TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0271

Number: P-18-0271
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: 2-Propanol, 1-butoxy-, 2,2'-ester

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (specific): Manufacture and process for use and use as a film-forming coalescent for architectural coatings, automotive Original Equipment Manufacturers (OEM) coatings, can and coil coatings, industrial wood coatings, floor polishes, industrial maintenance coatings, marine and wood coatings, and transportation coatings, and for use in printing inks and as a chemical intermediate to prepare ester plasticizers, consistent with the manufacturing, processing, use, distribution, and disposal information described in the PMN.

Known conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are known conditions of use and found none.

Reasonably foreseen conditions of use: Applying such factors as described in footnote 1, EPA has identified use as an oil field chemical for drilling muds/frothing agent/ore flotation as reasonably foreseen based on the submitter's amendment to the submission.

Summary: The chemical substance is not likely to present an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant by the Administrator under the conditions of use, based on the risk assessment presented below and the terms of the proposed Significant New Use Rule (SNUR) signed by EPA.[2]. Although EPA

[1] Under TSCA § 3(4), the term "conditions of use" means "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." In general, EPA considers the intended conditions of use of a new chemical substance to be those identified in the section 5(a) notification. Known conditions of use include activities within the United States that result from manufacture that is exempt from PMN submission requirements. Reasonably foreseen conditions of use are future circumstances, distinct from known or intended conditions of use, under which the Administrator expects the chemical substance to be manufactured, processed, distributed, used, or disposed of. The identification of "reasonably foreseen" conditions of use will necessarily be a case-by-case determination and will be highly fact-specific. Reasonably foreseen conditions of use will not be based on hypotheticals or conjecture. EPA's identification of conditions of use includes the expectation of compliance with federal and state laws, such as worker protection standards or disposal restrictions, unless case-specific facts indicate otherwise. Accordingly, EPA will apply its professional judgment, experience, and discretion when considering such factors as evidence of current use of the new chemical substance outside the United States, evidence that the PMN substance is sufficiently likely to be used for the same purposes as existing chemical substances that are structurally analogous to the new chemical substance, and conditions of use identified in an initial PMN submission that the submitter omits in a revised PMN. The sources EPA uses to identify reasonably foreseen conditions of use include searches of internal confidential EPA PMN databases (containing use information on analogue chemicals), other U.S. government public sources, the National Library of Medicine's Hazardous Substances Data Bank (HSDB), the Chemical Abstract Service STN Platform, REACH Dossiers, technical encyclopedias (e.g., Kirk-Othmer and Ullmann), and Internet searches.

[2] Reasonably foreseen conditions of use subject to a proposed SNUR are not likely to present an unreasonable risk of injury to health or the environment. Based on EPA's experience, it is the Agency's judgment that a new use

estimated that the new chemical substance could be persistent, the substance has a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Based on EPA's TSCA New Chemicals Program Chemical Category for Esters and Neutral Organics[3], estimated physical/chemical properties, data on analogous chemicals, and quantitative hazard data for a metabolite of the new chemical substance, EPA estimates that the chemical substance has moderate environmental hazard and potential for the following human health hazards: skin irritation and eye irritation. The PMN describes conditions of use that mitigate the human health and environmental risks. Therefore, EPA concludes that the new chemical is not likely to present unreasonable risk to human health or the environment under the intended conditions of use.

As set forth below, the information available to EPA is sufficient to permit the Agency to conduct a reasoned evaluation of the health and environmental effects of the chemical substance under the conditions of use that are not subject to the proposed SNUR, in order to determine that the chemical substance is not likely to present an unreasonable risk under those conditions of use. As such, EPA does not need to impose testing requirements to conduct this evaluation. Whether testing is needed to evaluate the effects of the intended, known, or reasonably foreseen conditions of use of a chemical substance subject to a PMN is determined on a case-by-case basis. To the extent that testing may be necessary to conduct a reasoned evaluation of the health or environmental effects of the reasonably foreseen conditions of use that are subject to the proposed SNUR, EPA will make the appropriate determination if a Significant New Use Notice (SNUN) is submitted following finalization of the SNUR.

