESI/MSMS). *Anal Chim Acta* 750: 152-160. <http://dx.doi.org/10.1016/j.aca.2012.04.009>
- Ames, BN; McCann, J; Yamasaki, E. (1975). Methods for detecting carcinogens and mutagens with the Salmonella/mammalian-microsome mutagenicity test. *Mutat Res* 31: 347-363.
- Anderson, SE; Franko, J; Anderson, KL; Munson, AE; Lukomska, E; Meade, BJ. (2013). Immunotoxicity and allergic potential induced by topical application of dimethyl carbonate (DMC) in a murine model. *J Immunotoxicol* 10: 59-66. <http://dx.doi.org/10.3109/1547691X.2012.691124>
- Anderson, SE; Munson, AE; Butterworth, LF; Germolec, D; Morgan, DL; Roycroft, JA; Dill, J; Meade, BJ. (2010). Whole-body inhalation exposure to 1-bromopropane suppresses the IgM response to sheep red blood cells in female B6C3F1 mice and Fisher 344/N rats. *Inhal Toxicol* 22: 125-132. <http://dx.doi.org/10.3109/08958370902953910>
- Apfel, MA; Ikeda, BH; Speckhard, DC; Frey, PA. (1984). Escherichia coli Pyruvate Dehydrogenase Complex. Thiamin Pyrophosphate-dependent Inactivation of 3-bromopyruvate. *J Biol Chem* 259: 2905-2909.
- Arakawa, S; Fujimoto, K; Kato, A; Endo, S; Fukahori, A; Shinagawa, A; Fischer, T; Mueller, J; Takasaki, W. (2012). Evaluation of hepatic glutathione transferase Mu 1 and Theta 1 activities in humans and mice using genotype information. *Drug Metab Dispos* 40: 497-503. <http://dx.doi.org/10.1124/dmd.111.042911>
- ATSDR. (2016). Draft toxicological profile for 1-bromopropane. Atlanta, GA: Division of Toxicology and Human Health Sciences, Environmental Toxicology Branch. <https://www.atsdr.cdc.gov/ToxProfiles/tp209.pdf>
- ATSDR. (2017). Toxicological profile for 1-bromopropane. Atlanta, GA: Division of Toxicology and Human Health Sciences, Environmental Toxicology Branch. <https://www.atsdr.cdc.gov/ToxProfiles/tp209.pdf>
- B Hymer, C; Cheever, KL. (2005). Development of a headspace gas chromatographic test for the quantification of 1- and 2-bromopropane in human urine. *J Chromatogr B Analyt Technol Biomed Life Sci* 814: 185-189. <http://dx.doi.org/10.1016/j.jchromb.2004.10.045>
- Baker, JP; Rabin, BR. (1969). Effects of Bromopyruvate on the control and catalytic properties of Glutamate Dehydrogenase. *11*: 154-159. <http://dx.doi.org/10.1111/j.1432-1033.1969.tb00753.x>
- Banu, S; Ichihara, S; Huang, F; Ito, H; Inaguma, Y; Furuhashi, K; Fukunaga, Y; Wang, Q; Kitoh, J; Ando, H; Kikkawa, F; Ichihara, G. (2007). Reversibility of the adverse effects of 1-bromopropane exposure in rats. *Toxicol Sci* 100: 504-512. <http://dx.doi.org/10.1093/toxsci/kfm245>
- Barber, ED; Donish, WH; Mueller, KR. (1981). A procedure for the quantitative measurement of the mutagenicity of volatile liquids in the Ames salmonella/microsome assay. *Mutat Res Genet Toxicol* 90: 31-48. [http://dx.doi.org/10.1016/0165-1218\(81\)90048-3](http://dx.doi.org/10.1016/0165-1218(81)90048-3)

- Barker, DJP. (2007). The origins of the developmental origins theory. *J Intern Med* 261: 412-417.
<http://dx.doi.org/10.1111/j.1365-2796.2007.01809.x>
- Barnsley, EA; Grenby, TH; Young, L. (1966). Biological Studies of Toxic Agents. The metabolism of 1- and 2-bromopropane. *Biochem J* 100: 282.
- Barnthouse, LW; Munns, RM, Jr.; Sorensen, MT. (2008). Population-level ecological risk assessment. Pensacola, FL: Taylor & Francis.
<http://www.crcpress.com/product/isbn/9781420053326>
- Batterman, S; Jia, C; Hatzivasilis, G. (2007). Migration of volatile organic compounds from attached garages to residences: A major exposure source. *Environ Res* 104: 224-240.
<http://dx.doi.org/10.1016/j.envres.2007.01.008>
- Belkin, S. (1992). BIODEGRADATION OF HALOALKANES. In International Workshop On The Use Of Microorganisms To Combat Pollution, Israel, May (pp. 10-18). (ISSN 0923-9820; EISSN 1572-9729; BIOSIS/93/26758). National Board of Labour Protection (Finland). <http://dx.doi.org/10.1007/BF00129090>
- Benigni, R; Bossa, C; Tcheremenskaia, O; Battistelli, CL; Crettaz, P. (2012). The new ISSMIC database on in vivo micronucleus and its role in assessing genotoxicity testing strategies [Review]. *Mutagenesis* 27: 87-92. <http://dx.doi.org/10.1093/mutage/ger064>
- BioReliance. (2015). Appendix III. Closed-System Ames Test on 1-Bromopropane Conducted at BioReliance and Sponsored by Albemarle Corporation FINAL REPORT. (AD58PU.503001.BTL).
- Blando, J; Schill, D; De La Cruz, P; Zhang, L; Zhang, J. (2009). PERC ban among dry cleaners leads to 1-bromopropane exposures with alternative "green" solvent. Presentation presented at Fall Regulatory Update: New Jersey Department of Environmental Protection, October 16, 2009, Trenton, NJ.
- Blando, JD; Schill, DP; De La Cruz, MP; Zhang, L; Zhang, J. (2010). Preliminary study of propyl bromide exposure among New Jersey dry cleaners as a result of a pending ban on perchloroethylene. *J Air Waste Manag Assoc* 60: 1049-1056.
<http://dx.doi.org/10.3155/1047-3289.60.9.1049>
- Boublík, T; Fried, V; Hála, E. (1984). The vapour pressures of pure substances: Selected values of the temperature dependence of the vapour pressures of some pure substances in the normal and low pressure region (2nd Revised ed.). Amsterdam, The Netherlands: Elsevier Science Publishers.
- Boyle, EB; Viet, SM; Wright, DJ; Merrill, LS; Alwis, KU; Blount, BC; Mortensen, ME; Moye, J; Dellarco, M. (2016). Assessment of Exposure to VOCs among Pregnant Women in the National Children's Study. *Int J Environ Res Public Health* 13: 376.
<http://dx.doi.org/10.3390/ijerph13040376>
- Bureau, USC. (2012). Statistics of U.S. businesses: Historical data available for downloading - 2012 [Website]. http://www.census.gov/econ/susb/data/download_susb2012.html
- Bureau, USC. (2015). Statistics of U.S. Businesses (SUSB).
<https://www.census.gov/data/tables/2015/econ/susb/2015-susb-annual.html>
- Burkholder, JB; Gilles, MK; Gierczak, T; Ravishankara, AR. (2002). The atmospheric degradation of 1-bromopropane (CH₃CH₂CH₂Br): The photochemistry of bromoacetone. *Geophys Res Lett* 29: 1822. <http://dx.doi.org/10.1029/2002GL014712>
- CARB. (2000). Initial statement of reasons for the proposed airborne toxic control measure for emissions of chlorinated toxic air contaminants from automotive maintenance and repair activities.

- CARB. (2011). Development of updated ARB solvent cleaning emissions inventories. Final Report: Agreement No. 06-322. In University of California, Riverside Bourns College of Engineering, Center for Environmental Research and Technology. Sacramento, CA. <http://www.arb.ca.gov/research/apr/past/06-322.pdf>
- Casazza, JP; Felver, ME; Veech, RL. (1984). The metabolism of acetone in rat. J Biol Chem 259: 231-236.
- CDC. (1997). Control of exposure to perchloroethylene in commercial drycleaning (Machine Design). (DHHS(NIOSH) Publication No. 97-154). Atlanta, GA: Centers for Disease Control and Prevention. <http://www.cdc.gov/niosh/docs/hazardcontrol/hc16.html>
- CDC. (2008). Neurologic illness associated with occupational exposure to the solvent 1-bromopropane--New Jersey and Pennsylvania, 2007-2008. MMWR Morb Mortal Wkly Rep 57: 1300-1302.
- CDC. (2016). Criteria for a recommended standard: Occupational exposure to 1-bromopropane. (CDC-2016-0003). Cincinnati, OH: National Institute for Occupational Safety and Health. https://www.cdc.gov/niosh/docket/review/docket057a/pdfs/ctd-1-bpcriteriadocument_final-012616.pdf
- CDC. (2019). Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, January 2019, Volume 2. Atlanta, GA: U.S. Department of Health and Human Services. <https://www.cdc.gov/exposurereport/>
- Cheever, KL; Marlow, KL; B'Hymer, C; Hanley, KW; Lynch, DW. (2009). Development of an HPLC-MS procedure for the quantification of N-acetyl-S-(n-propyl)-l-cysteine, the major urinary metabolite of 1-bromopropane in human urine. J Chromatogr B Analyt Technol Biomed Life Sci 877: 827-832. <http://dx.doi.org/10.1016/j.jchromb.2009.02.010>
- ClinTrials. (1997a). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat. (Report No. 91190). Canada.
- ClinTrials. (1997b). A 28-day inhalation toxicity study of a vapor formulation of ALBTA1 in albino rat. (Document No. 91198). Senneville, Quebec: Sponsored by Albemarle Corporation, Baton Rouge, LA.
- CRC Industries Inc. (2017). Docket ID # EPA-HQ-OPPT-2016-0741 [EPA Report]. (EPA-HQ-OPPT-2016-0741-0018.).
- Da Silva, APP; El-Bacha, T; Kyaw, N; Santos, RSd; Da-Silva, WS; Almeida, FCL; Poian, ATD; Galina, A. (2009). Inhibition of energy-producing pathways of HepG2 cells. Biochem J 417. <http://dx.doi.org/10.1042/BJ20080805>
- DHHS. (2017). Skin Notation (SK) Profile 1-Bromopropane. CDC.
- DOW. (2018). THERMAXTM Brand Insulation. <https://www.dow.com/en-us/products/thermaxbrandinsulation#sort=%40gtitle%20ascending>
- Durkee, J. (2014). Cleaning with solvents: Methods and machinery. In Cleaning with solvents: Methods and machinery. Oxford, UK: Elsevier Inc. <https://www.sciencedirect.com/book/9780323225205/cleaning-with-solvents-methods-and-machinery>
- ECHA. (2012). Substance Name: 1-bromopropane [n-propyl bromide]. CAS No: 106-94-5. Member State Committee Support Document for Identification of 1-bromopropane [n-propyl bromide] as a Substance of Very High Concern because of its CMR Properties. Helsinki, Finland: European Chemical Agency. <http://echa.europa.eu/documents/10162/54958f68-9718-473a-9d64-998c6e8b1d5c>

- ECHA. (2017). Registration dossier: 1-Bromopropane. Available online at <https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15004> (accessed August 29, 2017).
- Eisenberg, J; Ramsey, J. (2010). Evaluation of 1-Bromopropane Use in Four New Jersey Commercial Dry Cleaning Facilities. In New Jersey Department of Health and Senior Services, July 2010 (pp. pp.). (NTIS/12290078). National Board of Labour Protection (Finland). <http://www.cdc.gov/niosh/hhe/reports/pdfs/2008-0175-3111.pdf>
- Elf Atochem, SA. (1993a). Acute oral toxicity in rats. n-propyl bromide. Study No. 10611 Tar. Study director, Jack Clouzeau. Study performed by Centre International de Toxicologie, Miserey, France. November 3, 1993.
- Elf Atochem, SA. (1993b). Ames test--Reverse Mutation Assay on Salmonella typhimurium. n-Propyl Bromide. HIS1005/1005A. Study performed by Sanofi Recherche. Service de Toxicologie.
- Elf Atochem, SA. (1995). Micronucleus test by intraperitoneal route in mice. n-propyl bromide. Study No. 12122 MAS. Miserey, France: Elf Atochem Société Anonyme, Centre International de Toxicologie.
- Elf Atochem, SA. (1996a). In vitro mammalian cell gene mutation test in L5178y TK+/- mouse lymphoma cell of n-propyl bromide. Study no. 13293. Miserey, France. [http://yosemite.epa.gov/oppts/epatscat8.nsf/by+Service/B9769616121757CC85256F9400586E90/\\$File/88970000235.pdf](http://yosemite.epa.gov/oppts/epatscat8.nsf/by+Service/B9769616121757CC85256F9400586E90/$File/88970000235.pdf)
- Elf Atochem, SA. (1996b). In vitro mammalian cell gene mutation test in L5178Y TK+/- mouse lymphoma cells of n-propyl bromide. (88970000235).
- Elf Atochem, SA. (1997). Study of acute toxicity of n-propyl bromide administered to rats by vapour inhalation. Determination of the 50% lethal concentration (LC50/4 hours). INERIS-L.E.T.E. Study No. 95122. Study performed by Laboratoire d'Etudes de Toxicologie Experimentale.
- Emmerich, SJ; Gorfain, JE; Howard-Reed, C. (2003). Air and pollutant transport from attached garages to residential living spaces - literature review and field tests. Int J Vent 2: 265-276.
- Emoto, C; Murase, S; Sawada, Y; Jones, BC; Iwasaki, K. (2003). In vitro inhibitory effect of 1-aminobenzotriazole on drug oxidations catalyzed by human cytochrome P450 enzymes: A comparison with SKF-525A and ketoconazole. Drug Metab Pharmacokinet 18: 287-295. <http://dx.doi.org/10.2133/dmpk.18.287>
- Enviro Tech, I. (2019). Personal communication between R. Morford (Enviro Tech International, Inc.) and D. Parsons (U.S. EPA) [Personal Communication].
- Enviro Tech International. (2013). Drysolv spray testing & spotter. Material safety data sheet [Fact Sheet]. Melrose Park, IL. <http://nebula.wsimg.com/b5b721780e4046dae73c7753945cd994?AccessKeyId=F58D237F0A46DAC5AF87&disposition=0>
- Enviro Tech International. (2017). RE: 1-Bromopropane, Docket ID number EPA-HQ-OPPT 2016-0741. The Use of 1-bromopropane (nPB) in the Dry Cleaning Industry. (EPA-HQ-OPPT 2016-0741-0016).
- EPA, US. (2019a). Draft Risk Evaluation for 1-Bromopropane - 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Input Parameters.
- EPA, US. (2019b). Draft Risk Evaluation for 1-Bromopropane – 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Outputs.
- EPA, US. (2019c). Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Consumer Exposure Risk Calculations.

- [EPA, US.](#) (2019d). Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: ECHA Study Summaries for Environmental Hazard.
- [EPA, US.](#) (2019e). Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Human Health Benchmark Dose Modeling.
- [EPA, US.](#) (2019f). Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Consumer Exposure Assessment Public.
- [EPA, US.](#) (2019g). Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Occupational Exposure Assessment. (Docket EPA-HQ-OPPT-2019-0236).
- [EPA, US.](#) (2019h). Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Occupational Risk Calculator.
- [EPA, US.](#) (2019i). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction for Consumer Exposure.
- [EPA, US.](#) (2019j). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction Tables for Environmental Fate and Transport Studies.
- [EPA, US.](#) (2019k). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Consumer Exposure.
- [EPA, US.](#) (2019l). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies.
- [EPA, US.](#) (2019m). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies.
- [EPA, US.](#) (2019n). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data.
- [EPA, US.](#) (2019o). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data for Common Sources.
- [EPA, US.](#) (2019p). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies.
- [EPA, US.](#) (2019q). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiologic Studies.
- [EPA, US.](#) (2019r). Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Updates to the Data Quality Criteria for Epidemiological Studies.
- [ERG.](#) (2001). Draft generic scenario. Use of vapor degreasers. Chantilly, VA: Eastern Research Group.
- [ERG.](#) (2005). [Letter from Eric Goehl and Jennifer O'Neil, Eastern Research group, Inc, to Dry Cleaning Docket, Subject: Background information document]. Available online at <http://www3.epa.gov/airtoxics/dryperc/11-14-05background.pdf>
- [Federal Register.](#) (1999). 64 FR 60194: Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances (pp. 60194-60204). Register, F.
- [Fonda, M.](#) (1976). Bromopyruvate Inactivation of Glutamate Apodecarboxylase. *J Biol Chem* 251: 229-235.
- [Frasch, HF; Dotson, GS; Barbero, AM.](#) (2011). In vitro human epidermal penetration of 1-bromopropane. *J Toxicol Environ Health A* 74: 1249-1260.
<http://dx.doi.org/10.1080/15287394.2011.595666>
- [Fueta, Y; Fukuda, T; Ishidao, T; Hori, H.](#) (2004). Electrophysiology and immunohistochemistry in the hippocampal cal and the dentate gyrus of rats chronically exposed to 1-bromopropane,

- a substitute for specific chlorofluorocarbons. *Neuroscience* 124: 593-603.
<http://dx.doi.org/10.1016/j.neuroscience.2003.12.025>
- Fueta, Y; Fukunaga, K; Ishidao, T; Hori, H. (2002a). Hyperexcitability and changes in activities of Ca²⁺/calmodulin-dependent kinase II and mitogen-activated protein kinase in the hippocampus of rats exposed to 1-bromopropane. *Life Sci* 72: 521-529.
[http://dx.doi.org/10.1016/S0024-3205\(02\)02247-6](http://dx.doi.org/10.1016/S0024-3205(02)02247-6)
- Fueta, Y; Ishidao, T; Arashidani, K; Endo, Y; Hori, H. (2002b). Hyperexcitability of the hippocampal CA1 and the dentate gyrus in rats subchronically exposed to a substitute for chlorofluorocarbons, 1-bromopropane vapor. *J Occup Health* 44: 156-165.
<http://dx.doi.org/10.1539/joh.44.156>
- Fueta, Y; Ishidao, T; Kasai, T; Hori, H; Arashidani, K. (2000). Decreased paired-pulse inhibition in the dentate gyrus of the brain in rats exposed to 1-bromopropane vapor [Letter]. *J Occup Health* 42: 149-151. <http://dx.doi.org/10.1539/joh.42.149>
- Fueta, Y; Ishidao, T; Ueno, S; Yoshida, Y; Kunugita, N; Hori, H. (2007). New approach to risk assessment of central neurotoxicity induced by 1-bromopropane using animal models. *Neurotoxicology* 28: 270-273. <http://dx.doi.org/10.1016/j.neuro.2006.05.003>
- Fueta, Y; Ueno, S; Ishidao, T; Kanemitsu, M; Hori, H. (2013). Prenatal exposure to 1-Bromopropane changes basic excitability of hippocampus and inhibits the behaviors iduced by kainic acid and pentylenetetrazole in the rat offspring during lactation period. *Toxicologist* 132: Abstract No. 1389.
- Furuhashi, K; Kitoh, J; Tsukamura, H; Maeda, K; Wang, H; Li, W; Ichihara, S; Nakajima, T; Ichihara, G. (2006). Effects of exposure of rat dams to 1-bromopropane during pregnancy and lactation on growth and sexual maturation of their offspring. *Toxicology* 224: 219-228.
<http://dx.doi.org/10.1016/j.tox.2006.04.044>
- Ganapathy-Kanniappan, S; Geschwind, JFH; Kunjithapatham, R; Buijs, M; Vossen, J; Tchernyshyov, I; Cole, RH; Syed, LH; Rao, PP; Ota, S; Vali, M. (2009). Glyceraldehyde-3-phosphate Dehydrogenase (GAPDH). *Anticancer Res* 29: 4909-4918.
- Garner, CE; Liang, S; Yin, L; Yu, X. (2015). Physiologically based pharmacokinetic modeling for 1-bromopropane in F344 rats using gas uptake inhalation experiments. *Toxicol Sci* 145: 23-36. <http://dx.doi.org/10.1093/toxsci/kfv018>
- Garner, CE; Sloan, C; Sumner, SC; Burgess, J; Davis, J; Etheridge, A; Parham, A; Ghanayem, BI. (2007). CYP2E1-catalyzed oxidation contributes to the sperm toxicity of 1-bromopropane in mice. *Biol Reprod* 76: 496-505. <http://dx.doi.org/10.1095/biolreprod.106.055004>
- Garner, CE; Sumner, SC; Davis, JG; Burgess, JP; Yueh, Y; Demeter, J; Zhan, Q; Valentine, J; Jeffcoat, AR; Burka, LT; Mathews, JM. (2006). Metabolism and disposition of 1-bromopropane in rats and mice following inhalation or intravenous administration. *Toxicol Appl Pharmacol* 215: 23-36. <http://dx.doi.org/10.1016/j.taap.2006.01.010>
- Garner, CE; Yu, X. (2014). Species and sex-dependent toxicokinetics of 1-bromopropane: the role of hepatic cytochrome P450 oxidation and glutathione (GSH). *Xenobiotica* 44: 644-656.
<http://dx.doi.org/10.3109/00498254.2013.879624>
- Geiger, DL; Call, DJ; Brooke, LT. (1988). Acute toxicities of organic chemicals to fathead minnows (*Pimephales promelas*): Volume IV. Superior, WI: University of Wisconsin-Superior, Center for Lake Superior Environmental Studies.
- Guo, Y; Yuan, H; Jiang, L; Yang, J; Zeng, T; Xie, K; Zhang, C; Zhao, X. (2015). Involvement of decreased neuroglobin protein level in cognitive dysfunction induced by 1-bromopropane in rats. *Brain Res* 1600: 1-16. <http://dx.doi.org/10.1016/j.brainres.2014.12.046>

- Hanley, KW; Petersen, M; Curwin, BD; Sanderson, WT. (2006a). Urinary bromide and breathing zone concentrations of 1-bromopropane from workers exposed to flexible foam spray adhesives. *Ann Occup Hyg* 50: 599-607. <http://dx.doi.org/10.1093/annhyg/mel020>
- Hanley, KW; Petersen, M; Curwin, BD; Sanderson, WT. (2006b). Urinary bromide and breathing zone concentrations of 1-bromopropane from workers exposed to flexible foam spray adhesives.
- Hanley, KW; Petersen, MR; Cheever, KL; Luo, L. (2009). N-acetyl-S-(n-propyl)-l-cysteine in urine from workers exposed to 1-bromopropane in foam cushion spray adhesives. *Ann Occup Hyg* 53: 759-769. <http://dx.doi.org/10.1093/annhyg/mep051>
- Hanley, KW; Petersen, MR; Cheever, KL; Luo, L. (2010). Bromide and N-acetyl-S-(n-propyl)-L-cysteine in urine from workers exposed to 1-bromopropane solvents from vapor degreasing or adhesive manufacturing. *Int Arch Occup Environ Health* 83: 571-584. <http://dx.doi.org/10.1007/s00420-010-0524-4>
- Hansch, C. (1995). Fundamentals and applications in chemistry and biology - hydrophobic, electronic and steric constants. In *Exploring QSAR*. Washington DC: American Chemical Society Professional Reference Book/Oxford University Press.
- Hasspieler, B; Haffner, D; Stelljes, M; Adeli, K. (2006). Toxicological assessment of industrial solvents using human cell bioassays: assessment of short-term cytotoxicity and long-term genotoxicity potential. *Toxicol Ind Health* 22: 301-315. <http://dx.doi.org/10.1177/0748233706070312>
- Haynes, WM; Lide, DR. (2010). Editor CRC handbook of chemistry and physics: A ready-reference book of chemical and physical data (91st ed.). Boca Raton, FL: CRC Press.
- Honma, T; Suda, M; Miyagawa, M. (2003). Inhalation of 1-bromopropane causes excitation in the central nervous system of male F344 rats. *Neurotoxicology* 24: 563-575. [http://dx.doi.org/10.1016/S0161-813X\(03\)00049-4](http://dx.doi.org/10.1016/S0161-813X(03)00049-4)
- HSDB. (2017). Hazardous substances data bank: 1-Bromopropane [Database]. Rockville, MD: U.S. National Library of Medicine. Retrieved from <https://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm>
- HSIA. (2010). Petition to add n-propyl bromide to list of hazardous air pollutants regulate under section 112 of the Clean Air Act [with cover letter date 10/28/2010]. Arlington, VA. <http://www.hsia.org/news/nBPpetitionsigned.pdf>
- Huang, Z; Ichihara, S; Oikawa, S; Chang, J; Zhang, L; Hu, S; Huang, H; Ichihara, G. (2015). Hippocampal phosphoproteomics of F344 rats exposed to 1-Bromopropane. *Toxicol Appl Pharmacol* 282: 151-160. <http://dx.doi.org/10.1016/j.taap.2014.10.016>
- Huang, Z; Ichihara, S; Oikawa, S; Chang, J; Zhang, L; Subramanian, K; Mohideen, SS; Ichihara, G. (2012). Proteomic identification of carbonylated proteins in F344 rat hippocampus after 1-bromopropane exposure. *Toxicol Appl Pharmacol* 263: 44-52. <http://dx.doi.org/10.1016/j.taap.2012.05.021>
- Huang, Z; Ichihara, S; Oikawa, S; Chang, J; Zhang, L; Takahashi, M; Subramanian, K; Mohideen, SS; Wang, Y; Ichihara, G. (2011). Proteomic analysis of hippocampal proteins of F344 rats exposed to 1-bromopropane. *Toxicol Appl Pharmacol* 257: 93-101. <http://dx.doi.org/10.1016/j.taap.2011.08.023>
- Hughes, TJ; Simmons, DM; Monteith, LG; Claxton, LD. (1987). Vaporization technique to measure mutagenic activity of volatile organic chemicals in the Ames/Salmonella assay. *Environ Mutagen* 9: 421-441. <http://dx.doi.org/10.1002/em.2860090408>
- Huntingdon Life Sciences. (1999). A range-finding development/reproductive toxicity study of 1-Bromopropane in rats via whole body inhalation exposure. Final report. (Study No. 98-

4140. 8EHQ-0799-14346).
[http://yosemite.epa.gov/oppts/epatscat8.nsf/by+Service/D275E580BB932A308525695A0048BA00/\\$File/89990000271.pdf](http://yosemite.epa.gov/oppts/epatscat8.nsf/by+Service/D275E580BB932A308525695A0048BA00/$File/89990000271.pdf)
- [Huntingdon Life Sciences](#). (2001). A developmental toxicity study in rat via whole body inhalation exposure (with cover letter dated 9/18/2001). (Study No. 98-4141; docket number A-2001-07). East Millstone, NJ: Study sponsored by Brominated Solvents Committee (BSOC).
- [IARC](#). (1994). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Propylene oxide. vol. 60, pp. 181-213. Lyon, France.
<http://monographs.iarc.fr/ENG/Monographs/vol60/mono60-9.pdf>
- [IARC](#). (1999a). 1,2-dibromo-3-chloropropane [IARC Monograph]. In IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (pp. 479-500). Lyon, France: World Health Organization. <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-20.pdf>
- [IARC](#). (1999b). 1,2-dichloroethane [IARC Monograph]. In IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (pp. 501-529). Lyon, France: World Health Organization. <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-21.pdf>
- [IARC](#). (1999c). 1,2,3-tris(chloromethoxy)propane [IARC Monograph]. In IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (pp. 1549-1550). Lyon, France: World Health Organization. <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-115.pdf>
- [IARC](#). (1999d). Dichloromethane [IARC Monograph]. In IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans (pp. 251-315). Lyon, France: World Health Organization. <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-10.pdf>
- [IARC](#). (1999e). Ethylene dibromide (1,2-dibromoethane) [IARC Monograph]. In IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (pp. 641-669). Lyon, France: World Health Organization. <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-28.pdf>
- [IARC](#). (2000). Glycidol in some industrial chemicals in IARC monographs on the evaluation of carcinogenic risks to humans (pp. 469-489). Lyon, France.
<http://monographs.iarc.fr/ENG/Monographs/vol77/mono77-19.pdf>
- [IARC](#). (2018). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Some Industrial Chemicals. Lyon, France: World Health Organization.
<https://monographs.iarc.fr/wp-content/uploads/2018/06/mono115.pdf>
- [Ichihara, G; Kitoh, J; Yu, X; Asaeda, N; Iwai, H; Kumazawa, T; Shibata, E; Yamada, T; Wang, H; Xie, Z; Takeuchi, Y](#). (2000a). 1-Bromopropane, an alternative to ozone layer depleting solvents, is dose-dependently neurotoxic to rats in long-term inhalation exposure. Toxicol Sci 55: 116-123. <http://dx.doi.org/10.1093/toxsci/55.1.116>
- [Ichihara, G; Li, W; Ding, X; Peng, S; Yu, X; Shibata, E; Yamada, T; Wang, H; Itohara, S; Kanno, S; Sakai, K; Ito, H; Kanefusa, K; Takeuchi, Y](#). (2004a). A survey on exposure level, health status, and biomarkers in workers exposed to 1-bromopropane. Am J Ind Med 45: 63-75. <http://dx.doi.org/10.1002/ajim.10320>
- [Ichihara, G; Li, W; Shibata, E; Ding, X; Wang, H; Liang, Y; Peng, S; Itohara, S; Kamijima, M; Fan, Q; Zhang, Y; Zhong, E; Wu, X; Valentine, WM; Takeuchi, Y](#). (2004b). Neurologic abnormalities in workers of a 1-bromopropane factory. Environ Health Perspect 112: 1319-1325. <http://dx.doi.org/10.1289/ehp.6995>
- [Ichihara, G; Miller, JK; Ziolkowska, A; Itohara, S; Takeuchi, Y](#). (2002). Neurological disorders in three workers exposed to 1-bromopropane. J Occup Health 44: 1-7. <http://dx.doi.org/10.1539/joh.44.1>

- Ichihara, G; Wang, H; Zhang, L; Wakai, K; Li, W; Ding, X; Shibata, E; Zhou, Z; Wang, Q; Li, J; Ichihara, S; Takeuchi, Y. (2011). Dose-dependent neurologic abnormalities in workers exposed to 1-bromopropane: authors' response [Letter]. *J Occup Environ Med* 53: 1095-1098. <http://dx.doi.org/10.1097/JOM.0b013e3182300a4f>
- Ichihara, G; Yu, X; Kitoh, J; Asaeda, N; Kumazawa, T; Iwai, H; Shibata, E; Yamada, T; Wang, H; Xie, Z; Maeda, K; Tsukamura, H; Takeuchi, Y. (2000b). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats. *Toxicol Sci* 54: 416-423. <http://dx.doi.org/10.1093/toxsci/54.2.416>
- ICRP. (1975). Report of the task group on reference man. In ICRP Publication 23. Oxford, UK: Pergamon Press. http://ani.sagepub.com/site/includefiles/icrp_publications_collection.xhtml
- International, ET. (2017). Current Uses of 1-bromopropane (nPB) in the Cleaning Solvent Industry in the United States. (EPA-HQ-OPPT-2016-0741-0016). Enviro Tech International.
- IRTA. (2016). Alternative Compliance Strategies for Enclosed and ConveyORIZED Vapor Degreasers under a Prohibition of Trichloroethylene. Draft.
- Ishidao, T; Kunugita, N; Fueta, Y; Arashidani, K; Hori, H. (2002). Effects of inhaled 1-bromopropane vapor on rat metabolism. *Toxicol Lett* 134: 237-243. [http://dx.doi.org/10.1016/S0378-4274\(02\)00171-6](http://dx.doi.org/10.1016/S0378-4274(02)00171-6)
- Jain, RB. (2015). Distributions of selected urinary metabolites of volatile organic compounds by age, gender, race/ethnicity, and smoking status in a representative sample of U.S. adults. *Environ Toxicol Pharmacol* 40: 471-479. <http://dx.doi.org/10.1016/j.etap.2015.07.018>
- Janssen, DB; Jager, D; Witholt, B. (1987). Degradation of n-haloalkanes and alpha, omega-dihaloalkanes by wild-type and mutants of *Acinetobacter* sp. strain GJ70. *Appl Environ Microbiol* 53: 561-566.
- Jones, AR; Walsh, DA. (1979). The oxidative metabolism of 1-bromopropane in the rat. *Xenobiotica* 9: 763-772. <http://dx.doi.org/10.3109/00498257909042344>
- Kane, Ta. (2015). The Great Port Mismatch. U.S. Goods Trade and International Transportation. Tomer and Kane. <https://www.brookings.edu/wp-content/uploads/2015/06/brgkssrvygcifreightnetworks.pdf>
- Kanegsberg, B; Kanegsberg, E. (2011). Handbook of critical cleaning, applications, processes, and controls. In Handbook for critical cleaning, cleaning agents and systems. Boca Raton: CRC Press. <http://dx.doi.org/10.1201/b10858>
- Kaneko, T; Kim, HY; Wang, PY; Sato, A. (1997). Partition coefficients and hepatic metabolism in vitro of 1- and 2-bromopropanes. *J Occup Health* 39: 341-342. <http://dx.doi.org/10.1539/joh.39.341>
- Kawai, T; Takeuchi, A; Miyama, Y; Sakamoto, K; Zhang, ZW; Higashikawa, K; Ikeda, M. (2001). Biological monitoring of occupational exposure to 1-bromopropane by means of urinalysis for 1-bromopropane and bromide ion. *Biomarkers* 6: 303-312. <http://dx.doi.org/10.1080/13547500110034817>
- Khan, S; O'Brien, PJ. (1991). 1-Bromoalkanes as new potent nontoxic glutathione depletors in isolated rat hepatocytes. *Biochem Biophys Res Commun* 179: 436-441. [http://dx.doi.org/10.1016/0006-291X\(91\)91389-T](http://dx.doi.org/10.1016/0006-291X(91)91389-T)
- Kim, H; Chung, J; Chung, Y; Kim, K; Maeng, S; Hang, C; Lim, C; Lee, J; Kim, K; Lee, K; et al. (1998). Toxicological studies on inhalation of 1-bromopropane using rats. Report submitted to the Industrial Health Research Institute. Yongsan Gu, Republic of Korea: Korea Industrial Safety Corporation.