EPA found no known conditions of use, assessed the intended conditions of use, and addressed reasonably foreseen conditions of use by proposing a SNUR. Therefore, EPA determines the new chemical substance is not likely to present unreasonable risk to human health or the environment.

Fate: Environmental fate is the determination of which environmental compartment(s) a chemical moves to, the expected residence time in the environmental compartment(s) and removal and degradation processes. Environmental fate is an important factor in determining exposure and thus in determining whether a chemical may present an unreasonable risk. EPA estimated physical/chemical and fate properties of the new chemical substance using data for

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would not commence during the pendency of a proposed SNUR because web posting of a proposed SNUR serves as the cut-off date for a significant new use. Therefore, manufacturers and processors would not commence a prohibited new use that would be legally required to cease upon the finalization of the SNUR. Once a SNUR is final and effective, no manufacturer or processor – including the PMN submitter – may undertake the conditions of use identified as a significant new use of the PMN substance in the SNUR. EPA must first evaluate the new use in accordance with the requirements of TSCA Section 5 and (a) either conclude that the new use is not likely to present an unreasonable risk under the conditions of use; or (b) take appropriate action under section 5(e) or 5(f). If EPA were not to finalize the proposed SNUR, then that decision would be based on information and data provided to the Agency during the comment period demonstrating that the reasonably foreseen conditions of use subject to the proposed SNUR are not likely to present an unreasonable risk. Under either scenario, the reasonably foreseen condition of use is not likely present an unreasonable risk.

[3] TSCA New Chemicals Program (NCP) Chemical Categories. https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/chemical-categories-used-review-new.

analogue(s) ([claimed CBI] and other chemicals) and EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). In wastewater treatment, the new chemical substance is expected to be removed with an efficiency of 90% due to sorption and biodegradation. Removal of the new chemical substance by biodegradation is high and destruction (mineralization) of the new chemical substance by biodegradation is possible partial to complete. Sorption of the new chemical substance to sludge is expected to be strong and to soil and sediment is expected to be moderate. Migration of the new chemical substance to groundwater is expected to be moderate due to moderate sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the new chemical substance is expected to undergo negligible volatilization to air. Overall, these estimates indicate that the new chemical substance has low potential to volatilize to air and has moderate potential to migrate to groundwater.

Persistence[4]: Persistence is relevant to whether a new chemical substance is likely to present an unreasonable risk because chemicals that are not degraded in the environment at rates that prevent substantial buildup in the environment, and thus increase potential for exposure, may present a risk if the substance presents a hazard to human health or the environment. EPA estimated degradation half-lives of the new chemical substance using data for analogue(s) ([claimed CBI] and other chemicals). EPA estimated that the new chemical substance's aerobic biodegradation half-life is < 2 months and anaerobic biodegradation half-life is 2 to 6 months. These estimates indicate that the new chemical substance may have limited persistence in aerobic environments (e.g., surface water) and may be persistent in anaerobic environments (e.g., sediment).

Bioaccumulation[5]: Bioaccumulation is relevant to whether a new chemical substance is likely to present an unreasonable risk because substances that bioaccumulate in aquatic and/or terrestrial species pose the potential for elevated exposures to humans and other organisms via food chains. EPA estimated the potential for the new chemical substance to bioaccumulate using EPI Suite™. EPA estimated that the new chemical substance has low bioaccumulation potential based on BCFBAF model result < 1,000 (bioconcentration factor = 90 [estimated] and bioaccumulation factor = 110 [estimated]). Although EPA estimated that the new chemical substance could be persistent, the substance has a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

[4] Persistence: A chemical substance is considered to have limited persistence if it has a half-life in water, soil or sediment of less than 2 months or there are equivalent or analogous data. A chemical substance is considered to be persistent if it has a half-life in water, soil or sediments of greater than 2 months but less than or equal to 6 months or if there are equivalent or analogous data. A chemical substance is considered to be very persistent if it has a half-life in water, soil or sediments of greater than 6 months or there are equivalent or analogous data. (64 FR 60194; November 4, 1999)