- Kim, HY; Chung, YH; Jeong, JH; Lee, YM; Sur, GS; Kang, JK. (1999a). Acute and repeated inhalation toxicity of 1-bromopropane in SD rats. *J Occup Health* 41: 121-128.
<http://dx.doi.org/10.1539/Joh.41.121>
- Kim, JS; Ahn, KJ; Kim, JA; Kim, HM; Lee, JD; Lee, JM; Kim, SJ; Park, JH. (2008). Role of reactive oxygen species-mediated mitochondrial dysregulation in 3-bromopyruvate induced cell death in hepatoma cells : ROS-mediated cell death by 3-BrPA. *J Bioenerg Biomembr* 40: 607-618. <http://dx.doi.org/10.1007/s10863-008-9188-0>
- Kim, KW; Kim, HY; Park, SS; Jeong, HS; Park, SH; Lee, JY; Jeong, JH; Moon, YH. (1999b). Gender differences in activity and induction of hepatic microsomal cytochrome P-450 by 1-bromopropane in Sprague-Dawley rats. *J Biochem Mol Biol* 32: 232-238.
- Ko, YH; Smith, B; Wang, Y; Pomper, M; Rini, DA; Torbenson, MS; Hullihen, J; Pedersen, PL. (2004). Advanced cancers: eradication in all cases using 3-bromopyruvate therapy to deplete ATP. *Biochem Biophys Res Commun* 324: 269-275.
<http://dx.doi.org/10.1016/j.bbrc.2004.09.047>
- Krause, RJ; Glocke, SC; Elfarra, AA. (2002). Sulfoxides as urinary metabolites of S-ALLYL-L-CYSTEINE in rats: Evidence for the involvement of flavin-containing monooxygenases. *Drug Metab Dispos* 30: 1137-1142. <http://dx.doi.org/10.1124/dmd.30.10.1137>
- Lee, SK; Jeon, TW; Kim, YB; Lee, ES; Jeong, HG; Jeong, TC. (2007). Role of glutathione conjugation in the hepatotoxicity and immunotoxicity induced by 1-bromopropane in female BALB/c mice. *J Appl Toxicol* 27: 358-367. <http://dx.doi.org/10.1002/jat.1214>
- Li, W; Shibata, E; Zhou, Z; Ichihara, S; Wang, H; Wang, Q; Li, J; Zhang, L; Wakai, K; Takeuchi, Y; Ding, X; Ichihara, G. (2010). Dose-dependent neurologic abnormalities in workers exposed to 1-bromopropane. *J Occup Environ Med* 52: 769-777.
<http://dx.doi.org/10.1097/JOM.0b013e3181eade7>
- Liu, F; Ichihara, S; Mohideen, SS; Sai, U; Kitoh, J; Ichihara, G. (2009). Comparative study on susceptibility to 1-bromopropane in three mice strains. *Toxicol Sci* 112: 100-110.
<http://dx.doi.org/10.1093/toxsci/kfp173>
- Liu, F; Ichihara, S; Valentine, WM; Itoh, K; Yamamoto, M; Sheik Mohideen, S; Kitoh, J; Ichihara, G. (2010). Increased susceptibility of Nrf2-null mice to 1-bromopropane-induced hepatotoxicity. *Toxicol Sci* 115: 596-606. <http://dx.doi.org/10.1093/toxsci/kfq075>
- Lopachin, RM; Gavin, T; Petersen, DR; Barber, DS. (2009). Molecular mechanisms of 4-hydroxy-2-nonenal and acrolein toxicity: Nucleophilic targets and adduct formation [Review]. *Chem Res Toxicol* 22: 1499-1508. <http://dx.doi.org/10.1021/tx900147g>
- Lowe, PN; Perham, RN. (1984). Bromopyruvate as an active-site-directed inhibitor of the pyruvate dehydrogenase multienzyme complex from *Escherichia coli*. *Biochemistry* 23: 91-97.
<http://dx.doi.org/10.1021/Bi00296a015>
- Mabey, W; Mill, T. (1978). Critical review of hydrolysis of organic compounds in water under environmental conditions [Review]. *J Phys Chem Ref Data* 7: 383-415.
- Macchioni, L; Davidescu, M; Sciacaluga, M; Marchetti, C; Migliorati, G; Coaccioli, S; Roberti, R; Corazzi, L; Castigli, E. (2011). Mitochondrial dysfunction and effect of antiglycolytic bromopyruvic acid in GL15 glioblastoma cells. *J Bioenerg Biomembr* 43: 507-518.
<http://dx.doi.org/10.1007/s10863-011-9375-2>
- Majersik, JJ; Caravati, EM; Steffens, JD. (2007). Severe neurotoxicity associated with exposure to the solvent 1-bromopropane (n-propyl bromide). *Clin Toxicol* 45: 270-276.
<http://dx.doi.org/10.1080/15563650701226218>

- Marquart, H; Franken, R; Goede, H; Fransman, W; Schinkel, J. (2017). Validation of the dermal exposure model in ECETOC TRA. *Annals of Work Exposures and Health* 61: 854-871. <http://dx.doi.org/10.1093/annweh/wxx059>
- MassDEP. (2013). Alternative dry cleaning technologies comparative analysis worksheet. Boston, MA. <http://www.mass.gov/eea/docs/dep/service/online/dc-companal.pdf>
- Mathias, PI; Cheever, KL; Hanley, KW; Marlow, KL; Johnson, BC; B'Hymer, C. (2012). Comparison and evaluation of urinary biomarkers for occupational exposure to spray adhesives containing 1-bromopropane. *Toxicol Mech Meth* 22: 526-532. <http://dx.doi.org/10.3109/15376516.2012.686536>
- Meulenberg, CJ; Vijverberg, HP. (2000). Empirical relations predicting human and rat tissue: Air partition coefficients of volatile organic compounds. *Toxicol Appl Pharmacol* 165: 206-216. <http://dx.doi.org/10.1006/taap.2000.8929>
- Mitchell, AE; Zheng, J; Hammock, BD; Lo Bello, M; Jones, AD. (1998). Structural and functional consequences of haloenol lactone inactivation of murine and human glutathione S-transferase. *Biochemistry* 37: 6752-6759. <http://dx.doi.org/10.1021/bi971846r>
- Mohideen, SS; Ichihara, G; Ichihara, S; Nakamura, S. (2011). Exposure to 1-bromopropane causes degeneration of noradrenergic axons in the rat brain. *Toxicology* 285: 67-71. <http://dx.doi.org/10.1016/j.tox.2011.04.005>
- Mohideen, SS; Ichihara, S; Banu, S; Liu, F; Kitoh, J; Ichihara, G. (2009). Changes in neurotransmitter receptor expression levels in rat brain after 4-week exposure to 1-bromopropane. *Neurotoxicology* 30: 1078-1083. <http://dx.doi.org/10.1016/j.neuro.2009.06.007>
- Mohideen, SS; Ichihara, S; Subramanian, K; Huang, Z; Naito, H; Kitoh, J; Ichihara, G. (2013). Effects of exposure to 1-bromopropane on astrocytes and oligodendrocytes in rat brain. *J Occup Health* 55: 29-38. <http://dx.doi.org/10.1539/joh.12-0118-OA>
- Morgan, DL; Nyska, A; Harbo, SJ; Grumbein, SL; Dill, JA; Roycroft, JH; Kissling, GE; Cesta, MF. (2011). Multisite carcinogenicity and respiratory toxicity of inhaled 1-bromopropane in rats and mice. *Toxicol Pathol* 39: 938-948. <http://dx.doi.org/10.1177/0192623311416374>
- NCDOL. (2013). A Health and Safety Guide for 1-bromopropane (n-propyl bromide). In Occupational Safety and Health Division. Raleigh, NC: North Carolina Department of Labor. <http://digital.ncdcr.gov/cdm/ref/collection/p16062coll9/id/148494>
- Neafsey, P; Ginsberg, G; Hattis, D; Johns, DO; Guyton, KZ; Sonawane, B. (2009). Genetic polymorphism in CYP2E1: Population distribution of CYP2E1 activity [Review]. *J Toxicol Environ Health B Crit Rev* 12: 362-388. <http://dx.doi.org/10.1080/10937400903158359>
- NEWMOA. (2001). Pollution prevention technology profile - Closed loop vapor degreasing. Boston, MA. <http://www.newmoa.org/prevention/p2tech/ProfileVaporDegreasing.pdf>
- NFPA. (2010). Fire protection guide to hazardous materials (14th ed.). Quincy, MA.
- NIOSH. (1997). Control of health and safety hazards in commercial drycleaners: chemical exposures, fire hazards, and ergonomic risk factors. In Education and Information Division. (DHHS (NIOSH) Publication Number 97-150). Atlanta, GA. <http://www.cdc.gov/niosh/docs/97-150/>
- NIOSH. (2002a). Health Hazard Evaluation Report No. 98-0153-2883. Custom Products Inc. Mooreville, NC. (98-0153-2883). National Institute for Occupational Safety and Health. <http://www.cdc.gov/niosh/hhe/reports/pdfs/1998-0153-2883.pdf>
- NIOSH. (2002b). Health hazard evaluation report: HETA 2000-0410-2891, STN Cushion Company, Thomasville, North Carolina. (HETA 2000-410-2891.). Cincinnati, OH. <http://www.cdc.gov/niosh/hhe/reports/pdfs/2000-0410-2891.pdf>

- NIOSH. (2002c). Health Hazard Evaluation Report: HETA # 2000-0410-2891 STN Cushion Company, Thomasville, North Carolina. (HETA 2000-410-2891.). Cincinnati, OH. <http://www.cdc.gov/niosh/hhe/reports/pdfs/2000-0410-2891.pdf>
- NIOSH. (2003a). Hazard Evaluation Report : HETA 99-260-2906. Marx Industries Inc., Sawmills, NC. (HETA 99-260-2906). NIOSH Publication Office, Cincinnati, OH: National Institute for Occupational Health and Safety. <http://www.cdc.gov/niosh/hhe/reports/pdfs/1999-0260-2906.pdf>
- NIOSH. (2003b). NIOSH Health Hazard Evaluation Report: HETA No. 99-0260-2906, Marx Industries, Inc., Sawmills, North Carolina. In Hazard Evaluation and Technical Assistance Branch. (HETA 99-260-2906). Cincinnati, OH: National Institute for Occupational Health and Safety. <http://www.cdc.gov/niosh/hhe/reports/pdfs/1999-0260-2906.pdf>
- NIOSH. (2007). Workers' exposures to n-propyl bromide at an adhesives and coating manufacturer. Cincinnati, OH: NIOSH Division of Surveillance, Hazard Evaluation and Field Studies. <http://www.cdc.gov/niosh/nioshtic-2/20031869.html>
- NIOSH. (2010). Evaluation of 1-bromopropane use in four New jersey Commercial Dry Cleaning Facilities. (HETA 2008-0175-3111). <http://www.cdc.gov/niosh/hhe/reports/pdfs/2008-0175-3111.pdf>
- Niosh. (2017). NIOSH Skin Notation Profiles: 1-Bromopropane. By Hudson NL, Dotson GS. (DHHS (NIOSH) Publication No. 2017-187). Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health.
- NRC. (2001). Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals. http://www.nap.edu/catalog.php?record_id=10122
- NTP. (1989a). NTP Toxicology and Carcinogenesis Studies of Tribromomethane (Bromoform) (CAS No. 75-25-2) in F344/N Rats and B6C3F1 Mice (Gavage Studies). 350: 1-194.
- NTP. (1989b). Toxicology and carcinogenesis studies of bromoethane in F344/N rats and B6C3F1 mice (inhalation studies). (Report No. 363). RTP, NC: National Toxicology Program Technical Report Series. http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr363.pdf
- NTP. (1990). Toxicology and carcinogenesis studies of glycidol (CAS no. 556-52-5) in F344/N rats and B6C3Fi mice (gavage studies) [NTP]. (NIH Pub No. 90-2829; NTP TR 374). Research Triangle Park, NC: National Institute of Environmental Health Sciences. https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr374.pdf
- NTP. (2011a). NTP technical report on the toxicology and carcinogenesis studies of 1-bromopropane (CAS No. 106-94-5) in F344/N rats and B6C3F1 mice (inhalation studies). (NTP TR 564; NIH Publication No. 11-5906). Research Triangle Park, NC. http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr564.pdf
- NTP. (2011b). Toxicology and carcinogenesis studies of 1-bromopropane (CAS No. 106-94-5) in F344/N rats and B6C3F1 mice (inhalation studies) [NTP] (pp. 1-190). (ISSN 0888-8051 NTP TR 564; NIH Publication No. 11-5906). Research Triangle Park, NC. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/TR564.pdf
- NTP. (2013a). Draft report on carcinogens. monograph for 1-bromopropane. Research Triangle Park, NC. http://ntp.niehs.nih.gov/ntp/about_ntp/monopeerrvw/2013/march/draftroc1bpmonograph_508.pdf
- NTP. (2013b). Report on carcinogens. Monograph for 1-bromopropane (Final) (pp. 1-168). (NIH Publication No. 13-5982). Research Triangle Park, NC. http://ntp.niehs.nih.gov/ntp/roc/thirteenth/monographs_final/1bromopropane_508.pdf

- NTP. (2014). Report on Carcinogenes. 13th Edition.
<http://ntp.niehs.nih.gov/pubhealth/roc/roc13/index.html>
- O'Neil, MJ. (2013). The Merck index: An encyclopedia of chemicals, drugs, and biologicals. In MJ O'Neil (Ed.), (15th ed.). Cambridge, UK: Royal Society of Chemistry.
- OECD. (1997). OECD guidelines for the testing of chemicals Section 4: Test No. 471: Bacterial Reverse Mutation Test. Paris, France.
- OECD. (2013). OECD guidelines for the testing of chemicals Section 4: Test no. 488: Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays. Paris, France.
- Ohnishi, A; Ishidao, T; Kasai, T; Arashidani, K; Hori, H. (1999). [Neurotoxicity of 1-bromopropane in rats]. J UOEH 21: 23-28.
- OSHA. (2005). Reducing worker exposure to perchloroethylene (PERC) in dry cleaning. (OSHA 3253-05N). Washington, DC: U.S. Department of Labor, Occupational Safety & Health Administration. <https://www.osha.gov/dsg/guidance/perc.html>
- OSHA. (2013a). 1-Bromopropane Manufacturing Site Visit Report – Company A. Draft – Final. Prepared by Project Enhancement Corporation.
- OSHA. (2013b). 1-Bromopropane, Inspection/Case File Summary.
- OSHA. (2013c). OSHA/NIOSH hazard alert: 1-Bromopropane. (OSHA - HA-3676-2013). Washington, DC: Occupational Safety & Health Administration, National Institute for Occupational Safety and Health.
https://www.osha.gov/dts/hazardalerts/1bromopropane_hazard_alert.html
- OSHA. (2013d). OSHA/NIOSH Hazard Alert: 1-Bromopropane. 7.
https://hero.epa.gov/index.cfm?action=search.view&reference_id=5018565 OSHA; NIOSH. (2013). Hazard alert: 1-Bromopropane. Washington, DC: Occupational Safety and Health Administration & National Institute for Occupational Safety and Health.
<http://www.cdc.gov/niosh/nioshtic-2/20031537.html>
- OSHA. (2019). OSHA CEHD Monitoring Data provided by OSHA to EPA on 2/12/2019 (Version 1-BP sanitized OIS 1-24-2019.xlsx).
- Patty, FA; Fassett, DW; Irish, DD. (1963). Industrial hygiene and toxicology: Vol. II: Toxicology. In FA Patty; DW Fassett; DD Irish (Eds.), Industrial hygiene and toxicology: Vol II: Toxicology (2nd revised ed.). New York, NY: Interscience Publishers.
- Pearson, RG. (1990). Hard and soft acids and bases - the evolution of a chemical concept. Coord Chem Rev 100: 403-425. [http://dx.doi.org/10.1016/0010-8545\(90\)85016-L](http://dx.doi.org/10.1016/0010-8545(90)85016-L)
- Porter, LM; Jones, AR. (1995). Inhibition of glyceraldehyde 3- phosphate dehydrogenase in boar spermatozoa by bromohydroxypropanone. Reprod Fertil Dev 7: 107-111.
<http://dx.doi.org/10.1071/RD9950107>
- Qin, JZ; Xin, H; Nickoloff, BJ. (2010). 3-Bromopyruvate induces necrotic cell death in sensitive melanoma cell lines. Biochem Biophys Res Commun 396: 495-500.
<http://dx.doi.org/10.1016/j.bbrc.2010.04.126>
- Raymond, LW; Ford, MD. (2007). Severe illness in furniture makers using a new glue: 1-bromopropane toxicity confounded by arsenic. J Occup Environ Med 49: 1009-1019.
<http://dx.doi.org/10.1097/JOM.0b013e318145b616>
- Reh, CM; Mortimer, VD; Nemhauser, JB; Trout, D. (2002). NIOSH Health Hazard Evaluation Report: HETA No. 98-0153-2883, Custom Products, Inc. Mooresville, NC (pp. pp.). (NTIS/02928129). Cincinnati, OH: National Board of Labour Protection (Finland).
<http://www.cdc.gov/niosh/hhe/reports/pdfs/1998-0153-2883.pdf>

- Reh, CM; Nemhauser, JB. (2001). Health Hazard Evaluation Report: HETA 2000-0233-2845, Trilithic, Inc. Indianapolis, Indiana. (NTIS/02937573_a). Organisation for Economic Cooperation and Development (OECD).
- Reyes, L; Mañalich, R. (2005). Long-term consequences of low birth weight [Review]. *Kidney Int Suppl* 68: S107-S111. <http://dx.doi.org/10.1111/j.1523-1755.2005.09718.x>
- Saito-Suzuki, R; Teramoto, S; Shirasu, Y. (1982). Dominant lethal studies in rats with 1,2-dibromo-3-chloropropane and its structurally related compounds. *Mutat Res Genet Toxicol* 101: 321-327. [http://dx.doi.org/10.1016/0165-1218\(82\)90125-2](http://dx.doi.org/10.1016/0165-1218(82)90125-2)
- Sakuratani, Y; Yamada, J; Kasai, K; Noguchi, Y; Nishihara, T. (2005). External validation of the biodegradability prediction model CATABOL using data sets of existing and new chemicals under the Japanese Chemical Substances Control Law. 16: 403-431. <http://dx.doi.org/10.1080/10659360500320289>
- Samukawa, M; Ichihara, G; Oka, N; Kusunoki, S. (2012). A case of severe neurotoxicity associated with exposure to 1-bromopropane, an alternative to ozone-depleting or global-warming solvents. *Arch Intern Med* 172: 1257-1260. <http://dx.doi.org/10.1001/archinternmed.2012.3987>
- Sclar, G. (1999). Encephalomyeloradiculoneuropathy following exposure to an industrial solvent. *Clin Neurol Neurosurg* 101: 199-202. [http://dx.doi.org/10.1016/S0303-8467\(99\)00034-7](http://dx.doi.org/10.1016/S0303-8467(99)00034-7)
- Sebroski, JMM. (2017). Developing consensus standards for measuring chemical emissions from spray polyurethane foam (SPF) insulation. Washington, DC: ASTM International. <http://dx.doi.org/10.1520/STP1589-EB>
- Sekiguchi, S; Suda, M; Zhai, YL; Honma, T. (2002). Effects of 1-bromopropane, 2-bromopropane, and 1,2-dichloropropane on the estrous cycle and ovulation in F344 rats. *Toxicol Lett* 126: 41-49. [http://dx.doi.org/10.1016/S0378-4274\(01\)00429-5](http://dx.doi.org/10.1016/S0378-4274(01)00429-5)
- Shochat, E; Hermoni, I; Cohen, Z; Abeliovich, A; Belkin, S. (1993). Bromoalkane-degrading *Pseudomonas* strains. *Appl Environ Microbiol* 59: 1403-1409.
- Simmon, VF; Kauhanen, K; Tardiff, RG. (1977). Mutagenic activity of chemicals identified in drinking water. In D Scott; B Bridges; F Sobel (Eds.), *Developments in Toxicology and Environmental Science*, 2 (pp. 249-258). New York, NY: Elsevier/North Holland Press.
- Sohn, YK; Suh, JS; Kim, JW; Seo, HH; Kim, JY; Kim, HY; Lee, JY; Lee, SB; Han, JH; Lee, YM; Lee, JY. (2002). A histopathologic study of the nervous system after inhalation exposure of 1-bromopropane in rat. *Toxicol Lett* 131: 195-201. [http://dx.doi.org/10.1016/S0378-4274\(02\)00051-6](http://dx.doi.org/10.1016/S0378-4274(02)00051-6)
- Stewart. (1998). Airborne exposure assessment of 1-bromopropane (Sanitized). Stewart.
- Subramanian, K; Mohideen, SS; Suzumura, A; Asai, N; Murakumo, Y; Takahashi, M; Jin, S; Zhang, L; Huang, Z; Ichihara, S; Kitoh, J; Ichihara, G. (2012). Exposure to 1-bromopropane induces microglial changes and oxidative stress in the rat cerebellum. *Toxicology* 302: 18-24. <http://dx.doi.org/10.1016/j.tox.2012.07.006>
- Suda, M; Honma, T; Miyagawa, M; Wang, RS. (2008). Alteration of brain levels of neurotransmitters and amino acids in male F344 rats induced by three-week repeated inhalation exposure to 1-bromopropane. *Ind Health* 46: 348-359. <http://dx.doi.org/10.2486/indhealth.46.348>
- Suter, G. (2016). Weight of evidence in ecological assessment. (EPA100R16001). Washington, DC: U.S. Environmental Protection Agency. https://cfpub.epa.gov/si/si_public_record_report.cfm?dirEntryId=335523
- Tachizawa, H; MacDonald, TL; Neal, RA. (1982). Rat liver microsomal metabolism of propyl halides. *Mol Pharmacol* 22: 745-751.

- Tech Spray. (2003). nPB and aerosol exposure. Tech Spray, L.P. Management.
<http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OAR-2002-0064-0044>
- Thomas, AP; Halestrap, AP. (1981). Identification of the protein responsible for pyruvate transport into rat liver and heart mitochondria by specific labelling with [3H]N-phenylmaleimide. *Biochem J* 196: 471-479.
- Toraason, M; Lynch, DW; Debord, DG; Singh, N; Krieg, E; Butler, MA; Toennis, CA; Nemhauser, JB. (2006). DNA damage in leukocytes of workers occupationally exposed to 1-bromopropane. *Mutat Res Genet Toxicol Environ Mutagen* 603: 1-14.
<http://dx.doi.org/10.1016/j.mrgentox.2005.08.015>
- Trafalis, DT; Panteli, ES; Grivas, A; Tsigris, C; Karamanakos, P. (2010). CYP2E1 and risk of chemically mediated cancers [Review]. *Expert Opin Drug Metab Toxicol* 6: 307-319.
<http://dx.doi.org/10.1517/17425250903540238>
- TURI. (2012). Assessment of alternatives to the perchloroethylene for dry cleaning industry. Available online at
http://www.turi.org/TURI_Publications/TURI_Methods_Policy_Reports/Assessment_of_Alternatives_to_Perchloroethylene_for_the_Dry_Cleaning_Industry_2012
- U.S. BLS. (2015). Occupational employment statistics: May 2014 national industry-specific occupational employment and wage estimates [Website].
<https://web.archive.org/web/20150607155702/http://www.bls.gov/oes/current/oesrci.htm>
- U.S. BLS. (2016). May 2016 Occupational Employment and Wage Estimates: National Industry-Specific Estimates [Website]. <http://www.bls.gov/oes/tables.htm>
- U.S. BLS. (2017). Labor Force Statistics from the Current Population Survey. Current Population Survey (CPS) Tables. Annual averages. Characteristics of the Employed. Table 14 and 18b. Retrieved from <https://www.bls.gov/cps/tables.htm>
- U.S. EPA. (1977). Control of volatile organic emissions from solvent metal cleaning [EPA Report]. (EPA-450/2-77-022). Research Triangle Park, NC: U.S. Environmental Protection Agency, Office of Air and Waste Management, Office of Air Quality Planning and Standards.
- U.S. EPA. (1981). AP-42. Compilation of air pollutant emission factors. Chapter 4. 6: Solvent degreasing. Washington, DC. <http://www3.epa.gov/ttn/chief/ap42/ch04/final/c4s06.pdf>
- U.S. EPA. (1987). Household solvent products: A national usage survey. (EPA-OTS 560/5-87-005). Washington, DC: Office of Toxic Substances, Office of Pesticides and Toxic Substances.
<https://ntrl.ntis.gov/NTRL/dashboard/searchResults.xhtml?searchQuery=PB88132881>
- U.S. EPA. (1988). Recommendations for and documentation of biological values for use in risk assessment (pp. 1-395). (EPA/600/6-87/008). Cincinnati, OH: U.S. Environmental Protection Agency, Office of Research and Development, Office of Health and Environmental Assessment. <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=34855>
- U.S. EPA. (1994). Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry [EPA Report]. (EPA/600/8-90/066F). Research Triangle Park, NC: U.S. Environmental Protection Agency, Office of Research and Development, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.
<https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=71993&CFID=51174829&CFTOKEN=25006317>
- U.S. EPA. (1997). Solvent Cleaning. Volume III, Chapter 6. pp. 6.2.1. Washington, DC.
<http://www3.epa.gov/ttnchie1/eiip/techreport/volume03/iii06fin.pdf>

- U.S. EPA. (1998a). Guidelines for ecological risk assessment [EPA Report]. (EPA/630/R-95/002F). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. <https://www.epa.gov/risk/guidelines-ecological-risk-assessment>
- U.S. EPA. (1998b). Guidelines for neurotoxicity risk assessment [EPA Report] (pp. 1-89). (EPA/630/R-95/001F). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. <http://www.epa.gov/risk/guidelines-neurotoxicity-risk-assessment>
- U.S. EPA. (2001). Risk assessment guidance for superfund: Volume III - Part A, Process for conducting probabilistic risk assessment [EPA Report]. (EPA/540-R-02-002). Washington, DC: U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. http://www2.epa.gov/sites/production/files/2015-09/documents/rags3adt_complete.pdf
- U.S. EPA. (2002). A review of the reference dose and reference concentration processes (pp. 1-192). (EPA/630/P-02/002F). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. <http://www.epa.gov/osa/review-reference-dose-and-reference-concentration-processes>
- U.S. EPA. (2003). Protection of the stratospheric ozone: Listing of substances for ozone depleting substances - n-propyl bromide. Fed Reg 68: 33284-33316.
- U.S. EPA. (2005a). Guidelines for carcinogen risk assessment [EPA Report] (pp. 1-166). (EPA/630/P-03/001F). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. <http://www2.epa.gov/osa/guidelines-carcinogen-risk-assessment>
- U.S. EPA. (2005b). Supplemental guidance for assessing susceptibility from early-life exposure to carcinogens [EPA Report]. (EPA/630/R-03/003F). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. https://www3.epa.gov/airtoxics/childrens_supplement_final.pdf
- U.S. EPA. (2006a). Risk assessment for the halogenated solvent cleaning source category [EPA Report]. (EPA Contract No. 68-D-01-052). Research Triangle Park, NC: U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards. <http://www3.epa.gov/airtoxics/degrea/residrisk2008.pdf>
- U.S. EPA. (2006b). Significant new alternatives policy (SNAP) - Risk screen on substitutes for ozone depleting substances for adhesive, aerosol solvent, and solvent cleaning applications. Proposed substitute: n-Propyl bromide. In Office of Air and Radiation, Stratospheric Protection Division. Washington DC.
- U.S. EPA. (2007a). Analysis of Economic Impacts of Final nPB [1-Bromopropane] Rulemaking for Cleaning Solvent Sector [EPA Report]. https://hero.epa.gov/index.cfm?action=search.view&reference_id=2991013
- U.S. EPA. (2007c). Protection of stratospheric ozone: Listing of substances for ozone depleting substances - n-propyl bromide in adhesives, coatings and aerosols. Fed Reg 72: 30168-30207.
- U.S. EPA. (2011). Exposure factors handbook: 2011 edition (final) [EPA Report]. (EPA/600/R-090/052F). Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment. <http://cfpub.epa.gov/ncea/cfm/recorddisplay.cfm?deid=236252>
- U.S. EPA. (2012a). Benchmark dose technical guidance. (EPA/100/R-12/001). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. <https://www.epa.gov/risk/benchmark-dose-technical-guidance>
- U.S. EPA. (2012b). Estimation Programs Interface Suite for Microsoft Windows, v. 4.11. <https://www.epa.gov/tsca-screening-tools/download-epi-suitetm-estimation-program-interface-v411>

- U.S. EPA. (2012c). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11 [Computer Program]. Washington, DC. Retrieved from <https://www.epa.gov/tsca-screening-tools/epi-suite™-estimation-program-interface>
- U.S. EPA. (2012d). Non-Confidential 2012 Chemical Data Reporting. http://www.epa.gov/oppt/cdr/pubs/guidance/1st_CDR_basics_factsheet_5_23_2014.pdf
- U.S. EPA. (2012e). Sustainable futures P2 framework manual [EPA Report]. (EPA-748-B12-001). Washington DC. <http://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual>
- U.S. EPA. (2013a). ChemSTEER user guide - Chemical screening tool for exposures and environmental releases. Washington, D.C. https://www.epa.gov/sites/production/files/2015-05/documents/user_guide.pdf
- U.S. EPA. (2013b). Interpretive assistance document for assessment of discrete organic chemicals. Sustainable futures summary assessment [EPA Report]. Washington, DC. http://www.epa.gov/sites/production/files/2015-05/documents/05-iad_discretes_june2013.pdf
- U.S. EPA. (2013c). Use and market profile for 1-bromopropane in vapor degreasers, spray adhesives, and aerosol solvents [EPA Report]. Washington, DC.
- U.S. EPA. (2014a). Degreasing with TCE in commercial facilities: Protecting workers [EPA Report]. Washington, DC: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics. https://hero.epa.gov/index.cfm?action=search.view&reference_id=4565445
- U.S. EPA. (2014c). Framework for human health risk assessment to inform decision making. Final [EPA Report]. (EPA/100/R-14/001). Washington, DC: U.S. Environmental Protection, Risk Assessment Forum. <https://www.epa.gov/risk/framework-human-health-risk-assessment-inform-decision-making>
- U.S. EPA. (2014d). TSCA work plan chemical risk assessment. Trichloroethylene: Degreasing, spot cleaning and arts & crafts uses. (740-R1-4002). Washington, DC: Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. http://www2.epa.gov/sites/production/files/2015-09/documents/tce_opptworkplanchemra_final_062414.pdf
- U.S. EPA. (2016a). Public database 2016 chemical data reporting (May 2017 release). Washington, DC: US Environmental Protection Agency, Office of Pollution Prevention and Toxics. Retrieved from <https://www.epa.gov/chemical-data-reporting>
- U.S. EPA. (2016b). A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding the Draft Risk Assessment for TSCA Work Plan Chemical 1-Bromopropane (CASRN-106-94-5). (Chemical Safety Advisory Committee Minutes No. 2016-02).
- U.S. EPA. (2016c). TRI Basic Plus Data Files: 2016 Reporting Year (Version 15). Retrieved from <https://www.epa.gov/toxics-release-inventory-tri-program/tri-basic-plus-data-files-calendar-years-1987-2017>
- U.S. EPA. (2016d). TSCA work plan chemical risk assessment: Peer review draft 1-bromopropane: (n-Propyl bromide) spray adhesives, dry cleaning, and degreasing uses CASRN: 106-94-5 [EPA Report]. (EPA 740-R1-5001). Washington, DC. https://www.epa.gov/sites/production/files/2016-03/documents/1-bp_report_and_appendices_final.pdf
- U.S. EPA. (2017a). Chemical data reporting: 1-bromo-propane [Database]. Retrieved from <http://java.epa.gov/chemview>

- [U.S. EPA.](#) (2017b). Preliminary Data for 2017 Reporting Year.
- [U.S. EPA.](#) (2017c). Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane. Support document for Docket EPA-HQ-OPPT-2016-0741 [Comment]. (EPA-HQ-OPPT-2016-0741-0003). Washington, DC: Office of Chemical Safety and Pollution Prevention. <https://www.epa.gov/sites/production/files/2017-02/documents/1-bromopropane.pdf>
- [U.S. EPA.](#) (2017d). Scope of the risk evaluation for 1-Bromopropane [EPA Report]. (EPA- 740-R1-7009). https://www.epa.gov/sites/production/files/2017-06/documents/bp_scope_06-22-17.pdf
- [U.S. EPA.](#) (2017e). Strategy for conducting literature searches for 1-Bromopropane (1-bp): supplemental document to the TSCA scope document [EPA Report]. https://www.epa.gov/sites/production/files/2017-06/documents/1-bp_lit_search_strategy_053017_0.pdf
- [U.S. EPA.](#) (2017f). Toxicological review of benzo[a]pyrene [CASRN 50-32-8]. (EPA635R17003FA). Washington, DC: U.S. Environmental Protection Agency, Integrated Risk Information System. https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0136tr.pdf
- [U.S. EPA.](#) (2017g). Toxics Release Inventory (TRI), reporting year 2015. Retrieved from <https://www.epa.gov/toxics-release-inventory-tri-program/tri-data-and-tools>
- [U.S. EPA.](#) (2018a). Application of systematic review in TSCA risk evaluations. (740-P1-8001). Washington, DC: U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsc_a_05-31-18.pdf
- [U.S. EPA.](#) (2018c). Problem formulation of the risk evaluation for 1-bromopropane. (EPA-740-R1-7019). Washington, DC: Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. https://www.epa.gov/sites/production/files/2018-06/documents/1bp_problem_formulation_05-31-18.pdf
- [U.S. EPA.](#) (2018d). Strategy for assessing data quality in TSCA risk evaluations. Washington DC: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics.
- [U.S. EPA.](#) (2019a). Consumer Exposure Model (CEM) 2.1 User Guide. (EPA Contract # EP-W-12-010). Washington, DC.
- [U.S. EPA.](#) (2019b). Consumer Exposure Model (CEM) 2.1 User Guide - Appendices. (EPA Contract # EP-W-12-010). Washington, DC: U.S. EPA.
- [U.S. EPA.](#) (2019c). IECCU 1.1 User's Guide. In Simulation Program for Estimating Chemical Emissions from Sources and Related Changes to Indoor Environmental Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU). (EPA Contract # EP-W-12-010). Washington, DC: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics.
- [U.S. EPA.](#) (2019d). Multi-Chamber Concentration and Exposure Model (MCCCEM) User Guide. U.S. EPA.
- [U.S. EPA; ICF Consulting.](#) (2004). The U.S. solvent cleaning industry and the transition to non ozone depleting substances. <http://www.hsia.org/applications/ODS%20report.pdf>
- [Ueno, S; Yoshida, Y; Fueta, Y; Ishidao, T; Liu, J; Kunugita, N; Yanagihara, N; Hori, H.](#) (2007). Changes in the function of the inhibitory neurotransmitter system in the rat brain following subchronic inhalation exposure to 1-bromopropane. *Neurotoxicology* 28: 415-420. <http://dx.doi.org/10.1016/j.neuro.2006.03.006>

- Valentine, H; Amarnath, K; Amarnath, V; Li, WH; Ding, XC; Valentine, WM; Ichihara, G. (2007). Globin S-Propyl Cysteine and urinary N-acetyl-S-propylcysteine as internal biomarkers of 1-bromopropane exposure. *Toxicol Sci* 98: 427-435.
<http://dx.doi.org/10.1093/toxsci/kfm126>
- Van Raaij, MTM; Janssen, PAH; Piersma, AH. (2003). The relevance of developmental toxicity endpoints for acute limits settings (pp. 1-88). (RIVM Report 601900004). Netherlands: Netherlands National Institute for Public Health and the Environment.
<http://www2.epa.gov/sites/production/files/2014-04/documents/mtg35b.pdf>
- Von Grote, J; Hurlimann, JC; Scheringer, M; Hungerbuhler, K. (2003). Reduction of Occupational Exposure to Perchloroethylene and Trichloroethylene in Metal Degreasing over the Last 30 years: Influence of Technology Innovation and Legislation. *J Expo Anal Environ Epidemiol* 13: 325-340. <http://dx.doi.org/10.1038/sj.jea.7500288>
- Wadden, RA; Scheff, PA; Franke, JE. (1989). Emission Factors for Trichloroethylene Vapor Degreasers. *Am Ind Hyg Assoc J* 50: 495-500.
- Wang, H; Ichihara, G; Ito, H; Kato, K; Kitoh, J; Yamada, T; Yu, X; Tsuboi, S; Moriyama, Y; Sakatani, R; Shibata, E; Kamijima, M; Itohara, S; Takeuchi, Y. (2002). Biochemical changes in the central nervous system of rats exposed to 1-bromopropane for seven days. *Toxicol Sci* 67: 114-120. <http://dx.doi.org/10.1093/toxsci/67.1.114>
- Wang, H; Ichihara, G; Ito, H; Kato, K; Kitoh, J; Yamada, T; Yu, X; Tsuboi, S; Moriyama, Y; Takeuchi, Y. (2003). Dose-dependent biochemical changes in rat central nervous system after 12-week exposure to 1-bromopropane. *Neurotoxicology* 24: 199-206.
[http://dx.doi.org/10.1016/S0161-813X\(02\)00195-X](http://dx.doi.org/10.1016/S0161-813X(02)00195-X)
- Wang, QH; Zhong, ZX; Chen, JJ; Xie, KQ; Zhao, XL. (2012). [Development of peripheral neuropathy rat model induced by 1-bromopropane]. *Zhonghua Laodong Weisheng Zhiyebing Zazhi* 30: 751-755.
- Weinberg, JT. (2016). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation. (Laboratory Project ID WIL-266501). Melrose Park, IL, US: Enviro Tech International.
- Wheeler, MW; Bailer, AJ. (2007). Properties of model-averaged BMDLs: A study of model averaging in dichotomous response risk estimation. *Risk Anal* 27: 659-670.
<http://dx.doi.org/10.1111/j.1539-6924.2007.00920.x>
- Whittaker, SG; Johanson, CA. (2011). A profile of the dry cleaning industry in King County, Washington: Final report. (LHWMP 0048). Seattle, WA: Local Hazardous Waste Management Program in King County.
http://www.hazwastehelp.org/publications/publications_detail.aspx?DocID=Oh73%2fQilg9Q%3d
- WIL Research. (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats. (Study No. WIL-380001). Ashland, OH.
- Woo, YT; Lai, DY. (2003). Mechanism of action of chemical carcinogenes and their role in Structure-Activity Relationship (SAR) analysis and risk assessment. In R Benigni (Ed.), (pp. 41-80). Boca Raton, FL: CRC Press.
- Xin, QQ; Huang, Y; Li, J; Zhang, WJ; Yu, T; Wang, H; Zhang, C; Ye, DQ; Huang, F. (2010). Apoptosis contributes to testicular toxicity induced by two isomers of bromopropanes. *Toxicol Ind Health* 26: 513-524. <http://dx.doi.org/10.1177/0748233710373083>
- Yahagi, T; Nagao, M; Seino, Y; Matsushima, T; Sugimura, T. (1977). Mutagenicities of N-nitrosamines on Salmonella. *Mutat Res* 48: 121-129.

- Yalkowsky, SH; He, Y; Jain, P. (2010). Handbook of aqueous solubility data (2nd ed.). Boca Raton, FL: CRC Press. <http://dx.doi.org/10.1201/EBK1439802458>
- Yamada, T; Ichihara, G; Wang, H; Yu, X; Maeda, K; Tsukamura, H; Kamijima, M; Nakajima, T; Takeuchi, Y. (2003). Exposure to 1-bromopropane causes ovarian dysfunction in rats. Toxicol Sci 71: 96-103. <http://dx.doi.org/10.1093/toxsci/71.1.96>
- Yoshida, Y; Liu, JQ; Nakano, Y; Ueno, S; Ohmori, S; Fueta, Y; Ishidao, T; Kunugita, N; Yamashita, U; Hori, H. (2007). 1-BP inhibits NF-kappaB activity and Bcl-xL expression in astrocytes in vitro and reduces Bcl-xL expression in the brains of rats in vivo. Neurotoxicology 28: 381-386. <http://dx.doi.org/10.1016/j.neuro.2006.05.015>
- Young, ML. (2012). Pre-spotting step toward better cleaning. Available online at <https://americandrycleaner.com/articles/pre-spotting-step-toward-better-cleaning>
- Young, RR. (2016). In vivo mutation assay of n-propyl bromide at the cII locus in Big Blue® transgenic B6C3F1 mice exposed via whole-body inhalation. Provided by Julie Ownbey, ICL Industrial Products. Beer-Sheva, Israel: ICL-IP.
- Yu, WJ; Kim, JC; Chung, MK. (2008). Lack of dominant lethality in mice following 1-bromopropane treatment. Mutat Res Genet Toxicol Environ Mutagen 652: 81-87. <http://dx.doi.org/10.1016/j.mrgentox.2008.01.001>
- Yu, X; Ichihara, G; Kitoh, J; Xie, Z; Shibata, E; Kamijima, M; Takeuchi, Y. (2001). Neurotoxicity of 2-bromopropane and 1-bromopropane, alternative solvents for chlorofluorocarbons. Environ Res 85: 48-52. <http://dx.doi.org/10.1006/enrs.2000.4226>
- Zhang, L; Nagai, T; Yamada, K; Ibi, D; Ichihara, S; Subramanian, K; Huang, Z; Mohideen, SS; Naito, H; Ichihara, G. (2013). Effects of sub-acute and sub-chronic inhalation of 1-bromopropane on neurogenesis in adult rats. Toxicology 304: 76-82. <http://dx.doi.org/10.1016/j.tox.2012.12.009>
- Zhang, ZW; Kawai, T; Takeuchi, A; Miyama, Y; Sakamoto, K; Watanabe, T; Matsuda-Inoguchi, N; Shimbo, S; Higashikawa, K; Ikeda, M. (2001). Urinary bromide levels probably dependent to intake of foods such as sea algae. Arch Environ Contam Toxicol 40: 579-584. <http://dx.doi.org/10.1007/s002440010213>
- Zhao, WY; Aoki, K; Xie, TX; Misumi, J. (1999). Electrophysiological changes induced by different doses of 1-bromopropane and 2-bromopropane. J Occup Health 41: 1-7. <http://dx.doi.org/10.1539/joh.41.1>
- Zhong, Z; Zeng, T; Xie, K; Zhang, C; Chen, J; Bi, Y; Zhao, X. (2013). Elevation of 4-hydroxynonenal and malondialdehyde modified protein levels in cerebral cortex with cognitive dysfunction in rats exposed to 1-bromopropane. Toxicology 306: 16-23. <http://dx.doi.org/10.1016/j.tox.2013.01.022>
- Zong, C; Garner, CE; Huang, C; Zhang, X; Zhang, L; Chang, J; Toyokuni, S; Ito, H; Kato, M; Sakurai, T; Ichihara, S; Ichihara, G. (2016). Preliminary characterization of a murine model for 1-bromopropane neurotoxicity: Role of cytochrome P450. Toxicol Lett 258: 249-258. <http://dx.doi.org/10.1016/j.toxlet.2016.07.006>

Appendix A REGULATORY HISTORY

A.1 Federal Laws and Regulations

Table_Apx A-1. Federal Laws and Regulations

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
US EPA Regulations		
Toxic Substances Control Act (TSCA) – Section 6(b)	EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments.	1-BP is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016)
Toxic Substances Control Act (TSCA) – Section 8(a)	The TSCA section 8(a) Chemical Data Reporting (CDR) Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the US.	1-BP manufacturing, importing, processing, and use information is reported under the Chemical Data Reporting (CDR) rule (76 FR 50816, August 16, 2011).
Toxic Substances Control Act (TSCA) – Section 8(b)	EPA must compile, keep current, and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed, or imported in the United States.	1-BP was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process (60 FR 16309, March 29, 1995).
Toxic Substances Control Act (TSCA) – Section 8(e)	Manufacturers (including importers), processors, and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment.	Eleven notifications of substantial risk (Section 8(e)) received before 2001 (US EPA, ChemView. Accessed April 13, 2017).
Toxic Substances Control Act (TSCA) – Section 4	Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures.	One submission from a test rule (Section 4) received in 1981 (US EPA, ChemView. Accessed April 13, 2017).
Emergency Planning and Community Right-To-Know Act (EPCRA) – Section 313	Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process, or otherwise use a Toxics Release Inventory (TRI)-listed chemical in quantities above threshold levels.	1-BP is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 2016, with reporting due July 1, 2017 (80 FR 72906, November 23, 2015).
Clean Air Act (CAA) – Section 112(b)	This section lists 189 Hazardous Air Pollutants (HAPs) that must be addressed by EPA and includes authority for EPA to add or delete pollutants. EPA may, by rule, add pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse	EPA received petitions from the Halogenated Solvent Industry Alliance and the New York State Department of Environmental Conservation to list 1-BP as a <i>hazardous air pollutant</i> (HAP) under section 112(b)(1) of the Clean Air Act (80 FR 6676, February 6, 2015). On January 9, 2017, EPA published a draft notice on the rational for granting the petitions to add 1-BP to the list of hazardous air pollutants. Comments are due June 8, 2017 (82 FR 2354, January 9, 2017). Since 1-BP is not a HAP, currently, there are no

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	environmental effects. For all major source categories emitting HAP, the CAA requires issuance of technology-based standards and, 8 years later, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.	National Emissions Standards for Hazardous Air Pollutants (NESHAPs) that apply to the life cycle.
Clean Air Act (CAA) – Section 183(e)	Section 183(e) requires EPA to list the categories of consumer and commercial products that account for at least 80 percent of all VOC emissions in areas that violate the National Ambient Air Quality Standards (NAAQS) for ozone and to issue standards for these categories that require “best available controls.” In lieu of regulations, EPA may issue control techniques guidelines if the guidelines are determined to be substantially as effective as regulations.	1-BP is listed under the National Volatile Organic Compound Emission Standards for Aerosol Coatings (40 CFR part 59, subpart E). 1-BP has a reactivity factor of 0.35 g O ₃ /g VOC.
Clean Air Act (CAA) – Section 612	Under Section 612 of the Clean Air Act (CAA), EPA’s Significant New Alternatives Policy (SNAP) program reviews substitutes for ozone depleting substances within a comparative risk framework. EPA publishes lists of acceptable and unacceptable alternatives. A determination that an alternative is unacceptable, or acceptable only with conditions, is made through rulemaking.	Under EPA’s SNAP program, EPA evaluated 1-BP as an acceptable substitute for ozone-depleting substances. In 2007, EPA listed 1-BP as an acceptable substitute for chlorofluorocarbon (CFC)-113 and methyl chloroform in the solvent and cleaning sector for metals cleaning, electronics cleaning, and precision cleaning. EPA recommended the use of personal protective equipment, including chemical goggles, flexible laminate protective gloves and chemical-resistant clothing (72 FR 30142, May 30, 2007). In 2007, the Agency also proposed to list 1-BP as an unacceptable substitute for CFC-113, hydrochlorofluorocarbon (HCFC)- 114b and methyl chloroform when used in adhesives or in aerosol solvents; and in the coatings end use (subject to use conditions) (72 FR 30168, May 30, 2007). The proposed rule has not been finalized by the Agency. The rule identifies 1-BP as acceptable and unacceptable substitute for ozone-depleting substances in several sectors.
Other Federal Regulations		
Occupational Safety and Health Act (OSHA)	Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress, or unsanitary conditions.	OSHA has not issued a PEL for 1-BP. OSHA and the National Institute for Occupational Safety and Health (NIOSH) issued a Hazard Alert regarding 1-BP (OSHA-NIOSH, 2013) providing information regarding health effects, how workers are exposed, how to control the exposures and

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	Under the Act, OSHA can issue occupational safety and health standards including such provisions as Permissible Exposure Limits (PELs), exposure monitoring, engineering and administrative control measures, and respiratory protection.	how OSHA and NIOSH can help. The Hazard alert indicates that: "ACGIH currently recommends a 10 ppm time-weighted average threshold limit value but has proposed lowering the value to 0.1 ppm [ACGIH 2013]."
Department of Energy (DOE)	The Atomic Energy Act authorizes DOE to regulate the health and safety of its contractor employees.	10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. The 2005 TLV for 1-BP is 10 ppm (8hr Time Weighted Average).

A.2 State Laws and Regulations

Table Apx A-2. State Laws and Regulations

State Actions	Description of Action
State Air Regulations	Allowable Ambient Levels Rhode Island (Air Pollution Regulation No. 22) New Hampshire (Env-A 1400: Regulated Toxic Air Pollutants) New York has a de facto ban on the use of 1-BP in dry cleaning. New York will not issue an Air Facility Registration to any facility proposing to use that chemical as an alternative dry cleaning solvent as it is not an approved alternative solvent.
Chemicals of High Concern	Massachusetts designated 1-BP as a higher hazard substance requiring reporting starting in 2016 (301 CMR 41.00). Minnesota listed 1-BP as chemical of high concern to children (Minnesota Statutes 116.9401 to 116.9407).
State Permissible Exposure Limits	California PEL: 5 ppm as an 8-hr-time-weighted average (TWA) (California Code of Regulations, title 8, section 5155).
State Right-to-Know Acts	New Jersey (42 N.J.R. 1709(a)), Pennsylvania (Chapter 323. Hazardous Substance List).
Other	In California, 1-BP was added to proposition 65 list in December 2004 due to developmental, female and male, toxicity; and in 2016 due to cancer. (Cal. Code Regs. title 27, section 27001). 1-BP is listed as a Candidate Chemical under California's Safer Consumer Products Program (Health and Safety Code sections 25252 and 25253). California also selected 1-BP as the first chemical for early warning and prevention activities under SB 193 Early Warning Authority and issued a Health Hazard Alert for 1-BP (Hazard Evaluation System and Information Service, 2016). Oregon has adopted, and is considering, several state-specific statutes and regulations to manage the impacts of toxic and hazardous pollutants, including air toxics permits and benchmarks for industrial facilities, and the Toxics Use and Hazardous Waste Reduction planning requirements, which apply to large and small quantity generators of hazardous waste and Toxic Release Inventory reporters. The District of Columbia's Hazardous Waste Management Act includes provisions for toxic chemical source reporting and reduction. Businesses identified by the Standard

State Actions	Description of Action
	Industrial Classification (SIC) as the largest generators or within the top 25% of all hazardous waste generators within the District, or that release a toxic chemical subject to regulation are required to file an annual Toxic Release Inventory (TRI) Form R for each TRI-listed chemical it manufactures, processes or otherwise uses in quantities above the threshold reporting quantity. In addition, reporting facilities must prepare and submit a toxic chemical source reduction plan which must be updated every four years.

A.3 International Laws and Regulations

Table_Apx A-3. Regulatory Actions by other Governments and Tribes

Country /Organization	Requirements and Restrictions
European Union	In 2012, 1-BP was listed on the Candidate list as a Substance of Very High Concern (SVHC) under regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals due to its reproductive toxicity (category 1B). In June 2017, 1-BP was added to Annex XIV of REACH (Authorisation List) with a sunset date of July 4, 2020 (European Chemicals Agency (ECHA) database. Accessed December 6, 2017).
Australia	1-BP was assessed under Environment Tier II of the Inventory Multi-tiered Assessment and Prioritisation (IMAP) (National Industrial Chemicals Notification and Assessment Scheme (NICNAS), 2017, <i>Human Health Tier II Assessment for Propane, 1-bromo-</i> . Accessed April, 18 2017).
Japan	1-BP is regulated in Japan under the following legislation: Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL) Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof Industrial Safety and Health Act (ISHA) Air Pollution Control Law (National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 13, 2017).
Belgium, Canada, Finland, Japan, Poland, South Korea and Spain	Occupational exposure limits for 1-BP. (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017).
Basel Convention	Halogenated organic solvents (Y41) are listed as a category of waste under the Basel Convention – Annex I. Although the United States is not currently a party to the Basel Convention, this treaty still affects U.S. importers and exporters.
OECD Control of Transboundary Movements of Wastes Destined for Recovery Operations	Halogenated organic solvents (A3150) are listed as a category of waste subject to The Amber Control Procedure under Council Decision C (2001) 107/Final.

Appendix B LIST OF SUPPLEMENTAL DOCUMENTS

List of supplemental documents:

Associated Systematic Review Data Quality Evaluation Documents – Provides additional detail and information on individual study evaluations including criteria and scoring results.

1. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Updates to the Data Quality Criteria for Epidemiological Studies. ([EPA, 2019r](#)).
2. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies. ([EPA, 2019m](#)).
3. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Consumer Exposure ([EPA, 2019k](#)). .
4. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data. ([EPA, 2019n](#)).
5. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data for Common Sources. ([EPA, 2019o](#)).
6. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies. ([EPA, 2019l](#)).
7. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiologic Studies. ([EPA, 2019q](#)).
8. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies. EPA-HQ-OPPT-2019-0235 ([EPA, 2019p](#)).
9. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction Tables for Environmental Fate and Transport Studies. ([EPA, 2019j](#)).
10. Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction for Consumer Exposure ([EPA, 2019i](#)).

Associated Supplemental Information Documents – Provides additional details and information on engineering and exposure assessments.

1. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Consumer Exposure Assessment ([EPA, 2019f](#)). Provides additional details and information on the exposure assessment and analyses including modeling inputs and outputs.

2. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Consumer Exposure Assessment Modeling Input Parameters ([EPA, 2019a](#)).
3. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Consumer Exposure Assessment Model Outputs ([EPA, 2019b](#)).
4. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Consumer Exposure Risk Calculations ([EPA, 2019c](#)).
5. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: ECHA Study Summaries for Environmental Hazard. ([EPA, 2019d](#)).
6. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Occupational Exposure Assessment. ([EPA, 2019g](#)). This document provides additional details and information on the occupational exposure assessment, including estimates of number of sites and workers, summary of monitoring data, and exposure modeling equations, inputs and outputs.
7. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Occupational Risk Calculator. ([EPA, 2019h](#)).
8. Draft Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Human Health Benchmark Dose Modeling. ([EPA, 2019e](#)).

Appendix C FATE AND TRANSPORT

C.1 Fate in Air

If released to the atmosphere, 1-BP is expected to exist solely in the vapor-phase based on its vapor pressure. In the vapor phase, it is degraded by reaction with photochemically produced hydroxyl radicals. The half-life of this reaction is approximately 9 - 12 days assuming a hydroxyl radical concentration over a 12 hour day of 1.5×10^6 hydroxyl radicals per cubic centimeter of air (Version 4.10 EPISuite). Its atmospheric degradation and its photooxidation products were investigated for their ozone depletion potential ([Burkholder et al., 2002](#)). It was shown that the hydroxyl radical initiated degradation does not lead to long-lived bromine containing species that can migrate to the stratosphere. The major photodegradation products were bromoacetone, propanal and 3-bromopropanal. Bromoacetone was rapidly photolyzed releasing bromine which was removed from the atmosphere by wet deposition. 1-BP does not absorb light greater than 290 nm; therefore, degradation of this substance by direct photolysis is not expected to be an important fate process. The bromoacetone and propanal constitute about 90% of 1-BP that is degraded in the atmosphere, and they, as well as 3-bromopropanal, are expected to be rapidly degraded. Apparently, the major atmospheric degradative fate of 1-BP is the rapid and irreversible release of Br atoms. Based on the 1-BP estimated half-life of 9-12 days in air, it is possible that it can undergo long range transport via the atmosphere.

C.2 Fate in Water

When released to water, 1-BP is not expected to adsorb to suspended solids and sediment in the water column based upon its estimated Koc value of about 40 ([U.S. EPA, 2013b](#)). The rate of volatilization is expected to be rapid based on a Henry's Law constant of 7.3×10^{-3} atm-m³/mole. 1-BP was reported to achieve 70% of its theoretical biochemical oxygen demand (BOD) in the MITI (OECD 301C) test ([Sakuratani et al., 2005](#)) which is considered readily biodegradable. Bacterial strains isolated from organobromide-rich industrial wastewater were shown to degrade 1-BP ([Shochat et al., 1993](#)). *Arthrobacter* HA1 debrominated 1-BP under aerobic conditions yielding 1-propanol as a degradation product ([Belkin, 1992](#)) and *Acinetobacter* strain GJ70, isolated from activated sludge was able to utilize it as a carbon source ([Janssen et al., 1987](#)). These results suggest that 1-BP will undergo biodegradation in the environment under aerobic conditions. Hydrolysis of 1-BP is expected based on studies of ([Mabey and Mill, 1978](#)). A hydrolysis half-life of about 26 days was calculated at pH 7 and 25 degrees Celsius from its first-order neutral rate constant of 3.01×10^{-7} sec⁻¹. The expected hydrolysis product is propanol and the hydrodebromination product propene is also possible. Photooxidation in water has not been reported to be an important environmental fate process. 1-BP is not expected to be persistent in water.

C.3 Fate in Sediment and Soil

1-BP is expected to have high mobility in soil based on an estimated log Koc of 1.6. Volatilization is expected to be an important fate process given its relatively high Henry's law constant of 7.3×10^{-3} atm m³/mole and it is expected to volatilize from dry soil surfaces based upon its high vapor pressure. Its biodegradation is considered to be moderate in sediment and soil. 1-BP is not persistent in sediment or soil.

Appendix D CHEMICAL DATA REPORTING RULE DATA FOR 1-BP

EPA's [2012 Chemical Data Reporting \(CDR\)](#) reported a 1-BP production volume of 15.4 million pounds. Albemarle Corporation and a CBI company reported domestic manufacturing of 1-BP ([U.S. EPA, 2012d](#)). Dow Chemical Company, Special Materials Company, and ICL reported imports of 1-BP ([U.S. EPA, 2012d](#)). Data in Table_Apx D-D-1 through Table_Apx D-D-3 were extracted from the 2012 CDR records ([U.S. EPA, 2012d](#)).

Table_Apx D-1. National Chemical Information for 1-BP from 2012 CDR

Production Volume (aggregate)	15.4 million pounds
Maximum Concentration (at manufacture or import site)	>90%
Physical form(s)	Liquid
Number of reasonably likely to be exposed industrial manufacturing, processing, and use workers (aggregated)	>1,000
Was industrial processing or use information reported?	Yes
Was commercial or consumer use information reported?	Yes

Table_Apx D-2. Summary of Industrial 1-BP Uses from 2012 CDR

Industrial Sector (Based on NAICS)	Industrial Function	Type of Processing
Soap, Cleaning Compound, and Toilet Preparation Manufacturing	Solvents (for cleaning or degreasing)	Processing-repackaging
Soap, Cleaning Compound, and Toilet Preparation Manufacturing	Solvents (for cleaning or degreasing)	Processing-incorporation
Abbreviations: NAICS=North American Industry Classification System		

Table_Apx D-3. Commercial/Consumer Use Category Summary of 1-BP

Commercial/Consumer Product Category	Intended for Commercial and/or Consumer Uses or Both	Intended for Use in Children's Products in Related Product Category
Cleaning and Furnishing Care Products	Commercial	No
Electrical and Electronic Products	Commercial	No

Appendix E CONSUMER EXPOSURE ASSESSMENT

E.1 Consumer Exposure

Consumer exposure was evaluated utilizing a modeling approach because emissions and chemical specific personal monitoring data associated with consumer use of products containing 1-BP were not identified during data gathering and literature searches performed as part of Systematic Review. Three models were used to evaluate consumer exposures, EPA's consumer Exposure Model (CEM), EPA's Multi-Chamber Concentration and Exposure Model (MCCEM), and EPA's Indoor Environment Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model.

Numerous input parameters are required to generate exposure concentration estimates within each of the three models used. These parameters include physical-chemical properties of the chemical of concern, product information (product density, water solubility, vapor pressure, etc.), model selection and scenario inputs (pathways, CEM emission model(s), emission rate, activity pattern, product user, background concentration, etc.), product or article property inputs (frequency of use, aerosol fraction, etc.), environmental inputs (building volume, room of use, near-field volume in room of use, air exchange rates, etc.), and receptor exposure factor inputs (body weight, averaging time, exposure duration inhalation rate, etc.). Several of these input parameters have default values within the models based on the pre-defined use scenario selected. Default parameters within the models are a combination of high-end and mean or median values found within the literature or based on data taken from the Exposure Factors Handbook ([U.S. EPA, 2011](#)). Details on those parameters can be found within the respective model user guides and associated user guide appendices.

This section summarizes the input parameters used for each of the three models utilized in this evaluation. Many of these input parameters are also discussed in Section 2.3.2.3.2.

CEM Inputs:

CEM is a deterministic model. It predicts indoor air concentrations from consumer product use through a deterministic, mass-balance calculation derived from emission calculation profiles within the model. CEM is capable of providing a time-series air concentration profile for each run which are intermediate concentration values produced prior to applying pre-defined activity patterns and biological factors like breathing rate, body weight, etc. Selecting the intermediate time-series air concentration profile avoids the need to back-calculate from doses to determine the air concentration to which consumers are exposed.

The approach taken to evaluate consumer exposure is discussed in Section 2.3.2.3. In an effort to characterize a potential range of consumer inhalation exposures, EPA varied three key parameters within the CEM model while keeping all other input parameters constant. The key parameters varied were duration of use per event (minutes/use), amount of chemical in the product (weight fraction), and mass of product used per event (gram(s)/use). These key parameters were varied because they provide representative consumer behavior patterns for product use. Additionally, CEM is highly sensitive to two of these three parameters (duration of use and weight fraction).

Modeling covered all possible combinations of these three parameters with available data. This approach results in a maximum of 27 different iterations for each consumer use and are summarized in Table_Apx E-1.

Table_Apx E-1. Example Structure of CEM Cases Modeled for Each consumer Product/Article Use Scenario.

CEM Set	Scenario Characterization (Duration-Weight Fraction-Product Mass)	Duration of Product Use Per Event (min/use) [not scalable]	Weight Fraction of Chemical in Product (unitless) [scalable]	Mass of Product Used (g/use) [scalable]
Set 1 (Low Intensity Use)	Case 1: Low-Low-Low	Low	Low	Low
	Case 2: Low-Low-Mid			Mid
	Case 3: Low-Low-High			High
	Case 4: Low-Mid-Low		Mid	Low
	Case 5: Low-Mid-Mid			Mid
	Case 6: Low-Mid-High			High
	Case 7: Low-High-Low		High	Low
	Case 8: Low-High-Mid			Mid
	Case 9: Low-High-High			High
Set 2 (Moderate Intensity Use)	Case 10: Mid-Low-Low	Mid	Low	Low
	Case 11: Mid-Low-Mid			Mid
	Case 12: Mid-Low-High			High
	Case 13: Mid-Mid-Low		Mid	Low
	Case 14: Mid-Mid-Mid			Mid
	Case 15: Mid-Mid-High			High
	Case 16: Mid-High-Low		High	Low
	Case 17: Mid-High-Mid			Mid
	Case 18: Mid-High-High			High
Set 3 (High Intensity Use)	Case 19: High-Low-Low	High	Low	Low
	Case 20: High-Low-Mid			Mid
	Case 21: High-Low-High			High
	Case 22: High-Mid-Low		Mid	Low
	Case 23: High-Mid-Mid			Mid
	Case 24: High-Mid-High			High
	Case 25: High-High-Low		High	Low
	Case 26: High-High-Mid			Mid
	Case 27: High-High-High			High

A summary of parameters used for estimation of indoor air concentrations of 1-BP that were constant across all scenarios modeled with CEM are summarized in Table_Apx E-2.

Table Apx E-2. Non-varied CEM Modeling Parameters Across All Scenarios Modeled

Parameter	Units	Value / Description
CHEMICAL PROPERTY INPUTS		
Chemical of Interest	n/a	1-Bromopropane
CAS Number	n/a	106-94-5
Vapor Pressure	torr	146.26
Molecular Weight	g/mol	122.99
Chemical Saturation Concentration in Air	mg/m ³	966,000 (CEM Estimate)
MODEL SELECTION / SCENARIO INPUTS		
Pathways Selected	n/a	Inhalation (except coin cleaner and AC Auto Flush) and Dermal
Emission Model	n/a	E3: Product Sprayed
Inhalation Model	n/a	P_INH2: Near-Field Used in Zone 1
Emission Rate	n/a	Let CEM Estimate Emission Rate
Dermal Model	n/a	P-DER1b: Permeability
Product User (s)	n/a	Adult (≥21 yrs) and Youth (Age 11-20 yrs)
Activity Pattern		Stay-At-Home
Product Use Start Time	n/a	9:00 AM
Background Concentration	mg/m ³	0
PRODUCT/ARTICLE PROPERTY INPUTS		
Frequency of Use	--	Acute: 1 events/day (CEM default)
Aerosol (Overspray) Fraction	unitless	0.06 (CEM default)
Fraction Product Ingested	n/a	0
Skin Permeability Coefficient	cm/hr	0.00905 (2017)
Product Dilution Factor	unitless	1 (i.e., no dilution)
ENVIRONMENT INPUTS		
Building Volume (Residence)	m ³	492 (CEM default)
Near-Field Volume in Room of Use	m ³	1 (CEM default)
Air Exchange Rate, Zone 1 (Residence)	hr ⁻¹	0.45 (CEM default)
Air Exchange Rate, Zone 2 (Residence)	hr ⁻¹	0.45 (CEM default)
Air Exchange Rate, Near-Field Boundary	hr ⁻¹	402 (CEM default)
RECEPTOR EXPOSURE FACTOR INPUTS		
Averaging Time (parameter evaluated at 1 and scaled outside CEM)	--	Acute: 1 day
Exposure Duration (parameter evaluated at 1 and scaled outside CEM)	--	Acute: 1 day
Inhalation Rate During Use	m ³ /hr	CEM default, refer to CEM User Guide
Inhalation Rate After Use	m ³ /hr	CEM default, refer to CEM User Guide

A summary of parameters used for estimation of indoor air concentrations of 1-BP that were scenario specific when modeled with CEM are summarized in Table_Apx E-3. These parameters may vary across scenarios, but were kept constant within a given scenario.

Table Apx E-3. Scenario Specific CEM Modeling Parameters

Scenario	MODEL SELECTION / SCENARIO INPUTS			PRODUCT/ARTICLE INPUTS	ENVIRONMENT INPUTS		RECEPTOR EXPOSURE FACTOR INPUTS
	CEM Product/Article (Emission Model)	Near-Field Option	Product/Article Environment of Use ¹	Product Density (g/cm ³) ³	Use Environment Volume (m ³) ²	Interzone Ventilation Rate (m ³ /hr) ²	Body Part Impacted ⁴
1. Adhesive Accelerant	Generic Product (E3)	Yes	Utility Room	1.35	20	107.01	
2. General Spray	All Purpose Spray Cleaner (E3)	Yes	Utility Room	1.32	20	107.01	
3. Spot Cleaner-Stain Remover	Generic Product (E3)	Yes	Utility Room	1.32	20	107.01	
4. Mold Cleaning-Release Product	Generic Product (E3)	Yes	Utility Room	1.3	20	107.01	
5. General Cleaner-Degreaser	Degreasers (E3)	Yes	Garage	1.3	90	109	10% of Hand
6. Degreasers-Electronic	Degreasers (E3)	Yes	Living Room	1.32	50	109	
7. Coin-Cleaner	n/a	n/a	n/a	1.32	n/a	n/a	10% of Hand
8. AC Auto Flush	n/a	n/a	n/a	1.21	n/a	n/a	Face Hands and Arms
1. The environment of use (or room of use) was selected based on results from the Westat consumer product survey for Scenarios 1-6. Refer to Table 1 which identifies the consumer product category selected from the Westat survey as a surrogate for each 1-BP exposure scenario. If the survey indicated the primary use environment as "Other Inside Room", the utility room was selected as a surrogate based on professional judgment. Additionally, "outdoor" use environments were modeled using the garage as a conservative measure. For Scenarios 7-8, the frequency of use was assumed to be the low CEM default because a surrogate Westat scenario was not available. The frequency of use parameter was run at 1 in CEM and scaled outside CEM. 2. The volume of the room of use and the interzone ventilation rate are model defaults based on the selected room of use. 3. Product densities were obtained from SDS identified in Systematic Review. If not available, defaults from the CEM User Guide were used. 4. The body part impacted is based off the CEM defaults for similar scenarios and/or professional judgement. Refer to the CEM User Guide for the Surface Area to Body Weight Ratios for each receptor based on the impacted body part.							

A summary of parameters used for estimation of indoor air concentrations of 1-BP that were scenario specific when modeled with CEM and varied within each consumer use are summarized in Table_Apx E-4. These parameters are also provided in Table 2-43 but copied here so input parameters are readily accessible in this Appendix. These parameters represent the three parameters varied to capture a broad spectrum of consumer use patterns.

Table_Apx E-4. Scenario Specific CEM Modeling Parameters Varied by Consumer Use

Consumer Use	Duration of Use			Mass of Product Used			Amount of Chemical In Product		
	(minutes/use)			(gram(s)/use)			(weight fraction)		
	10 th	50 th	95 th	10 th	50 th	95 th	Low	Mean	High
Adhesive Accelerant	0.5	4.25	60	1.20	9.98	172.45		0.99 (single)	
General Spray Cleaner	2	15	120	21.86	126.86	1249.04		0.94 (single)	
Spot Cleaner/Stain Remover	0.5	5	30	9.76	51.91	434.43	0.276	0.58	0.922
Mold Cleaning/Release	0.5	2	30	3.84	21.14	192.21	0.32	0.6	0.915
General Cleaner-Degreaser	5	15	120	111.86	445.92	1845.17	0.109	0.505	0.9505
Degreaser-Electronic	0.5	2	30	1.56	19.52	292.74	0.496	0.72	0.972

MCCEM Inputs:

MCCEM was used to model inhalation exposure for two of the nine consumer scenarios evaluated (coin cleaner/scissors cleaner and Automobile AC Flush). The approach used for these two consumer use scenarios was to evaluate exposure due to evaporation from a pool of material. Exposure from this approach is dependent on surface area of the pool rather than chemical mass (mass of product used and percent of chemical within product).

Inputs needed for MCCEM include: (1) the emission rate; (2) product amount and duration of use; (3) house and zone volumes; and (3) airflows to and from each zone. These inputs, and associated inputs needed to calculate these inputs are discussed in Section 2.3.2.3.2 but summarized in Table_Apx E-5.

Table_Apx E-5. Summary of Input Parameters Used in MCCEM for Estimating Indoor Air Concentrations of 1-BP

Parameter	Value	Units	
Chemical of Interest	1-Bromopropane	N/A	
CAS Number	106-94-5	N/A	
Vapor Pressure	146.26	torr	
Molecular Weight	122.99	grams/mole	
Saturation Concentration in Air	966,000	mg/m ³	
Coin/Scissors Cleaner			
Container Diameter (Bowl)	4	inches	
Characteristic Length (Bowl)	9	cm	
Source Area (Bowl)	81	cm ²	
Product Density	1.32	g/cm ³	
Mass transfer coefficient	6.01	m/hr	Estimated
Emission Rate	47,026	mg/hr	

Quantity Available	5-8	ounces	
Product Mass Used	319	grams	
High Intensity Use	60	minutes	
Moderate Intensity Use	30	minutes	
Low Intensity Use	15	minutes	
Automobile AC Flush			
Conatiner Diameter (Bucket)	12	inches	
Characteristic Length (Bucket)	27	cm	
Source Area (Bucket)	730	cm ³	
Product Density (AC Flush)	1.21	g/cm ³	
Mass Transfer Coefficient (AC Flush)	3.47	m/hr	Estimated
Emission Rate (AC Flush)	244,697	mg/hr	
Quantity Available	6-16	ounces	
Product Mass Used	639	grams	
High Intensity Use	30	minutes	
Moderate Intensity Use	15	minutes	
Low Intensity Use	5	minutes	

Zone Definitions, Volumes, and Airflow Rates for both the coin/scissors cleaner and Automobile AC Flush are discussed in Section 2.3.2.3.2 and summarized in Table_Apx E-6 through Table_Apx E-9.

Table_Apx E-6. Zone Descriptions and Volumes for Coin/Scissors Cleaner Scenario

Zone	Description	Volum (m ³)	Total Flow In (m ³ /hr)	Total Flow Out (m ³ /hr)
0	Outside	N/A	N/A	N/A
1	Near Field	1	100	100
2	Far Field	19	216.1	216.1
3	Rest of House	426	298.8	298.8

Table_Apx E-7. Inter-Zonal Air Flow Rates (m³/hr) for Coin/Scissors Cleaner Scenario

Air Flow From Zone	Air Flow To Zone			
	Zone 0	Zone 1	Zone 2	Zone 3
Zone 0	N/A	0	9	191.7
Zone 1	0	N/A	100	0
Zone 2	9	100	N/A	107.1
Zone 3	191.7	0	107.1	N/A

Table_Apx E-8. Zone Descriptions and Volumes for Automobile AC Flush Scenario

Zone	Description	Volum (m ³)	Total Flow In (m ³ /hr)	Total Flow Out (m ³ /hr)
0	Outside	N/A	N/A	N/A
1	Garage Near Field	4	507	507
2	Garage Far Field	114	909	909
3	Rest of House	446	308	308

Table Apx E-9. Inter-Zonal Air Flow Rates (m3/hr) for Automobile AC Flush Scenario

Air Flow From Zone	Air Flow To Zone			
	Zone 0	Zone 1	Zone 2	Zone 3
Zone 0	N/A	0	295	201
Zone 1	0	N/A	507	0
Zone 2	295	507	N/A	107
Zone 3	201	0	107	N/A

Appendix F ENVIRONMENTAL HAZARDS

F.1 Systematic Review

As part of the systematic review process, EPA identified and reviewed one ecotoxicity study for 1-bromopropane according to the data quality evaluation criteria found in [The Application of Systematic Review in TSCA Risk Evaluations](#) (U.S. EPA, 2018a). This (acute fish) study was determined to be high quality following data evaluation (Geiger et al., 1988). The data quality evaluation for this fish ecotoxicity study can be found in the *Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies* (EPA, 2019l). The data quality evaluation results, showing only acceptable studies, for 1-BP environmental hazard are presented in Table_Apx F-1. In addition, five data summaries were identified in the European Chemicals Agency (ECHA) Database. EPA was unable to obtain the full study reports that accompany the studies summarized in the ECHA database, so these study summaries were not evaluated for data quality. As a result, the data presented in these summaries were only considered potentially relevant data/information sources and were used qualitatively to characterize risks of 1-BP. Copies of these study summaries are available in the docket (EPA-HQ-OPPT-2016-0741-0047), and the results are presented and discussed below (EPA, 2019d).

Table_Apx F-1. Aquatic toxicity studies that were evaluated for 1-BP

Test Species	Test System	Duration	End-point	Conc. (mg/L)	Test Analysis	Effect	Reference	Data Quality Evaluation Result*
<i>Fish</i>								
Fathead minnow (<i>Pimphales promelas</i>)	Freshwater, flow-through	96 hours	LC ₅₀	67.3	Measured	Mortality	(Geiger et al., 1988)	High

* = This table shows the results of the data quality evaluation according to criteria found in *The Application of Systematic Review in TSCA Risk Evaluations*. A data quality evaluation was conducted on Geiger (1988), but not on the data summarized in the ECHA database due to the inability to obtain the full study reports. Consequently, the ECHA summary reports were not evaluated or presented in this table.

F.2 Hazard Identification- Aquatic

During problem formulation, EPA identified aquatic (aqueous-only) data reported in the scientific literature and in the ECHA database to assess the aquatic hazard of 1-BP (U.S. EPA, 2018c). These endpoints are summarized in Table_Apx F-2. Based on the available data that were identified and evaluated for study quality, the 96-hour LC₅₀ value for fish following acute exposure to 1-BP is 67.3 mg/L (Geiger et al., 1988).

The ECHA database presented endpoints for fish, aquatic invertebrates, algae and microorganisms (sludge) following acute exposure to 1-BP. The LC₅₀ for fish following acute exposure to 1-BP is 24.3 mg/L (ECHA, 2017) (EPA, 2019d). The acute aquatic invertebrate EC₅₀ for 1-BP was 99.3 mg/L (ECHA, 2017) (EPA, 2019d). The EC₅₀ for the algae toxicity test was 52.4 mg/L (biomass) and 72.3 mg/L (growth rate) based on summary data from ECHA (2017) (EPA, 2019d). The NOEC for the algae toxicity test was 12.4 mg/L (ECHA, 2017). The EC₅₀ and NOEC for microorganisms toxicity study for a 5-minute time period was 270 mg/L and 100 mg/L (ECHA, 2017), respectively.

Table Apx F-2. Ecological Hazard Characterization of 1-BP

Duration	Test organism	Endpoint	Hazard value ¹	Units	Effect Endpoint	Citation
Acute	Fish	LC ₅₀	24.3	mg/L	Mortality	(ECHA, 2017) (EPA, 2019d)
			67.3	mg/L		(Geiger et al., 1988)
	Aquatic invertebrates	EC ₅₀	99.3	mg/L	Immobilization	(ECHA, 2017) (EPA, 2019d)
	Algae	EC ₅₀	52.4 / 72.3	mg/L	Biomass / growth rate	(ECHA, 2017) (EPA, 2019d)
	Algae	EC ₅₀	>54.98 ²	mg/L	Growth rate	(ECHA, 2017) (EPA, 2019d)
	Microorganism	EC ₅₀	270	mg/L	Respiration	(ECHA, 2017) (EPA, 2019d)
	Acute COC		4.86	mg/L		(ECHA, 2017) (EPA, 2019d)
			13.46	mg/L		(Geiger et al., 1988)
Chronic	Fish	ChV	2.43	mg/L	Acute to chronic ratio of 10	(ECHA, 2017) (EPA, 2019d)
	Fish	ChV	6.73	mg/L	Acute to chronic ratio of 10	(Geiger et al., 1988)
	Aquatic invertebrates	ChV	9.93	mg/L	Acute to chronic ratio of 10	(ECHA, 2017) (EPA, 2019d)
	Algae	NOEC	12.4	mg/L	Growth rate	(ECHA, 2017) (EPA, 2019d)
		NOEC	0.93 ²³	mg/L		
	Microorganism	NOEC	100	mg/L	Respiration	(ECHA, 2017) (EPA, 2019d)
	Chronic COC		0.24	mg/L		(ECHA, 2017) (EPA, 2019d)
			0.67	mg/L		(Geiger et al., 1988)

¹ Values in the tables are presented as reported by the study authors. Copies of these study summaries are available in the docket ([EPA-HQ-OPPT-2016-0741-0047](#))

² These algae toxicity values were identified in ECHA following the publication of the Problem Formulation. This algae study was not evaluated for study quality, but the ECHA summary report for this endpoint indicated that study quality was questionable due to “incomplete reporting or methodological deficiencies.”

³ Algae data were not used to calculate the hazard aquatic organisms from chronic exposure, because durations normally considered acute for other species (e.g. 48, 72 hours) can encompass several generations of algae.

F.3 Concentrations of Concern (COC)

The acute and chronic concentrations of concern (COCs) for aquatic species were calculated based on the results of the high confidence study (Geiger et al., 1988). For risk characterization purposes, COCs were also calculated with summarized environmental hazard data for 1-BP in the ECHA (European Chemicals Agency) Database. The calculation of the environmental COCs are based on a weight of evidence approach as well as EPA methods (Suter, 2016) (U.S. EPA, 2012e) (U.S. EPA, 2013b). For a particular environment (e.g., aquatic environment), the COCs are based on the most sensitive species or the species with the lowest toxicity value reported in that environment.

After selecting the lowest relevant toxicity values, an uncertainty factor (UF; also referred to as an assessment factor (AF)) is applied according to EPA methods (Suter, 2016) (U.S. EPA, 2012e)

([U.S. EPA, 2013b](#)). The application of AFs provides a lower bound effect level that would likely encompass more sensitive species not specifically represented by the available experimental data. AFs also account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. These assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group. The assessment factors are often standardized in risk assessments conducted under TSCA, since the data available for most industrial chemicals are limited. The acute COC for the aquatic plant endpoint is calculated based on the lowest value in the dataset divided by an assessment factor (AF) of 4. For fish and aquatic invertebrates (e.g., daphnia), the acute COC values are divided by an AF of 5. For chronic COCs, an AF of 10 is used.

F.4 Hazard Estimations for Acute Exposure Durations

As described above, the 96-hour LC₅₀ value for 1-BP that was reported in the high confidence study is 67.3 mg/L ([Geiger et al., 1988](#)). This high confidence value was then divided by the AF of 5 for fish. The lowest value for the 96-hour fish toxicity LC₅₀ (67.3 mg/L) / AF of 5 = 13.64 mg/L or 13,640 µg/L or ppb.

To provide additional characterization of potential hazards to aquatic organisms, the lowest acute toxicity value for aquatic organisms (i.e., most sensitive species) for 1-BP was also used to calculate a COC. This was calculated using a 96-hour fish toxicity study presented in ECHA, where the LC₅₀ is 24.3 mg/L ([ECHA, 2017](#)) ([EPA, 2019d](#)). This toxicity value was used in the screening-level analysis presented in the Problem Formulation ([U.S. EPA, 2018c](#)). The lowest value for the 96-hour fish toxicity LC₅₀ (24.3 mg/L) / AF of 5 = 4.86 mg/L or 4,860 µg/L or ppb. The acute COC of 4,860 µg/L, derived from experimental fish endpoint, is used as the conservative (screening-level) hazard level in this risk evaluation for 1-BP.

F.5 Hazard Estimations for Chronic Exposure Durations

Since there are no long-term chronic studies for 1-BP, the fish 96-hr LC₅₀ of 67.3 mg/L (the value in the dataset derived from the high confidence toxicity study; is divided by an acute-to-chronic ratio (ACR) of 10 to obtain a chronic value (ChV) for fish ([Geiger et al., 1988](#)). The fish ChV is then divided by an AF (10) to obtain a chronic COC. The highest confidence value for the fish 96-hr LC₅₀ (67.3 mg/L) / 10 (ACR) / AF of 10 = 0.673 mg/L or 673 µg/L or ppb.

To provide additional characterization of potential hazards to aquatic organisms, the fish 96-hr LC₅₀ of 24.3 mg/L (the lowest acute value in the dataset; is also use divided by an acute-to-chronic ratio (ACR) of 10 to obtain a chronic value (ChV) for fish ([EPA, 2019d](#)) ([ECHA, 2017](#)). The fish ChV is then divided by an AF (10) to obtain a chronic COC. This toxicity value was used in the screening-level analysis presented in the Problem Formulation ([U.S. EPA, 2018c](#)). The lowest value for the fish 96-hr LC₅₀ (24.3 mg/L) / 10 (ACR) / AF of 10 = 0.243 mg/L or 243 µg/L or ppb. The chronic COC of 243 µg/L, derived from experimental fish endpoint, is used as the conservative (screening-level) hazard level in this risk evaluation for 1-BP.

F.6 Summary of Environmental Hazard

The acute (13,460 ppb) and chronic COCs (670 ppb) are based on environmental toxicity endpoint values (e.g., LC₅₀) from the highest confidence study that was evaluated according to the systematic review criteria ([Geiger et al., 1988](#)). This indicates that 1-BP presents a moderate hazard to environmental receptors. This conclusion is supported by data summarized in the

ECHA database that represent the lowest bound and therefore most conservative hazard value of all reasonably available 1-BP data. These COC values are (4,860 ppb) and chronic COC (243 ppb) based on environmental toxicity endpoint values (e.g., LC₅₀) ([ECHA, 2017](#)) ([ECHA, 2017](#)).

Appendix G ESTIMATES OF SURFACE WATER CONCENTRATION

SCENARIO 1. REPORTED RELEASES TO TRI

Estimating Surface Water Concentrations

Surface water concentrations were estimated for multiple scenarios using E-FAST which can be used to estimate site-specific surface water concentrations based on estimated loadings of 1-bromopropane into receiving water bodies. For TRI, the reported releases are based on monitoring, emission factors, mass balance and/or other engineering calculations. These reported annual loading amounts (lbs/year) were first converted to release inputs required by E-FAST (kg/day) by converting from lbs to kgs and dividing by the number of release days for a given scenario.

E-FAST incorporates stream dilution at the point of release using stream flow distribution data contained within the model. The stream flow data have not been updated recently and may differ from current values obtained from NHD or USGS gages. Site-specific stream flow data are applied using a National Pollutant Discharge Elimination System (NPDES) code. If a specific discharger's NPDES code could not be identified within the E-FAST database, a surrogate site or generic Standard Industrial Classification (SIC) code was applied (i.e., Industrial POTW).

E-FAST 2014 can incorporate wastewater treatment removal efficiencies. Wastewater treatment removal is assumed to be 0% for this exercise, as reported direct loadings/releases are assumed to account for any pre-release treatment. Because the days of release and/or operation are not reported in these sources, E-FAST is run assuming hypothetical release-day scenarios. Refer to the E-FAST 2014 Documentation Manual for equations used in the model to estimate surface water concentrations ([U.S. EPA, 2014b](#)).

The modeled surface water concentrations presented below in Table_Apx G-1 are associated with a low flow – 7Q10, which is an annual minimum seven-day average stream flow over a ten-year recurrence interval. The 10th percentile 7Q10 stream flow is used to derive the presented surface water concentrations. No post-release degradation or removal mechanisms (e.g., hydrolysis, aerobic degradation, photolysis, volatilization) are applied in the calculation of the modeled surface water concentrations.

Modeled Surface Water Concentrations

It is assumed that these modeled surface water concentrations are higher than those that would be present from non-point sources based on the conservative nature of the estimation approaches including the following: surface water concentrations would be expected to decrease downstream and this modeling analysis does not account for downstream transport and fate processes; non-zero wastewater removal rates would be applied for any indirect releases that pass through a treatment facility before release; and assuming a low-end number of release days (i.e., 1 day per year) assumes the total annual loading estimate occurs over 1 day.

For 1-BP, there is one facility reporting water releases from the 2016 TRI reporting period, the Flint Hills Resources facility. This facility, located in Corpus Christi, TX, has reported 1 lb of 1-BP released to the Neuces River with 100% from stormwater on an annual basis. They also reported 4 lbs of 1-BP released to an unnamed water body with 83% from stormwater on an annual basis.

These are direct releases to water and thus are presumed to be untreated at a POTW. A quick calculation of site-specific surface water concentration was performed using E-FAST assuming that the total release occurs over 1 day, 20 days or 100 days. Two receiving waters were used:

- Neuces River – the NPDES permit for Corpus Christi City POTW TX0047082 was used as a surrogate for this direct release. 0% removal was assumed since this is listed as a direct release.
- Unnamed Waterbody – the NPDES permit for the reporting facility was available in EFAST with the receiving water body listed as the Corpus Christi Bay. Acute dilution factors were used to estimate the surface water concentration, again with 0% removal.

The resulting estimated surface water concentrations presented below in Table_Apx G-1 are based on the reported releases and locations and are well below the acute and chronic concentrations of concern even if the annual release amount occurs over 1 day. The maximum estimated surface water concentration is 78 µg/L for this scenario. The acute concentration of concern is 4860 ppb and the chronic concentration of concern is 243 ppb.

Table_Apx G-1. Estimated Surface Concentrations from Water Releases Reported to TRI

SCENARIO 1: REPORTED RELEASES TO TRI

Acute COC = 4860 ppb

Chronic COC = 243 ppb

From TRI reporting: 1 reporting facility: Flint Hills Resources Corpus Christi LLC – West Plant

1 lb to Neuces River (100% from stormwater);

4 lbs to ‘unnamed water body’ (83% from stormwater)

Wastewater Treatment Removal= 0%; direct release

(Note: NPDES for Corpus Christi City POTW used as surrogate for Neuces River. Flint Hills Resources facility modeled directly)

	Neuces River (Corpus Christi City - TX0047082)				Flint Hills Resources - Corpus Christi Bay, (TX0006289)		
	7Q10 SWC µg/L				SWC* µg/L		
Annual Release Amount lb (kg)	1 day/yr	20 days/yr	100 days/yr		1 day/yr	20 days/yr	100 days/yr
1 (0.45)	7.86	0.39	0.08		19.4	0.97	0.19
4 (1.81)	31.60	1.58	0.31		77.90	3.90	0.77
					*Acute dilution factor for bay		

Appendix H TOXICOKINETICS

The studies summarized in this section were identified for consideration in the human health hazard assessment, as described in Section 3.2.3.

Empirical evidence from rodent toxicity studies and from occupational exposure studies indicate that 1-BP is absorbed by both inhalation and dermal routes. Additional evidence of the systemic uptake of 1-BP via the oral route has been reported ([Lee et al., 2007](#)). Absorption is rapid by all routes, and a significant portion of the absorbed dose (39% to 48% in mice and 40% to 70% in rats) is eliminated in exhaled breath as unspecified volatile organic compounds ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). Garner and Yu ([2014](#)) provided supplemental evidence on the toxicokinetics of BP in rodents. Rodents exposed to 1-BP via intravenous injection or inhalation exhibited rapid systemic clearance and elimination that decreased as the dose increased. Previous studies showed that the remaining absorbed dose is eliminated, unchanged, in urine (humans) or as metabolites in the urine and exhaled breath of all species studied ([Garner et al., 2006](#); [Kawai et al., 2001](#)). Available toxicokinetic data indicate that glutathione (GSH) conjugation and oxidation via cytochrome P450 (CYP450) significantly contribute to the metabolism of 1-BP ([Garner and Yu, 2014](#); [Garner et al., 2006](#)).

H.1 Absorption

The detection of carbon-containing metabolites and elevated bromide ion concentrations in urine samples of workers exposed to 1-BP by inhalation and dermal contact provides qualitative evidence that 1-BP is absorbed by the respiratory tract and the skin in humans ([Hanley et al., 2010, 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006a](#)). In addition, reports of neurological and other effects in occupationally exposed subjects provide indirect evidence of absorption of 1-BP ([Samukawa et al., 2012](#); [CDC, 2008](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [NIOSH, 2003a](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)).

Dermal absorption characteristics estimated in human epidermal membranes mounted on static diffusion cells included steady-state fluxes averaging 625–960 $\mu\text{g cm}^{-2} \text{hour}^{-1}$ with pure 1-BP and 441–722 $\mu\text{g cm}^{-2} \text{hour}^{-1}$ with a commercial dry cleaning solvent, an average dermal penetration of about 2% from an applied dose of 13.5 mg/cm² under non-occluded conditions, and a dermal permeability coefficient for 1-BP in water of 0.257 cm/hour ([Frasch et al., 2011](#)).

Animal studies provide qualitative evidence of absorption by the gastrointestinal and respiratory tracts ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). ¹³C-labeled metabolites were detected in urine collected from rats and mice exposed by inhalation to 800 ppm [1,2,3-¹³C]-1-BP for 6 hours ([Garner et al., 2006](#)). A number of mercapturic acid derivative metabolites were detected in pooled urine samples collected from rats given oral doses of 200 mg 1-BP/kg/day in arachis oil for five days ([Jones and Walsh, 1979](#)).

No other human or animal studies were located that determined the rate or extent of 1-BP absorption following inhalation, oral, or dermal exposure.

H.2 Distribution

Metabolic disposition studies in rats and mice given single intravenous injections of [1,2,3-¹³C]-1-BP indicate that 1-BP is not expected to accumulate in tissues ([Garner et al., 2006](#)). Following intravenous injection of [1-¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity

remaining in the carcass 48 hours after dose administration accounted for about 6, 6, and 2% of the administered dose in rats, and 4, 2, and 4% in mice ([Garner et al., 2006](#)). In these studies, most of the administered radioactivity was exhaled (as the parent material or CO₂) or excreted as metabolites in urine.

H.3 Metabolism

The metabolism of 1-BP in mammals involves: (1) conjugation, principally with glutathione, leading to the release of bromide ions and formation of mercapturic acid derivatives and (2) cytochrome P-450 mediated oxidation leading to formation of metabolites with hydroxyl, carbonyl, and sulfoxide groups, as well as CO₂. These concepts are based on studies of urinary metabolites in workers exposed to 1-BP ([Hanley et al., 2010, 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006a](#)), *in vivo* metabolic disposition studies in rats and mice ([Garner et al., 2007](#); [Garner et al., 2006](#); [Ishida et al., 2002](#); [Jones and Walsh, 1979](#); [Barnsley et al., 1966](#)), and *in vitro* metabolism studies with rat liver preparations ([Kaneko et al., 1997](#); [Tachizawa et al., 1982](#); [Jones and Walsh, 1979](#)).

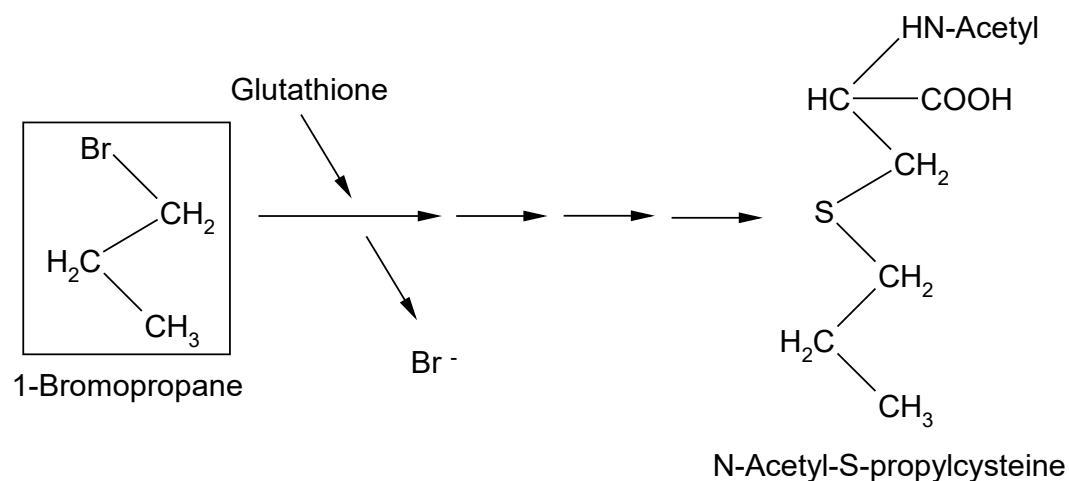
N-Acetyl-S-propylcysteine has been identified in urine samples from workers in a 1-BP manufacturing plant ([Valentine et al., 2007](#)), in foam fabricating plants using spray adhesives containing 1-BP ([Hanley et al., 2010, 2009](#); [Hanley et al., 2006a](#)), and in degreasing operations in plants using 1-BP as a cleaning solvent in the manufacture of aerospace components, hydraulic equipment, optical glass, and printed electronic circuit assemblies ([Hanley et al., 2009](#)). Other urinary metabolites identified in 1-BP workers are the bromide ion ([Hanley et al., 2010](#)) and three oxygenated metabolites present at lower urinary concentrations than N-acetyl-S-propylcysteine: N-acetyl-S-propylcysteine-S-oxide (also known as N-acetyl-3-(propylsulfinyl) alanine), N-acetyl-S-(2-carboxyethyl) cysteine, and N-acetyl-S-(3-hydroxy-propyl) cysteine ([Cheever et al., 2009](#); [Hanley et al., 2009](#)). The correlations between time weighted average workplace air concentrations of 1-BP and urinary levels of bromide and N-acetyl-S-propylcysteine ([Hanley et al., 2010, 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006a](#)) support the hypothesis that conjugation with glutathione is an important pathway in humans (see Figure 3-3). The detection of oxygenated metabolites in urine samples indicates that oxidation pathways also exist in humans (see Figure 3-3 for structures of identified oxygenated metabolites).

Results from metabolic disposition studies in rats and mice illustrate that the metabolism of 1-BP in mammals is complex, involving initial competing conjugation or oxidation steps, followed by subsequent conjugation, oxidation, or rearrangement steps. Figure 3-3 presents proposed metabolic pathways based on results from studies of F-344 rats and B6C3F1 mice exposed to [1-¹⁴C]-1-BP by intravenous injection or [1,2,3-¹³C]-1-BP by inhalation or intravenous injection ([Garner et al., 2006](#)).

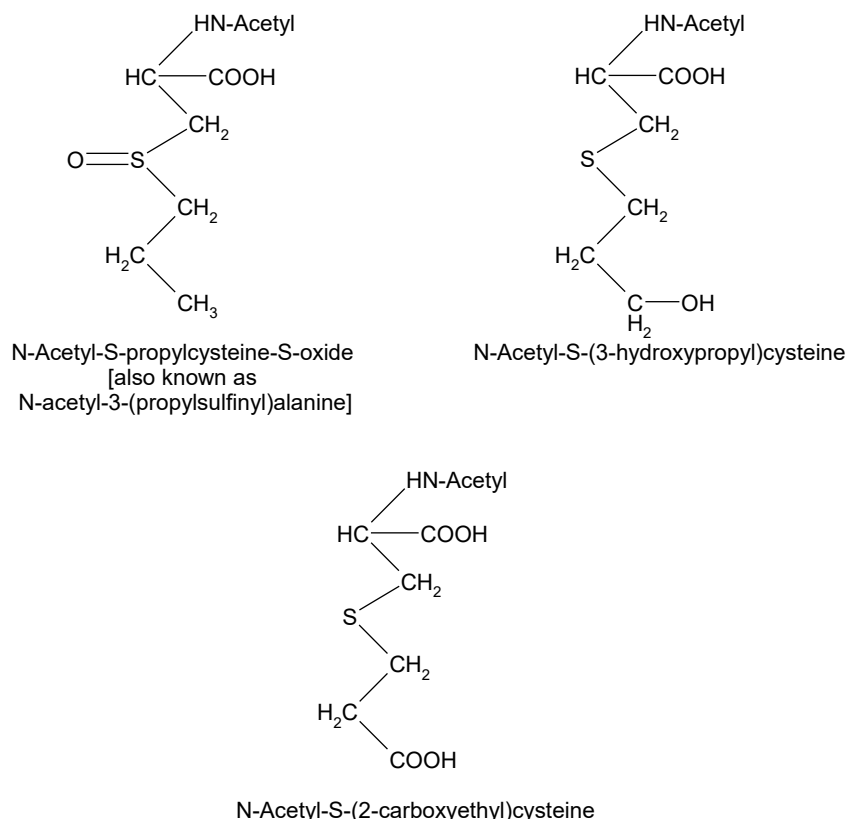
The metabolic scheme shows an oxidation path to CO₂ formation which involves cytochrome P450 (CYP) oxidation steps to 1-bromo-2-propanol and bromoacetone. This path is proposed based on several findings:

1. Following intravenous injection of ¹⁴C-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity in CO₂ exhaled within 48 hours accounted for approximately 28, 31, and 10% of the administered dose in rats, and 22, 26, and 19% in mice ([Garner et al., 2006](#)). (These data also indicate that oxidative metabolism of 1-BP in rats is more dependent on dose than oxidative metabolism in mice; the decrease in percentage dose exhaled as CO₂ at the highest dose is greater in rats than mice.)

2. Pretreatment of rats with 1-aminobenzotriazole (ABT) before administration of a single intravenous dose of ~20 mg/kg ^{14}C -1-BP or inhalation exposure to 800 ppm ^{13}C -1-BP for 6 hours caused decreased exhalation of radioactivity as CO_2 and decreased formation of oxidative urinary metabolites ([Garner et al., 2006](#)). ABT is an inhibitor of a number of CYP enzymes ([Emoto et al., 2003](#)).
3. Urinary metabolites derived from 1-bromo-2-propanol accounted for over half of all carbon-containing urinary metabolites identified in rats and mice exposed by inhalation or intravenous injection of ^{13}C -1-BP, and no 1-bromo-2-propanol-derived metabolites were found in urine of ABT-pretreated rats exposed to ^{13}C -1-BP ([Garner et al., 2006](#)). 1-Bromo-2-propanol and bromoacetone themselves were not detected in urine of 1-BP-exposed rodents.



Figure_Apx H-1 Formation of N-Acetyl-S-Propylcysteine from 1-Bromopropane Via Conjugation with Reduced Glutathione (GSH)



Figure_Apx H-2 Mercapturic Acid Metabolites with a Sulfoxide Group or a Hydroxyl or Carbonyl Group on the Propyl Residue Identified in Urine Samples of 1-Bromopropane-Exposed Workers

Sources: ([Cheever et al., 2009](#); [Hanley et al., 2009](#))

Results from metabolic disposition studies indicate that 1-BP is eliminated from the body by exhalation of the parent material and metabolically derived CO₂ and by urinary excretion of metabolites ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). Following intraperitoneal injection of 200 mg/kg of [1-¹⁴C]-1-BP in rats, about 60 and 1.4% of the administered dose was recovered as the parent material and CO₂ respectively, in air expired within 6 hours; about 15% of the administered dose was recovered in urine collected over a 48- hour period ([Jones and Walsh, 1979](#)). Following intravenous injection of [1-¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, the radioactivity in CO₂ exhaled within 48 hours accounted for approximately 28, 31, and 10% of the administered dose in rats, and 22, 26, and 19% in mice ([Garner et al., 2006](#)). Radioactivity in the exhaled parent material accounted for about 25, 32, and 71% of the administered dose in rats, and 45, 39, and 48% in mice ([Garner et al., 2006](#)). Radioactivity in urine collected for 48 hours accounted for about 17, 19, and 13% of the administered dose in rats, and 23, 19, and 14% in mice ([Garner et al., 2006](#)). Radioactivity in feces accounted for <4% of administered doses, regardless of dose level, in both species ([Garner et al., 2006](#)).

Animal studies also show rapid elimination of 1-BP from the body ([Garner and Yu, 2014](#); [Garner et al., 2006](#); [Ishidao et al., 2002](#)). Following intravenous injection of [1-¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity remaining in the carcass 48 hours after dose administration

accounted for about 6, 6, and 2% of the administered dose in rats, and 4, 2, and 4% in mice ([Garner et al., 2006](#)). ([Garner et al., 2006](#)) proposed that radioactivity remaining in the carcass could represent covalently bound residues from interactions with reactive metabolites or incorporation of ^{14}C into cellular macromolecules. Following intravenous injection of 5 or 20 mg 1-BP/kg doses into rats, the mean half-life for 1-BP elimination from blood was 0.39 or 0.85 hours, respectively ([Garner and Yu, 2014](#)). In gas uptake studies with male and female rats, 1-BP elimination was rapid, with a decrease in the elimination half-life observed with increasing air concentrations of 1-BP ([Garner and Yu, 2014](#)). Pretreatment of female rats with ABT, an inhibitor of CYP metabolism (intraperitoneal injection of 50 mg 1-BP/kg 4 hours prior to gas uptake measurements) or buthionine sulfoxime, an inhibitor of glutathione synthesis (1,000 mg 1-BP/kg/day orally for 3 days before gas uptake), resulted in longer elimination half-times: 9.6 hours with ABT and 4.1 hours with D,L-buthionine(S,R)-sulfoximine (BSO), as compared with 2.0 hours in females not pretreated with ABT or BSO prior to 1-BP exposure at 800 ppm in the gas uptake chamber ([Garner and Yu, 2014](#)). These results suggest that oxidative metabolism and glutathione conjugation play an important role in the elimination of 1-BP. Blood levels decreased rapidly (to detection limits) < 1 hour after the cessation of exposure in Wistar rats exposed to 700 or 1,500 ppm 1-BP 6 hours/day for ≥ 3 weeks ([Ishida et al., 2002](#)). Clearance of bromide ions from blood and urine showed slower elimination kinetics; the elimination half-life for bromide was 4.7-15 days in blood and 5.0-7.5 days in urine ([Ishida et al., 2002](#)).

Based on urinary metabolites identified with nuclear magnetic resonance spectroscopy, liquid chromatography-tandem mass spectrometry, and high-performance liquid chromatography ([Garner et al., 2006](#)), the scheme in Figure 3-3 also shows an initial conjugation of 1-BP with glutathione leading to N-acetyl-S-propylcysteine, an oxidation step from 1-bromo-2-propanol to alpha-bromohydrin, a glucuronic acid conjugation step from 1-bromo-2-propanol to 1-bromo-2-hydroxypropane-O-glucuronide, and glutathione conjugation of 1-bromo-2-propanol and bromoacetone followed by oxidation steps leading to metabolites with sulfoxide groups (e.g., N-acetyl-3-[(2-hydroxypropyl)sulfinyl] alanine). The steps involving oxidation of sulfur in the glutathione conjugate derivatives were proposed to be catalyzed by CYP oxygenases or flavin-containing monooxygenases (FMO) as suggested by Krause et al. ([2002](#)).

Catalysis of the oxidation steps by a number of CYP enzymes is supported by results from metabolic disposition studies in wild-type and *Cyp2e1*^{-/-} knock-out mice (F1 hybrids of 129/Sv and C57BL/6N strains) exposed by inhalation to 800 ppm ^{13}C -1-BP for 6 hours ([Garner et al., 2007](#)). Three major metabolites were identified in urine collected from wild-type mice during exposure: N-acetyl-S-(2-hydroxypropyl) cysteine (34 μmoles in collected urine), 1-bromo-2-hydroxypropane-O-glucuronide (5 μmoles), and N-acetyl-S-propylcysteine (8 μmoles). In *Cyp2e1*^{-/-} mice, the amounts of these metabolites in collected urine were changed to 21, 2, and 24 μmoles , respectively. The ratio of 2-hydroxylated metabolites to N-acetyl-S-propylcysteine was approximately 5:1 in wild-type and 1:1 *Cyp2e1*^{-/-} mice. The results indicate that the elimination of CYP2E1 increased the relative importance of the glutathione conjugation pathway, but did not eliminate the formation of oxygenated metabolites, suggesting the involvement of other CYP enzymes, in addition to CYP2E1, in oxidation steps illustrated in Figure 3-5. Evidence for the initial conjugation of 1-BP with glutathione leading to the formation of N-acetyl-S-propylcysteine comes from a number of studies in rats and mice ([Garner et al., 2007](#); [Garner et al., 2006](#); [Khan and O'Brien, 1991](#); [Jones and Walsh, 1979](#)).

1. N-Acetyl-S-propylcysteine was detected in the urine of wild-type and *Cyp2e1*^{-/-} mice exposed to 800 ppm 1-BP for 6 hours, at molar ratios to hydroxylated metabolites of 5:1 and 1:1 ([Garner et al., 2007](#)).
2. N-Acetyl-S-propylcysteine and N-acetyl-3-(propylsulfinyl) alanine (i.e., N-acetyl-S-propylcysteine-S-oxide) accounted for approximately 39 and 5% of excreted urinary metabolites, respectively, in urine collected for 24 hours after inhalation exposure of rats to 800 ppm 1-BP for 6 hours ([Garner et al., 2006](#)).
3. N-Acetyl-S-propylcysteine was a relatively minor urinary metabolite in rats given single 5-mg 1-BP/kg intravenous doses, but accounted for >80% of urinary metabolites following administration of 100 mg 1-BP/kg ([Garner et al., 2006](#)).
4. N-Acetyl-S-propylcysteine and N-acetyl-S-propylcysteine-S-oxide were among the six mercapturic acid derivatives identified in urine from rats given 200 mg 1-BP/kg by gavage (in arachis oil) for 5 days ([Jones and Walsh, 1979](#)). The structures of the other four mercapturic acid derivatives identified were consistent with glutathione conjugation of oxygenated metabolites of 1-BP, rather than 1-BP itself. These included N-acetyl-S-(2-hydroxypropyl) cysteine, N-acetyl-S-(3-hydroxypropyl) cysteine, and N-acetyl-S-(2-carboxyethyl) cysteine ([Jones and Walsh, 1979](#)). The techniques used in this study did not determine the relative amounts of the urinary mercapturic acid derivatives.
5. Isolated hepatocytes incubated for 60 minutes with 1-BP showed a decrease in glutathione content (from 58.4 to 40.8 nmol/10⁶ cells), consistent with the importance of glutathione conjugation in metabolic disposition of 1-BP in mammals ([Khan and O'Brien, 1991](#)).

Other studies have identified other metabolites, not included in Figure 3-3, in urine from rats and mice exposed to 1-BP Ishidao ([Ishidao et al., 2002](#); [Jones and Walsh, 1979](#)) and in *in vitro* systems ([Kaneko et al., 1997](#); [Tachizawa et al., 1982](#); [Jones and Walsh, 1979](#)). ([Jones and Walsh, 1979](#)) reported detecting metabolites in urine from rats orally exposed to 1-BP that are consistent with the initial oxidation of the 3-C of 1-BP: N-acetyl-S-(3-hydroxypropyl) cysteine, 3-bromopropionic acid, and N-acetyl-S-(2-carboxyethyl) cysteine. ([Garner et al., 2006](#)) were not able to detect these metabolites in urine following administration of single intravenous doses up to 100 mg 1-BP/kg in rats or exposure to 800 ppm for 6 hours in rats or mice. ([Garner et al., 2006](#)) proposed that the apparent discrepancy may have been due to an amplification of minor metabolites from the pooling, concentration, and acid hydrolysis processes used in the earlier study. Glycidol (1,2-epoxy-3-propanol) was detected in urine of Wistar rats exposed by inhalation 6 hours/day to 700 ppm for 3 or 4 weeks or 1,500 ppm for 4 or 12 weeks; but no determination of the amount of this compound was made, and the report did not mention the detection of any other carbon-containing metabolites ([Ishidao et al., 2002](#)). ([Kaneko et al., 1997](#)) monitored the formation of n-propanol during incubation of rat liver microsomes with 1-BP. 3-Bromopropanol and 3-bromopropionic acid were detected when 1-BP was incubated in an *in vitro* oxidizing system, but 1-BP metabolism with rat liver homogenates was not examined due to the low water solubility of 1-BP ([Jones and Walsh, 1979](#)). Propene, 1,2-epoxypropane, 1,2-propanediol, and propionic acid were detected when liver microsomes from phenobarbital-treated rats were incubated with 1-BP, and the addition of glutathione to the reaction mixture led to formation of S-(1' propyl)glutathione and S-(2' hydroxyl-1' propyl) glutathione ([Tachizawa et al., 1982](#)). ([Garner et al., 2006](#)) reported that propene,

propylene oxide, propanediol, and propionic acid were not detected in liver homogenate incubations with 1-BP; they suggested that the use of phenobarbital as a CYP inducer may have resulted (in the ([Tachizawa et al., 1982](#)) studies) in the formation of metabolites not generated by constitutive CYP enzymes.

1-BP may be converted to either of two epoxide metabolites (see section O-5-7), glycidol (which was found in the urine of 1-BP-exposed rats, see above) and propylene oxide. Metabolic pathways by which propylene oxide may be generated from 1-BP are shown in Jones and Walsh ([Jones and Walsh, 1979](#)), NTP ([2013b](#)), and IARC ([2018](#)) and a pathway by which glycidol may be generated from 1-BP is shown in IARC ([2018](#)).

H.4 Elimination

Results from animal metabolic disposition studies indicate that 1-BP is eliminated from the body by exhalation of the parent material and metabolically derived CO₂ and by urinary excretion of metabolites ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). Following single intraperitoneal injections of 200 mg/kg doses of [¹⁴C]-1-BP in rats, about 60 and 1.4% of the administered dose was in parent material and CO₂ in air expired within 6 hours, respectively, and about 15% of the administered dose was in urine collected for 48 hours ([Jones and Walsh, 1979](#)). Following intravenous injection of [¹⁴C] 1 bromopropane at nominal doses of 5, 20, or 100 mg/kg, radioactivity in CO₂ exhaled in 48 hours accounted for about 28, 31, and 10% of the administered dose in rats, and 22, 26, and 19% in mice ([Garner et al., 2006](#)). Radioactivity in exhaled parent material accounted for about 25, 32, and 71% of the administered dose in rats, and 45, 39, and 48% in mice ([Garner et al., 2006](#)). Radioactivity in urine collected for 48 hours accounted for about 17, 19, and 13% of the administered dose in rats, and 23, 19, and 14% in mice ([Garner et al., 2006](#)). Radioactivity in feces accounted for <4% of administered doses, regardless of dose level, in both species ([Garner et al., 2006](#)).

Animal studies also show that the elimination of 1-BP from the body is rapid and accumulation in the body is not expected ([Garner and Yu, 2014](#); [Garner et al., 2006](#); [Ishidao et al., 2002](#)). Following intravenous injection of [¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity remaining in the carcass 48 hours after dose administration accounted for about 6, 6, and 2% of the administered dose in rats, and 4, 2, and 4% in mice ([Garner et al., 2006](#)). ([Garner et al., 2006](#)) proposed that radioactivity remaining in the carcass could represent covalently bound residues from reactive metabolites or incorporation of ¹⁴C into cellular macromolecules from intermediate metabolic pathways. Following intravenous injection of 5 or 20 mg 1-BP/kg doses into rats, the mean half-times of elimination of 1-BP from the blood were 0.39 and 0.85 hours, respectively ([Garner and Yu, 2014](#)). In gas uptake studies with male and female rats, calculated half-times of elimination for 1-BP were rapid and decreased with increasing air concentrations of 1-BP ([Garner and Yu, 2014](#)). Terminal elimination half-times were 0.5, 0.6, 1.1, and 2.4 hours for males, and 1.0, 1.0, 2.0, and 6.1 hours for females, exposed to initial air concentrations of 70, 240, 800, and 2,700 ppm, respectively. Pretreatment of female rats with ABT to inhibit CYP metabolism (intraperitoneal injection of 50 mg 1-BP/kg 4 hours prior to gas uptake measurements) or buthionine sulfoxime, an inhibitor of glutathione synthesis (1,000 mg 1-BP/kg/day orally for 3 days before gas uptake), resulted in longer elimination half-times: 9.6 hours with ABT and 4.1 hours with D,L-buthionine(S,R)-sulfoximine (BSO), compared with 2.0 hours in untreated females at 800 ppm 1 bromopropane in the gas uptake chamber ([Garner and Yu, 2014](#)). The results with the inhibitors show that both CYP mediated oxidative metabolism and glutathione conjugation play

important roles in the elimination of 1-BP. Levels of 1-BP in blood decreased rapidly to detection limits within 0.7 hours after exposure stopped in Wistar rats exposed to 700 or 1,500 ppm 1-BP 6 hours/day for ≥ 3 weeks ([Ishidao et al., 2002](#)). Clearance of the bromide ion from blood and urine, however, showed slower elimination kinetics: elimination half-times for bromide were 4.7–15.0 days in blood and 5.0–7.5 days in urine ([Ishidao et al., 2002](#)).

Appendix I ANIMAL AND HUMAN TOXICITY STUDIES CONSIDERED FOR USE IN RISK ASSESSMENT

The 1-BP hazard information subjected to data quality evaluation consisted primarily of studies designed to examine the effects of repeated inhalation exposure (e.g., liver and kidney toxicity) and specialized repeated-dose studies of reproductive and developmental toxicity, neurotoxicity and carcinogenesis. Most of the available laboratory animal studies were considered useful for characterizing the potential human health hazards of 1-BP exposure; however, limitations were noted in some studies. This hazard information is summarized in the evidence tables shown in Table_Apx I-2. Additional information regarding the data evaluation results for individual studies can be found in the *Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies*. EPA-HQ-OPPT-2019-0235 ([EPA, 2019p](#)). Any study evaluation concerns thought to have influenced the reliability or interpretation of a specific hazard endpoint are discussed in the synthesis of evidence for a given hazard (See section 3.2.8). All endpoints considered for dose-response analysis were obtained from toxicity studies that scored high during data evaluation.

I.1 Reproductive Toxicity

A two-generation reproduction study in rats reported adverse effects on male and female reproductive parameters ([WIL Research, 2001](#)). The majority of these effects exhibited a dose-response beginning at 250 ppm, with statistical significance observed at 500 ppm. The F₀ generation showed significant dose-related decreases in male and female fertility indices at 500 ppm (fertility was 52% and 0% at 500 and 750 ppm, respectively). A significant increase in the number of females that displayed evidence of mating without delivery was also observed at 500 (10 of 25, 40%) and 750 ppm (17 of 25, 68%) in the F₀ generation. In the F₁ generation, the number of females that displayed evidence of mating without delivery was greater than controls, but not statistically significant at 500 ppm (8 of 25, 32% versus 3/25, 12% in treated and control dams, respectively). The number of males in the F₀ generation that did not sire a litter numbered 2, 0, 3, 12 and 25 (8, 0, 12, 48 and 100%) in the control, 100, 250, 500 and 750 ppm groups respectively. In addition, two females treated at 500 ppm showed evidence of mating, and were gravid, but did not deliver litters. The number of implantation sites, the actual number of litters produced, and live litter size were significantly reduced at 500 ppm in the F₀ and F₁ generations.

Significant changes in female reproductive parameters included a decrease in absolute and relative ovary weights at 750 ppm in the F₀ generation and an increase in estrous cycle length in F₀ and F₁ females (500 ppm). Estrous cycling was not observed in two F₀ females in the 500 ppm group, three F₀ females in the 750 ppm group, three F₁ females in the 250 ppm group, and four F₁ females in the 500 ppm group. This finding is supported by an inhalation study which showed significant treatment-related effects on estrous cycling in female rats and mice following three months of 1-BP inhalation exposure at ≥ 250 ppm ([NTP, 2011a](#)).

The toxicological significance of these findings is underscored by related findings at comparable doses in F₀ and F₁ generations:

- Decreased fertility (significant in 500 and 750 ppm groups). Because both males and females were treated, the observed decreases in fertility could be due in part, to dose-related impairment of male reproductive function.

- An increase in the number of primordial follicles at the highest dose evaluated (750 ppm in F₀ and 500 ppm in F₁) and a decrease in the number of corpora lutea in F₀ females at ≥ 500 ppm (significant at 750 ppm; endpoint was not measured at 100 or 250 ppm).
- No difference in the numbers of corpora lutea was observed in F₁ females treated at 500 ppm as compared to control (no other doses were evaluated for this endpoint).
- A significantly decreased number of implantation sites in F₀ and F₁ females at ≥ 500 ppm (no implantations observed at 750 ppm).
- Decreased live litter size (significant at 500 ppm in F₀ and F₁ treatment groups).

Statistically significant changes in male reproductive and spermatogenic endpoints included:

- Decreased sperm motility and morphologically normal sperm in the F₀ (≥ 500 ppm) and F₁ generations (500 ppm)
- Reduced absolute weight of the left and right cauda epididymides at ≥ 500 ppm in F₀/F₁
- Decreased absolute prostate weight in F₀ (≥ 250 ppm) and F₁ males (500 ppm)
- Decreased seminal vesicle weight in F₀ (750 ppm) and F₁ males (250 ppm)
- Decreased mean epididymal sperm numbers in F₀ males at 750 ppm

These findings positively correlate with the negative effects on fertility observed at 500 ppm, and the complete lack of fertility observed in F₀ mating pairs treated at 750 ppm.

([Zong et al., 2016](#)) investigated the potential effects of 1-aminobenzotriazole (1-ABT), a general inhibitor of cytochrome P450s, on the induction of toxicity to the reproductive system of male mice that were exposed by inhalation to vapors of 1-bromopropane (1-BP). Groups of six 10-week-old male C57BL/6J mice were exposed whole-body to 1-BP for 8 hours/day, 7 days/week for 4 weeks at vapor concentrations of 0, 50, or 250 ppm with twice-daily s.c. injections of saline and at 0, 50, 250, or 1200 ppm with twice-daily s.c. injections of 50 mg 1-ABT/kg in saline. Timing of 1-ABT/saline injections was not indicated. The only treatment-related effect on body weight at the end of exposure was significantly lower mean body weight in mice exposed to 1200 ppm 1-BP/1-ABT, compared with the 1-ABT-treated control. Weights of prostate plus seminal vesicle were significantly decreased at 250 ppm 1-BP without 1-ABT treatment and at 250 ppm and 1200 ppm 1-BP with 1-ABT treatment. No other organ weights were affected in mice that were exposed to 1-BP in the absence of 1-ABT treatment. However, in mice treated with 1-ABT, spleen weights were significantly decreased at 50, 250, and 1200 ppm 1-BP and testes and epididymide weights were significantly decreased at 1200 ppm 1-BP. Epididymal sperm count and percent mobile sperm were significantly decreased at 250 ppm 1-BP in the absence of 1-ABT treatment but were not decreased at 250 ppm 1-BP in the 1-ABT-treated mice. In mice exposed to 1200 ppm 1-BP and treated with 1-ABT, epididymal sperm count, percent mobile sperm, and the number of round spermatids per seminiferous tubule were significantly decreased, and percent morphologically abnormal epididymal sperm was significantly increased. The number of retained elongated spermatids per seminiferous tubule was significantly increased at 50 and 250 ppm 1-BP without 1-ABT treatment, but only at 1200 ppm 1-BP with 1-ABT treatment. The number of periodic acid-Schiff (PAS)-positive round structures per seminiferous tubule was significantly increased at 250 ppm 1-BP in the absence of 1-ABT treatment and at 250 and 1200 ppm 1-BP in mice treated with 1-ABT. In 1-ABT treated mice, the numbers of retained elongated spermatids per tubule at 50 and 250 ppm 1-BP and PAS-positive round structures per tubule at 250 ppm were significantly lower than in the mice not treated with 1-ABT. The study authors concluded that treatment of male mice with 1-ABT, a general inhibitor of cytochrome P450s, inhibited the decreased epididymal sperm

count, decreased epididymal sperm motility, increased retained elongated spermatids per seminiferous tubule, and increased PAS-positive round structures per seminiferous tubule that were found in mice exposed to 50 and 250 ppm 1-BP in the absence of 1-ABT treatment.

I.2 Neurotoxicity

A number of laboratory animal studies report that both acute and repeated inhalational exposure to high concentrations of 1-BP produce peripheral neurotoxicity indicated by changes in both function and structure of the peripheral nervous system. The degree or severity of peripheral neurotoxicity produced by 1-BP depends on the concentration as well as duration of exposure. Most studies using concentrations of ≥ 1000 ppm report ataxia progressing to severely altered gait, hindlimb weakness or loss of hindlimb control, convulsions, and death (e.g., ([Banu et al., 2007](#); [Yu et al., 2001](#); [Fueta et al., 2000](#); [Ichihara et al., 2000a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). Concentrations of 400-1000 ppm produce neuropathological changes including peripheral nerve degeneration, myelin sheath abnormalities, and spinal cord axonal swelling ([Wang et al., 2002](#); [Yu et al., 2001](#); [Ichihara et al., 2000a](#)).

Physiological and behavioral measures have been used to characterize and develop dose-response data for this peripheral neurotoxicity. Motor nerve conduction velocity and latency measured in the rat tail nerve were altered at ≥ 800 ppm with progressive changes observed from 4 to 12 weeks of exposure ([Yu et al., 2001](#); [Ichihara et al., 2000a](#)). These findings in rats agree with neurological symptoms reported in exposed humans, including peripheral weakness, tingling in extremities, and gait disturbances. The nerve conduction velocity endpoint that was altered in rats ([Yu et al., 2001](#); [Ichihara et al., 2000a](#)) is directly comparable to the increased latencies and lower conduction velocity measured in a population of female factory workers exposed to 1-BP ([Li et al., 2010](#); [Ichihara et al., 2004b](#)).

Behavioral tests such as grip strength, landing foot splay, traction (hang) time, and gait score provide dose-response data and appear somewhat more sensitive than neuropathology or physiological changes. Ichihara et al. ([2000a](#)) reported progressively worsening effects over 13 weeks of exposure at 400 and 800 ppm including decreased hindlimb and forelimb grip strength, and inability to walk on a slightly-sloped plane; exposure at 200 ppm significantly decreased hindlimb grip only at 4 weeks and otherwise was without effect. Hindlimb grip was preferentially decreased compared to forelimb as is often observed with peripheral neuropathy. Similarly decreased hindlimb strength was reported by Banu et al. ([2007](#)) after 6 weeks of 1-BP exposure at 1000 ppm (but not 400 ppm); these changes had not recovered at 14 weeks post exposure. Honma et al. ([2003](#)) measured the time for a rat to hang onto a suspended bar, which they called a traction test. The average time to hang appeared to be decreased following 21 days of exposure to 50 ppm, and was significantly so with 200 and 1000 ppm; these changes were still evident when animals were tested 7 days later. The ability to stay on a rotarod was not altered in these rats, suggesting that the weakness is peripherally mediated.

Results reported following oral dosing with 1-BP are similar to those reported following inhalation exposure. Over 16 weeks of dosing (200-800 mg/kg/d), Wang et al. ([2012](#)), reported progressively decreased hindlimb grip strength, wider landing foot splay, and increased gait abnormalities. The high-dose group was too debilitated to test after 14 weeks, but at that time their grip strength was decreased by 42%, somewhat comparable to the 56% decrease reported with 13 weeks of 800 ppm inhalational exposure ([Ichihara et al., 2000a](#)). Rats exposed to the lowest concentration of 200

mg/kg/d showed less, but still statistically significant changes in gait and decreased (9%) hindlimb grip strength. Subcutaneous administration of 455 or 1353 mg/kg/d (said to be equal to inhalation of 300 or 1000 ppm) over a 4 week period also produced changes in tail motor nerve function ([Zhao et al., 1999](#)) similar to the effects reported by others following inhalation exposure.

Some behavioral assays conducted in rats exposed to 1-BP reflect involvement of central as well as peripheral nervous systems. Increased motor activity levels were measured following inhalation of 50 or 200 ppm for three weeks ([Honma et al., 2003](#)). Spatial learning and memory measured in a Morris water maze was severely impaired while rats were receiving oral doses of 200 mg/kg/d and greater ([Guo et al., 2015](#); [Zhong et al., 2013](#)). Guo et al. (2015) also reported that these cognitive deficits correlated with lowered levels of neuroglobin and glutathione depletion indicative of oxidative stress in the same rats. During inhalational exposure, water maze performance was impaired at concentrations of 200 ppm and above ([Honma et al., 2003](#)). However, these concentrations also produced neuromotor difficulties, which would interfere with performance of the task. There were no changes in water maze performance when training was initiated after exposure ended. Furthermore, there were no differences in memory of a passive avoidance task when the initial learning took place before exposures began ([Honma et al., 2003](#)).

A number of features reflecting CNS neurotoxicity have been reported for 1-BP. Brain pathology has been reported in several, but not all, studies, which may be due to experimental differences such as tissue sampling, staining, and measurement. Histological examination of the brain showed widespread pathology at 1000 and 1600 ppm, and mild myelin vacuolization at 400 ppm, following 28 days of exposure ([ClinTrials, 1997b](#)); however, the same testing laboratory reported no neuropathology with exposures up to 600 ppm for 13 weeks ([ClinTrials, 1997a](#)). In the cerebellum, exposure at 400 ppm and higher produced degeneration of Purkinje cells ([Mohideen et al., 2013](#); [Ohnishi et al., 1999](#)) without morphological changes in the hippocampus ([Mohideen et al., 2013](#)). Similar exposure levels decreased noradrenergic but not serotonergic axonal density in frontal cortex and amygdala ([Guo et al., 2015](#); [Mohideen et al., 2011](#)). In contrast to these reports, no degeneration was observed across several brain sections up to 800 ppm despite marked peripheral and spinal cord changes in the same rats ([Wang et al., 2002](#); [Ichihara et al., 2000a](#)). In two other studies conducted in the same laboratory, one reported no histological or morphological changes in brain following exposures up to 1250 ppm for 13 weeks ([Sohn et al., 2002](#)) and another reported no neuropathology after daily exposures of 1800 ppm for up to eight weeks ([Kim et al., 1999a](#)), even though in the latter study other indicators of neurotoxicity were observed.

Decreased absolute brain weight has been reported in several studies, both in the context of adult exposures and long-term exposures during a 2-generation reproductive study. Studies involving exposures from 4 to 12 weeks reported decreased brain weight at 800 and 1000 ppm ([Subramanian et al., 2012](#); [Wang et al., 2003](#); [Ichihara et al., 2000a](#)). Kim et al. (1999a) also reported decreased brain weight at 300 ppm for 8 weeks, but only provided relative brain:body weight data. In the parental generation of a 2-generation study, exposure for at least 16 weeks also produced brain weight changes, with males being more sensitive (NOAEL=100 ppm, LOAEL=250 ppm) than females (NOAEL=250 ppm) ([WIL Research, 2001](#)). The F₁ generation, which was exposed during gestation and at least 16 weeks after weaning, had lower brain weight at 100 ppm in males, and again females were less sensitive (NOAEL=250 ppm). Histopathological evaluations in the WIL study revealed no correlative macroscopic or microscopic alterations in unperfused brain tissue. Two studies have measured brain weight and reported no effects: 1) ([Wang et al., 2002](#)), in which

exposure was only 7 days and may not have been a sufficient exposure duration, and 2) the 13-wk study of ([ClinTrials, 1997a](#)), even though the same laboratory reported decreased brain weight at the same concentration with only 4 weeks of exposure.

Fueta and colleagues ([Fueta et al., 2007](#); [Ueno et al., 2007](#); [Fueta et al., 2004](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Fueta et al., 2000](#)), reported a series of studies using electrophysiological measures of hippocampal slices (dentate gyrus and CA1 regions) from rats exposed to 1-BP for four to 12 weeks. Concentrations of 400 ppm and higher showed disinhibition in paired-pulse population spikes, and the effect was dependent on exposure concentration and duration. This hyperexcitability appeared to be due to a reduction in feedback inhibition rather than a change in excitatory synaptic drive. There was a moderate correlation with the level of bromide ion in the brain. Pharmacological probes, proteins and receptor mRNA levels suggest that these effects are related to actions on the GABA and NMDA neural systems, and/or intracellular signaling cascades ([Ueno et al., 2007](#); [Fueta et al., 2004](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#)). A recent Society of Toxicology presentation (abstract only available) reported similar effects in hippocampal slices from 14-day old rat pups whose mothers were exposed to 400 or 700 ppm during gestation ([Fueta et al., 2013](#)).

A number of investigators have probed potential molecular mechanisms for some of these CNS effects. Exposures of 200 ppm and greater produce changes in biomarkers and proteome expressions suggesting alterations in the function and maintenance of neural and astrocytic cell populations. Some of these include indicators of oxidative stress (reactive oxygen species, glutathione depletion), ATP loss, protein damage, altered apoptotic signaling, neurotransmitter dysregulation, decreased hippocampal neurogenesis, and others ([Huang et al., 2015](#); [Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Zhong et al., 2013](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Yoshida et al., 2007](#); [Wang et al., 2003](#); [Wang et al., 2002](#)). Concentrations as low as 50 ppm for three weeks were reported to decrease levels of the serotonin metabolite 5-HIAA in frontal cortex and taurine in midbrain, while concentrations of 200 ppm and greater impacted additional markers (protein levels, mRNA) of monoaminergic and amino acid neurotransmitter systems ([Zhang et al., 2013](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Ueno et al., 2007](#)). Overall these data suggest several and perhaps overlapping cellular and molecular mechanisms that could contribute to the functional and structural alterations reported for 1-BP. ([Zong et al., 2016](#)), citing studies from the literature, noted that the potential of 1-bromopropane (1-BP) to induce neurotoxicity in mice had not been studied because 1-BP induced lethal hepatotoxicity in mice before the appearance of potential overt evidence of neurotoxicity. To develop a murine model of neurotoxicity, ([Zong et al., 2016](#)) proposed treatment of mice with 1-aminobenzotriazole (1-ABT), a general inhibitor of cytochrome P450s, to reduce severe hepatotoxicity and allow studies on the effects of 1-BP on the mouse brain. A preliminary experiment showed that subcutaneous (s.c) or intraperitoneal injections of male C57BL/6J mice with 50 mg/kg 1-ABT twice daily for three days inhibited CYP2E1 activity by 62-64% in the brain and by 92-96% in the liver, compared with values in saline-injected control mice. Since the route of injection had no significant effect on the extent of CYP2E1 activity inhibition, the s.c. route of 1-ABT administration was chosen for model development to minimize potential for damage of internal organs. For the main study, groups of six 8-week-old male C57BL/6J mice were exposed whole-body to 1-BP for 8 hours/day for 4 weeks at vapor concentrations of 0, 50, or 250 ppm with s.c. injections of saline before and after each inhalation exposure and at 0, 50, 250, or 1200 ppm with s.c. injections of 50 mg 1-ABT/kg in saline before and after each inhalation exposure (100 mg

1-ABT/kg-day). The only treatment-related effect on body weight was significant loss of body weight on day 28 in mice exposed to 1200 ppm 1-BP/1-ABT. In mice not treated with 1-ABT, mild histological changes in hepatocytes included centrilobular degeneration and nuclear and cytoplasmic changes at 50 ppm 1-BP. Exposure to 250 ppm without 1-ABT produced severe pathological changes in the liver including macroscopic and microscopic liver necrosis, hemorrhage, and foci of hepatocyte degeneration. In contrast, no serious histopathological changes were found in the livers of 1-ABT-treated mice that were exposed to 50, 250, or 1200 ppm 1-BP. Absolute mean liver weights were significantly decreased at 50 ppm 1-BP in the absence of 1-ABT treatment and at 250 and 1200 ppm 1-BP in animals treated with 1-ABT. Absolute mean brain weight was significantly lower than control in the group treated with 1-ABT and exposed to 1200 ppm 1-BP, but brain weights were unaffected in other exposure groups. Cerebral cortex and hippocampal expression of Ran, GRP78, γ -enolase, and c-Fos proteins was determined by western blotting analysis in all treated mouse groups. Studies from the literature showed that expression of these four proteins was altered in brain tissues of rats exposed to 1-BP in the absence of treatment with 1-ABT. In the male C57BL/6J mice treated with 1-ABT, hippocampal Ran expression and cortex GRP78 expression were significantly increased at 1200 ppm 1-BP and hippocampal Ran expression was significantly increased at 250 ppm 1-BP. No changes in Ran or GRP78 expression occurred in other mouse groups, including those treated with 50 or 250 ppm 1-BP in the absence of 1-ABT treatment. No treatment-related changes were found in the expression of γ -enolase or c-Fos in the hippocampus or cerebral cortex. The treatment of mice in this study with 1-ABT, a general inhibitor of cytochrome P450s, reduced the severe hepatotoxicity/lethality of 1-BP to mice, thus allowing mouse survival at 1-BP exposure concentrations as high as 1200 ppm for 8 hours/day for 28 days and the study of the effects of 1-BP on the mouse brain.

I.3 Human Case Reports

Several case studies have reported various neurological effects in workers exposed to 1-BP ([Samukawa et al., 2012](#); [CDC, 2008](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)). Some of the neurological effects experienced by workers included peripheral neuropathy, muscle weakness, pain, headaches, numbness, gait disturbance, confusion, ocular symptoms, slowed mental activity, and dizziness. In some instances, the effects were still observed many months after exposure had ceased or had been reduced.

Workers described in the case reports were exposed to 1-BP in the following activities: metal cleaning, circuit board cleaning, and gluing foam cushions or furniture. In almost all of the cases reported in the table below, personal protective equipment was not used and air concentrations of 1-BP, when available, were greater than 100 ppm. Bromide levels, both serum and in a few cases, urinary, were provided in some of the studies and are included in the table below. Bromide concentrations have been used as a biomarker of exposure to 1-BP. A description of the use of bromide levels and the investigation into using other biomarkers of exposure are included in Section 2.2.

([Raymond and Ford, 2007](#)) reported high levels of urinary arsenic, as well as serum bromide, in the workers described in their case report of four employees who required hospitalization, suggesting arsenic and bromide synergism. All four of the workers had total (organic and inorganic) urinary arsenic levels greater than 200 $\mu\text{g/L}$, but the source of the arsenic could not be identified. NIOSH reported on these 4 employees in a HHE on a plant where workers applied spray adhesive to

cushions, and concluded that the exposure was likely not occupational and could not have been the sole cause of ataxia and paresthesias that the four hospitalized workers experienced

Table Apx I-1. Case Reports on 1-BP

Reference ¹	# Cases	Primary Symptoms	Activity	Air levels	Serum Bromide levels (mg/dL) ²
(Majersik et al., 2007)	6	Headache, nausea, dizziness, lower extremity numbness, pain, paresthesias, difficulty walking/balance	Foam cushion gluing at furniture plant (glue contained 70% 1-BP)	130 ppm (range, 91-176); TWA 108 ppm (range, 92-127)	Peak range: 44-170
(Sclar, 1999)	1	Peripheral neuropathy, weakness of lower extremities and hand, numbness, dysphagia	Metal stripping (degreasing and cleaning)	Not available	Not available
(CDC, 2008)	2	Confusion, dysarthria, dizziness, paresthesias, ataxia; Headache, nausea, dizziness, malaise	Cleaning circuit boards (spray) Solvent in dry cleaning	178 ppm 75-250x background levels	48 mg/dL and not available for case #2
(Samukawa et al., 2012)	1	Muscle weakness, pain, numbness in lower extremities, gait disturbance	Metal cleaning	553 ppm, mean TWA (range, 353-663)	58 µg/mL (peak)
(Raymond and Ford, 2007) (4 cases from NIOSH (2003a) HHE report on Marx Industries)	4	Dizziness, anorexia, dysesthesias, nausea, numbness, ocular symptoms, unsteady gait, weakness, weight loss	Gluing in furniture making	Mean 107 ppm (range, 58-254 ppm) collected 9 months after workers became ill	3.0 - 12.5 mEq/L (100 mg/dL) Arsenic levels > 200 µg/L for all 4 employees ³
(NIOSH, 2003a)	16 (incl. 4 from Raymond (2007))	Headache, anxiety, feeling “drunk”, numbness and “pins and needles” sensation in legs and feet	Spray application of glue to polyurethane foam to make cushions	1999 (16 personal breathing zone samples): GM 81.2 ppm (range, 18-254 ppm); 2001 (13 PBZ samples): GM 45.7 ppm (range, 7-281 ppm)	Serum GM: 4.8 mg/dL (2.7-43.5; n=39); Urinary: 46.5 mg/dL (15.4-595.4, n=40) Includes both exposed and “unexposed workers
(Ichihara et al., 2002)	3	Staggering gait, paresthesia in lower extremities, numbness in legs, headache, urinary incontinence, decr in vibration sense in legs	Spray application of glue to polyurethane foam to make cushions	Mean 133 ppm, (range, 60-261 ppm daily TWA); avg over 11 days 133 ± 67 ppm--after ventilation improved	Not available

Table Apx I-1. Case Reports on 1-BP

Reference ¹	# Cases	Primary Symptoms	Activity	Air levels	Serum Bromide levels (mg/dL) ²
Biomarker Studies also Containing Case Report Data					
(Hanley et al., 2006a)	13	(focused on exposure and urinary Br)	Spray application of glue to polyurethane foam to make cushions	Mean 92 ppm (range, 45-200 ppm)	Urinary: 190 (43-672; composite of 2 days)
(Ichihara et al., 2004b ; Ichihara et al., 2004a)	24 female 13 male China	Nose, throat, eye irritation; malaise, headache, dizziness	1-BP production	3.3-90.2 ppm No severe neurological effects < 170 ppm	Urinary bromide measured but not reported

¹EPA has not published systematic review criteria for reports/case studies, therefore data quality evaluation for these reports are not available

²Serum bromide unless otherwise indicated; Reference ranges vary by report

³Arsenic Reference range: <0.06

I.4 Human Epidemiology Studies

The 1-BP database includes three epidemiological studies of workers occupationally exposed to 1-BP ([Li et al., 2010](#); [Toraason et al., 2006](#); [Ichihara et al., 2004b](#)), two of the studies report neurologic effects and the third describes DNA damage in workers' leukocytes. The evaluation of 1-BP epidemiology studies by each of the five aspects of study design – study population characteristics and representativeness, exposure measures, outcome measures, confounding, and analysis – is discussed below; additional information regarding the data evaluation results for individual studies can be found in the *Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies*. EPA-HQ-OPPT-2019-0235 ([EPA, 2019p](#)). Twenty-three female workers involved in 1-BP production in China were surveyed in 2001 and compared with age-matched controls from a beer factory located in the same city ([Ichihara et al., 2004b](#)). The study authors did not report the method of recruitment. Neurological tests (vibration sensation, electrophysiologic studies), blood tests, neurobehavioral tests and postural sway tests were administered. Passive sampling indicated individual exposure levels ranging from 0.34 – 49.2 ppm in an 8-hour shift (median 1.61 ppm; geometric mean 2.92 ppm). Some of the employees in this plant were also exposed to 2-BP and were analyzed separately. Although some of the neurologic measures indicated reduced function in exposed workers compared to controls, because of the past exposures to 2-BP and the small number of cases who entered the study after 2-BP was no longer used (n= 12 pairs), it was difficult to interpret the results of this study. In workers who were employed at the plant after 2-BP was no longer used, Benton visual memory test scores, POMS depression, and POMS fatigue were significantly different. It is not clear whether this indicates a lack of power to detect differences in the larger group or whether the exposure to 2-BP affected the results.

As a follow-up to the Ichihara study ([Ichihara et al., 2004b](#)) described above, ([Li et al., 2010](#)) combined data from three 1-BP production facilities in China to analyze a larger sample of workers. Sixty female and 26 male workers and controls from other types of factories matched by age, sex and geographic region were analyzed from four time periods (2001, 2003, 2004, 2005).

Data were collected over 3 days between 2001 and 2005. The authors did not describe the recruitment process, and it is not clear whether the same workers included in the Ichihara 2004 study were recruited for this study. The authors reported that none of the workers had a history of diabetes.

Exposures were measured for each plant using passive samplers. Exposure was measured either once or twice over 8 or 12 hour work shifts. TWA exposure concentrations to 1-BP ranged from 0.07-106.4 ppm for female workers and 0.06-114.8 ppm for male workers. It was reported that none of the workers wore gloves or masks in the plant. However, the authors later clarified that some workers wore gloves ([Ichihara et al., 2011](#)). Employees were placed into low-, medium-, and high-exposure groups (for females) to include equal numbers. Median exposures for the three groups (n=20 per group) were 1.28, 6.60 and 22.58 ppm for females and 1.05 (low) and 12.5 (high) ppm for males (n=13 per group). Ambient exposure levels varied by job and by plant and were collected in different years for each plant. For example, the ambient concentrations of “raw product collection” were more than 3 times higher at the Yancheng plant (analyzed in 2003) than at the Yixing plant ([Li et al., 2010](#)).

Clinical chemistries were obtained, and electrophysiological studies and neurological and neurobehavioral tests were conducted for each employee. A single neurologist performed most of the neurological assessments except for those collected in 2004 from one plant, which included 5 female workers. Electrophysiological tests conducted included: motor nerve conduction velocity, distal latency (DL), F-wave conduction velocity in the tibial nerve, sensory nerve conduction velocity in the sural nerve (SNCV), and amplitude of the electromyogram induced by motor nerve stimulation, F-wave, and potential of sensory nerve. Vibration sense, reflex, and muscle strength were measured using a tuning fork on the big toe. Neurobehavioral tests and blood tests were also performed.

In regression analyses, the authors reported a statistically significant increase ($p<0.05$) in mean tibial motor distal latency and a decrease in mean sural nerve conduction velocity in women in the middle exposure group only (compared to controls). Statistically significant decreased vibration sense in toes (vibration loss) was reported in all exposure groups compared to controls. In addition, thyroid stimulating hormone (TSH) was significantly different in the middle and high exposure groups compared to controls and FSH in low and medium exposure groups in females. Red blood cell count was significantly decreased in all exposure groups compared to controls in females. In males, the only statistically significant difference between the high exposure group and controls was for blood urea nitrogen.

Analyses of cumulative exposure measures (exposure level x duration) indicated statistically significant ($p<0.05$) increases in vibration sense in toes in females across all exposure levels when compared to controls (5.6 ± 4.3 , 6.4 ± 3.8 , and 6.5 ± 3.4 secs, mean $\pm$ SD for low, medium and high cumulative exposure groups, respectively). In females, only the high cumulative exposure group for tibial motor DL was statistically higher than in controls and only the low cumulative exposure group for sural NCV. Analyses to adjust for other factors that could influence vibration loss (examining neurologist, age, height, body weight, alcohol consumption) were conducted using analysis of covariance in female workers. The effect of 1-BP exposure on vibration loss was significant ($p = 0.0001$ or $p = 0.0002$) based on cumulative exposures as well as exposures not

considering duration of exposure, respectively, but the effect of examining neurologist was also significant ($p < 0.0001$).

Both of the neurological studies described above ([Li et al., 2010](#); [Ichihara et al., 2004b](#)) showed neurological effects related to 1-BP exposure. The co-exposures to 2-BP and the small sample size of workers exposed only to 1-BP was a limitation in the Ichihara et al. 2004 study. Li et al. ([2010](#)) selected workers exposed to 1-BP from 3 plants to include more study participants; however, the exposure data reported by plant were limited, the job activities were somewhat different between plants (but for those jobs with similar activities between plants, some exposures were more than 3 times higher at one plant than another), and ambient exposure levels of 1-BP and 2-BP reported by job and by plant were collected in different years for each plant. Several of these issues could lead to exposure misclassification of the workers. TWAs (8- and 12- hour) were used to assign exposure groups, based on either 1 or 2 samples. Using the TWA does not account for the fluctuations or potential peaks that may have occurred during the shift. In addition, the median exposure level of the high exposure group for females was 22.58 ppm but the range was 15.28-106.4 ppm, indicating that some of the workers were exposed to levels much higher than the lowest exposed workers in that group. In addition, the cumulative exposure measures were based on only 1-3- day measurements of individual exposure levels.

Skin temperature is important when conducting electrophysiological studies; however, the only control for temperature in this study was to acclimate study participants to 24° C in a room for 30 minutes. Individual skin temperatures should have been taken at the site of the test (on the foot) because the results are affected by temperature. Vibration sense can be influenced by BMI, but it was not reported or controlled in the study. As acknowledged in the report by the study authors, vibration sense is inherently imprecise (based on the sensitivity of the subject relative to the examiner). Evidence of a high degree of variability was shown in the large standard deviations reported for vibration sense in females (2.9 ± 3.9 , mean $\pm$ SD for controls; 5.6 ± 4.4 , low exposure group). Other than RBC, only vibration sense in females using the cumulative exposure measure was concentration-dependent. RBC in females could have been influenced by other factors (e.g., menstruation, dehydration) that were not examined in the study.

Toraason et al. ([2006](#)) analyzed DNA damage in peripheral leukocytes of workers exposed to 1-BP during spray application of adhesives in the manufacture of foam cushions for upholstered furniture. Sixty-four workers (18 males, 46 females) at two plants were included in the analysis. There were no unexposed groups. Fifty of 64 workers wore personal air monitors for 1-3 days. Workers employed as sprayers had the highest exposures; 1-BP 8-hr TWA concentrations were substantially higher (4 times) for sprayers at one of the plants than the other. TWA exposures ranged from 0.2 to 271 ppm across both plants. DNA damage was assessed using comet assay. DNA damage was measured by tail moment in leukocytes of workers. At both the start and end of the work week, DNA leukocyte damage was higher for sprayers than non-sprayers but the increases were not statistically significant. In addition, the facility with lower exposures had higher measures of DNA damage than the higher exposure facility at the beginning of the week but not the end. Tail moment dispersion coefficients did not indicate an exposure-response relationship. Three different biomarkers of exposure, 1-BP TWA concentrations and serum and urinary bromide levels, were evaluated in multivariate analyses. After controlling for various potential confounders, starting and ending work week comet tail moments in leukocytes were significantly associated with serum bromide quartiles and ending work week values of 1-BP TWA concentrations. None of

the models that examined associations between DNA damage and dispersion coefficients was statistically significant. There was a slight risk for DNA damage in workers' leukocytes in vitro in workers exposed to 1-BP but the results of the in vivo data were not consistent.

Table Apx I-2. Summary of the Toxicological Database for 1-BP

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Mortality	Acute	Rat, Wistar, M/F (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	LC ₅₀ = 7000	Mortality (acute inflammatory response and alveolar edema)	(Elf Atochem, 1997)	N/A
Mortality	Acute	Rat, Sprague-Dawley, M/F (n=10/group)	Inhalation, whole body, vapor	0, 511,000, 13,000, 15,000 or 17,000 ppm	4 hours	LC ₅₀ = 14,374	Mortality	(Kim et al., 1999a)	N/A
Mortality	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250 (M)	Decreased survival	(NTP, 2011a)	High
Mortality	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 250	Decreased survival	(NTP, 2011a)	High
Mortality	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/week for 4 weeks	NOAEL= 110	Mortality (two of three strains affected)	(Liu et al., 2009)	High
Mortality	Short-term/Subchronic	Mouse, B6C3F1, F (n=5-8/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	NOAEL= 250 (F)	Mortality (first week on study)	(Anderson et al., 2010)	Medium
Mortality	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250	Decreased survival rate	(NTP, 2011a)	High
Mortality	Acute	Rat, Sprague-Dawley, F (n=10/group)	Oral	0 or 2000 mg/kg	Single exposure	LD ₅₀ > 2000 mg/kg (F)	Mortality	(Elf Atochem, 1993a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Acute	Rat, M (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 8500 (M)	No effects on body weight	(Elf Atochem, 1997)	N/A
Body weight	Short-term	Rat, Wistar, M (n=8/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day for 7 days	NOAEL= 400 (M)	Decreased body weight	(Wang et al., 2002)	N/A
Body weight	Short-term	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day for 7 days	NOAEL= 400 (M)	Decreased body weight	(Zhang et al., 2013)	High
Body weight	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 1000	Decreased body weight	(NTP, 2011a)	High
Body weight	Short-term	Rat, F344, M (n=5/group)	Inhalation, whole body, vapor	0, 10, 50, 200 or 1000 ppm	8 hours/day, 7 days/week for 3 weeks	NOAEL= 50 (M)	Increased body weight	(Honma et al., 2003)	Low
Body weight	Short-term	Rat, F344, F (n=7-8/group)	Inhalation, whole body, vapor	0, 50, 200 or 1000 ppm	8 hours/day, 7 days/week for 3 weeks	NOAEL= 1000 (F)	No effects on body weight	(Sekiguchi et al., 2002)	N/A
Body weight	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/week for 4 weeks	NOAEL= 398	Decreased weight gain	(ClinTrials, 1997b)	N/A
Body weight	Short-term	Rat, Wistar-ST, M (n=12/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/week for 4 weeks	NOAEL= 800 (M)	Decreased body weight	(Subramanian et al., 2012)	N/A
Body weight	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/week for 5 or 7 weeks	LOAEL= 1000 (M)	Decreased body weight	(Yu et al., 2001)	Medium
Body weight	Subchronic	Rat, Wistar, M (n=24/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/week for 6 weeks	NOAEL= 400 (M)	Decreased body weight	(Banu et al., 2007)	N/A
Body weight	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/week for 8 weeks	NOAEL= 300	Decreased body weight	(Kim et al., 1999b)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/week for 12 weeks	NOAEL= 200 (M)	Decreased body weight	(Ichihara et al., 2000a)	High
Body weight	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/week for 12 weeks	NOAEL= 1200 (M)	Decreased body weight	(Wang et al., 2003)	N/A
Body weight	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/week for up to 12 weeks	NOAEL= 400 (F)	Decreased body weight	(Yamada et al., 2003)	High
Body weight	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/week for 13 weeks	NOAEL= 600	No effects on body weight	(ClinTrials, 1997a)	High
Body weight	Chronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 200, 500 or 1250 ppm	6 hours/day, 5 days/week for 13 weeks	NOAEL= 1250	No effects on body weight	(Sohn et al., 2002)	N/A
Body weight	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500 (M)	Decreased body weight	(NTP, 2011a)	High
Body weight	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on body weight	(NTP, 2011a)	High
Body weight	Developmental	Rat, Albino Crl:CD(SD)IGS BR, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 199, 598 or 996 ppm	6 hours/day on GDs 6-19 and lactation days 4-20	NOAEL= 100 (F)	Decreased body weight gain during gestation	(Huntingdon Life Sciences, 1999)	N/A
Body weight	Developmental	Rat, F (n=25/group)	Inhalation	0, 103, 503 or 1005 ppm	6 hours/day on GDs 6-19	NOAEL= 103 (F)	Decreased body weight gain during gestation	(Huntingdon Life Sciences, 2001)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Developmental	Rat, Wistar-Imamichi, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 400 or 800 ppm	8 hours/day during gestation (GDs 0-20) and lactation (PNDs 1-20)	NOAEL= 400 (F)	Decreased body weight at PND 21	(Furuhashi et al., 2006)	N/A
Body weight	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0/group, 49-50 F1 adults/group/generation; 30-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥ 70 days), through mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 250 (F)	Decreased body weight (F ₀ and F ₁ adults)	(WIL Research, 2001)	High
Body weight	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 500 (M)	Decreased body weight gain	(NTP, 2011a)	High
Body weight	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/ week for 4 weeks	NOAEL= 250 (M)	No effects on body weight	(Liu et al., 2009)	High
Body weight	Short-term/Subchronic	Mouse, B6C3F1, F (n=5-8/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	LOAEL= 125 (F)	Decreased body weight	(Anderson et al., 2010)	Medium

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on body weight	(NTP, 2011a)	High
Body weight	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on body weight	(NTP, 2011a)	High
Body weight	Acute	Rat (n=10/group)	Oral	0 or 2000 mg/kg	Single exposure	NOAEL= 2000 mg/kg	No effects on body weight	(Elf Atochem, 1993a)	
Body weight	Short-term	Rat, Wistar, M (n=10/group)	Oral, gavage (corn oil vehicle)	0, 200, 400 or 800 mg/kg-day	12 days	NOAEL= 400 mg/kg-day (M)	Decreased final body weight; used for weight of evidence; no route-to-route extrapolation	(Zhong et al., 2013)	Low
Body weight	Short-term	Rat, Sprague-Dawley, M (n=7/group)	Intra-peritoneal	0 or 1000 mg/kg-day	14 days	LOAEL= 1000 mg/kg-day (M)	Decreased body weight	(Xin et al., 2010)	N/A
Body weight	Chronic	Rat, M (n=10/group)	Oral	0, 200, 400 or 800 mg/kg-day	16 weeks	NOAEL= 400 mg/kg-day (M)	Decreased body weight	(Wang et al., 2012)	N/A
Body weight	Short-term	Rat, Wistar, M (n=14/group)	Oral, gavage	0, 100, 200, 400 or 800 mg/kg-day	12 days	NOAEL= 400 mg/kg-day (M)	Decreased body weight	(Guo et al., 2015)	High
Body weight	Acute	Mouse, BALB/c, F (n=5/group)	Oral, gavage (corn oil vehicle)	0, 200, 500 or 1000 mg/kg	Single exposure; necropsy after 6, 12, 24 or 48 hours	NOAEL= 1000 mg/kg (F)	No effects on body weight	(Lee et al., 2007)	N/A
Cardio-vascular	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on heart weight or histo-pathology	(Ichihara et al., 2000b)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Cardio-vascular	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on heart weight or histo-pathology	(Kim et al., 1999a)	N/A
Cardio-vascular	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on heart weight or histo-pathology	(ClinTrials, 1997a)	High
Cardio-vascular	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on heart weight	(NTP, 2011a)	High
Cardio-vascular	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Cardio-vascular	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 2000 (M)	Decreased absolute and relative heart weight	(NTP, 2011a)	High
Cardio-vascular	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on heart weight or histo-pathology	(NTP, 2011a)	High
Cardio-vascular	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Skin	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Skin	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Endocrine	Short-term	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day for 7 days	NOAEL= 1000 (M)	No effects on adrenal gland weight or plasma corticosterone	(Zhang et al., 2013)	High
Endocrine	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on organ weights or histopathology	(Kim et al., 1999a)	N/A
Endocrine	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on organ weights or histopathology	(Ichihara et al., 2000a ; Ichihara et al., 2000b)	High
Endocrine	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	NOAEL= 800 (F)	No effects on organ weights or histopathology	(Yamada et al., 2003)	High
Endocrine	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on organ weights or histopathology	(ClinTrials, 1997a)	High
Endocrine	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on organ weights	(NTP, 2011a)	High
Endocrine	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Endocrine	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0/group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 500 (M)	Decreased absolute weights of adrenals and pituitary (F ₁)	(WIL Research, 2001)	High
Endocrine	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250 (F)	Necrosis of adrenal cortex (moderate to marked)	(NTP, 2011a)	High
Endocrine	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Gastro-intestinal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Gastro-intestinal	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Hemato-logical	Acute	Rat, M (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 8500 (M)	No effects on hematology parameters	(Elf Atochem, 1997)	N/A
Hemato-logical	Short-term	Rat (n=20/group)	Inhalation	0, 398, 984 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 398	Decreased erythrocyte parameters	(ClinTrials, 1997b)	N/A
Hemato-logical	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/ week for 5 or 7 weeks	LOAEL= 1000 (M)	Decreased mean corpuscular volume	(Yu et al., 2001)	Medium
Hemato-logical	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 300	Decreased WBCs, RBCs, hematocrit and MCV; increased Hgb and MCH	(Kim et al., 1999a)	N/A
Hemato-logical	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 400 (M)	Decreased MCHC; increased MCV	(Ichihara et al., 2000b)	High
Hemato-logical	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 400 (F)	Decreased WBC and absolute lymphocytes (at 6 weeks)	(ClinTrials, 1997a)	High
Hemato-logical	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on hematology parameters	(NTP, 2011a)	High
Hemato-logical	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on hematology parameters	(NTP, 2011a)	High

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Immune	Short-term/Subchronic	Rat, F344/N, F (n=8/group)	Inhalation, whole body, vapor	0, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	NOAEL= 500 (F)	Decreased spleen IgM response to SRBC; decreased T cells	(Anderson et al., 2010)	Medium
Immune	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on histopathology (thymus and spleen)	(Kim et al., 1999a)	N/A
Immune	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on organ weights or histopathology (spleen and thymus)	(Ichihara et al., 2000b)	High
Immune	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	NOAEL= 800 (F)	No effects or organ weights or histopathology (spleen and thymus)	(Yamada et al., 2003)	High
Immune	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No immune effects	(ClinTrials, 1997a)	High
Immune	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High
Immune	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Immune	Reproductive/Developmental	Rat, CrI:CD(SD)IGS BR, M/F (n=50 F0/group; 49-50 F1 adults/group; 41-47 F1 weanlings/group; 30-44 F2 weanlings/group))	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 750	Increased brown pigment in the spleen	(WIL Research, 2001)	High
Immune	Short-term/Subchronic	Mouse, B6C3F1, F (n=5-8/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	LOAEL= 125 (F)	Decreased spleen IgM response to SRBC	(Anderson et al., 2010)	Medium
Immune	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High
Immune	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Immune	Acute	Mouse, BALB/c, F (n=5/group)	Oral, gavage (corn oil vehicle)	0, 200, 500 or 1000 mg/kg	Single exposure; necropsy after 6, 12, 24 or 48 hours	LOAEL= 200 mg/kg (F)	Reduced antibody response to T-antigen; used for weight of evidence; no route-to-route extrapolation	(Lee et al., 2007)	N/A
Hepatic	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 125 (M)	Increased absolute and relative liver weights	(NTP, 2011a)	High
Hepatic	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/week for 5 or 7 weeks	LOAEL= 1000 (M)	No effects on histopathology	(Yu et al., 2001)	Medium
Hepatic	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/week for 8 weeks	NOAEL= 50 (M)	Increased relative liver weight	(Kim et al., 1999b)	N/A
Hepatic	Subchronic	Rat, Wistar, M (n=10/group)	Inhalation, whole body, vapor	0, 700 or 1500 ppm	6 hours/day, 5 days/ week for 4 and 12 weeks	LOAEL= 700 (M)	Decreased plasma ALT activity	(Fucta et al., 2002b)	N/A
Hepatic	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 400 (M)	Increased absolute and relative liver weight	(Ichihara et al., 2000b)	High
Hepatic	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	LOAEL= 1016 mg/m3 (F)	Increased absolute and relative liver weight	(Yamada et al., 2003)	High

Target Organ/System	Study Type	Species/ Strain/Sex (Number/ group) ¹	Exposure Route	Doses/ Concentrations ²	Duration ³	Effect Dose/ Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Hepatic	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	LOAEL= 100 (M)	Increased incidence of cytoplasmic vacuolization	(ClinTrials, 1997a)	High
Hepatic	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 125 (F)	Increased liver weight; increased incidence of cytoplasmic vacuolization	(NTP, 2011a)	High
Hepatic	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Hepatic	Repro- ductive/ Develop- mental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0/group; 49- 50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre- mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 100 (M)	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	(WIL Research, 2001)	High
Hepatic	Repro- ductive/ Develop- mental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0/group; 49- 50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre- mating (≥70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	NOAEL= 250 (F)	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	(WIL Research, 2001)	High
Hepatic	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 250 (M)	Centrilobular necrosis (mild to moderate)	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Hepatic	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 50 (M)	Hepatocellular degeneration and focal necrosis	(Liu et al., 2009)	High
Hepatic	Short-term	Mouse, C57BL/6J (<i>Nrf2</i> -null and wild-type), M (n=8/genotype/group)	Inhalation, whole body, vapor	0, 100 or 300 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 100 (M)	Necrosis and hepatocyte degeneration	(Liu et al., 2010)	N/A
Hepatic	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250	Necrosis and hepatocyte degeneration	(NTP, 2011a)	High
Hepatic	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Hepatic	Chronic	Rat, M (n=10/group)	Oral	0, 200, 400 or 800 mg/kg-day	16 weeks	LOAEL= 200 mg/kg-day (M)	Increased relative liver weight; used for weight of evidence; no route-to-route extrapolation	(Wang et al., 2012)	N/A
Hepatic	Acute	Mouse, BALB/c, F (n=5/group)	Oral, gavage (corn oil vehicle)	0, 200, 500 or 1000 mg/kg	Single exposure; necropsy after 6, 12, 24 or 48 hours	NOAEL= 200 mg/kg (F)	Centrilobular hepatocyte swelling	(Lee et al., 2007)	N/A
Metabolic	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on electrolyte or glucose levels	(ClinTrials, 1997a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Musculo-skeletal	Subchronic	Rat, Wistar, M (n=2/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 400 (M)	Alteration in soleus muscle myofilaments	(Ichihara et al., 2000a)	High
Musculo-skeletal	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Musculo-skeletal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Musculo-skeletal	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Musculo-skeletal	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Musculo-skeletal	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Neurological	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 50 (M)	Decreased relative brain weight	(Kim et al., 1999a)	N/A
Neurological	Acute	Rat, Sprague-Dawley, M/F (n=10/group)	Inhalation, whole body, vapor	0, 11,000, 13,000, 15,000 or 17,000 ppm	4 hours	LOAEL= 11,000	Ataxia, lacrimation, decreased activity	(Kim et al., 1999a)	N/A
Neurological	Short-term	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day for 7 days	LOAEL= 200 (M)	Altered neuron-specific proteins and ROS	(Wang et al., 2002)	N/A
Neurological	Short-term	Rat, Wistar, M (n=12/group)	Inhalation, whole body, vapor	0, 200, 400, 800 or 1000 ppm	8 hours/day for 7 or 28 days	LOAEL= 200 (M)	Decreased hippocampal glucocorticoid receptor expression	(Zhang et al., 2013)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term	Rat, Wistar, M (n=6-13/exposure group; n=6-10/control group)	Inhalation, whole body, vapor	0 or 1500 ppm	6 hours/day, 5 days/ week for 1, 3 or 4 weeks	LOAEL= 1500 (M)	Paired pulse disinhibition (DG and CA1 pyramidal neuron); neuronal dysfunction in dentate gyrus; convulsive behaviors	(Fueta et al., 2002a ; Fueta et al., 2002b)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 1 or 4 weeks	LOAEL= 400 (M)	Altered regulation and expression of hippocampal proteins	(Huang et al., 2011)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 1 or 4 weeks	LOAEL= 400 (M)	Increased hippocampal ROS levels	(Huang et al., 2012)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 1 or 4 weeks	LOAEL= 400 (M)	Altered regulation and expression of hippocampal proteins	(Huang et al., 2015)	N/A
Neurological	Short-term	Rat, F344, M (n=2/group)	Inhalation, whole body, vapor	0, 10, 50 or 200 ppm	8 hours/day, 7 days/week for 3 weeks	NOAEL= 10 (M)	Increased spontaneous locomotor activity	(Honma et al., 2003)	High
Neurological	Short-term	Rat, F344, M (n=5/group)	Inhalation, whole body, vapor	0, 10, 50, 200 or 1000 ppm	8 hours/day, 7 days/ week for 3 weeks	NOAEL= 50 (M)	Decreased time hanging from a suspended bar	(Honma et al., 2003)	High
Neurological	Short-term	Rat, F344, M (n=4-5/group)	Inhalation, whole body, vapor	0, 50, 200 or 1000 ppm	8 hours/day, 7 days/ week for 3 weeks	LOAEL= 50 (M)	Altered neurotransmitter and metabolites	(Suda et al., 2008)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	LOAEL= 398	Histo-pathological abnormalities in the CNS	(ClinTrials, 1997b)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 4 weeks	NOAEL= 400 (M)	Changes in the mRNA expression of serotonin, dopamine, and GABA receptors	(Mohideen et al., 2009)	N/A
Neurological	Short-term	Rat, F344, M (n=6/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 4 weeks	NOAEL= 400 (M)	Decreased density of noradrenergic axons in frontal cortex and amygdala	(Mohideen et al., 2011)	N/A
Neurological	Short-term	Rat, F344, M (n=12/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/week for 4 weeks	LOAEL= 400 (M)	Increased astrogliosis	(Mohideen et al., 2013)	High
Neurological	Short-term	Rat, Wistar-ST, M (n=12/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 400 (M)	Morphological changes in cerebellar microglia and increased ROS	(Subramania n et al., 2012)	N/A
Neurological	Short-term	Rat, M (n=8/group)	Inhalation, whole body	0 or 1500 ppm	6 hours/day, 5 days/ week for 4 weeks	LOAEL= 1500 (M)	Decreased activity, behavioral abnormalities, movement disorders, histo-pathological changes in Purkinje cells	(Ohnishi et al., 1999)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term/Subchronic	Rat, Wistar, M (n=7-14/group)	Inhalation, whole body, vapor	0 or 700pm	6 hours/day, 5 days/week for 4, 8 or 12 weeks	LOAEL= 700 (M)	Paired pulse disinhibition in ex vivo hippocampal slices (DG and CA1 pyramidal neuron)	(Fucta et al., 2004)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/ week for 5 or 7 weeks	LOAEL= 1000 (M)	Movement disorder, altered motor nerve conduction velocity and distal nerve latency in tail nerve); histo-pathological changes to CNS and PNS	(Yu et al., 2001)	Medium
Neurological	Subchronic	Rat, Wistar, M (n=24/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/ week for 6 weeks	NOAEL= 400 (M)	Movement disorder, decreased hind limb grip strength	(Banu et al., 2007)	N/A
Neurological	Subchronic	Rat, Wistar M (n=12/group)	Inhalation, whole body, vapor	0 or 700 ppm	6 hours/day, 5 days/ week for 8 weeks	LOAEL= 700 (M)	Paired pulse disinhibition in ex vivo hippocampal slices (DG and CA1 pyramidal neuron); increased protein kinase activities	(Fucta et al., 2002a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Subchronic	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0, 200 or 400 ppm	6 hours/day, 5 days/ week for 8 or 12 weeks	NOAEL= 200 (M)	Paired pulse disinhibition in ex vivo hippocampal slices (DG and CA1 pyramidal neuron)	(Fueta et al., 2007)	Medium
Neurological	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on brain histopathology	(Kim et al., 1999a)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	LOAEL= 200 (M)	Decreased hind limb grip strength	(Ichihara et al., 2000a)	High
Neurological	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	LOAEL= 200 (M)	Altered neuron-specific proteins and increased ROS	(Wang et al., 2003)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0 or 400 ppm	6 hours/day, 5 days/ week for 12 weeks	LOAEL= 400 (M)	Changes in gene expression of anti-apoptotic proteins in astrocytes	(Yoshida et al., 2007)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=8/group)	Inhalation, whole body, vapor	0 or 400 ppm	6 hours/day, 5 days/ week for 12 weeks	LOAEL= 400 (M)	Decreased paired pulse inhibition in ex vivo hippocampal slices (dentate gyrus)	(Ueno et al., 2007)	N/A

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No changes based on functional observational battery, motor activity, organ weight, or histopathology	(ClinTrials, 1997a)	High
Neurological	Chronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 200, 500 or 1250 ppm	6 hours/day, 5 days/week for 13 weeks	NOAEL= 1250	No effects histopathology of central or peripheral nervous tissues	(Sohn et al., 2002)	N/A
Neurological	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 1000	Hindlimb splay	(NTP, 2011a)	High
Neurological	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects	(NTP, 2011a)	High
Neurological	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0 /group; 49-50 F1 adults/group; 41-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 100	Decreased brain weight (F ₀)	(WIL Research, 2001)	High
Neurological	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50/group/generation)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	LOAEL= 100 (M)	Decreased brain weight (weanling and adult F ₁)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0 /group; 49-50 F1 adults/group; 41-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 250	Decreased brain weight (weanling F ₂)	(WIL Research, 2001)	High
Neurological	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.1 hours/day, 5 days/week for 17 days	NOAEL= 2000	No effects	(NTP, 2011a)	High
Neurological	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects	(NTP, 2011a)	High
Neurological	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects	(NTP, 2011a)	High
Neurological	Short-term	Rat, Wistar, M (n=14/group)	Oral, gavage	0, 100, 200, 400 or 800 mg/kg-day	12 days	LOAEL= 100 mg/kg-day (M)	Impaired spatial learning and memory; neuron loss in prelimbic cortex; increased ROS in cerebral cortex	(Guo et al., 2015)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term	Rat, Wistar, M (n=10/group)	Oral, gavage (corn oil vehicle)	0, 200, 400 or 800 mg/kg-day	12 days	LOAEL= 200 mg/kg-day (M)	Impaired spatial learning and memory. Used for weight of evidence	(Zhong et al., 2013)	Low
Neurological	Chronic	Rat, M (n=10/group)	Oral	0, 200, 400 or 800 mg/kg-day	16 weeks	LOAEL= 200 mg/kg-day (M)	Decreased hindlimb grip strength; increased gait score; used for weight of evidence; no route-to-route extrapolation	(Wang et al., 2012)	N/A
Neurological	Short-term	Rat, Wistar, M (n=7-9/group)	Sub-cutaneous	0, 3.7 or 11 mmol/kg-day	4 weeks	LOAEL= 3.7 mmol/kg-day (M)	Increased tail motor nerve latency	(Zhao et al., 1999)	N/A
Ocular	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Ocular	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Ocular	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Ocular	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Ocular	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Renal	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	LOAEL= 125 (F)	Increased relative kidney weight	(NTP, 2011a)	High
Renal	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 398	Changes in BUN, total bilirubin, and total protein levels	(ClinTrials, 1997b)	N/A
Renal	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/week for 5 or 7 weeks	NOAEL= 1000 (M)	No effects on histopathology	(Yu et al., 2001)	Medium
Renal	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50 to 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 300	Decreased urobilinogen (males); increased bilirubin (females)	(Kim et al., 1999a)	N/A
Renal	Reproductive	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on kidney weight or histopathology	(Ichihara et al., 2000b)	High
Renal	Reproductive	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	LOAEL= 200 (F)	Increased absolute and relative kidney weight	(Yamada et al., 2003)	High
Renal	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600 (M)	No effects on urinalysis parameters, or organ weights	(ClinTrials, 1997a)	High
Renal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500 (F)	Increased absolute and relative kidney weights	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Renal	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Renal	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100 to 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL = 100 (M)	Increased incidence of pelvic mineralization (F ₀)	(WIL Research, 2001)	High
Renal	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	NOAEL = 100 (F)	Increased incidence of pelvic mineralization (F ₀)	(WIL Research, 2001)	High
Renal	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 500 (F)	Increased absolute and relative kidney weights	(NTP, 2011a)	High
Renal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250 (F)	Increased absolute and relative kidney weights	(NTP, 2011a)	High
Renal	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 350	No effects on histopathology	(NTP, 2011a)	High

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Acute	Rat, M (n=5/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 8500 (M)	No effects on histopathology of the testes	(Elf Atochem, 1997)	N/A
Reproductive	Short-term	Rat, F344, F (n=7-8/group)	Inhalation, whole body, vapor	50, 200 or 1000 ppm	8 hours/day, 7 days/ week for 3 weeks	NOAEL= 1000 (F)	No effects on number of days per estrous cycle or ovary and uterus weights	(Sekiguchi et al., 2002)	N/A
Reproductive	Short-term	Rat, M (n=10/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 1000 (M)	Microscopic lesions in male reproductive system	(ClinTrials, 1997b)	N/A
Reproductive	Subchronic	Rat, Wistar, M (n=24/group)	Inhalation, whole body, vapor	400, 800 or 1000 ppm	8 hours/day, 7 days/ week for 6 weeks	LOAEL= 400 (M)	Decreased epididymal sperm count	(Banu et al., 2007)	N/A
Reproductive	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/ week for 5 or 7 weeks	NOAEL= 1000 (M)	No effects on testis histopathology	(Yu et al., 2001)	Medium
Reproductive	Reproductive	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	LOAEL= 200 (F)	Decreased number of antral follicles	(Yamada et al., 2003)	High
Reproductive	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	50-1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 300	Increased relative ovary weight	(Kim et al., 1999a)	N/A
Reproductive	Reproductive	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	LOAEL = 200 (M)	Decreased relative seminal vesicle weight	(Ichihara et al., 2000b)	High

Target Organ/System	Study Type	Species/ Strain/Sex (Number/ group) ¹	Exposure Route	Doses/ Concentrations ²	Duration ³	Effect Dose/ Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on organ weights	(ClinTrials, 1997a)	High
Reproductive	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	LOAEL= 250 (M)	Decreased sperm motility	(NTP, 2011a)	High
Reproductive	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	LOAEL= 250 (F)	Alterations in estrous cycles	(NTP, 2011a)	High
Reproductive	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology of reproductive organs	(NTP, 2011a)	High
Reproductive	Repro- ductive/ Develop- mental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre- mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 250 (M)	Decreased percent motile sperm (F ₀)	(WIL Research, 2001)	High
Reproductive	Repro- ductive/ Develop- mental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre- mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 250 (M)	Decreased percent normal sperm morphology (F ₀)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0/group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 100 (M)	Decreased absolute prostate weight (F ₀)	(WIL Research, 2001)	High
Reproductive	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0/group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	NOAEL= 250 (F)	Increase in estrous cycle length (F ₀)	(WIL Research, 2001)	High
Reproductive	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 50 (M)	Decreased sperm count and motility and/or increased abnormal sperm	(Liu et al., 2009)	High
Reproductive	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/ week for 14 weeks	NOAEL= 125 (M)	Decreased epididymis weight and sperm motility	(NTP, 2011a)	High
Reproductive	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	LOAEL= 125 (F)	Alterations in estrous cycles	(NTP, 2011a)	High

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology of reproductive organs	(NTP, 2011a)	High
Reproductive	Short-term	Rat, Sprague-Dawley, M (n=7/group)	Intra-peritoneal	0 or 1000 mg/kg-day	14 days	LOAEL= 1000 (M)	Decreased epididymal sperm count; decreased epididymis and prostate + seminal vesicle weights	(Xin et al., 2010)	N/A
Respiratory	Acute	Rat (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 6040	Pulmonary edema and emphysema	(Elf Atochem, 1997)	N/A
Respiratory	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 100 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 250 (M)	Nasal lesions (including suppurative inflammation and respiratory epithelial necrosis)	(NTP, 2011a)	High
Respiratory	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 994	Histo-pathological changes in nasal cavities	(ClinTrials, 1997b)	N/A
Respiratory	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on lung weight or histopathology	(Ichihara et al., 2000b)	High

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Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Respiratory	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on lung weight or histopathology	(Kim et al., 1999a)	N/A
Respiratory	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on lung weight or histopathology	(ClinTrials, 1997a)	High
Respiratory	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on lung weight or histopathology	(NTP, 2011a)	High
Respiratory	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	LOAEL= 635 mg/m3	Chronic active nasal inflammation and squamous metaplasia in the larynx	(NTP, 2011a)	High
Respiratory	Reproductive/ Developmental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in F ₀ males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in F ₀ females	NOAEL= 750	No effects on lung weight or histopathology	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Respiratory	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 250	Lesions in the lung and nose	(NTP, 2011a)	High
Respiratory	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250	Cytoplasmic vacuolization in the nose, larynx, trachea, and lung	(NTP, 2011a)	High
Respiratory	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	LOAEL= 62.5	Histo-pathological lesions in the nasal respiratory epithelium, larynx, trachea, and bronchioles	(NTP, 2011a)	High
Developmental Effects	Developmental	Rat, Wistar-Imamichi, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 400 or 800 ppm	8 hours/day during gestation (GDs 0-21) and lactation (PNDs 1-21)	NOAEL= 100	Decreased survival during lactation	(Furuhashi et al., 2006)	N/A
Developmental Effects	Developmental	Rat, Albino Crl:CD(SD)IG S BR, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 199, 598 or 996 ppm	6 hours/day on GDs 6-19; PNDs 4-20	NOAEL= 199	Decreased body weight gain in pups	(Huntingdon Life Sciences, 1999)	N/A
Developmental Effects	Developmental	Rat (n=25/group)	Inhalation	0, 103, 503 or 1005 ppm	6 hours/day on GDs 6-19; PNDs 4-20	LOAEL = 103	Decreased fetal weight	(Huntingdon Life Sciences, 2001)	N/A

Target Organ/System	Study Type	Species/ Strain/Sex (Number/ group) ¹	Exposure Route	Doses/ Concentrations ²	Duration ³	Effect Dose/ Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Develop- mental Effects	Repro- ductive/ Develop- mental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre- mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 250	Decreased live litter size (F ₁ females)	(WIL Research, 2001)	High
Develop- mental Effects	Repro- ductive/ Develop- mental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre- mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL = 100	Decreased pup body weights (F ₁ PND 28 males)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Developmental Effects	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL = 250	Decreased pup body weights (F ₂ PNDs 14 and 21 males)	(WIL Research, 2001)	High
Developmental Effects	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL = 250	Decreased pup body weights (F ₂ PNDs 14 and 21 females)	(WIL Research, 2001)	High

¹Species/strain, sex of animals included in the study.²Doses and concentrations – values were reported in [2016 Draft Risk Assessment \(U.S. EPA, 2016d\)](#) for 1-BP.³Acute exposures defined as those occurring within a single day (<24 hr). Short-term exposures are defined as 1-30 days. Subchronic exposures are defined as 30-90 days. Chronic exposures are defined as >90 days, or 10% or more of a lifetime.⁴Units are mg/m³ for inhalation exposure and mg/kg-day for oral exposure; sex is identified if one sex has a lower POD; this includes only the PODs identified by the study authors.

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⁵The effect(s) listed were the most sensitive effects observed for that target organ/system in that study (i.e., the effect(s) upon which the POD was based).

⁶This column lists the primary reference for the reported data.

⁷Information included in this column is the result of the data quality evaluation for all acceptable studies (those with an overall rating of high, medium or low). Unacceptable studies are not included in this table.

⁸N/A: Only key and supporting studies carried forward for dose-response analysis in the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016d](#)) for 1-BP, in addition to any new studies since that time, went through systematic review.

I.5 Carcinogenicity and Mutagenicity

There are no epidemiological studies on the effects of 1-BP exposure on human cancer.

The carcinogenicity of 1-BP has been studied in rats and mice in a two-year bioassay by the National Toxicology Program ([NTP, 2011a](#)). Groups of 50 male and 50 female rats and mice were exposed to 1-BP vapor at concentrations of 62.5, 125, or 250 ppm (mice) and 125, 250, or 500 ppm (rats), 6 hours per day, 5 days per week for up to 105 weeks. Similar groups of 50 animals were exposed to clean air in the same inhalation chambers as the control groups. All animals were observed twice daily. Clinical findings were recorded for all animals every 4 weeks through week 93, every 2 weeks thereafter, and at the end of the studies. Rats and mice were weighed initially, weekly for the first 13 weeks, then every 4 weeks through week 93, every 2 weeks thereafter, and at the end of the studies. Complete necropsies and microscopic examinations were performed on all rats and mice.

At the end of the two-year bioassay, there were treatment-related skin tumors in male rats and large intestine tumors in female rats. Significantly increased incidence of lung tumors was found in female mice. Based on increased incidences of tumors in rats and mice, at multiple sites and the occurrence of rare tumors, it has been concluded that there is sufficient evidence of carcinogenicity in experimental animals for 1-BP. Each of these tumor types is described below.

I.5.1 Skin Tumors

In male rats, there were exposure concentration treatment-related increased incidences of keratoacanthoma, keratoacanthoma or squamous cell carcinoma (combined); and keratoacanthoma, basal cell adenoma, basal cell carcinoma, or squamous cell carcinoma (combined). The incidences of keratoacanthoma and of keratoacanthoma or squamous cell carcinoma (combined) in 250 ppm (12%) and 500 ppm (12%) males were significantly increased as compared to the controls (0% and 2%), and exceeded the historical control ranges (0-8%) for inhalation studies. The incidences of keratoacanthoma, basal cell adenoma, basal cell carcinoma, or squamous cell carcinoma (combined) were significantly increased in all exposed groups of males (125 ppm: 14%; 250 ppm: 18%; and 500 ppm: 20%) as compared to the controls (2%) and exceeded the historical control range (0-10%) for inhalation studies. In female rats, there were increased incidences of squamous cell papilloma, keratoacanthoma, basal cell adenoma, or basal cell carcinoma (combined) in the 500 ppm group (8%) as compared to the control (2%). Although the increased incidences were not significant, they exceeded the respective historical control ranges for inhalation studies.

I.5.2 Large Intestine Tumors

Large intestine tumors are rare tumors in the rat. The incidence of adenoma of the large intestine (colon or rectum) in 500 ppm females (5/50, 10%) was significantly greater than that in the controls (0%). The incidences in the 250 ppm (2%) and 500 ppm (4%) groups of females exceeded the historical controls in inhalation studies (0.1%). In 250 (4%) and 500 (2%) ppm males, the incidences of adenoma of the large intestine were slightly increased compared to that in the controls (0%); although the increases were not statistically significant, the incidence in the 250 ppm group (4%) exceeded the historical control ranges (0-2%) for inhalation studies.

I.5.3 Lung Tumors

In the female mice, there were treatment-related increased incidences of alveolar/bronchiolar adenoma, alveolar/bronchiolar carcinoma, and alveolar/bronchiolar adenoma or carcinoma

(combined). The incidence of alveolar/bronchiolar adenoma in 250 ppm females (20%) and the incidences of alveolar/bronchiolar carcinoma in 62.5 ppm (14%) and 125 ppm (10%) females were significantly increased as compared to the controls (0-2%). The incidences of alveolar/bronchiolar adenoma or carcinoma (combined) were significantly increased in all exposed groups (18%, 16% and 28% in low-, mid- and high-dosed groups) as compared to the controls (2%).

I.5.4 Pancreatic Tumors

The evidence that 1-BP exposure was associated with an increased incidence of pancreatic islet adenoma in male rats was equivocal. Although the incidences of pancreatic islet adenoma were significantly increased in all exposed groups compared to the chamber controls (0%, 10%, 8%, 10%), the incidences were within the historical control ranges for inhalation studies (0% to 12%). The incidences of pancreatic islet carcinoma in exposed male rats were not significantly different from that in the chamber controls and were not considered treatment related. The incidences of pancreatic islet adenoma or carcinoma (combined) were significantly increased only in the low-dose (20%) and mid-dose groups (18%) as compared with the chamber controls (6%); only the incidence in the low-dose group (20%) exceeded the historical control ranges for inhalation studies (6% to 18%).

I.5.5 Malignant Mesothelioma

There were increased incidences of malignant mesothelioma in male rats exposed to 1-BP as compared to the chamber controls: control, 0%; low-dose, 4%; mid-dose, 4%; and high-dose, 8%. The incidence of malignant mesothelioma in high-dose group (8%) was significantly greater than that of the chamber controls (0%) and exceeded that of the historical controls (0-6%) in inhalation studies. The overall strength of this evidence was considered equivocal because the increased incidence in the high-dose (500 ppm) group was barely outside the historical control range (0% to 6%).

Under the conditions of these 2-year inhalation studies, there was clear evidence of carcinogenic activity of 1-BP in female F344/N rats based on increased incidences of adenoma of the large intestine. Increased incidences of skin neoplasms may also have been related to 1-BP exposure. There was some evidence of carcinogenic activity of 1-BP in male F344/N rats based on the increased incidences of epithelial neoplasms of the skin (keratoacanthoma, squamous cell carcinoma, and basal cell neoplasms). Increased incidences of malignant mesothelioma and pancreatic islet adenoma and carcinoma (combined) may also have been related to 1-BP exposure. There was clear evidence of carcinogenic activity of 1-BP in female B6C3F1 mice based on increased incidences of alveolar/bronchiolar neoplasms. There was no evidence of carcinogenic activity of 1-BP in male B6C3F1 mice exposed to concentrations of 62.5, 125, or 250 ppm 1-BP. Based on increased incidences of tumors in rats and mice, at multiple sites and the occurrence of rare tumors, it has been concluded that there is sufficient evidence of carcinogenicity in experimental animals for 1-BP. The compound has been considered to be “reasonably to be anticipated as a human carcinogen” and will be listed in the next issue of Report on Carcinogens of the National Toxicology Program ([NTP, 2013a](#)).

The tumor data on the skin, large intestine and lung in male and female rats and female mice (Table_Apx I-3) may be used for quantitative assessment of the potential risk of humans exposed to 1-BP.

Table Apx I-3. Tumors induced by 1-BP in Rats and Mice

Animal	Tumor	Concentration (ppm)	Incidence
F344/N rats, male	Skin (keratoacanthoma, squamous-cell carcinoma, basal-cell adenoma or carcinoma combined)	0	1/50 (2%)
		125	7/50* (14%)
		250	9/50** (18%)
		500	10/50** (20%)
		Trend	$p=0.003$
F344/N rats, female	Large intestine (colon or rectum adenoma)	0	0/50 (0%)
		125	1/50 (2%)
		250	2/50 (4%)
		500	5/50* (10%)
		Trend	$p=0.004$
B6C3F1 mice, female	Lung (alveolar /bronchiolar adenoma or carcinoma combined)	0	1/50 (2%)
		62.5	9/50** (18%)
		125	8/50* (16%)
		250	14/50*** (28%)
		Trend	$p<0.001$

* $p<0.05$; ** $p<0.01$; *** $p<0.001$

I.5.6 Genotoxicity

1-BP has been shown to bind covalently to DNA to form N7-guanine adducts in an *in vitro* system using calf thymus DNA ([Lee et al., 2007](#)). This is supportive of possible genotoxic potential; however, further studies are needed, particularly *in vivo* studies, to provide further information for MOA consideration.

Mixed results have been reported in genotoxicity tests using bacteria. 1-BP was mutagenic in a dose-dependent manner in *Salmonella typhimurium* (*S. typhimurium*) strains TA100 and TA1535 when the assay was conducted using closed chambers/desiccators specifically designed for testing volatile substances ([Barber et al., 1981](#)). The data suggest that 1-BP may be a direct-acting mutagen since similar responses were observed both with and without metabolic activation. A number of other studies reported negative responses in *S. typhimurium* and *Escherichia coli* (*E. coli*) but some of these studies were not conducted using the appropriate methodology (*i.e.*, treatment and incubation in a closed chamber) for testing a volatile substance ([NTP, 2011a](#); [Kim et al., 1998](#); [Elf Atochem, 1993b](#)). An NTP peer review committee considered Barber ([1981](#)) to be a well conducted study ([NTP, 2013a](#)).

1-BP was shown to induce base-pair mutations in the L5178Y mouse lymphoma cell assay, with and without S9 metabolic activation ([Elf Atochem, 1996b](#)). Using the comet assay, ([Toraason et al., 2006](#)) demonstrated DNA damage in human leukocytes exposed to 1 mM 1-BP *in vitro*; there was also limited evidence that leukocytes from workers exposed to 1-BP may present risk for increased DNA damage. In contrast to the positive *in vitro* studies, negative results were reported with *in vivo* micronucleus assays in mice exposed to 1-BP via intraperitoneal (ip) injection ([Kim et al., 1998](#)), and in rats exposed via inhalation ([NTP, 2011a](#); [Elf Atochem, 1995](#)). It should be noted, however, that a recent compilation of *in vivo* micronucleus data by ([Benigni et al., 2012](#)) showed a low correlation between *in vivo* micronucleus data and carcinogenicity, suggesting a potential for

“false negative” predictions. 1-BP was also produced negative results in dominant lethal mutation assays conducted in ICR mice ([Yu et al., 2008](#)) and Sprague-Dawley rats ([Saito-Suzuki et al., 1982](#)).

Weinberg ([2016](#)) determined mutation frequencies at the *cH* gene in the liver, lung, and colon in groups of 7 female B6C3F1 heterozygous transgenic Big Blue® mice (mutations were evaluated in 6 mice/group) that were exposed by whole-body inhalation to target 1-BP vapor concentrations of 0 (concurrent control), 62.5, 125, or 250 ppm (mean measured concentrations of 0, 62.8, 125, and 258 ppm, respectively) for 6 hours/day, 5 days/week for 4 weeks. Liver, lung, and colon tissues were collected for DNA isolation and determination of mutation frequencies on the third day after the final exposure. Compared with controls, groups exposed to 1-BP showed no statistically significant elevations in mutation frequencies at the *cH* gene in liver, lung, or colon and showed no treatment-related effects on clinical observations, body weights, food consumption, or organ weights. Mutation frequencies in the liver, lung, and colon from concurrent negative control mice were comparable to values found in historical negative controls. In a positive control group that received 40 mg/kg of the direct-acting mutagen ethyl nitrosourea by gavage on study days 1, 2, and 3, mutation frequencies on study day 31 were statistically significantly elevated in liver, lung, and colon, thus demonstrating the ability of this test system to detect mutations.

Young ([2016](#)) evaluated mutation frequencies at the *cH* gene in the liver and lung in groups of 6 female B6C3F1 heterozygous transgenic Big Blue® mice (mutations were evaluated in 5-6 mice/group) exposed by whole-body inhalation to target 1-BP vapor concentrations of 0 (concurrent control), 62.5, 125, or 250 ppm (mean measured concentrations of 0, 63.0, 128, and 251 ppm, respectively) for 6 hours/day, 7 days/week for 4 weeks. Liver and lung tissues were collected for DNA isolation and determination of mutation frequencies on the third day after the final exposure. Compared with controls, groups exposed to 1-BP showed no statistically significant elevations in mutation frequencies at the *cH* gene in liver or lung and showed no treatment-related effects on clinical observations, body weights, food consumption, or organ weights. Mutation frequencies in the liver and lung from concurrent negative control mice were comparable to values found in historical negative controls. In a positive control group that received 40 mg/kg of the direct-acting mutagen ethyl nitrosourea by gavage on study days 1, 2, and 3, mutation frequencies on study day 31 were statistically significantly elevated in liver and lung, thus demonstrating the ability of this test system to detect mutations.

Several known or proposed metabolites of 1-BP have been shown to be mutagenic ([NTP, 2014](#); [IARC, 2000, 1994](#)). For example, both glycidol and propylene oxide are mutagenic in bacteria, yeast, *Drosophila*, and mammalian cells. These compounds have also been shown to induce DNA and chromosomal damage in rodent and human cells, and can form DNA adducts *in vitro*. α -Bromohydrin and 3-bromo-1-propanol were mutagenic in the *S. typhimurium* reversion assay, and 3-bromo-1-propanol and 1-bromo-2-propanol induced DNA damage in *E. coli*. The available *in vivo* test results for glycidol indicate that it induces micronucleus formation, but not chromosomal aberrations in mice. Studies of propylene oxide indicated chromosomal damage evidenced by positive responses for micronucleus induction in mouse bone marrow and chromosomal aberration tests; DNA damage was evident in the sister chromatid exchange (SCE) assay.

Table Apx I-4. Genotoxicity of 1-BP In Vitro

Species (test system)	End point	Results		Reference
		With activation	Without activation	
Prokaryotic organisms:				
<i>S. typhimurium</i> TA98, TA100, TA1535, TA1537, TA1538	Reverse mutation	– (open test system)	– (open test system)	(Barber et al., 1981)
<i>S. typhimurium</i> TA100, TA1535	Reverse mutation	+ (closed test system)	+ (closed test system)	(Barber et al., 1981)
<i>S. typhimurium</i> TA97, TA98, TA100, TA 1535	Reverse mutation	–	–	(NTP, 2011a)
<i>Escherichia coli</i> Wp2 uvrA/pKM101	Reverse mutation	–	–	(NTP, 2011a)
Mammalian cells:				
Human hepatoma cell-line (HepG2)	DNA damage and repair, single strand breaks	–		(Hasspieler et al., 2006)
Human hepatoma cell-line (HepG2)	DNA damage and repair, repair activity	–		(Hasspieler et al., 2006)
Human leukocyte cells	DNA damage and repair	+		(Toraason et al., 2006)
+ = positive results; – = negative results				

1.5.7 Comparison of Bacterial Reverse Mutation Studies

Two bacterial reverse mutation studies of 1-BP both used test systems characterized as ‘closed’ but yielded different results for mutagenicity. In a study by Barber et al. ([1981](#)), a positive mutagenicity result was observed for 1-BP in *Salmonella typhimurium* strains TA 1535 and TA 100 (but not TA 1537, TA 1538, or TA 98) in the presence and absence of metabolic activation. In contrast, a study by BioReliance ([2015](#)) found no evidence of mutagenicity in *S. typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537 or *Escherichia coli* strain WP2 uvrA (a DNA repair-deficient strain) in the presence or absence of metabolic activation.

In many respects, both studies adhered to OECD TG 471 (Bacterial Reverse Mutation Test ([2019p](#))), although only the BioReliance ([2015](#)) study indicated that it conformed to the test guidelines. However, the procedures outlined in the guideline pertain primarily to standard plate incorporation or preincubation methods; OECD TG 471 ([2019p](#)) notes that certain classes of mutagens (including volatile chemicals, such as 1-BP) are not detected using these methods. In these ‘special cases’, the guideline recommends the use of alternative approaches. The studies by Barber et al. ([1981](#)) and BioReliance ([2015](#)) used different methods in an effort to circumvent issues with respect to the volatility of the test substance.

The primary differences between the two studies were the method of exposure, the duration of exposure of test organisms to 1-BP, methods used to control for the volatility of the test substance, and differences between the studies in maintenance of effective concentrations of 1-BP during test organism exposure. Barber et al. ([1981](#)) indicated that the study followed the standard methods

originally described by Ames et al. (1975); only the method of chemical application was modified. Rather than using a standard plate-incorporation test, Barber designed a chemically inert, closed incubation system to test the mutagenicity of volatile chemicals, applied as a vapor. The test system consisted of several Pyrex containers, each designed to accommodate a metal rack housing up to 12 glass plates. The glass plates were considered chemically inert with respect to adsorption of halogenated hydrocarbons, in contrast to plastic plates. The Pyrex containers were fitted with Teflon tops with valve and septum assemblies. A blank plate, containing only sterile distilled water, was inserted into each test system and was used for measurement of the aqueous 1-BP concentration at the end of exposure. Test plates were prepared by mixing an inoculum of an overnight growth culture (growth phase not reported) with top agar (with or without S9 mix) and pouring the mixture onto a plate containing Vogel-Bonner Medium E and agar. The plates were allowed to solidify at room temperature and then placed onto a stainless-steel rack. The racks filled with plates were placed into the Pyrex containers and the containers were sealed. Under a partial vacuum, the liquid test substance was added through the septum using a syringe and was observed to vaporize, after which time air was reintroduced into each incubation system. The test systems were then incubated at 37°C for 48 hours, with continuous stirring to mix the internal atmosphere. Samples of the vapor, as well as aqueous samples, were taken from the test systems at the end of the 48-hour incubation period and analyzed by gas-liquid chromatography (GLC). The GLC results for the aqueous samples were used to calculate the amount of chemical dissolved per plate (i.e., 1.1, 2.3, 4.9, 9.0, or 20.3 $\mu\text{moles/plate}$, or about 0, 140, 280, 600, 1100, and 2500 $\mu\text{g/plate}$, based on a molecular weight for 1-BP of 122.9 g/mol). Numbers of revertant colonies were tabulated using a colony counter at the end of the 48-hour incubation period. The study authors indicated that advantages of using this system included: 1) an enhanced ability to detect mutagenicity of volatile chemicals in the closed system compared to the standard plate-incorporation test; 2) decreased exposure of laboratory personnel to volatile chemicals that are potentially mutagenic; 3) better simulation of actual exposure (frequently as a vapor); and 4) the purity of the test substance is obtained as part of the analytical result, minimizing the chance of false positives due to mutagenic impurities.

The BioReliance (2015) study tested the mutagenicity of 1-BP using a preincubation method, as described by Yahagi et al. (1977). After an initial toxicity-mutation assay, two confirmatory mutagenicity assays were conducted. Target concentrations of 1-BP tested were 1.5-5000 $\mu\text{g/plate}$ for the initial toxicity-mutation assay and 50-5000 $\mu\text{g/plate}$ for the confirmatory mutagenicity assays. To prepare the dosing formulations, the test substance was diluted in ethanol; the test substance was determined to be stable in this solvent at room temperature for at least 3.25 hours. Dosing formulations were prepared immediately before use. For the repeat test of the confirmatory assay, dilutions of 1-BP were prepared in screw-capped tubes with minimal headspace; it was unclear whether these measures to reduce volatilization were taken during the first confirmatory assay due to a lack of documentation. To prepare the preincubation solutions, the diluted test substance or vehicle (ethanol), S9, or sham mix (containing phosphate buffer), and the tester strain (late log growth phase) were added to glass culture tubes preheated to $37\pm 2^\circ\text{C}$. Tubes receiving the test substance were capped using screw caps (amount of headspace not reported) during the preincubation period, which lasted for 90 ± 2 minutes at $37\pm 2^\circ\text{C}$. Samples for analysis of test substance concentrations by gas chromatography (GC) were taken from the dosing formulations, as well as from the solutions in preincubation tubes (without metabolic activation) at the beginning and end of the preincubation period, from the vehicle control and lowest and highest exposure concentrations (positive controls not evaluated). Measured concentrations of 1-BP in dosing

formulations met acceptability criteria (85% to 115% of target concentrations, with < 5% relative standard deviation [RSD]), except for the low concentration of the second confirmatory assay (>5% RSD). A small peak of test substance was detected in the vehicle control dosing formulation used in the second confirmatory assay. Measured concentrations of 1-BP in preincubation tubes were much lower than target (nominal) concentrations. For the first confirmatory assay, the measured concentrations of 1-BP at the beginning of the preincubation period were 37% and 9% of the target concentrations at the lowest and highest exposure concentrations, respectively; by the end of the preincubation period, the measured concentrations had declined to 3% and 2%, respectively, of the target concentrations. For the second confirmatory assay, the measured concentrations at the beginning of the preincubation period were 7% and 4% of the target concentrations at the lowest and highest exposure concentrations, respectively; the measured concentrations at the end of the preincubation period were 5% and 3%, respectively, of the target concentrations. Following preincubation, top agar was added to the tube and the mixture was overlaid onto minimal bottom agar (Vogel-Bonner minimal medium E). Once solidified, plates containing the test substance were inverted and placed in desiccators by dose level for 48 to 72 hours at $37\pm 2^{\circ}\text{C}$ prior to scoring. Additional plates were prepared using only test substance, vehicle, S9, or sham mix to confirm the sterility of these solutions. Revertant colonies were counted either entirely by automatic colony counter or entirely by hand unless the plate exhibited toxicity (except for positive controls). Plates not scored immediately following the incubation period were stored at $2-8^{\circ}\text{C}$ until counting occurred. Although it was noted in the study report that the use of screw caps, intended to prevent evaporation of the test substance, was not documented in the initial confirmatory assay (and the assay was repeated), the conclusion of both confirmatory assays was the same; no mutagenicity was detected in any strain in the presence or absence of metabolic activation.

In some regards, there were similarities between the two studies. Both studies tested at least 5 concentrations of the test substance, with negative and standard, non-volatile positive controls used (see below for additional information). However, neither study used volatile positive control substances for explicitly demonstrating that their specific test protocols were optimized for detection of volatile chemical mutagens. The purity of the test substance was > 99% in both studies. Although both studies used at least 5 strains of bacteria, only the BioReliance study ([2015](#)) included a DNA repair-deficient strain of *E. coli*. In both studies, the metabolic activation system used S9 from Aroclor-induced rat livers and plates were incubated for 48 to 72 hours prior to the scoring of revertant colonies. The BioReliance study ([2015](#)) used target exposure concentrations up to 5000 $\mu\text{g}/\text{plate}$, as recommended by test guidelines; the highest concentration of 5000 $\mu\text{g}/\text{plate}$ was determined to be cytotoxic to all strains in the second confirmatory mutagenicity test. In contrast, Barber et al. ([1981](#)) tested concentrations up to 20.3 $\mu\text{moles}/\text{plate}$ (approximately 2500 $\mu\text{g}/\text{plate}$ based on a molecular weight for 1-BP of 122.9 g/mol) and detected mutagenicity even in the absence of cytotoxicity. The criteria for a positive or negative result were somewhat different for the two studies. Barber et al. ([1981](#)) indicated that a result was determined to be positive based on observed increases in the numbers of revertant colonies per plate in comparison to negative controls (not further specified). Statistical analyses (i.e., Student's t-test tables) were used to determine the minimum significant number of revertants per plate for each strain (data not shown), which was used to calculate the minimum vapor concentration with a positive result (i.e., "minimum detectable vapor concentration", equivalent to 31.2 ppm for TA 1535 and 106.5 ppm for TA 100). The BioReliance study ([2015](#)) stated that a result was deemed positive if there was a dose-related increase in the mean number of revertants per plate in at least one strain at two

increasing concentrations of the test substance; a three-fold increase in the mean number of revertants was required for *S. typhimurium* strains TA 1535 and TA 1537, while a two-fold change was considered positive for all other strains tested. If the criteria for the BioReliance study (2015) were applied to the data provided by Barber et al. (1981), 1-BP would be deemed mutagenic in strains TA 1535 and TA 100 in the presence and absence of metabolic activation (mean data were shown only for *S. typhimurium* strains TA 1535, TA 98, and TA 100); this is the same conclusion reached by Barber et al. (1981).

The guideline pertaining to this type of assay (OECD 471; (2019p)) indicates that a result can be considered positive for mutagenicity based on observed concentration-related increases in revertants over the range of concentrations tested, and/or a reproducible increase in the number of revertants/plate at one or more concentrations in at least one strain with or without metabolic activation (OECD, 1997). The OECD 471 (2019p) test guideline recommends that biological relevance be considered first; statistical analyses may also be used, but should not be the sole determinant for identifying a positive response. Therefore, although the two studies differed with respect to the classification of a positive versus a negative response, these differences do not suggest that one study followed guideline recommendations while the other did not. The Barber et al. (1981) study used statistics to determine vapor concentrations corresponding to a significantly increased number of revertants. Although the BioReliance (2015) study did not use statistical methods to evaluate mutagenicity, specific criteria for identifying a positive result were provided in the study report. These criteria closely adhere to those set forth in the guidelines, as described above.

In both studies, standard (non-volatile) chemicals were used as positive controls. Barber et al. (1981) used 2-aminoanthracene as a positive control for all strains when metabolic activation was used. In the absence of activation, positive controls were ICR-191 for *S. typhimurium* TA 98, methyl-N-nitro-N'-nitrosoguanidine for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and picrolonic acid for TA 1538. Positive and negative control data were provided by Barber et al. (1981); however, no criteria for establishing the validity of the positive control data were reported. For the BioReliance study (2015), 2-aminoanthracene was also identified as the positive control substance for all strains tested in the presence of metabolic activation. The positive controls used in the absence of metabolic activation included 2-nitrofluorene for *S. typhimurium* TA 98, sodium azide for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and methyl methanesulfonate for *E. coli* WP2 uvrA. The study report specified that positive controls were subjected to the preincubation process and plated concurrently with each assay (in duplicate in the initial toxicity-mutagenicity assay and in triplicate for subsequent confirmatory assay). The BioReliance study (2015) indicated that the mean number of revertants/plate for each positive control needed to be at least three times higher than the mean value for the respective vehicle control group for the mutagenicity test to be considered valid. Based on this criteria, positive controls responded appropriately in both the study by Barber et al. (1981) and in all three assays in the BioReliance study (2015). The mean numbers of revertants per plate that were observed for negative and positive controls are provided in Table_Apx I-5.

Table_Apx I-5. Comparison of Mean Numbers of Revertants/Plate for Controls in Reverse Mutation Assays

Mean numbers of revertants/plate for controls in reverse mutation assays								
Species and Strain	Barber et al. (1981)				BioReliance (2015) ^a			
	Negative control		Positive control		Negative control		Positive control	
	- S9	+ S9	- S9	+ S9	- S9	+ S9	- S9	+ S9
<i>S. typhimurium</i> TA 98	38	38	170	415	22	32	768	490
<i>S. typhimurium</i> TA 100	85	96	285	678	106	100	1057	554
<i>S. typhimurium</i> TA 1535	20	19	148	267	15	31	463	105
<i>S. typhimurium</i> TA 1537	6	9	265	402	6	5	115	87
<i>S. typhimurium</i> TA 1538	8	21	72	495	NT	NT	NT	NT
<i>E. coli</i> WP2 uvrA	NT	NT	NT	NT	32	41	614	402

^a Values are provided for the repeat (second) confirmatory assay of BioReliance (BioReliance, 2015), which was the only assay that documented the use of screw-capped tubes for preparation of dosing formulations.

NT = This strain was not tested for mutagenicity.

In summary, the studies by Barber et al. (1981) and BioReliance (2015) conformed to most of the recommendations provided in OECD TG 471 (2019p). The major differences in experimental design between the two studies are the method of test substance application (vapor exposure of plated bacteria for 48 hours in the Barber et al. study (1981) versus aqueous preincubation exposure for 90 minutes in the BioReliance study (2015) study and the methods used to achieve a ‘closed’ system to account for the inherent volatility of 1-BP (fully enclosed test chamber versus preparation of solutions in screw-capped tubes). Although the guideline indicates that volatile chemicals should be considered special cases, the alternative methods that should be used to test these types of test substances are not outlined in OECD TG 471 (2019p). It is likely that the varied mutagenicity results from the two studies (i.e., positive results in the Barber et al. study (1981) study and negative results in the BioReliance study (2015) are due to differences in the methods used for exposure and to compensate for the volatility of 1-BP in the bacterial reverse mutation assay.

Based on the following primary differences in methodology, the preincubation exposure test by BioReliance study (2015) had inadequate sensitivity to assess the mutagenic potential of volatile chemicals such as 1-BP, in contrast to the closed system plate vapor exposure test by Barber et al. (1981):

1. The BioReliance study report (2015) stated that “The test system was exposed to the test article via the preincubation methodology described by Yahagi et al. (1977)” but this method was not designed to retain a volatile test substance such as 1-BP within the test system during preincubation (prior to plating) with the bacterial test strains. In contrast, the Barber et al. (1981) study was explicitly designed to retain vapors of the volatile 1-BP test substance in contact with the bacterial test strains throughout plate incubation.
2. The BioReliance study (2015) study attempted to circumvent the volatility of 1-BP by using screw-capped tubes for test substance dilutions (documented in the second confirmatory assay only) and during the 90-minute preincubation period in contact with test strains (prior to plating). While the use of minimal headspace was documented for preparation of dosing formulations, it was unclear whether preincubation tubes contained minimal headspace; in the absence of this precaution, 1-BP would be expected to volatilize into the headspace. In contrast, the closed system used in the Barber et al. (1981) study

generated conditions that permitted the test strains to be exposed to 1-BP as a vapor for the entirety of the 48-hour exposure period (i.e., without loss due to volatility); analyses of 1-BP in aqueous samples from blank incubation plates by GLC were used to calculate the 1-BP concentrations in plates.

3. The results of analytical measurements of 1-BP suggest that bacteria were exposed to much higher concentrations of 1-BP in the study that found evidence of mutagenicity in two of five bacterial strains ([Barber et al., 1981](#)) than in the study that found no evidence of mutagenicity in five bacterial strains ([BioReliance, 2015](#)). Barber et al. ([1981](#)) tested measured concentrations up to 20.3 $\mu\text{moles/plate}$ (approximately 2500 $\mu\text{g/plate}$ based on a molecular weight for 1-BP of 122.9 g/mol) and detected mutagenicity in two of five bacterial strains in the absence of cytotoxicity. In the BioReliance study ([2015](#)) study, analytical measurements by GC confirmed that concentrations of 1-BP in dosing formulations were within 85-115% of target concentrations. However, despite the use of screw-capped tubes to reduce 1-BP loss via volatilization during preincubation with the bacterial test strains, analytical concentrations of 1-BP in preincubation tubes during the BioReliance study ([2015](#)) confirmatory assays were far below target, with 4-37% of target concentrations at the beginning of the preincubation period and 2-5% of target concentrations by the end of the preincubation period. At the highest target exposure concentration of 5000 $\mu\text{g/plate}$, the measured concentrations during preincubation correspond to approximately 100-450 $\mu\text{g/plate}$ (2-9% of the target concentration) in the BioReliance study ([2015](#)) and no evidence of mutagenicity was seen at this or lower concentrations.
4. The duration of exposure of bacteria to 1-BP was much longer in the study that showed mutagenicity from 1-BP exposure Barber et al. study ([1981](#)) than in the study that found no evidence of mutagenicity from 1-BP exposure ([BioReliance, 2015](#)). The closed system used in the positive Barber et al. ([1981](#)) study generated conditions that permitted the tester strains to be exposed to 1-BP as a vapor for the entirety of the 48-hour exposure period (i.e., without loss due to volatility). In contrast, bacteria were exposed to 1-BP in solution for 90 minutes in the negative BioReliance study ([2015](#)).
5. Neither Barber et al. ([1981](#)) nor BioReliance ([2015](#)) included volatile positive control chemicals in their assays. This does not appear to be an issue for the Barber et al. study ([1981](#)), which demonstrated mutagenicity for the volatile 1-BP test substance and for six other volatile halogenated alkane solvents in the presence and absence of metabolic activation. However, given that the Barber et al. study ([1981](#)) method was sufficient to detect the mutagenicity of 1-BP and related volatile chemicals, but the BioReliance study ([2015](#)) method found no evidence of 1-BP mutagenicity and did not show that their method could detect mutagenicity of volatile positive controls, there is uncertainty that the BioReliance study ([2015](#)) protocols and specific methodology were capable of adequately assessing the mutagenic potential of 1-BP. Thus, in the absence of data for volatile positive control chemicals³¹ in the BioReliance study ([2015](#)) study, it is possible that the lack of demonstrated 1-BP mutagenicity in this study was a false negative.

The differences in results, including both cytotoxicity and mutagenicity, between these two studies (described above and summarized in Table_Apx I-6) suggest that the design of the experimental

³¹ For examples of volatile positive control mutagens see Hughes et al. ([1987](#)), which was cited by OECD TG 471 ([2019p](#)) as an appropriate method for testing of gaseous or volatile substances.

system used for exposure and retention of the volatile test substance within the test system significantly influenced the response of the test organisms.

Table Apx I-6. Comparison of Mutagenicity Studies of 1-BP

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
Doses	Measured 1-BP concentrations were 0, 1.1, 2.3, 4.9, 9.0, and 20.3 μmoles/plate (equivalent to approximately 0, 140, 280, 600, 1100, and 2500 μg/plate). There was no indication of cytotoxicity at the highest tested concentration.	Target 1-BP concentrations were 0, 1.5, 5.0, 15, 50, 150, 500, 1500, and 5000 μg/plate (initial toxicity-mutagenicity assay); 0, 50, 150, 500, 1500, 2000, 3000, and 5000 μg/plate (confirmatory mutagenicity assays). 1-BP concentrations measured in confirmation mutagenicity assay preincubation tubes at the beginning and end of the 90-minute exposure were much lower than target (see row “Compound dose confirmation and purity”) and much lower than the highest test concentration used in the study by Barber et al. (1981). In the initial assay, cytotoxicity was observed at 5000 μg/plate (all strains); cytotoxicity was also observed at 3000 and 5000 μg/plate in the repeat of the confirmatory assay.	At least 5 test concentrations of the test substance should be used. The recommended highest test concentration for non-cytotoxic substances is 5000 μg/plate; or, for non-cytotoxic substances that are insoluble at that concentration, a concentration(s) that is insoluble in final treatment mixture. Cytotoxic substances should be tested up to a cytotoxic concentration.
Negative controls	Plates in a closed system with no added test or positive control chemical With the exception of not adding chemical to the system, untreated controls were treated the same as treatment groups. Negative controls were used for each strain, with and without metabolic activation. Average spontaneous reversion rates from negative control plates were reported.	Exposure to vehicle only (ethanol) in preincubation tubes Negative controls were included for each strain, with and without activation, and were treated the same as treatment groups. Raw data (number of revertant colonies per plate) were provided for negative controls. In the repeat of the confirmatory assay, a small peak of the test substance was detected in the vehicle control sample (~0.03 mg/mL). This was noted as a study deviation.	Concurrent strain-specific negative controls, with and without metabolic activation, should be included in each assay. Negative controls, consisting of solvent or vehicle alone, without test substance, should be included and should otherwise be treated the same as treatment groups.
Positive controls	<u>With activation:</u> 2-Aminoanthracene (all strains). No mutagen requiring activation by microsomal enzymes was tested. <u>Without activation:</u> ICR-191 for <i>Salmonella typhimurium</i> TA 98, methyl-N-nitro-N'-nitrosoguanidine for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and picrolonic acid for TA 1538. 9-Aminoacridine and ICR-191 are listed as strain-	<u>With activation:</u> 2-Aminoanthracene (all strains). No mutagen requiring activation by microsomal enzymes was tested; however, each bulk preparation of S9 was assayed for its ability to metabolize benzo(a)pyrene to forms mutagenic to <i>S. typhimurium</i> TA 100. <u>Without activation:</u> 2-Nitrofluorene for <i>S. typhimurium</i> TA 98, sodium azide for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and methyl methanesulfonate for <i>Escherichia coli</i> WP2 <i>uvrA</i>. All except methyl methanesulfonate for <i>E. coli</i> WP2 <i>uvrA</i>	Concurrent strain-specific positive controls, with and without metabolic activation, should be included in each assay. Examples of chemicals that can be used as positive controls in the presence and absence of metabolic activation are recommended by guideline (other appropriate reference substances may be used). It is noted that 2-aminoanthracene should not be used as the sole indicator of the efficacy of the S9 mix; each batch should also be characterized using a

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
	specific positive controls for TA 1537 and TA 97 (but not TA 98) according to OECD TG 471. The other chemicals are not listed in OECD TG 471. The solvent(s) used for positive control substances were not specified. No criteria were provided for a valid response of positive controls.	were listed as strain-specific positive controls according to OECD TG 471. Positive controls were diluted in DMSO except sodium azide, which was diluted in sterile water. The study indicated that for the test to be valid, positive controls had to show a 3-fold increase in the number of revertants compared to the respective vehicle control; however, there were no vehicle controls for DMSO or water.	mutagen that requires metabolic activation by microsomal enzymes (i.e., benzo(a)pyrene, dimethylbenzanthracene).
Compound dose confirmation & purity	Purity of 1-BP (as per GLC) = 99.85% <u>Dose confirmation:</u> Plates containing only sterile distilled water were included in the closed system containers for GLC analysis of aqueous 1-BP concentrations at the end of the 48-hour incubation period. Samples of the vapor were also taken from the closed system containers at the end of the 48-hour incubation period and analyzed by GLC. The GLC results from the aqueous samples were used to calculate the amount of chemical dissolved per plate.	Purity of 1-BP (determined by sponsor) > 99% <u>Dose confirmation:</u> Samples of dosing formulations and preincubation solutions (at 0 and 90 minutes) were analyzed by GC (vehicle control, low- and high-dose groups only). 1-BP concentrations in dosing formulations were similar to target concentrations, but 1-BP concentrations measured in preincubation solutions were shown to be far below target concentrations. At 0 minutes in the confirmatory mutagenicity assays, 1-BP concentrations in preincubation tubes at the highest target level (5000 µg/plate) were 4% to 9% of target, which corresponds to 1-BP concentrations of 200-450 µg/plate; by the end of the 90-minute preincubation exposure period, measured 1-BP concentrations at the highest target level (5000 µg/plate) were 2% to 3% of target, which corresponds to 1-BP concentrations of approximately 100-150 µg/plate. No analysis of 1-BP concentrations was conducted at the end of the plate incubation period (after 48-72 hours), but negligible 1-BP concentrations would be expected since no volatility control was used during the plate incubation period.	OECD TG 471 indicates that the test report must include specific types of information, including purity of the test substance. Given the volatility of 1-BP, it may be especially important to verify concentrations of the test substance as a 'special case'.
Methods reporting details provided	<u>Not provided:</u> Bacterial titers (cells/mL); raw data (i.e., individual plate counts); revertants/plate data for the two strains in which no mutagenicity was observed (i.e., <i>S. typhimurium</i> strains TA 1537 and TA 1538); standard deviations for	<u>Not provided:</u> None (items recommended by OECD TG 471 were reported)	The guideline indicates a number of items that must be included in the test report (with respect to the test substance, solvent/vehicle, strains, test conditions, and results).

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
	mean numbers of revertants/plate (except positive and negative controls); historical control data. Negative control results were noted to have been in good agreement with those found in an interlaboratory survey (de Serres and Shelby, 1979) and those presented by Ames et al. (1975).		
Closed-system protocol details	<u>System used:</u> Modified plate-incorporation test. Pyrex containers with circular Teflon tops (drilled and threaded to accommodate valve and septum assemblies and containing a sampling port); containers accommodated a metal rack holding up to 12 glass plates. An O-ring was used to ensure a good seal between the container and the top; clamps were used to hold tops in place. <u>Addition of 1-BP:</u> Under a hood, prepared plates (with or without activation) were introduced to the Pyrex containers. A plate containing sterile, distilled water (30 mL) was added to each container for GLC analysis of 1-BP concentrations at the end of the exposure period. After sealing the containers and drawing a partial vacuum, 1-BP was added through the septum using a syringe. Once the liquid vaporized (ascertained visually), air was added via the valve until the pressure inside the containers was equal to ambient pressure. Containers were removed from the hood and incubated for 48 hours at 37°C (with continuous stirring of the	<u>System:</u> Preincubation method. Screw-capped tubes during preincubation; minimal head space documented for the second confirmatory mutagenicity assay only. <u>Addition of 1-BP:</u> Dosing formulations of 1-BP were prepared in screw-capped tubes with minimal headspace; use of minimal headspace was documented only for the second of two confirmatory assays. To prepare preincubation solutions, 1-BP dosing formulations or vehicle (ethanol), S9 or sham mix, and the tester bacterial strain were added to glass culture tubes preheated to 37±2°C. Tubes containing 1-BP were capped using screw caps (amount of headspace not reported) during the preincubation period (90 minutes at 37°C). Following preincubation, top agar was added, and the mixture was overlaid onto minimal bottom agar. Once solidified, plates were inverted and placed in desiccators by dose level for 48 to 72 hours at 37°C.	OECD TG 471 indicates that certain classes of mutagens (including gases and volatile chemicals) are not always detected using standard procedures such as the plate incorporation or preincubation methods; therefore, these are considered 'special cases' and alternative procedures (scientifically justified) should be used for their detection. Gases or volatile substances should be tested by appropriate methods, such as in sealed vessels.

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
	atmosphere in each container).		
Activation system	Aroclor-induced rat liver S9 The concentration of S9 in S9 mix was not reported. For plates with metabolic activation, top agar contained 0.2 mL overnight culture, 2.0 mL agar, and 0.5 mL S9 mix.	Aroclor 1254-induced rat liver S9 (male Sprague-Dawley rats) The S9 mix contained a final S9 concentration of 10% v/v. Preincubation tubes contained 0.5 mL S9 or sham mix, 100 μL tester strain, and 25 μL vehicle or test substance dilution, to which 2.0 mL agar was added after the 90-minute preincubation period.	Bacteria should be exposed to the test substance in the presence and absence of an appropriate metabolic activation system. The most commonly used system is a cofactor-supplemented post-mitochondrial fraction (S9) prepared from the livers of rodents treated with enzyme-inducing agents such as Aroclor 1254 or a combination of phenobarbitone and β-naphthoflavone. The post-mitochondrial fraction is usually used at concentrations in the range from 5 to 30% v/v in the S9 mix. Usually, 0.05 or 0.1 mL of test substance/solution, 0.1 mL bacteria, and 0.5 mL S9 mix or sterile buffer are mixed with 2.0 mL of top agar.
Bacterial strains	<i>S. typhimurium</i> strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 This combination of strains conforms to the guideline except that TA 1538 was used in lieu of <i>E. coli</i> WP2 <i>uvrA</i> or <i>E. coli</i> WP2 <i>uvrA</i> (pKM101) or <i>S. typhimurium</i> TA 102. The test plates were prepared from overnight growth cultures (phase of growth not reported); the number of cells/mL was not specified.	<i>S. typhimurium</i> strains TA 98, TA 100, TA 1535, and TA 1537; <i>E. coli</i> strain WP2 <i>uvrA</i> This combination of strains conforms to the guideline. To assure that cultures were harvested in the late log phase, the length of incubation was controlled and monitored. Each culture was monitored spectrophotometrically for turbidity and harvested at a percent transmittance yielding a titer $\geq 0.3 \times 10^9$ cells/mL. Actual titers were determined by viable counts assays (actual counts were 1.3 to 5.7×10^9 cells/mL).	Fresh cultures grown up to the late exponential or early stationary phases of growth should be used (approximately 10^9 cells/mL; not late stationary). At least 5 strains of bacteria should be used. These should include 4 strains of <i>S. typhimurium</i> (TA 1535, TA 1537 or TA 97a or TA 97, TA 98, and TA 100). These strains have GC base pairs at the primary reversion site and may not detect certain oxidizing mutagens, cross-linking agents, and hydrazines. Such substances may be detected using <i>E. coli</i> WP2 strains or <i>S. typhimurium</i> TA 102, which have an AT base pair at the primary reversion site. To detect cross-linking mutagens, it may be preferable to include TA 102 or a DNA repair-deficient strain of <i>E. coli</i>, such as WP2 or WP2 (pKM101). The guideline specifies a recommended combination of strains (<i>S. typhimurium</i> TA 1535; <i>S. typhimurium</i> TA 1537 or TA 97a or TA 97; <i>S. typhimurium</i> TA 98; <i>S. typhimurium</i> TA 100; and <i>E. coli</i>

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
			WP2 uvrA or <i>E. coli</i> WP2 uvrA (pKM101) or <i>S. typhimurium</i> TA 102).
Duration of exposure	48 hours at 37°C	90±2 minutes at 37±2°C (preincubation period with test article or controls); 48-72 hours at 37°C (plate incubation period)	For the preincubation method, cultures should be incubated for 20 minutes or more at 30-37°C prior to mixing with top agar. All plates should be incubated at 37°C for 48 to 72 hours.
Time of assessment	Number of revertant colonies/plate was counted after 48 hours incubation	Number of revertant colonies counted after 48-72 hours incubation (plates that were not counted immediately were stored at 2-8°C)	All plates should be incubated at 37°C for 48 to 72 hours. After the incubation period, the number of revertant colonies per plate is counted.
Type of assessment	Revertant colonies counted using a colony counter. <u>Criteria for a positive result:</u> Increased revertants/plate compared to controls; statistical analysis (Student's t-test tables) was used to determine the minimum vapor concentration that significantly increased the number of revertant colonies.	Revertant colonies counted either entirely by automated colony counter or entirely by hand (except positive controls). <u>Criteria for a positive result:</u> Dose-related increases in the numbers of revertants/plate in at least one strain over a minimum of two increasing concentrations of 1-BP; at least 3-fold increase in revertants for <i>S. typhimurium</i> strains TA 1535 and 1537 and at least 2-fold increases for all other strains.	After the incubation period, the number of revertant colonies per plate is counted (method of counting not specified). Criteria for determining a positive result include a concentration-related increase over the range tested and/or a reproducible increase at one or more concentrations in at least one strain with or without activation. Biological relevance should be considered first; statistical methods may be used but should not be the only determining factor. Any result that does not meet these criteria is considered negative. Data should be presented as the mean number of revertant colonies per plate and standard deviation. There is no requirement for verification of a clear positive result. Equivocal results should be clarified by modifying experimental conditions, whenever possible. Negative results need to be confirmed on a case-by-case basis; if not confirmed, justification should be provided.

GLC = gas-liquid chromatography; GC = gas chromatography

I.5.8 Metabolism, Structure-Activity Relationships and Mechanism/Mode of Action

Studies in experimental animals and humans indicate that 1-BP can be absorbed following inhalation, oral, or dermal exposure (Cheever et al., 2009; NIOSH, 2007). Metabolism studies show that oxidation by P450 enzymes (e.g., CYP2E1) and glutathione conjugation are the primary metabolic pathways (Garner et al., 2006; Ishidao et al., 2002). Over 20 metabolites have been identified in rodent studies, including the four metabolites that can be detected in urine samples of workers exposed to 1-BP (Hanley et al., 2009). Besides being a direct-acting alkylating agent, 1-

BP may be converted to either of two epoxide metabolites, glycidol and propylene oxide, by oxidation followed by cyclization of the resulting α -bromohydrin intermediates. Both the 2- and 3- positions on 1-bromopropane are susceptible to oxidation by cytochrome P450 (NTP, 2013b). Oxidation at the 3-position results in the formation of 3-bromo-1-propanol. Further oxidation of this intermediate at the 2-position yields 3-bromo-1,2-propanediol, which can cyclize to form glycidol. Propylene oxide may be formed by a similar, though shorter pathway. Oxidation of 1-bromopropane at the 2-position yields 1-bromo-2-propanol. This bromohydrin intermediate may then be cyclized to form propylene oxide. Glycidol was detected in urine of rats exposed 6 hours/day to 1-BP by inhalation for 3 to 12 weeks (Ishidao et al., 2002). Metabolic pathways by which propylene oxide may be generated from 1-BP are shown in Jones and Walsh (1979), NTP (2013b), and IARC (2018) and a pathway by which glycidol may be generated from 1-BP is shown in IARC (2018). Epoxide intermediates such as propylene oxide and glycidol are expected to have more mutagenic activity than 1-BP (IARC, 2018, 2000, 1994).

Mice appear to have a greater capacity to oxidize 1-BP than rats (Garner et al., 2006). This species difference in metabolic capacity may explain why mice were found to be more sensitive to 1-BP toxicity than rats. The identified or putative reactive intermediates for 1-BP include the epoxides noted above (glycidol, and propylene oxide), α -bromohydrin and 2-oxo-1-BP (NTP, 2014; Ishidao et al., 2002; Mitchell et al., 1998). Detoxification of 1-BP metabolites occurs primarily via glutathione-S-transferase (GST) -mediated conjugation with glutathione (NTP, 2014; Liu et al., 2009; Garner et al., 2006).

1-BP is expected to be a good alkylating agent because bromine is a good leaving group. Two of its closest homologs, bromoethane and 1-bromobutane, were both shown to be mutagenic in the Ames Salmonella test; in both cases, use of desiccators was needed to show positive results (NTP, 1989b; Simmon et al., 1977). Bromoethane is a known carcinogen via the inhalation route of exposure (NTP, 1989b), whereas 1-bromobutane has not been tested for carcinogenic activity. 1-BP is a relatively soft electrophile which is expected to preferentially react with sulfhydryl (-SH) residues on glutathione and proteins before binding to DNA. Besides being a direct-acting alkylating agent, 1-BP may be metabolically activated to genotoxic intermediates (see above). A number of other structurally-related halogenated alkanes such as 1,2-dibromoethane (ethylene dibromide) (IARC, 1999e), dichloromethane (IARC, 1999d), 1,2-dichloroethane (IARC, 1999b), 1,2-dibromo-3-chloropropane (IARC, 1999a) and 1,2,3-trichloropropane (IARC, 1999c) have been classified as “probably carcinogenic to humans (group 2A)” or “possibly carcinogenic to human carcinogens” (group 2B) by the International Agency for Research on Cancer; however, some of these chemicals may have different mechanisms.

The exact mechanism/mode of action for 1-BP carcinogenesis is not clearly understood. More research (e.g., organ-specific *in vivo* DNA adduct studies, oxidative stress) is needed to identify key molecular events. Since 1-BP can induce tumors in multiple organs and can act directly as an alkylating agent, as well as indirectly via metabolically activated reactive intermediates such as glycidol and propylene oxide, it may have different mechanisms in different target organs. Whereas the reasonably available data/information and the weight of evidence support a mutagenic mode of action for 1-BP carcinogenesis, at least three additional mechanisms, oxidative stress, immunosuppression, and cell proliferation can act synergistically with mutagenicity and may contribute to the multi-stage process of carcinogenesis (NTP, 2013b).

As discussed in the previous section on genotoxicity, 1-BP and its genotoxic reactive intermediates can induce DNA mutations and/or chromosome aberrations. Although the results are not as clear cut for 1-BP itself, some of the discrepancies may be explained by testing limitations. Available *in vitro* DNA binding studies and structure-activity relationship analyses support the genotoxic potential of 1-BP. The induction of tumors in multiple targets by 1-BP is also a common characteristic of genotoxic carcinogens. Overall, the weight of scientific evidence supports a mutagenic mode of action for 1-BP carcinogenesis.

Oxidative stress due to cellular glutathione depletion could contribute to the carcinogenicity of 1-BP ([Morgan et al., 2011](#)). Oxidative stress is an important epigenetic mechanism that can contribute to all three stages of carcinogenesis - oxidation can induce initiation (as a result of DNA damage), promotion (as a result of compensatory cell proliferation in response to cell necrosis), and progression (via oxidative changes in signal transduction and gene expression; *rev.* ([Woo and Lai, 2003](#))). Exposure to 1-BP has also been shown to deplete glutathione in various tissues (e.g., ([Liu et al., 2009](#); [Lee et al., 2007](#); [Wang et al., 2003](#))), which can lead to a loss of protection against electrophiles.

As summarized in the previous section on genotoxicity, 1-BP did not induce mutations at the *cH* gene of female B6C3F1 transgenic Big Blue® mice following whole-body inhalation exposures to 1-BP vapor concentrations of 62.5, 125, or 250 ppm 5 days/week for 28 days ([Weinberg, 2016](#)); or 7 days/week for 28 days ([Young, 2016](#)). The guideline for transgenic rodent somatic and germ cell gene mutation assays ([OECD, 2013](#)) indicates that daily exposures to test substance are needed in a repeated-dose protocol of at least 28 days based on “observations that mutations accumulate with each treatment”. Thus, the 5 days/week exposure protocol used in the study by Weinberg ([2016](#)) was deficient but the 7 days/week exposure protocol of Young ([2016](#)) conformed to the ([OECD, 2013](#)) guidance to use daily exposures to test substance.

Due to the following issues, the negative Big Blue® rodent mutation assay in female B6C3F1 mice of Young ([2016](#)) does not provide clear evidence against a mutagenic mode of action of 1-BP carcinogenicity:

- (a) The study protocol was not optimal for detection of mutations because the highest test concentration of 250 ppm was not a Maximum Tolerated Dose (MTD). The MTD is defined as the dose producing signs of toxicity such that higher dose levels, based on the same dosing regimen, would be expected to produce lethality ([OECD, 2013](#)). Given that Young ([2016](#)) showed no treatment-related effects on survival, clinical observations, body weights, food consumption, or organ weights, the highest 1-BP test concentration was not an MTD and the study needs to be repeated to include a top concentration at the MTD.
- (b) The study assessed only females but it is possible that males may also be sensitive to mutagenicity/carcinogenicity from exposure to 1-BP. Indeed, the NTP ([2011b](#)) 2-year inhalation study found statistically-significant increases in tumor incidence not only in female B6C3F1 mice but also in both male and female F344/N rats.
- (c) The study assessed only mice, at a maximum 1-BP exposure concentration of 250 ppm, but the 3-month toxicity studies that preceded the NTP 2-year bioassay showed that F344/N rats tolerated a higher repeated-dose inhalation concentration (500 ppm) than B6C3F1 mice (250 ppm). Thus to provide higher sensitivity for detection of potential mutagenicity in rodents, an additional *in vivo* mutation assay using Big Blue® F344/N rats could be conducted using a higher maximum inhalation concentration than that used in the mouse

study, i.e., 500 ppm should be part of the range tested in Big Blue® F344/N rats. According to (OECD, 2013), “the use of transgenic rat models should be considered”, for example, “when investigating the mechanism of carcinogenesis for a tumour seen only in rats”. The NTP (2011b) 2-year bioassay of 1-BP reported that neoplasms of skin (in both sexes), large intestines (in females), and pancreas (in males) as well as increased incidences of malignant mesotheliomas (in males) occurred only in F344/N rats, which provides additional justification for 1-BP mutagenicity testing in Big Blue® F344/N rats of both sexes.

- (d) The Big Blue® assay typically evaluates fast and slow mutation fixation/repairing tissue types. Young (2016) assessed mutagenicity only in lung and liver but, because of differences in metabolic enzymes/cytochrome p450s among mammalian organs and tissues and different species, several tissues of rats and mice should be sampled for mutations in the Big Blue® rodent mutagenicity assay of 1-BP to minimize the possibility of false negative mutagenicity results. The NTP (2011b) 2-year study for 1-BP included neoplasm findings for skin, large intestines, lung, and pancreas. Before concluding that a mutagenic mode of action of 1-BP is not operable for all target sites, additional target sites, including skin, pancreas, and intestines at a minimum, would need to be assessed for 1-BP in Big Blue® models for both B6C3F1 mice and F344/N rats.
- (e) Test chemical exposures of longer than 28 days may be needed for “detecting mutations in slowly proliferating organs” (OECD, 2013). Further research may be needed to determine if 1-BP exposure periods of more than 28 days are needed for detection of potential mutations in the Big Blue® assay.
- (f) The Big Blue® rodent assay may fail to detect mutagens if the post-exposure fixation time is too short to allow fixing of DNA damage into stable mutations. Likewise, the assay can fail to detect mutagens if a rapid cell turnover in a particular tissue, together with longer post-exposure time, decrease the frequency of cells that carry mutations in reporter genes. As indicated in (OECD, 2013) administration of the test agent “is usually followed by a period of time, prior to sacrifice, during which the agent is not administered and during which unrepaired DNA lesions are fixed into stable mutations. In the literature, this period has been variously referred to as the manifestation time, fixation time, or expression time.” In the Big Blue® mouse study by Young (2016), the post-exposure fixation time was 3 days, which may provide adequate sensitivity for detection of mutagenicity in some tissues but not others. (OECD, 2013) recognizes the issue of potential underestimation of mutagenic potential, noting that the fixation period is tissue-specific and that “maximum mutant frequency may not manifest itself in slowly proliferating tissues” when a 3-day fixation period is used. To address the possibility of underreporting mutagenic potential for slowly proliferating tissues, (OECD, 2013) indicates that “a later sampling time of 28 days following the 28 day administration period may be more appropriate.” Further research is needed on the lengths of fixation periods needed to manifest mutagenicity in each tissue sampled in future Big Blue® rodent assays of 1-BP.
- (g) The Big Blue® assay lacks a body of data on mutagenic and carcinogenic chemicals with structural similarity to 1-BP. One of the closest homologs of 1-BP, bromoethane, is positive in closed-system testing in the Ames *Salmonella* mutagenicity assay (NTP, 1989b; Simmon et al., 1977) and is carcinogenic by the inhalation route (NTP, 1989b). To enhance confidence that the methods used for 1-BP testing in the Big Blue® assays are sufficient to prevent false negative mutagenicity findings, mutagenicity data from Big Blue® assays of rats and mice are needed from independent testing of bromoethane (and other known mutagenic carcinogens with structural similarity to 1-BP) or these 1-BP analogs could be

included as potentially-positive controls in additional Big Blue® studies of 1-BP. If mutagenic and carcinogenic structural analogs of 1-BP are not mutagenic in Big Blue® rodent assays, it can be concluded that these assays are not suitable for assessing the mutagenicity of 1-BP.

Besides genotoxicity and oxidative stress, 1-BP has been shown to cause immunosuppression in rodents ([Anderson et al., 2010](#); [Lee et al., 2007](#)). Immunosuppression can facilitate tumor progression by lowering the immunosurveillance process against tumor growth. There is also some evidence that 1-BP can cause γ -aminobutyric acid (GABA) dysfunction and thereby impact cell proliferation, differentiation and migration of neuronal cells ([NTP, 2013a](#)).

Several known or proposed metabolites of 1-BP have been shown to be mutagenic ([NTP, 2014](#); [IARC, 2000, 1994](#)). For example, both glycidol and propylene oxide are mutagenic in bacteria, yeast, *Drosophila*, and mammalian cells. These compounds have also been shown to induce DNA and chromosomal damage in rodent and human cells, and can form DNA adducts *in vitro*. α -Bromohydrin and 3-bromo-1-propanol were mutagenic in the *S. typhimurium* reversion assay, and 3-bromo-1-propanol and 1-bromo-2-propanol induced DNA damage in *E. coli*. The available *in vivo* test results for glycidol indicate that it induces micronucleus formation, but not chromosomal aberrations in mice. Studies of propylene oxide indicated chromosomal damage evidenced by positive responses for micronucleus induction in mouse bone marrow and chromosomal aberration tests; DNA damage was evident in the sister chromatid exchange (SCE) assay.

Appendix J 1-BP: Mutagenic MOA Analysis

According to the Cancer Guidelines and the Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens ([U.S. EPA, 2005a, b](#)), individuals exposed during early life stages (i.e., development) to carcinogens with a mutagenic mode of action are assumed to have an increased risk for cancer. The framework for the weight of the scientific evidence for mutagenicity is used to consider the available data ([U.S. EPA, 2005a](#)). Age-Dependent Adjustment Factors (ADAFs) are then applied for carcinogens with evidence supporting a mutagenic mode of action and/or for carcinogens with available data indicating increased susceptibility after developmental life stage exposure ([U.S. EPA, 2005b](#)) if relevant to potentially exposed populations.

According to the Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens ([U.S. EPA, 2005b](#); see Figure_Apx J-1 below), chemicals are considered for whether there is evidence of a mutagenic MOA in animal studies. This figure illustrates the considerations and decision logic for whether ADAFs are applied. While there are some negative results in some assays, the positive findings are from in vitro assays conducted under conditions considered to be appropriate for assessing a volatile chemical. Specifically, 1-BP was mutagenic in closed-system testing in the presence or absence of metabolic activation, induced DNA damage and repair in human cells in culture in the presence of metabolic activation, and induced mutations in mammalian cells in culture in the presence or absence of metabolic activation. The available animal toxicology studies for 1-BP provide support for the association between chronic inhalation exposure and lung, large intestinal, and skin cancer ([NTP, 2011b](#)). Further 1-BP metabolites, that may include epoxide intermediates, such as propylene oxide and glycidol, are known to have mutagenic activity ([IARC, 2018, 2000, 1994](#)). Rodent metabolic studies have shown that 1-BP can be converted into at least five mutagenic intermediates by CYP2E1. Although it is possible that additional MOAs are operative and contribute to the carcinogenic responses, the weight-of-the-evidence supports that the MMOA is at least plays a contributing role for 1-BP and its epoxide intermediates in inducing key mutagenic precursor cancer events in target tissues.

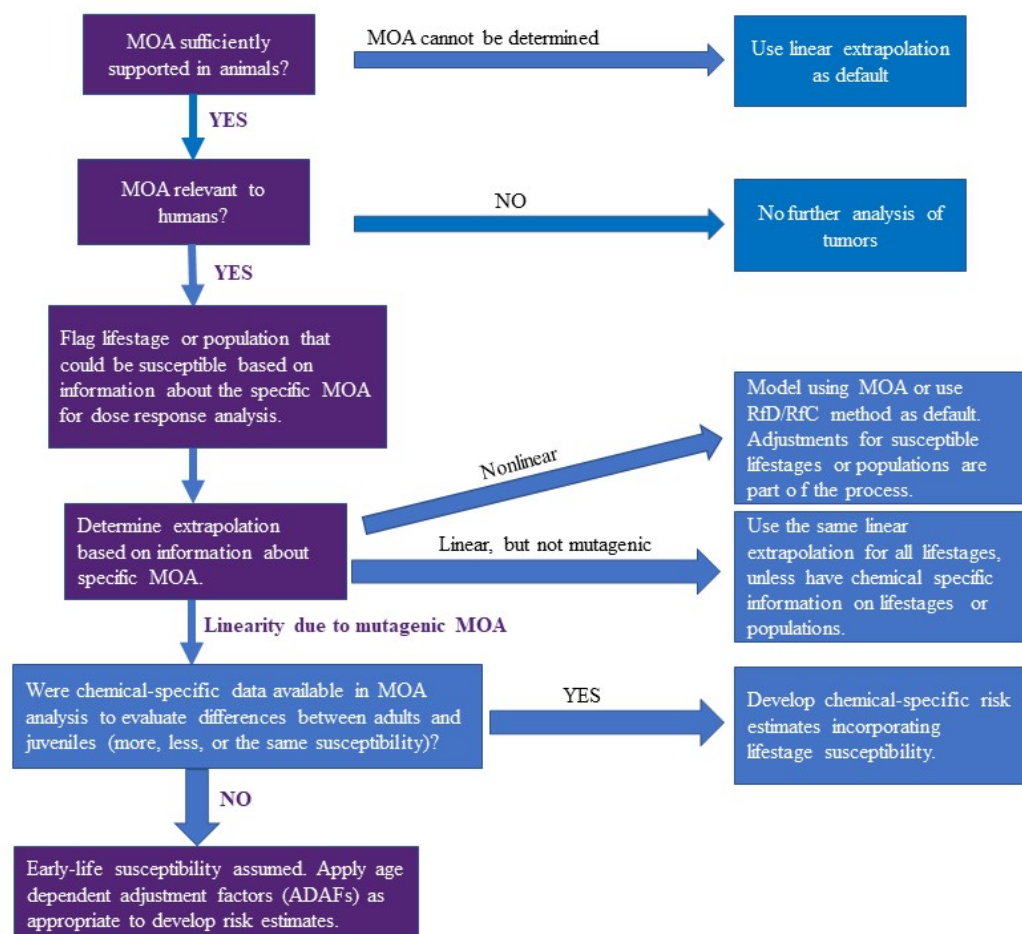
1-BP was then considered for whether there is human relevance of the mutagenic MOA ([U.S. EPA, 2005b](#)). In a human occupational study, there is limited evidence of DNA damage in leukocytes. There are occupational studies indicating increased lifetime cancer risk, there are no additional studies that assessed mutagenicity in humans. In the absence of such data, human relevance of cancer is made (“...tumors observed in animals are generally assumed to indicate that an agent may produce tumors in humans”; ([U.S. EPA, 2005a](#)), p. 2-22). Further, “...site concordance is not always assumed between animals and humans.” ([U.S. EPA, 2005a](#)), p. 2-22). Based on these assumptions about cross-species cancer formation, while not specifically about the mutagenic MOA, EPA assumes the mutagenic MOA is operative in humans.

The next step was to determine extrapolation based on information about specific MOA. Linearity was selected based on the mutagenic MOA for 1-BP.

1-BP was then considered for whether there are data to indicate an increased susceptibility to cancer after developmental exposure or for another population. Similar to benzo-a-pyrene ([U.S. EPA, 2017f](#)), 1-BP lacks data to evaluate age-specific exposure differences in susceptibility to cancer. In the absence of adequate chemical-specific data to evaluate differences in age-specific susceptibility, the Supplemental Guidance for Assessing Susceptibility from Early Life Exposure

to Carcinogens ([U.S. EPA, 2005b](#)) recommends that age-dependent adjustment factors (ADAFs) be applied in estimating cancer risk. The ADAFs are 10- and 3-fold adjustments that are combined with age specific exposure estimates when estimating cancer risks from early life (<16 years of age) exposures.

Another population that may have increased susceptibility to 1-BP are individuals with polymorphisms in cyp2E1. CYP2E1 is important in the activation of mutagenic 1-BP intermediates. Therefore, individuals with altered activation of 1-BP intermediates may be at increased cancer risk. Cancer outcomes in this population have not been identified.



Figure_Apx J-1. 1-BP Mutagenic MOA Weight of the Scientific Evidence Determination Following the Supplemental Guidance¹ for Assessing Susceptibility from Early-Life Exposure to Carcinogens

¹EPA's Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#)) includes a framework to establish MOA(s) for a chemical. Purple boxes indicate the decisions made for 1-BP based on the available animal and human cancer studies and mechanistic studies. Blue boxes indicate options in the supplemental guidance that were not supported by the available 1-BP data. The WOE for 1-BP supports mutagenic MOA that is relevant to humans. Therefore, ADAFs are applied per the Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens ([U.S. EPA, 2005b](#)). This figure was adapted from Figure 1-1. Flow chart for early-life risk assessment using mode of action framework in the Supplemental guidance ([U.S. EPA, 2005b](#)).

Table_Apx J-1. Decisions and justification for mutagenic mode of action for 1-BP (see Figure 1 from [\(U.S. EPA, 2005b\)](#))

Decision	Justification	Document; p. #
MOA sufficiently supported in animals	WOE indicates mutagenic MOA. Although there are mixed study findings, the positive results were in the higher quality studies using the more appropriate assay for assessing volatiles. But note that: “An agent may work by more than one mode of action, both at different sites and at the same tumor site.” (U.S. EPA, 2005a)	Section 3.2.7.2
MOA relevant to humans	EPA guidelines that state that you assume human relevance if the MOA occurs in animal studies and there is an absence of human data. A lack of site concordance across species is not a reason to assume no human relevance.	(U.S. EPA, 2005a) , p. 2-22
Exposure during early lifestages expected to be more susceptible than adults. Apply to dose response analysis.	For carcinogens with a mutagenic MOA assumes, greater susceptibility from exposure during childhood/development is expected (U.S. EPA, 2005a) . Humans with a polymorphism in Cyp2E1 may be at increased susceptibility.	(U.S. EPA, 2005b)
Determine extrapolation based on information about specific MOA: Linearity.	Due to mutagenic MOA	
Early-life susceptibility assumed. Apply age dependent adjustment factors (ADAFs) as appropriate to develop risk estimates.	No chemical-specific data available in MOA analysis to evaluate differences between adults and juveniles (more, less, or the same susceptibility).	(U.S. EPA, 2017f) for BaP precedent. (U.S. EPA, 2005b) .

There are uncertainties in the 1-BP database associated with the mutagenic MOA for carcinogenesis. Data gaps exist regarding *in vitro* mutagenicity study results and the mutagenic properties of 1-BP and its metabolites, studies of mutation in workers exposed to 1-BP over time, studies of the human population with cyp2E1 polymorphisms and cancer, and studies to evaluate developmental life stage exposure and cancer in childhood and adulthood. Further research is required at the molecular level to demonstrate that the cellular events are operative, development of a set of key events to understand the adverse outcome pathway from chemical exposure to phenotypic changes that ultimately lead to cancer.