[5] Bioaccumulation: A chemical substance is considered to have a low potential for bioaccumulation if there are bioconcentration factors (BCF) or bioaccumulation factors (BAF) of less than 1,000 or there are equivalent or analogous data. A chemical substance is considered to be bioaccumulative if there are BCFs or BAFs of 1,000 or greater and less than or equal to 5,000 or there are equivalent or analogous data. A chemical substance is considered to be very bioaccumulative if there are BCFs or BAFs of 5,000 or greater or there are equivalent or analogous data. (64 FR 60194; November 4 1999)

Human Health Hazard[6]: Human health hazard is relevant to whether a new chemical substance is likely to present an unreasonable risk because the significance of the risk is dependent upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. Absorption of the new chemical substance is expected to be poor via the lungs and moderate via the skin and gastrointestinal (GI) tract based on physical/chemical properties. For the new chemical substance, EPA identified irritation, kidney toxicity, and liver toxicity as hazards based on the expected metabolite (propylene glycol *n*-butyl ether). EPA identified, for the expected metabolite, a NOAEL of 350 mg/kg/day for oral exposure based on liver and kidney effects, a No Observed Adverse Effect Concentration (NOAEC) of 3,244 mg/m^3 for inhalation exposure based on no observed effects at the highest tested concentration, and a NOAEL of 1,000 mg/kg/day for dermal exposure based on no effects at the highest tested dose, which were used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below. EPA qualitatively assessed irritation.

Environmental Hazard[7]: Environmental hazard is relevant to whether a new chemical substance is likely to present unreasonable risk because the significance of the risk is dependent upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. EPA estimated environmental hazard of this new chemical substance using the Ecological Structure Activity Relationships (ECOSAR) Predictive Model

[6] A chemical substance is considered to have low human health hazard if effects are observed in animal studies with a No Observed Adverse Effect Level (NOAEL) equal to or greater than 1,000 mg/kg/day or if there are equivalent data on analogous chemical substances; a chemical substance is considered to have moderate human health hazard if effects are observed in animal studies with a NOAEL less than 1,000 mg/kg/day or if there are equivalent data on analogous chemical substances; a chemical substance is considered to have high human health hazard if there is evidence of adverse effects in humans or conclusive evidence of severe effects in animal studies with a NOAEL of less than or equal to 10 mg/kg/day or if there are equivalent data on analogous chemical substances. EPA may also use Benchmark Dose Levels (BMDL) derived from benchmark dose (BMD) modeling as points of departure for toxic effects. See https://www.epa.gov/bmds/what-benchmark-dose-software-bmds. Using this approach, a BMDL is associated with a benchmark response, for example a 5 or 10 % incidence of effect. The aforementioned characterizations of hazard (low, medium, high) would also apply to BMDLs. In the absence of animal data on a chemical or analogous chemical substance, EPA may use other data or information such as from in vitro assays, chemical categories (e.g., Organization for Economic Co-operation and Development, 2014 Guidance on Grouping of Chemicals, Second Edition. ENV/JM/MONO(2014)4. Series on Testing & Assessment No. 194. Environment Directorate, Organization for Economic Co-operation and Development, Paris, France. (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en)), structure-activity relationships, and/or structural alerts to support characterizing human health hazards.

[7] A chemical substance is considered to have low ecotoxicity hazard if the Fish, Daphnid and Algae LC50 values are greater than 100 mg/L, or if the Fish and Daphnid chronic values (ChVs) are greater than 10.0 mg/L, or there are not effects at saturation (occurs when water solubility of a chemical substance is lower than an effect concentration), or the log Kow value exceeds QSAR cut-offs. A chemical substance is considered to have moderate ecotoxicity hazard if the lowest of the Fish, Daphnid or Algae LC50s is greater than 1 mg/L and less than 100 mg/L, or where the Fish or Daphnid ChVs are greater than 0.1 mg/L and less than 10.0 mg/L. A chemical substance is considered to have high ecotoxicity hazard, or if either the Fish, Daphnid or Algae LC50s are less than 1 mg/L, or any Fish or Daphnid ChVs is less than 0.1 mg/L (Sustainable Futures https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual).

(https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model); specifically the QSAR for esters and neutral organics. This substance falls within the TSCA New Chemicals Category of Esters and Neutral Organics. Acute toxicity values estimated for fish, aquatic invertebrates, and algae are 4.6 mg/L, 7.5 mg/L, and 3.6 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are 0.35 mg/L, 1.1 mg/L, and 1.3 mg/L, respectively. These toxicity values indicate that the new chemical substance is expected to have moderate environmental hazard. Application of assessment factors of 4 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern of 0.9 mg/L (900 ppb) and 0.035 mg/L (35 ppb), respectively.

Exposure: The exposure to a new chemical substance is potentially relevant to whether a new chemical substance is likely to present unreasonable risks because the significance of the risk is dependent upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance.

EPA estimates occupational exposure and environmental release of the new chemical substance under the intended conditions of use described in the PMN using ChemSTEER (Chemical Screening Tool for Exposures and Environmental Releases; https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases). EPA uses EFAST (the Exposure and Fate Assessment Screening Tool; https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-version-2014) to estimate general population, consumer, and environmental exposures.

EPA considers workers to be a potentially exposed or susceptible subpopulation (PESS) on the basis of greater exposure potential compared to the general population. EPA also considers PESS in conducting general population drinking water exposures by evaluating risks associated with water intake rates for multiple age groups, ranging from infants to adults. EPA considers consumers of specific products to be a potentially exposed or susceptible subpopulation on the basis of greater exposure potential compared to the general population who do not use specific products.

For this new chemical assessment, EPA assessed worker exposure via dermal and inhalation exposure. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via drinking water ingestion, fish ingestion, and groundwater ingestion via landfill leaching. Exposure to the general population via inhalation was not assessed because releases to air were expected to be negligible (below modeling thresholds). Exposure to consumers was assessed via oral, dermal, and inhalation exposure.

Risk Characterization: EPA applies a margin of exposure approach to calculate potential human health risks of new chemicals. A benchmark (acceptable) margin of exposure (MOE) is derived by applying uncertainty factors (UFs) for the following types of extrapolations: intra-species extrapolation (UF_H = 10 to account for variation in sensitivity among the human population), inter-species extrapolation (UF_A = 10 to account for extrapolating from experimental animals to humans) and Lowest Observed Adverse Effect Level (LOAEL)-to-NOAEL extrapolation (UF_L = 10 to account for using a LOAEL when a NOAEL is not available). Hence, in the New Chemicals Program, a benchmark MOE is typically 100 and 1,000 when NOAELs and LOAELs, respectively, are used to identify hazard. When allometric scaling

or pharmacokinetic modeling is used to derive an effect level, the UF_H may be reduced to 3, for a benchmark MOE of 30. The benchmark MOE is used to compare to the MOE calculated by comparing the toxicity NOAEL or LOAEL to the estimated exposure concentrations. When the calculated MOE is equal to or exceeds the benchmark MOE, the new chemical substance is not likely to present an unreasonable risk. EPA assesses risks to workers considering engineering controls described in the PMN but in the absence of personal protective equipment (PPE) such as gloves and respirators. If risks are preliminarily identified, EPA then considers whether the risks would be mitigated by the use of PPE (e.g., impervious gloves, respirator).

Risks to human health for the new chemical substances were evaluated using the route-specific effect levels (i.e., NOAELs and NOAEC) described above. Based on the hazard determination and available qualitative risk information, EPA did not identify risks for the new chemical substance.

Risks were not identified for workers for liver and kidney effects via inhalation exposure based on quantitative hazard data for a metabolite of the new chemical substance, propylene glycol *n*-butyl ether (MOE =28,385; benchmark MOE = 100). Risks were not calculated for workers exposed via the dermal route because the quantitative hazard data on a metabolite of the new chemical substance (i.e., propylene glycol *n*-butyl ether) indicated a low hazard. Eye and skin irritation hazards to workers were identified based on analogue data and a structural alert for solvents. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. However, exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including (impervious gloves and eye protection). EPA expects that employers will require and that workers will use appropriate PPE consistent with the Safety Data Sheet (SDS) prepared by the new chemical submitter, in a manner adequate to protect them.

Risks were not identified for the general population for liver and kidney effects via oral ingestion (drinking water, landfill leachate and fish) based on quantitative hazard data for a metabolite of the new chemical substance, propylene glycol *n*-butyl ether (MOEs > 27,685; benchmark MOE = 100). Risks to the general population via inhalation exposure were not evaluated because exposures are expected to be negligible (below modeling thresholds). Irritation hazards to the general population are not expected via oral ingestion due to dilution of the chemical substance in the media.

EPA assumes that eye and skin irritation is possible from exposure to the consumer product because the new chemical substance is an ingredient in the consumer product at concentration levels ≥ 3% and therefore its irritating properties are assumed to persist even in the presence of other unknown components.[8] Risks were not quantified for consumers exposed via the dermal

[8] EPA is using the *Globally Harmonized System of Classification and Labeling of Chemicals (GHS): Eighth Revised Edition (*UN, New York, https://doi.org/10.18356/f8fbb7cb-en, Chapter 3.2 and 3.3), to establish the cut-off value for the new chemical substance's skin and eye irritation effects in consumer products. EPA will consider a mixture to be irritating to the skin or eye when the concentration of the new chemical substance is ≥ 3% in the mixture. When selecting the cut-off value, EPA assumes that a mixture containing irritant ingredients cannot be classified based on the additivity approach. The theory of additivity assumes that each ingredient contributes to the overall irritant properties of the mixture in proportion to its potency and concentration. However, there are types of chemicals that the theory of additivity might not apply. Annex 5 of the GHS document states *"[e]stimates of*

route because the quantitative hazard data on a metabolite of the new chemical substance (i.e., propylene glycol *n*-butyl ether) indicated a low hazard concern based on no effects observed at the highest tested dose in two repeated-dose dermal studies. Risks were not identified for consumers for liver and kidney effects via oral exposure from toner uses (MOE = 27,778; benchmark MOE = 100). Risks were not identified for consumers for liver and kidney effects via inhalation from paint (MOEs = 676, benchmark = 100). Although skin and eye irritation are possible from exposure to the consumer products, the final products contain [claimed CBI]% in formulation of the new chemical substance, which is close to the cutoff value of ≥ 3% in formulation for irritation effects in consumer products. Therefore, EPA concludes that unreasonable risk to consumers from irritation is not likely.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks from acute exposure to the environment were not identified due to releases to water that did not exceed the acute COC. Risks from chronic exposure to the environment were not identified since the predicted environmental concentration (surface water concentration (SWC)) of 16 ppb is less than the chronic COC of 35 ppb (manufacturing scenario). Risks from chronic exposure to the environment were not identified due to releases to water (SWC of 97 ppb) that exceeded the chronic COC of 35 ppb for less than 20 days/year (10/108 days/year; processing scenario).[9]

It is reasonably foreseen, based on information included in the original submission which was subsequently amended, that the new chemical substance could have other uses that could result in higher environmental releases. The SNUR that has been proposed for this chemical substance defines certain conditions of use as significant new uses. The proposed significant new uses include use other than as described in the PMN. Conditions of use that fall under the restrictions of the proposed SNUR are not likely to present unreasonable risk of injury to health or the environment because (1) those conditions of use are not likely to be commenced during the pendency of the proposed SNUR, and (2) upon finalization of the SNUR, those conditions of use would be prohibited unless and until EPA makes an affirmative determination that the significant new use is not likely to present an unreasonable risk or takes appropriate action under section 5(e) or 5(f).

5/29/2020
Date:

/s/
Tala R. Henry, Ph.D.
Deputy Director for Programs
Office of Pollution Prevention and Toxics

possible exposures and risk to consumers should be based on conservative, protective assumptions to minimize the possibility of underestimating exposure or risks [Section A5.2.1(c)].” Thus, EPA selected the cut-off value (≥ 3%) under the assumption that the additivity approach does not apply for the new chemical substance in relation to the other ingredients in the consumer product.

[9] The 20-day criterion for concluding chronic risk is not likely is based on partial life cycle tests (daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration.