United States
Environmental Protection Agency

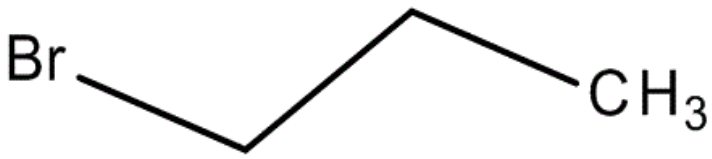
Office of Chemical Safety and
Pollution Prevention

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

Systematic Review Supplemental File:

Data Quality Evaluation of Human Health Hazard Studies – Animal and *In Vitro* Studies

CASRN: 106-94-5



August 2020

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1 Acute (<24 hr)

Table 1: **Animal toxicity evaluation results of Garner et al 2007 for an acute inhalation reproductive-sperm study on reproductive outcomes**

Study Citation:	Garner, C. E., Sloan, C., Sumner, S. C., Burgess, J., Davis, J., Etheridge, A., Parham, A., Ghanayem, B. I. (2007). CYP2E1-catalyzed oxidation contributes to the sperm toxicity of 1-bromopropane in mice Biology of Reproduction, 76(3), 496-505
Data Type:	Acute inhalation reproducive-sperm
HERO ID:	1519112

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by name and form (radiolabel and neat).
	Metric 2:	Test Substance Source	High	× 1	1	The source was reported and identify confirmed by GCMS.
	Metric 3:	Test Substance Purity	High	× 1	1	The reported purity was such that effects likely due to the test substance.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Not Rated	NA	NA	Controls were used, but not described. However, the purpose of the study was to determine the contribution of CYP2E1 to the kinetics of elimination via comparison of Cyp2e1 knockout and wild-type mice. This limitation is unlikely to have a major impact on results.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation methods were not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	The method and equipment used to generate the test gas were reported and appropriate.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was consistent.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	The initial concentration was reported and graphical depiction of chamber concentrations over time was provided. The methods used to measure chamber concentrations were reported, and based on the graph, the initial concentrations were approximately 20% above target. Because both of the groups used for comparison (wild type and knockout) received the same exposure, this limitation is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Duration was reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Not Rated	NA	NA	Only a single exposure concentration was used.

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Study Citation:	Garner, C. E., Sloan, C., Sumner, S. C., Burgess, J., Davis, J., Etheridge, A., Parham, A., Ghanayem, B. I. (2007). CYP2E1-catalyzed oxidation contributes to the sperm toxicity of 1-bromopropane in mice Biology of Reproduction, 76(3), 496-505
Data Type:	Acute inhalation reproducive-sperm
HERO ID:	1519112

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 12:	Exposure Route and Method	Low	× 1	3	It is unclear of the air changes/hour in the chamber.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, strain, sex, and age were reported. Initial body weight and health status were not reported. Cyp2e1 mice were included in the study along with WT mice.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	All conditions except room air changes were reported.
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group was appropriate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methodology was described and appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently.
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not required.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	No confounding variables were reported, but respiratory rate and body temperature were not measured or reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	× 1	2	No health outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	The methods were reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data were adequately reported.
Overall Quality Determination‡			High		1.5	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 2: **Animal toxicity evaluation results of Honma et al 2003 for an inhalation neurotoxicity - traction time study on neurological/behavior outcomes**

Study Citation:	Honma, T., Suda, M., Miyagawa, M. (2003). Inhalation of 1-bromopropane causes excitation in the central nervous system of male F344 rats NeuroToxicology, 24(4-5), 563-575					
Data Type:	Inhalation neurotoxicity - traction time					
HERO ID:	1519108					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Source identified.
	Metric 3:	Test Substance Purity	Medium	× 1	2	Identified as GR grade.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	Medium	× 1	2	Animals were allocated so minimize mean body weight differences across groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Not Rated	NA	NA	Inhalation exposure information as described in Sekiguchi et al., 2002 and Tsuga and Honma, 2000.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Animals exposed during the same time. Inhalation exposure information as described in Sekiguchi et al., 2002 and Tsuga and Honma, 2000.
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Only target and converted concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	The frequency and duration were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of groups and spacing were reported and the highest concentration was based on a previous study.
	Metric 12:	Exposure Route and Method	Not Rated	NA	NA	Inhalation exposure information as described in Sekiguchi et al., 2002 and Tsuga and Honma, 2000.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strain, age, sex, and initial body weight were reported. Health status was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	All conditions were reported except for room air changes.
	Metric 15:	Number per Group	Medium	× 1	2	The number of animals per experiment (n=4-5) was lower than they typical number used in studies of similar type (N=10)

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Study Citation:	Honma, T., Suda, M., Miyagawa, M. (2003). Inhalation of 1-bromopropane causes excitation in the central nervous system of male F344 rats NeuroToxicology, 24(4-5), 563-575
Data Type:	Inhalation neurotoxicity - traction time
HERO ID:	1519108

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methodology was reported clearly (rat forced to hand from suspended bar, time until rat fell was recorded). Standard motor/strength test
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently.
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate for the number of evaluations per exposure group.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not required for this endpoint (objective measure of traction time).
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Respiratory rate was not measured.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were reported and are appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data were reported.
Overall Quality Determination‡			High		1.6	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

2 Short-term (1-30 days)

Table 3: **Animal toxicity evaluation results of Liu et al 2009 (1519113) for a 28-day inhalation-3 strains male mice, liver and repro study on hepatic, reproductive, and body weight outcomes**

Study Citation:	Liu, F., Ichihara, S., Mohideen, S. S., Sai, U., Kitoh, J., Ichihara, G. (2009). Comparative study on susceptibility to 1-bromopropane in three mice strains Toxicological Sciences, 112(1), 100-110
Data Type:	28-day inhalation-3 strains male mice, liver and repro
HERO ID:	1519113

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Source identified.
	Metric 3:	Test Substance Purity	High	× 1	1	The reported purity was such that effects likely due to test substance.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Concurrent negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Study did not report the method used to randomly allocate animals to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Preparation of the test material was reported; storage was not.
	Metric 8:	Consistency of Exposure Administration	Not Rated	NA	NA	Exposures were conducted during the same time each day. The inhalation exposure system was as described in Ichihara et al., 1997 and Takeuchi et al. 1989.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and mean measured concentrations were reported
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration were adequate.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	The number of groups and spacing were reported and based on preliminary experiments.
	Metric 12:	Exposure Route and Method	Not Rated	NA	NA	The inhalation exposure system was as described in Ichihara et al., 1997 and Takeuchi et al. 1989.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strains, sex, and age were reported. Initial body weight and health status were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	All conditions except room air changes were reported.

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Study Citation:	Liu, F., Ichihara, S., Mohideen, S. S., Sai, U., Kitoh, J., Ichihara, G. (2009). Comparative study on susceptibility to 1-bromopropane in three mice strains Toxicological Sciences, 112(1), 100-110
Data Type:	28-day inhalation-3 strains male mice, liver and repro
HERO ID:	1519113

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group is appropriate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methodology was reported and appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently.
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate.
	Metric 19:	Blinding of Assessors	High	× 1	1	Histopathological examinations were performed by investigators blinded to the strain and treatment type.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses responded appropriately.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not reported or measured.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to treatment were reported or inferred.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data were reported.
Overall Quality Determination‡			High		1.5	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 4: **Animal toxicity evaluation results of Zhong et al 2013 for a 12-day oral gavage neurotoxicity study in rats on nutrition and metabolic/adult exposure body weight, and neurological/behavior outcomes**

Study Citation:	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(0), 16-23					
Data Type:	12 day oral gavage neurotoxicity study in rats					
HERO ID:	1717375					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test material identified by unambiguous name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Test substance obtained from manufacturer; lot number not provided and certification of authenticity not reported.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity reported to be 99.99%
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Sham-treated controls received vehicle.
	Metric 5:	Positive Controls	Not Rated	NA	NA	A strict requirement for use of a positive control in Morris water maze testing was not identified in guidance.
	Metric 6:	Randomized Allocation	Low	× 1	3	Method used for allocation of animals in test groups not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	1-BP was dissolved in corn oil; no further details were reported.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	No inconsistencies in exposure administration were noted. Time of day of gavage administration was not reported.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Gavage doses reported in mg/kg bw
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Daily administration for 12 days; duration was sufficient to elicit effect.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	3 nonzero dose groups spanning a range of 4- fold were used; effects were seen at all doses, so the low dose may not have been low enough. Dose selection was based on preliminary experiments.
	Metric 12:	Exposure Route and Method	High	× 1	1	
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The test animal species, strain, sex, lifestage, and starting body weight were reported, and the test animal was obtained from a commercial source. Health status and specific age were not reported. Only male rats were tested.

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Study Citation:	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(0), 16-23
Data Type:	12 day oral gavage neurotoxicity study in rats
HERO ID:	1717375

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	Animal husbandry conditions were reported and adequate, except number of animals per cage.
	Metric 15:	Number per Group	High	× 1	1	10 males/group were tested.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	× 2	4	The only neurotoxicity metric tested was the Morris water maze. The procedure was described adequately.
	Metric 17:	Consistency of Outcome Assessment	Low	× 1	3	Time of day of testing was not reported, so the consistency of outcome assessment is uncertain.
	Metric 18:	Sampling Adequacy	High	× 1	1	All animals were evaluated for all endpoints.
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Study did not report blinding, but Morris water maze test is evaluated with largely objective metrics (escape latency, distance traveled)
	Metric 20:	Negative Control Response	High	× 1	1	Negative control response was reported and appeared to be appropriate. Control response in the MWM was variable, but not so variable that significant differences were masked.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	No information on food or water intake was provided.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were noted. There was no animal attrition.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical analysis methods were described and appropriate.
	Metric 24:	Reporting of Data	Medium	× 2	4	Data are presented graphically with overlapping SD bars that preclude digitizing data for independent analysis.
Overall Quality Determination‡			~~High~~ ⟶ Low§		~~1.6~~	
Extracted			Yes			

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Study Citation:	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(0), 16-23
Data Type:	12 day oral gavage neurotoxicity study in rats
HERO ID:	1717375

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "The only metric that was unacceptable was test substance preparation and storage. The study used gavage administration, so test substance preparation and storage are of lower concern."

Table 5: **Animal toxicity evaluation results of Zhang et al 2013 for 7-day and 4-week inhalation studies on neurological/behavior, and endocrine outcomes**

Study Citation:	Zhang, L., Nagai, T., Yamada, K., Ibi, D.,Ichihara, S., Subramanian, K., Huang, Z., Mohideen, S. S., Naito, H., Ichihara, G. (2013). Effects of sub-acute and sub-chronic inhalation of 1-bromopropane on neurogenesis in adult rats Toxicology, 304(0), 76-82
Data Type:	7-day and 4-week inhalation studies
HERO ID:	1717376

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by chemical name.
	Metric 2:	Test Substance Source	Low	× 1	3	No details were provided on the source of the test substance.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative air controls
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not needed for this study design.
	Metric 6:	Randomized Allocation	Low	× 1	3	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Method and equipment was briefly described (further details were provided in another paper (Ichihara et al, 2000)
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Analytical concentrations were not reported; however, chamber concentrations were measured by GC every 10 seconds and electronically controlled to within +/- 5%.
	Metric 10:	Exposure Frequency and Duration	Medium	× 1	2	8h/day for 1 or 4 weeks. Days per week was not specified for the 4-week studies.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 concentrations plus control. Concentrations were not justified, but a range of responses was observed.
	Metric 12:	Exposure Route and Method	Not Rated	NA	NA	The inhalation exposure system was as described in Ichihara et al., 2000). Dynamic whole-body chamber.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	Species, strain, sex, age, and starting body weight were reported (commercial source)
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Husbandry conditions were reported and appropriate.

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Study Citation:	Zhang, L., Nagai, T., Yamada, K., Ibi, D.,Ichihara, S., Subramanian, K., Huang, Z., Mohideen, S. S., Naito, H., Ichihara, G. (2013). Effects of sub-acute and sub-chronic inhalation of 1-bromopropane on neurogenesis in adult rats Toxicology, 304(0), 76-82
Data Type:	7-day and 4-week inhalation studies
HERO ID:	1717376

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 15:	Number per Group	High	× 1	1	12/group (6 for biochemistry; 6 for histopathology)
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	6/group for biochemistry; 6/group for histopathology
	Metric 19:	Blinding of Assessors	High	× 1	1	Histopath. examiner was blinded to exposure group.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not measured and 1-BP is expected to be a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.5	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 6: **Animal toxicity evaluation results of Mohideen et al 2013 for a 28-day inhalation study on neurological/behavior outcomes**

Study Citation:	Mohideen, S. S., 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 Journal of Occupational Health, 55(1), 29-38
Data Type:	28-day inhalation
HERO ID:	1717378

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by name, CASRN and analytically verified by NMR.
	Metric 2:	Test Substance Source	High	× 1	1	Manufacturer was identified without lot. no.; however analytical verification was referenced.
	Metric 3:	Test Substance Purity	High	× 1	1	99.81%
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative air control was included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not needed for 28-day inhalation study.
	Metric 6:	Randomized Allocation	Low	× 1	3	Method used to randomly allocate animals to study groups was not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Preparation of test substance was reported; storage was not.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Vapor concentration was measured every 10 sec. by GC and was digitally contolled within +/- 5% of the target concnetration.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	8h/day, 7d/wk, 4 wk
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 exposure group plus control; produced a range of responses.
	Metric 12:	Exposure Route and Method	Not Rated	NA	NA	The inhalation exposure system was as described in Ichihara et al.,2000.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	Rat strain and initial body weight were provided (commercial source).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Husbandry condidtions were reported and appropriate.
	Metric 15:	Number per Group	Medium	× 1	2	3 rats/group for histopathology (3 brain sections. 9/group for brain biochemistry.
Domain 5: Outcome Assessment						

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Study Citation:	Mohideen, S. S., 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 Journal of Occupational Health, 55(1), 29-38
Data Type:	28-day inhalation
HERO ID:	1717378

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Immunohistochemistry, and counting by cell type.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Assessments were conducted consistently across dose groups.
	Metric 18:	Sampling Adequacy	High	× 1	1	
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Blinding was not reported, but outcomes were objective.
	Metric 20:	Negative Control Response	High	× 1	1	A negative control was included and responded appropriately.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not reported and 1-BP is anticipated to be a respiratory irritant'.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	Medium	× 2	4	Some Western blot and mRNA data were not shown.
Overall Quality Determination‡			High		1.4	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 7: **Animal toxicity evaluation results of NTP 2011 for a 2-week inhalation dose range finding study in rats and mice on mortality, nutrition and metabolic/adult exposure body weight, neurological/behavior, respiratory, cardiovascular, renal, hepatic, and hematological and immune outcomes**

Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	2-week inhalation dose range finding study in rats and mice
HERO ID:	1737813

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Chambers analyzed for particles to ensure form of 1-BP was vapor.
	Metric 2:	Test Substance Source	High	× 1	1	
	Metric 3:	Test Substance Purity	High	× 1	1	
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not typical for this study type
	Metric 6:	Randomized Allocation	Medium	× 1	2	Random allocation into groups with approximately equal initial mean body weights
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	No inconsistencies in administration were reported.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations were reported and within 10% of nominal. Chamber air analyzed by GC every 20 min during exposure
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	5 nonzero exposure levels were used, ranging 16-fold and yielding effects at the higher concentrations.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Study does not explicitly state whether nose-only or whole body, but it appears to be dynamic whole body chamber with 15 air changes/hr.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	5/sex/group; appropriate number for study duration/purpose.
Domain 5: Outcome Assessment						

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Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	2-week inhalation dose range finding study in rats and mice
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment described in detail; appropriate methods used.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were reported.
	Metric 18:	Sampling Adequacy	High	× 1	1	Histopathology examined on all control and high exposure animals, and to a no effect level for organs affected at the highest exposure level.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	No subjective endpoints evaluated apart from clinical signs of toxicity.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature and were respiratory rates not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 8: **Animal toxicity evaluation results of Guo et al 2015 for a 12-day oral gavage study on neurological/behavior outcomes**

Study Citation:	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 Research, 1600 1-16
Data Type:	12-day oral gavage study
HERO ID:	2990971

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by chemical name
	Metric 2:	Test Substance Source	Medium	× 1	2	Manufacturer was reported without lot/batch no.
	Metric 3:	Test Substance Purity	High	× 1	1	99.99% pure
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	A negative control group was used; however, it was not stated whether it was a vehicle (i.e., corn oil) or untreated control group.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not needed for neurotoxicity studies.
	Metric 6:	Randomized Allocation	Low	× 1	3	Study did not report the method used to allocate animals to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	1-BP was dissolved in corn oil; no further details were reported.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Gavage volume was not reported.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	
	Metric 10:	Exposure Frequency and Duration	Medium	× 1	2	Daily gavage administration for 12 consecutive days differs from typical neurotoxicity study designs.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	4 Treatment groups, plus control. Dose levels and spacing were not justified, but a range of responses was observed.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Dosing volumes were not reported.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	Species, strain and starting body weight were reported; health status and age were not. (commercial source).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Husbandry conditions were reported and appropriate.
	Metric 15:	Number per Group	High	× 1	1	14/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Behavioral tests and estimation of neuronal loss.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	

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Study Citation:	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 Research, 1600 1-16
Data Type:	12-day oral gavage study
HERO ID:	2990971

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 18:	Sampling Adequacy	Medium	× 1	2	10/group for behavior; 4/group for immunohistochemistry.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding was not reported, but outcomes were objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	High	× 2	2	No differences in initial body weight
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.4	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 9: **Animal toxicity evaluation results of Zong et al 2016 for a 28-day inhalation study on neurological/behavior and hepatic outcomes**

Study Citation:	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 Toxicology Letters, 258 249-258
Data Type:	28-day inhalation study
HERO ID:	3539685

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by chemical name and CASRN.
	Metric 2:	Test Substance Source	High	× 1	1	Manufacturer and lot no. were reported.
	Metric 3:	Test Substance Purity	High	× 1	1	>98% pure
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not needed for repeat dose inhalation studies.
	Metric 6:	Randomized Allocation	Low	× 1	3	The study authors did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Not Rated	NA	NA	Methods were briefly described. Equipment and methods used for vapor generation are reported in other publications.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Measured concentrations were not reported; however, concentrations were measured every 5 seconds by GC and were digitally controlled to be within +/-5% of the target.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Days/week was not reported but assumed to be 7 days/week. 8h/day for 28 days.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	Concentrations were justified by previous data. 2 concentrations plus control. A range of responses was noted.
	Metric 12:	Exposure Route and Method	High	× 1	1	
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	Species, strain, sex and starting age was reported; initial body weight was not (commercial source).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	Husbandry conditions (except number of animals per cage) were reported.
	Metric 15:	Number per Group	High	× 1	1	5-6/group

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Study Citation:	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 Toxicology Letters, 258 249-258
Data Type:	28-day inhalation study
HERO ID:	3539685

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	
	Metric 19:	Blinding of Assessors	Low	× 1	3	Blinding was not reported for subjective endpoints.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not measured; 1-BP is expected to cause respiratory irritation.
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported for each study group.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	Medium	× 2	4	Incidence data were not provided for histopathology data.
Overall Quality Determination‡			High		1.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 10: **Animal toxicity evaluation results of Zong et al 2016 for a 28-day inhalation study on reproductive, hematological, immune, renal, and hepatic outcomes**

Study Citation:	Zong, C; Zhang, X; Huang, C; Chang, J; Garner, CE; Sakurai, T; Kato, M; Ichihara, S; Ichihara, G (2016). Role of cytochrome P450s in the male reproductive toxicity of 1-bromopropane Toxicology Research, 5(6), 1522-1529
Data Type:	28-day inhalation
HERO ID:	3554790

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by chemical name and CASRN.
	Metric 2:	Test Substance Source	High	× 1	1	Manufacturer and lot no. were provided.
	Metric 3:	Test Substance Purity	High	× 1	1	99.81% pure
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative air controls were used.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not generally used for repeat dose inhalation studies.
	Metric 6:	Randomized Allocation	Low	× 1	3	Study authors did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Not Rated	NA	NA	Details on equipment were not reported (provided in another study;
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Measured concentrations were not reported; however, chamber concentrations were monitored every 5 seconds by GC. Values ranged from +/- 11 to 14%.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	8 h/day, 7 days/wk for 4 weeks
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	2 concentrations plus control. Concentrations were not justified. Use of 3 test groups and a control are generally recommended.
	Metric 12:	Exposure Route and Method	Not Rated	NA	NA	The inhalation exposure system was as described in Ichihara et al., 2000. (Whole body exposure.) Analytical concentrations showed significant variability (std deviation > 10%) in mean air concentrations
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	Species, strain, sex and starting age were reported, but not body weight (commercial source).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	Husbandry conditions (except # animals per cage) were reported.
	Metric 15:	Number per Group	High	× 1	1	6/group

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Study Citation:	Zong, C; Zhang, X; Huang, C; Chang, J; Garner, CE; Sakurai, T; Kato, M; Ichihara, S; Ichihara, G (2016). Role of cytochrome P450s in the male reproductive toxicity of 1-bromopropane Toxicology Research, 5(6), 1522-1529
Data Type:	28-day inhalation
HERO ID:	3554790

Domain	Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 5: Outcome Assessment					
	Metric 16: Outcome Assessment Methodology	High	× 2	2	
	Metric 17: Consistency of Outcome Assessment	High	× 1	1	
	Metric 18: Sampling Adequacy	High	× 1	1	
	Metric 19: Blinding of Assessors	Low	× 1	3	Blinding was not reported; some sperm parameters may be considered subjective.
	Metric 20: Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control					
	Metric 21: Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not reported and 1-BP is expected to cause respiratory irritation.
	Metric 22: Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported for each study group
Domain 7: Data Presentation and Analysis					
	Metric 23: Statistical Methods	High	× 1	1	
	Metric 24: Reporting of Data	High	× 2	2	
Overall Quality Determination[‡]		High		1.5	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 11: **Animal toxicity evaluation results of Weinberg 2016 for a 4-week somatic mutation gene inhalation study in transgenic mice study on hepatic and body weight outcomes**

Study Citation:	Weinberg, JT (2016). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation					
Data Type:	4-week somatic mulation gene inhalation study in transgenic mice					
HERO ID:	4140180					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identity and CAS number clearly stated.
	Metric 2:	Test Substance Source	High	× 1	1	Commercial source, lot# provided
	Metric 3:	Test Substance Purity	High	× 1	1	0.999
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Filtered air control
	Metric 5:	Positive Controls	High	× 1	1	Positive control included
	Metric 6:	Randomized Allocation	High	× 1	1	computer randomized
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Comprehensive study details were provided
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Study includes details on methods used to generate test atmospheres for inhalation exposures. Variability (>20% CV) observed in 62.5 ppm treatment group.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations provided
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	6hrs/day 5 days/week for 4 weeks
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	Three exposure groups and a control; justification provided.
	Metric 12:	Exposure Route and Method	High	× 1	1	Whole body inhalation exposure; no aerosol formation detected.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	Transgenic mice were appropriate for the purpose of the study (in vivo genotoxicity; study authors provide justification for use of females only
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Clearly reported and acceptable.
	Metric 15:	Number per Group	High	× 1	1	7 animals per group
Domain 5: Outcome Assessment						

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Study Citation:	Weinberg, JT (2016). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation
Data Type:	4-week somatic mulation gene inhalation study in transgenic mice
HERO ID:	4140180

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	It is not clear how outliers were verified. DNA sequencing data was not used to determine whether 'jackpots' are the cause of high inter-individual variation. bioassay.
	Metric 17:	Consistency of Outcome Assessment	Low	× 1	3	Mutant frequency in negative controls comparable to historical controls; however, because manifestation time varies by tissue type, the relevance of a negative assay result for lung tissue is uncertain.
	Metric 18:	Sampling Adequacy	High	× 1	1	Liver/lung weights and body weights reported for all animals; samples from the first 5 treated or control from each group were processed for DNA isolation. Tissues from the sixth animal per group were retained.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Not necessary
	Metric 20:	Negative Control Response	Low	× 1	3	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported for each study group.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods acceptable
	Metric 24:	Reporting of Data	High	× 2	2	Raw data tables provided
Overall Quality Determination‡			~~High~~ ⟶ Medium§		~~1.5~~	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "The reviewer downgraded this study's overall quality rating. They noted: It is unclear whether the protocol was adequate to identify the intended result, as the maximum tolerated dose was not evaluated (OPP recommends testing at concentrations up to 1.5 times the maximum tolerated dose reported in the 2-year cancer bioassay). The sensitivity of the transgenic test system is also influenced by the duration of the post-exposure observation period.. Although a score was calculated, it is not presented here because the final rating was changed based on professional judgement."

3 Other

Table 12: **Animal toxicity evaluation results of Ishidao et al 2002 for an ADME - metabolism after inhalation study on ADME/PBPK outcomes**

Study Citation:	Ishidao, T., Kunugita, N., Fueta, Y., Arashidani, K., Hori, H. (2002). Effects of inhaled 1-bromopropane vapor on rat metabolism Toxicology Letters, 134(1-3), 237-243					
Data Type:	ADME - metabolism after inhalation					
HERO ID:	1717491					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by chemical name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Manufacturer was indicated without lot no.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Not Rated	NA	NA	Negative controls were not needed for metabolism studies.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not needed for metabolism studies.
	Metric 6:	Randomized Allocation	Low	× 1	3	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Vapor generation method and equipment were reported.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Nominal and analytical concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	6h/day, 5 days/wk, 3, 4, or 12 weeks (also single day exposure).
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	Adequate for ADME; however, high and low concentration had different exposure durations ((700 ppm for 4 and 12 weeks; 1500 ppm for 3 weeks)..
	Metric 12:	Exposure Route and Method	Low	× 1	3	The inhalation exposure system was as described in Hori et al., 1999.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	Commercial source (species, strain, age reported).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	Husbandry conditions were not reported.
	Metric 15:	Number per Group	High	× 1	1	10/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	

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Study Citation:	Ishidao, T., Kunugita, N., Fueta, Y., Arashidani, K., Hori, H. (2002). Effects of inhaled 1-bromopropane vapor on rat metabolism Toxicology Letters, 134(1-3), 237-243
Data Type:	ADME - metabolism after inhalation
HERO ID:	1717491

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	Medium	× 1	2	
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding was not reported; however, outcomes were objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not measured and 1-BP is expected to be a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported for each study group.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.7	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

4 Subchronic (30-90 days)

Table 13: **Animal toxicity evaluation results of Ichihara et al 2000 for a 12 week inhalation reproductive toxicity study in male rats on hematological and immune outcomes**

Study Citation:	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. (2000). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats Toxicological Sciences, 54(2), 416-423
Data Type:	12 week inhalation reproductive tox study in male rats (Hematol and immune)
HERO ID:	1309569

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by unambiguous name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Test substance source reported but without certification or analytical verification of identity.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity reported to be 99.81%
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	A concurrent negative control group was reported but it is unclear whether the control was sham-treated or untreated. SO: Controls were untreated (i.e., animals received fresh air).
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not typical for study type
	Metric 6:	Randomized Allocation	Low	× 1	3	Authors report random allocation; however, randomization method was not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Low	× 1	3	Some information on the method used to generate the test atmosphere was cited to prior studies. There was no description of the exposure chamber; however, chamber concentrations were measured every 10 sec during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	No inconsistencies in exposure administration were noted.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations reported; mean values were within 10% of nominal
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency was reported to be 8 hr/d for 12 weeks.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	3 nonzero exposure groups ranging 4-fold were used; max concentration selected based on prior study. Effect seen at lowest exposure level, so it may not have been low enough.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Inhalation exposure information as described in Ichihara et al., 1997; Takeuchi et al., 1989. Exposure concentrations were verified analytically.

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Study Citation:	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. (2000). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats Toxicological Sciences, 54(2), 416-423
Data Type:	12 week inhalation reproductive tox study in male rats (Hematol and immune)
HERO ID:	1309569

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The test animal species, strain, sex, health status, and age, were reported and appropriate, and the test animal was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	Temp, humidity, and photoperiod were reported and appropriate; cages, housing, and diet were not described.
	Metric 15:	Number per Group	Medium	× 1	2	9 males/group were tested.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	× 2	4	Hematology endpoints and spleen and thymus weights evaluated; no histopathology
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were noted.
	Metric 18:	Sampling Adequacy	High	× 1	1	All endpoints evaluated in all animals
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Endpoints were not subjective
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Respiratory rates, initial body weights, and food and water intake were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	One control rat was excluded due to splenoma
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical analysis methods were reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 14: **Animal toxicity evaluation results of Anderson et al 2010 for a 4 and 10 week inhalation immunotoxicity study in mice and rats on mortality, nutrition and metabolic/adult exposure body weight, and hematological and immune outcomes**

Study Citation:	Anderson, S.E., Munson, A.E., Butterworth, L.F., Germolec, D., Morgan, D.L., Roycroft, J.A., Dill, J., Meade, B.J. (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 Inhalation Toxicology, 22(2), 125-132
Data Type:	4 and 10 week inhalation immunotoxicity study in mice and rats
HERO ID:	1717420

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by name and CASRN
	Metric 2:	Test Substance Source	Medium	× 1	2	Test substance obtained from commercial source without lot number and analyzed for purity by GC and elemental analysis.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity analyzed by elemental analysis and GC to be 99.5% or higher
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Sham-treated negative controls were exposed to filtered conditioned air.
	Metric 5:	Positive Controls	Low	× 1	3	positive controls are recommended but not mandatory for immunotoxicity testing
	Metric 6:	Randomized Allocation	Low	× 1	3	Paper reports animals were randomized but allocation method not detailed.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Test substance preparation and storage reported and appropriate; stability during storage was tested and no degradation found.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Details of the chamber used for exposures, and time of day of exposures, were not reported. However, concentrations were monitored continuously via on-line GC-FID.
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Neither analytical concentrations nor variation of measured values from nominal concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	3 nonzero concentrations were used, with 4-fold range. Effects were seen at the lowest exposure, so it is not clear that it was low enough.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Animals were exposed via whole-body inhalation (15 air changes per hour were reported); The chamber size was not reported.

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Study Citation:	Anderson, S.E., Munson, A.E., Butterworth, L.F., Germolec, D., Morgan, D.L., Roycroft, J.A., Dill, J., Meade, B.J. (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 Inhalation Toxicology, 22(2), 125-132
Data Type:	4 and 10 week inhalation immunotoxicity study in mice and rats
HERO ID:	1717420

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The test animal species, strain, sex, and age were reported, and the test animal was obtained from a commercial source. Only females were tested. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Husbandry conditions were reported, appropriate, and consistent across groups.
	Metric 15:	Number per Group	High	× 1	1	8 females/group were exposed. This is the number recommended by EPA for immunotoxicity testing
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	× 2	4	Thymus weights were not measured; remaining endpoints are sensitive and appropriate
	Metric 17:	Consistency of Outcome Assessment	Medium	× 1	2	The only deviation from the test plan was failure to perform PFC assay on rat spleens after 4 wks, due to a shipping error.
	Metric 18:	Sampling Adequacy	High	× 1	1	Experiment was replicated, enabling analysis of 8/group immunized spleens for IgM response to SRBC and 8/group unimmunized spleens to splenocyte phenotyping and NK cell activity.
	Metric 19:	Blinding of Assessors	Low	× 1	3	Blinding is recommended for PFC assay; study does not report blinding.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Authors note that PFC and serum IgM response peak on different days (4 or 5-6 days after immunization) but spleen and serum were collected the same day (3 days after immunization).
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	× 1	3	Authors report that there were 3 deaths among mice exposed to the highest concentration during the first week of the 4 week exposure. It is unclear why the number of animals was reported to be 5 for both the 4 week and 10 week spleen weight and PFC assays, as these should have been two separate groups, unless there were 3 additional deaths in the group exposed for 10 weeks.
Domain 7: Data Presentation and Analysis						

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Study Citation:	Anderson, S.E., Munson, A.E., Butterworth, L.F., Germolec, D., Morgan, D.L., Roycroft, J.A., Dill, J., Meade, B.J. (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 Inhalation Toxicology, 22(2), 125-132
Data Type:	4 and 10 week inhalation immunotoxicity study in mice and rats
HERO ID:	1717420

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 23: Statistical Methods	High	× 1	1	Statistical analysis methods were reported and appropriate. Data enabling independent analysis were reported.
	Metric 24: Reporting of Data	High	× 2	2	
Overall Quality Determination‡		Medium		1.7	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 15: **Animal toxicity evaluation results of Ishidao et al 2002 for an acute, short-term and subchronic inhalation studies study on hematological and immune, and hepatic outcomes**

Study Citation:	Ishidao, T., Kunugita, N., Fueta, Y., Arashidani, K., Hori, H. (2002). Effects of inhaled 1-bromopropane vapor on rat metabolism Toxicology Letters, 134(1-3), 237-243
Data Type:	acute, short-term and subchronic inhalation studies
HERO ID:	1717491

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identified by chemical name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Manufacturer was indicated without lot no.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Not Rated	NA	NA	Air controls.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not needed for repeat dose studies.
	Metric 6:	Randomized Allocation	Low	× 1	3	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Vapor generation method and equipment were reported.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Measured concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	6h/day, 5 days/wk, 3, 4, or 12 weeks (also single day exposure).
	Metric 11:	Number of Exposure Groups and Dose Spacing	Low	× 1	3	High and low concentrations were not exposed for the same durations (700 ppm for 4 and 12 weeks; 1500 ppm for 3 weeks).
	Metric 12:	Exposure Route and Method	High	× 1	1	
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	Commercial source (species, strain, age reported).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	Husbandry conditions were not reported.
	Metric 15:	Number per Group	High	× 1	1	10/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Unacceptable	× 2	8	Hematological parameters were limited to (RBC, WBC, Hb and Hct). Serum ALT and AST were the only hepatic endpoints evaluated (i.e., no liver wt. or histopathology).

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Study Citation:	Ishidao, T., Kunugita, N., Fueta, Y., Arashidani, K., Hori, H. (2002). Effects of inhaled 1-bromopropane vapor on rat metabolism Toxicology Letters, 134(1-3), 237-243
Data Type:	acute, short-term and subchronic inhalation studies
HERO ID:	1717491

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	Medium	× 1	2	Data were not reported for (4 week) 1500 ppm exposure group.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding was not reported; however, outcomes were objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not measured and 1-BP is expected to be a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on attrition and/or health outcomes unrelated to exposure were not reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			~~Unacceptable~~⋆⋆ ⟶ Low§		~~1.9~~	
Extracted			No			

⋆⋆ Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Although the evaluation of hematological parameters is limited, the study results are acceptable."

Table 16: **Animal toxicity evaluation results of NTP 2011 for a 3-month inhalation study in rats and mice study on mortality, skin and connective tissue, ocular and sensory, nutrition and metabolic/adult exposure body weight, respiratory, cardiovascular, renal, hepatic, hematological and immune, clinical chemistry/biochemical, endocrine, gastrointestinal, reproductive, and thyroid outcomes**

Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	3-month inhalation study in rats and mice
HERO ID:	1737813

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Chambers analyzed for particles to ensure form of 1-BP was vapor.
	Metric 2:	Test Substance Source	High	× 1	1	
	Metric 3:	Test Substance Purity	High	× 1	1	
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not typical for this study type
	Metric 6:	Randomized Allocation	Medium	× 1	2	Random allocation into groups with approximately equal initial mean body weights
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	No inconsistencies in administration were reported.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations were reported and within 10% of nominal. Chamber air analyzed by GC every 20 min during exposure
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	5 nonzero exposure levels were used, ranging 16-fold and yielding effects at the higher concentrations.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Study does not explicitly state whether exposure is nose-only or whole body, but it appears to be a dynamic whole body chamber with 15 air changes/hr.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	10/sex/group; appropriate number for study duration/purpose.

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Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	3-month inhalation study in rats and mice
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment described in detail and sensitive.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were reported.
	Metric 18:	Sampling Adequacy	High	× 1	1	Histopathology examined on all control and high exposure animals, and to a no effect level for organs affected at the highest exposure levels.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	No subjective endpoints evaluated apart from clinical signs of toxicity.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature and respiratory rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 17: **Animal toxicity evaluation results of Ichihara et al 2000 for a 12 week inhalation reproductive toxicology study in male rats on renal, hepatic, and endocrine outcomes**

Study Citation:	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. (2000). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats Toxicological Sciences, 54(2), 416-423
Data Type:	12 week inhalation reproductive tox study in male rats (renal, hepatic, endocrine)
HERO ID:	1309569

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by unambiguous name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Test substance source reported (99.81% purity); however, no analytical verification or lot number was provided.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity reported to be 99.81%
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Medium	× 2	4	Negative control group was reported. Animals were untreated (i.e., exposed to fresh air).
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not typically used for this study type.
	Metric 6:	Randomized Allocation	High	× 1	1	Authors report random allocation
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Low	× 1	3	Some information on the method used to generate the test atmosphere was cited to prior studies. There was no description of the exposure chamber; however, chamber concentrations were measured via gas chromatography every 10 seconds during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	No inconsistencies in exposure administration were noted.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations reported; mean values were within 10% of nominal
	Metric 10:	Exposure Frequency and Duration	Low	× 1	3	Weekly frequency was not reported. Frequency was reported to be 8 hr/d for 12 weeks.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	3 nonzero exposure groups ranging 4-fold were used; max concentration selected based on prior study. Effect seen at lowest exposure level, so it may not have been low enough.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Inhalation exposure information as described in Ichihara et al., 1997; Takeuchi et al., 1989. Exposure concentrations were verified analytically.
Domain 4: Test Organism						

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Study Citation:	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. (2000). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats Toxicological Sciences, 54(2), 416-423
Data Type:	12 week inhalation reproductive tox study in male rats (renal, hepatic, endocrine)
HERO ID:	1309569

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The test animal species, strain, sex, health status, and age, were reported and appropriate, and the test animal was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	Temperature, humidity, and photoperiod were reported and appropriate; the number of animals per cage, , and diet were not described.
	Metric 15:	Number per Group	Medium	× 1	2	9 males/group were tested.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	The only renal, endocrine, and hepatic endpoints evaluated were organ weights (no clinical chemistry or histopathology)
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were noted.
	Metric 18:	Sampling Adequacy	High	× 1	1	All endpoints evaluated in all animals
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Endpoints were not subjective
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Respiratory rates, initial body weights, and food and water intake were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	One control rat was excluded due to splenoma
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical analysis methods were reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.7	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 18: **Animal toxicity evaluation results of Ichihara et al 2000 for a 12 week inhalation reproductive toxicity study in male rats on nutrition and metabolic/adult exposure body weight, and reproductive outcomes**

Study Citation:	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. (2000). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats Toxicological Sciences, 54(2), 416-423
Data Type:	12 week inhalation reproductive tox study in male rats
HERO ID:	1309569

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by unambiguous name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Test substance source reported but without certification or analytical verification of identity.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity reported to be 99.81%
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Low	× 2	6	A concurrent negative control group was reported but it is unclear whether the control was sham-treated or untreated.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not typical for study type
	Metric 6:	Randomized Allocation	High	× 1	1	Authors report random allocation
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Some information on the method used to generate the test atmosphere was cited to prior studies. There was no description of the exposure chamber. However, chamber concentrations were measured every 10 sec during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	No inconsistencies in exposure administration were noted.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	analytical concentrations reported; mean values were within 10% of nominal
	Metric 10:	Exposure Frequency and Duration	Low	× 1	3	Weekly frequency was not reported. Frequency was reported to be 8 hr/d for 12 weeks.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	3 nonzero exposure groups ranging 4-fold were used; max concentration selected based on prior study. Effect seen at lowest exposure level, so it may not have been low enough.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Inhalation exposure information as described in Ichihara et al., 1997; Takeuchi et al., 1989. Exposure concentrations were verified analytically.
Domain 4: Test Organism						

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Study Citation:	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. (2000). Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats Toxicological Sciences, 54(2), 416-423
Data Type:	12 week inhalation reproductive tox study in male rats
HERO ID:	1309569

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The test animal species, strain, sex, health status, and age, were reported and appropriate, and the test animal was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	Temp, humidity, and photoperiod were reported and appropriate; cages, housing, and diet were not described.
	Metric 15:	Number per Group	Medium	× 1	2	9 males/group were tested.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	× 2	4	Some methods were cited to prior publications.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were noted.
	Metric 18:	Sampling Adequacy	High	× 1	1	Study examined 12 seminiferous tubules per rat, which is more than the 10 recommended in prior studies (according to authors). All endpoints evaluated in all animals
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Most endpoints were not subjective
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rates, initial body weights, and food and water intake were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	× 1	2	One control rat was excluded due to splenoma
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical analysis methods were reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			Medium		1.8	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 19: **Animal toxicity evaluation results of Yu et al 2001 for a neurotoxicity-inhalation study for 5 or 7 weeks on neurological outcomes**

Study Citation:	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 Environmental Research, 85(1), 48-52					
Data Type:	Neurotoxicity-inhalation 5 or 7 weeks					
HERO ID:	1519105					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name.
	Metric 2:	Test Substance Source	Medium	× 1	2	Source identified.
	Metric 3:	Test Substance Purity	High	× 1	1	Reported purity such that effects likely due to the test substance.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative control animals were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation methods were not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Not Rated	NA	NA	The inhalation exposure system was described in Takeuchi et al., 1989, and Ichihara et al., 1997.
	Metric 8:	Consistency of Exposure Administration	Low	× 1	3	Exposure was discontinued because rats became emaciated after 5-7 weeks of exposure.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and measured vapor concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Exposure frequency and duration were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Low	× 1	3	Only one concentration group was exposed.
	Metric 12:	Exposure Route and Method	Low	× 1	3	The exposure route and method described in Takeuchi et al., 1989, and Ichihara et al., 1997.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strain, age, sex, and initial body weight were reported. Health status was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	All conditions except room air changes were reported.
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group was appropriate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methodology was reported.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently.

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Study Citation:	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 Environmental Research, 85(1), 48-52
Data Type:	Neurotoxicity-inhalation 5 or 7 weeks
HERO ID:	1519105

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding was not required.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	High	× 2	2	No confounding variables in test design were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to treatment were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data were reported.
Overall Quality Determination‡			~~High~~ ⟶ Medium§		~~1.6~~	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Only one concentration was evaluation (1000 ppm)."

Table 20: **Animal toxicity evaluation results of Yamada et al 2003 for an inhalation female reproductive study on reproductive outcomes**

Study Citation:	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 Toxicological Sciences, 71(1), 96-103
Data Type:	Inhalation female reproductive
HERO ID:	1519107

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name only.
	Metric 2:	Test Substance Source	Medium	× 1	2	The source was identified.
	Metric 3:	Test Substance Purity	High	× 1	1	The reported purity (> 99.5%), analyzed by GC, is such that effects likely due to the test substance.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Medium	× 2	4	Concurrent negative controls were included; however, limited details were provided in the study.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation method was not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Not Rated	NA	NA	The inhalation exposure system was described in Huang et al., 1989, 1990, and Takauchi et al., 1989.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Animals were exposed during the same time daily. The inhalation exposure system was described in Huang et al., 1989, 1990, and Takauchi et al., 1989.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	The target and actual concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration were adequate.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of exposure groups were reported and were adequate to show result; however, rats of the 800 ppm group were excluded from analysis because they became ill and were euthanized before study completion (8th week).
	Metric 12:	Exposure Route and Method	Low	× 1	3	The inhalation exposure system was described in Huang et al., 1989, 1990, and Takauchi et al., 1989.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	Animal source, species, strain, age and sex was reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	All husbandry conditions except room air changes were reported.
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group was appropriate.

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Study Citation:	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 Toxicological Sciences, 71(1), 96-103
Data Type:	Inhalation female reproductive
HERO ID:	1519107

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methodology was described and appropriate.
	Metric 17:	Consistency of Outcome Assessment	Medium	× 1	2	Outcomes were assessed consistently; however, rats of the 800 ppm treatment group were excluded from analysis because they became ill and were euthanized before study completion (8th week). .
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding was not reported; however, no subjective endpoints were evaluated.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Respiratory rate and body temperature was not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were reported or inferred.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data were reported.
Overall Quality Determination‡			High		1.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 21: **Animal toxicity evaluation results of Honma et al 2003 for an inhalation neurotoxicity study on neurological/behavior outcomes**

Study Citation:	Honma, T., Suda, M., Miyagawa, M. (2003). Inhalation of 1-bromopropane causes excitation in the central nervous system of male F344 rats NeuroToxicology, 24(4-5), 563-575
Data Type:	Inhalation neurotoxicity
HERO ID:	1519108

Domain		Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name only.
	Metric 2:	Test Substance Source	Medium	× 1	2	Source identified.
	Metric 3:	Test Substance Purity	Medium	× 1	2	Identified as GR grade.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	Medium	× 1	2	Method used for randomization not reported; however, animals were allocated to minimize mean body weight differences across groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Inhalation exposure information as described in Sekiguchi et al., 2002 and Tsuga and Honma, 2000.
	Metric 8:	Consistency of Exposure Administration	Not Rated	NA	NA	Animals exposed during the same time as described in Sekiguchi et al., 2002 and Tsuga and Honma, 2000.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Only target and converted concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	Medium	× 1	2	The frequency and duration were reported; however, the duration of exposure did not span a 28-day period in the repeated-dose inhalation study.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	The number of groups and spacing were reported and the highest concentration was based on a previous study.
	Metric 12:	Exposure Route and Method	Low	× 1	3	Inhalation exposure information as described in Sekiguchi et al., 2002 and Tsuga and Honma, 2000.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strain, age, sex, and initial body weight were reported. Health status was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	All conditions were reported except for the number of room air changes.

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Study Citation:	Honma, T., Suda, M., Miyagawa, M. (2003). Inhalation of 1-bromopropane causes excitation in the central nervous system of male F344 rats NeuroToxicology, 24(4-5), 563-575
Data Type:	Inhalation neurotoxicity
HERO ID:	1519108

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 15:	Number per Group	Medium	× 1	2	The number of animals per dose group (n=4-5) was lower than the typical number used in studies of similar type (N=10)
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methodology was reported.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently.
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate for the number of evaluations per exposure group.
	Metric 19:	Blinding of Assessors	Unacceptable	× 1	4	Blinding was not reported for the functional observation experiments (e.g., passive avoidance, open field behavior).
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Although respiratory rate was not measured; body temperature was monitored and may serve as a proxy for changes in respiration rate.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were reported and are appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data were reported.
Overall Quality Determination‡			~~Unacceptable~~** ⟶ Low§		~~1.7~~	
Extracted			No			

** Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Although blinding is important, some FOB parameters were measured objectively via computer."

Table 22: **Animal toxicity evaluation results of Fueta et al 2007 for an inhalation neurotoxicity-disinhibition and regional sensitivity study on neurological/behavior outcomes**

Study Citation:	Fueta, Y., Ishidao, T., Ueno, S., Yoshia, Y., Kunugita, N., Hori, H. (2007). New approach to risk assessment of central neurotoxicity induced by 1-bromopropane using animal models NeuroToxicology, 28(2), 270-273					
Data Type:	Inhalation neurotoxicity-disinhibition and regtional sensitivity					
HERO ID:	1519111					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name.
	Metric 2:	Test Substance Source	Low	× 1	3	Source not identified.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity and/or grade was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation methods were not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Not Rated	NA	NA	Inhalation exposure methods were as described in Fueta et al., 2004 (1717472) which referenced Ishidao et al., 2002.
	Metric 8:	Consistency of Exposure Administration	Not Rated	NA	NA	Inhalation exposure methods were as described in Fueta et al., 2004 (1717472) which referenced Ishidao et al., 2002.
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Actual exposure concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and exposure were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	The number of groups and spacing were reported and justified.
	Metric 12:	Exposure Route and Method	Low	× 1	3	Inhalation exposure methods were as described in Fueta et al., 2004 (1717472) which referenced Ishidao et al., 2002.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strain, sex, and age were reported. Initial body weight and health status were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	Husbandry conditions were not reported.
	Metric 15:	Number per Group	Medium	× 1	2	The number of animals per group was reported but not clearly stated for all experiments.
Domain 5: Outcome Assessment						

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Study Citation:	Fueta, Y., Ishidao, T., Ueno, S., Yoshia, Y., Kunugita, N., Hori, H. (2007). New approach to risk assessment of central neurotoxicity induced by 1-bromopropane using animal models NeuroToxicology, 28(2), 270-273
Data Type:	Inhalation neurotoxicity-disinhibition and regtional sensitivity
HERO ID:	1519111

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	Medium	× 2	4	Outcome assessment methodology was as described in Fueta et al., 2002 (1733939) and 2004 (1717472). Treatment of hippocampal slices was different in both studies.
	Metric 17:	Consistency of Outcome Assessment	Medium	× 1	2	Reporting of outcome assessment and protocol execution were incomplete.
	Metric 18:	Sampling Adequacy	Low	× 1	3	Details regarding sampling were not reported.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not required.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not reported or measured.
	Metric 22:	Health Outcomes Unrelated to Exposure	Not Rated	NA	NA	Data on health outcomes unrelated to exposure were not reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were reported and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	× 2	2	Data were presented for the outcomes of interest.
Overall Quality Determination‡			Medium		2.1	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

5 Chronic (>90 days)

Table 23: **Animal toxicity evaluation results of NTP 2011 for a 2 year inhalation study in rats and mice study on mortality, skin and connective tissue, ocular and sensory, nutrition and metabolic/adult exposure body weight, respiratory, cardiovascular, renal, hepatic, hematological and immune, endocrine, gastrointestinal, reproductive, thyroid, and cancer outcomes**

Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	2 yr inhalation study in rats and mice
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Chambers analyzed for particles to ensure form of 1-BP was vapor.
	Metric 2:	Test Substance Source	High	× 1	1	
	Metric 3:	Test Substance Purity	High	× 1	1	
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not typical for this study type
	Metric 6:	Randomized Allocation	Medium	× 1	2	Random allocation into groups with approximately equal initial mean body weights
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	No inconsistencies in administration were reported.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations were reported and within 10% of nominal. Chamber air analyzed by GC every 20 min during exposure.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 nonzero exposure levels were used, ranging 4-fold; effect levels were identified.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Study does not explicitly state whether nose-only or whole body; dynamic whole-body chamber with 15 air changes/hr.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	50/sex/group; appropriate number for study duration/purpose.

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Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	2 yr inhalation study in rats and mice
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment was sensitive and described in detail; limited to BW and histopath (no organ weights, hematology, or clinical chemistry).
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were reported.
	Metric 18:	Sampling Adequacy	High	× 1	1	All evaluations performed on all animals
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	No subjective endpoints evaluated apart from clinical signs of toxicity.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature and respiratory rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 24: **Animal toxicity evaluation results of WIL Research 2001 for a 2-generation inhalation study on liver outcomes**

Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats					
Data Type:	2-generation inhalation - liver					
HERO ID:	2990994					
Domain		Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	
	Metric 2:	Test Substance Source	High	× 1	1	Commercial source, manufacturer and lot numbers provided.
	Metric 3:	Test Substance Purity	High	× 1	1	At least 99.8% pure.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative control exposed to filtered air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not used for 2-gen repro. studies.
	Metric 6:	Randomized Allocation	High	× 1	1	Animals were allocated to study groups using a computerized randomization procedure.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Preparation and storage conditions were described; exposure concentrations were measured by GC every 35 minutes during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and mean analytical concentrations were reported; no information was provided for range or variance.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 treatment groups and negative control; dose spacing was adequate.
	Metric 12:	Exposure Route and Method	High	× 1	1	Appropriate number of air changes/hr. No aerosol formation detected in exposure chambers.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	25/sex/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Methods were well- described and appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	

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Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats
Data Type:	2-generation inhalation - liver
HERO ID:	2990994

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Blinding of assessors was not reported; however, substantial impacts are not anticipated as most endpoints are objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No significant differences in initial bw and food consumption; body temperature and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were clearly described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 25: **Animal toxicity evaluation results of WIL Research 2001 for a 2-generation inhalation study on kidney outcomes**

Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats					
Data Type:	2-generation inhalation - kidney					
HERO ID:	2990994					
Domain		Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	
	Metric 2:	Test Substance Source	High	× 1	1	Commercial source, manufacturer and lot numbers provided.
	Metric 3:	Test Substance Purity	High	× 1	1	At least 99.8% pure.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative control exposed to filtered air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not used for 2-gen repro. studies.
	Metric 6:	Randomized Allocation	High	× 1	1	Animals were allocated to study groups using a computerized randomization procedure.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Preparation and storage conditions were described and exposure concentrations were measured by GC every 35 minutes during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and mean analytical concentrations were reported; no information was provided for variance (CV).
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 treatment groups and negative control; dose spacing was adequate.
	Metric 12:	Exposure Route and Method	High	× 1	1	Appropriate number of air changes/hr. No aerosol formation detected in exposure chambers.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	25/sex/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Methods were well- described and appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	

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Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats
Data Type:	2-generation inhalation - kidney
HERO ID:	2990994

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Blinding of assessors was not reported; however, substantial impacts are not anticipated. Most endpoints are objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No significant differences in initial bw and food consumption; body temperature and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were clearly described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 26: **Animal toxicity evaluation results of WIL Research 2001 for a 2-generation inhalation study on neurological outcomes**

Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats					
Data Type:	2-generation inhalation - neuro					
HERO ID:	2990994					
Domain		Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	
	Metric 2:	Test Substance Source	High	× 1	1	Commercial source, manufacturer and lot numbers provided.
	Metric 3:	Test Substance Purity	High	× 1	1	At least 99.8% pure.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative control exposed to filtered air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not used for 2-gen repro. studies.
	Metric 6:	Randomized Allocation	High	× 1	1	Animals were allocated to study groups using a computerized randomization procedure.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Preparation and storage conditions were described and exposure concentrations were measured by GC every 35 minutes during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and mean analytical concentrations were reported; no information was provided for variance.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 treatment groups and negative control; dose spacing was adequate.
	Metric 12:	Exposure Route and Method	High	× 1	1	Appropriate number of air changes/hr. No aerosol formation detected in exposure chambers.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	25/sex/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Methods were well- described and appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	

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Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats
Data Type:	2-generation inhalation - neuro
HERO ID:	2990994

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Blinding of assessors was not reported; however, substantial impacts are not anticipated as most endpoints are objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No significant differences between study groups in initial bw and food consumption; body temperature and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were clearly described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 27: **Animal toxicity evaluation results of ClinTrials 1997 for a 13 week inhalation exposure study in rats on hematological and immune, neurological/behavior, renal, hepatic, ocular and sensory, cardiovascular, clinical chemistry/biochemical, endocrine, nutrition and metabolic/adult exposure body weight, respiratory, and thyroid outcomes**

Study Citation:	ClinTrials (1997). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat
Data Type:	13 wk inhalation exposure in rats
HERO ID:	2991104

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by CASRN. and tradename (ALBTA1)
	Metric 2:	Test Substance Source	Low	× 1	3	Test substance was provided by study sponsor. Batch number, receipt date, and test substance form as received were reported. Test substance characterization was the responsibility of the sponsor; laboratory did not verify identity and/or composition, nor was information from the sponsor regarding characterization provided in the report.
	Metric 3:	Test Substance Purity	Low	× 1	3	Test substance purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	A sham-treated control group was exposed to room air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive control not typical for this study type.
	Metric 6:	Randomized Allocation	Medium	× 1	2	Animals assigned based on randomization procedure designed to ensure homogeneity of body weights.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Test substance preparation and storage were fully reported and adequate.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	For 2 of the 3-month exposure duration, an incorrect T95 value (15 min vs correct value of 25 min) was used, which reduced the animals' exposures during that time period; however this is not expected to significantly impact outcome.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations (measured by Miran Infrared gas analyzer) were reported and within 10% of nominal.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	Four non-zero exposure groups spanning a 6-fold range were used. Effect levels were identified by the study authors suggesting that the high and low doses were appropriate.

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Study Citation: ClinTrials (1997). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat
Data Type: 13 wk inhalation exposure in rats
HERO ID: 2991104

Domain		Metric	Rating†	MWF⋆	Score	Comments††
	Metric 12:	Exposure Route and Method	Low	× 1	3	Dynamic whole-body exposure was used; chamber air change rate was 7.4/hr, below the recommended 10-15/hr.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	The test animal species, strain, sex, health status, age, and starting body weight were reported, the test animal was obtained from a commercial source, and the species and strain were typical for the study type.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	Intermittent deviations from the prescribed humidity (n=13 occasions), temperature (n=3), and photoperiod (n=15) ranges were noted. but not expected to significantly influence the results.
	Metric 15:	Number per Group	High	× 1	1	15 rats/sex/group were used; this number is higher than recommended by EPA guidance
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methods and timing were reported in detail. Sensitive and thorough outcome metrics were evaluated.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were noted.
	Metric 18:	Sampling Adequacy	Medium	× 1	2	FOB and motor activity were assessed on first 10 animals/group. Histopathology was evaluated on comprehensive organs for control and high dose only; in remaining groups, respiratory tissues, liver, and gross lesions were examined microscopically.
	Metric 19:	Blinding of Assessors	High	× 1	1	Study reports that technicians performing FOB assessments were blinded to treatment group.
	Metric 20:	Negative Control Response	High	× 1	1	Control response reported and appeared to be appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature, and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	× 1	2	Animal attrition was limited to 4 animals that apparently died as a consequence of the orbital bleeding procedure or anesthesia. These animals were essentially evenly distributed across exposure groups.
Domain 7: Data Presentation and Analysis						

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Study Citation:	ClinTrials (1997). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat
Data Type:	13 wk inhalation exposure in rats
HERO ID:	2991104

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods and results were reported and appropriate to the data, and data enabling independent analysis were also provided.
	Metric 24:	Reporting of Data	High	× 2	2	Data were reported at both group and individual levels.
Overall Quality Determination‡			High		1.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 28: **Animal toxicity evaluation results of ClinTrials 1997 for a 13-week inhalation exposure study in rats on reproductive outcomes**

Study Citation:	ClinTrials (1997). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat					
Data Type:	13 wk inhalation exposure in rats					
HERO ID:	2991104					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by CASRN. and tradename (ALBTA1)
	Metric 2:	Test Substance Source	Low	× 1	3	Test substance was provided by study sponsor. Batch number, receipt date, and test substance form as received were reported. Test substance characterization was the responsibility of the sponsor; laboratory did not verify identity and/or composition, nor was information from the sponsor regarding characterization provided in the report.
	Metric 3:	Test Substance Purity	Low	× 1	3	Test substance purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	A sham-treated control group was exposed to room air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive control not typical for this study type.
	Metric 6:	Randomized Allocation	Medium	× 1	2	Animals assigned based on randomization procedure designed to ensure homogeneity of body weights.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Test substance preparation and storage were fully reported and adequate.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	For 2 of the 3-month exposure duration, an incorrect T95 value (15 min vs correct value of 25 min) was used, which reduced the animals' exposures during that time period; however, this is not expected to significantly impact outcome.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations (measured by Miran Infrared gas analyzer) were reported and within 10% of nominal.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Exposure frequency and duration were adequate.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	Four non-zero exposure groups spanning a 6-fold range were used. Effect levels were identified by the study authors suggesting that the high and low doses were appropriate.

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Study Citation: ClinTrials (1997). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat
Data Type: 13 wk inhalation exposure in rats
HERO ID: 2991104

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 12:	Exposure Route and Method	Low	× 1	3	Dynamic whole-body exposure was used; chamber air change rate was 7.4/hr, below the recommended 10-15/hr.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	The test animal species, strain, sex, health status, age, and starting body weight were reported, the test animal was obtained from a commercial source, and the species and strain were typical for the study type.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	× 1	2	Intermittent deviations from the prescribed humidity (n=13 occasions), temperature (n=3), and photoperiod (n=15) ranges were noted. but not expected to significantly influence the results.
	Metric 15:	Number per Group	High	× 1	1	15 rats/sex/group were used; this number is higher than recommended by EPA guidance
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methods and timing were reported in detail. Reproductive endpoints were limited to gonad, prostate and uterine weights and histopathology.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	No inconsistencies in outcome assessment were noted.
	Metric 18:	Sampling Adequacy	Medium	× 1	2	Histopathology was evaluated on reproductive organs for control and high dose only.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	No subjective reproductive outcomes were evaluated.
	Metric 20:	Negative Control Response	High	× 1	1	Control response reported and appeared to be appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	× 1	2	Animal attrition was limited to 4 animals that apparently died as a consequence of the orbital bleeding procedure or anesthesia. These animals were essentially evenly distributed across exposure groups.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods and results were reported and appropriate to the data, and data enabling independent analysis were also provided.

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Study Citation:	ClinTrials (1997). A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the Albino Rat
Data Type:	13 wk inhalation exposure in rats
HERO ID:	2991104

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 24: Reporting of Data	High	× 2	2	Data were reported at both group and individual levels.
Overall Quality Determination‡		High		1.6	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 29: **Animal toxicity evaluation results of Anonymous 1998 for a neurological study on neurological/behavior outcomes**

Study Citation:	Anonymous, (1998). Follow-up submission: Neurotoxicity and effects of beta-amyloid protein translation					
Data Type:	Neurological					
HERO ID:	4158104					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	Test substance identified by name.
	Metric 2:	Test Substance Source	Low	× 1	3	Source not reported.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative control group was included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	High	× 1	1	Animals were randomly allocated.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Unacceptable	× 1	4	The method and equipment used to generate test atmospheres was not reported.
	Metric 8:	Consistency of Exposure Administration	Unacceptable	× 1	4	No details were reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and actual exposure levels were reported, but no analytical methods were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration data were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of groups and spacing were reported but not justified.
	Metric 12:	Exposure Route and Method	Low	× 1	3	Actual concentrations were reported but no information about the inhalation chamber was provided.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Low	× 2	6	The species, strain, and sex were reported, but source was not reported..
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	No information was reported.
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group was appropriate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	Reporting was incomplete, especially in terms of assessing grip strength and sperm counts.
	Metric 17:	Consistency of Outcome Assessment	Low	× 1	3	Assessment details were not fully reported.
	Metric 18:	Sampling Adequacy	Low	× 1	3	Details were not reported.
	Metric 19:	Blinding of Assessors	Low	× 1	3	Blinding of grip strength was not reported.
	Metric 20:	Negative Control Response	High	× 1	1	Negative responses were appropriate for the data reported.

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Study Citation: Anonymous, (1998). Follow-up submission: Neurotoxicity and effects of beta-amyloid protein translation
Data Type: Neurological
HERO ID: 4158104

Domain	Metric	Rating†	MWF⋆	Score	Comments††
Domain 6: Confounding / Variable Control					
	Metric 21: Confounding Variables in Test Design and Procedures	Low	× 2	6	Initial body weight and respiratory rate were not reported.
	Metric 22: Health Outcomes Unrelated to Exposure	Low	× 1	3	Data were not reported.
Domain 7: Data Presentation and Analysis					
	Metric 23: Statistical Methods	High	× 1	1	Statistical methods were described and appropriate.
	Metric 24: Reporting of Data	High	× 2	2	Data were reported.
Overall Quality Determination‡		Unacceptable⋆⋆		2.3	
Extracted		No			

⋆⋆ Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

6 Genetic toxicity studies

Table 30: **Animal toxicity evaluation results of NTP 2011 for mutagenesis**

Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	In vivo MN (3-month inhalation study in mice)
HERO ID:	1737813

Domain		Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance was identified by chemical name, CASRN and structure.
	Metric 2:	Test Substance Source	High	× 1	1	The commercial source and lot no. of the test substance was reported.
	Metric 3:	Test Substance Purity	High	× 1	1	The overall purity of the lot utilized for this study was determined to be approximately 99% via gas chromatography.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Air controls were included for both male and female mice.
	Metric 5:	Positive Controls	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 6:	Randomized Allocation	High	× 1	1	Animals were randomly allocated into groups with approximately equal initial mean body weights.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Vapor generation from the test substance was adequately described.
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Time of day of exposures was not reported. No inconsistencies in administration were reported.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Analytical concentrations were reported and within 10% of nominal. Chamber air analyzed by GC every 20 min during exposure
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	The exposure frequency and duration were reported and appropriate.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	4 nonzero exposure levels were used, ranging 16-fold.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	Study does not explicitly state whether nose-only or whole body, but it appears to be dynamic whole body chamber with 15 air changes/hr. Based on its BP of 71 dec C, 1-BP may condense at room temperature.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	The test model (B6C3F1 mice) was reported and appropriate.

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Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	In vivo MN (3-month inhalation study in mice)
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Animal husbandry conditions were reported in detail and appropriate.
	Metric 15:	Number per Group	High	× 1	1	10/sex/group; appropriate number for study duration/purpose.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology is appropriate for this endpoint.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	The outcome was assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling for this endpoint was adequate (2,000 normochromatic erthyrocytes per animal).
	Metric 19:	Blinding of Assessors	High	× 1	1	The slides were coded prior to analysis.
	Metric 20:	Negative Control Response	High	× 1	1	Negative responses were observed from negative controls.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	Respiratory rates were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were identified.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	The data were appropriately analyzed by Cochran-Armitage trend test, followed by pairwise comparisons between each exposed group and the chamber control group. An individual trial was considered positive of trend test $p < 0.025$ or if single exposed group $p < (0.025/\text{number of exposed groups})$.
	Metric 24:	Reporting of Data	High	× 2	2	All data were reported adequately.
Overall Quality Determination‡			High		1.1	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 31: **Animal toxicity evaluation results of Young 2016 for in vivo mutation assay**

Study Citation:	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					
Data Type:						
HERO ID:	4140181					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	Medium	× 2	4	CAS number reported. in Section 3.1. GLP Compliance statement on page 3 notes that the characterization analyses for the test substance were not conducted according to GLP standards. The test article was from a commercial batch.
	Metric 2:	Test Substance Source	Low	× 1	3	The sponsor was identified as the source of the test substance which was received by WIL Research (now Charles River Ashland). [Section 3.1]
	Metric 3:	Test Substance Purity	High	× 1	1	Purity reported as 99.9% (provided to study authors by the Sponsor and on file at Charles River Ashland). [Section 3.1]
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Vehicle controls were exposed under the same conditions to humidified filtered air. [Sections 3.1 & 3.2]
	Metric 5:	Positive Controls	High	× 1	1	Positive controls exposed to ethyl nitrosourea (ENU, a potent, direct acting mutagen, with mutagenicity observed in target organs).
	Metric 6:	Randomized Allocation	Medium	× 1	2	Animals were assigned to groups at random based on body weight stratification into a block design using a computer program [Appendix A].
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Study provides details on the method and equipment used to generate vapors [Section 1.3 and Appendix C]. Test article storage also reported [Appendix A Study Protocol Section 7].
	Metric 8:	Consistency of Exposure Administration	Medium	× 1	2	Study includes details on methods for generating atmospheres for inhalation exposures. Positive control (not characterized in the certificate of analysis) administered via the oral route.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Nominal concentrations calculated daily. Exposure concentrations were analyzed at 45-minute intervals using GC. Mean nominal and mean analyzed exposure concentrations are presented in the study (text tables 2 & 3; Section 9.5 Appendix A; Appendix C).

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Study Citation: 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

Data Type:

HERO ID: 4140181

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	6 hours/day for 7 days/week for a 28-day period; consistent with OECD TG 488
	Metric 11:	Number of Exposure Groups and Dose Spacing	Low	× 1	3	Maximum tolerated dose was not achieved. OPPT recommends use of dose at least 1.5 times higher than the highest dose used in the NTP 2-year cancer bioassay.
	Metric 12:	Exposure Route and Method	Low	× 1	3	Whole-body inhalation chamber; no mention of condensation in the exposure chamber. Study authors report variable distribution of test article and < 15 air changes per hour.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	The study includes details regarding the age, health status, and starting body weights. The study also provides justification for selection of the species and strain used for this study.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Same conditions for all exposure groups. Mice were housed in an accredited facility and received certified feed and reverse osmosis- treated drinking water.
	Metric 15:	Number per Group	Medium	× 1	2	Six female mice/exposure group. The sample size is small, but adequate for the purposes of this study. DNA analysis conducted in five mice/group. Tissues from one of the mice were retained frozen in reserve and not processed further unless needed.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	It is unclear how outliers were verified as DNA sequencing data was not used to determine whether 'jackpots' were the cause of high inter- individual variation.
	Metric 17:	Consistency of Outcome Assessment	Low	× 1	3	Mutant frequency in negative controls comparable to historical controls; however, because manifestation time varies by tissue type, the relevance of the negative assay result for lung tissue is uncertain.
	Metric 18:	Sampling Adequacy	High	× 1	1	Evaluations were conducted on all exposure groups, including the negative l and positive control groups. The individual animal was considered the experimental unit.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Plates were scored visually for number of plaques per plate. Blinding not described in study, but not required for evaluation of an objective endpoint. Not expected to have a substantial impact on results.

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Study Citation:	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
Data Type:	
HERO ID:	4140181

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 20: Negative Control Response	High	× 1	1	Mutant frequency in negative controls was comparable to historical controls.
Domain 6: Confounding / Variable Control					
	Metric 21: Confounding Variables in Test Design and Procedures	Low	× 2	6	Body temperature and respiration rate were not reported.
	Metric 22: Health Outcomes Unrelated to Exposure	High	× 1	1	Body weight losses were noted in all test substance-treated groups from Days 6 to 13 (relative to Test Site Study Day 0); however, the changes were limited in magnitude and did not occur in a dose-related manner; therefore, are not considered treatment related.
Domain 7: Data Presentation and Analysis					
	Metric 23: Statistical Methods	Medium	× 1	2	Statistical approaches for evaluating results were clearly described in the study; however, analysis for jackpot mutations was not presented.
	Metric 24: Reporting of Data	High	× 2	2	Data presented in summary tables, and raw data included in appendices.
Overall Quality Determination‡		~~Medium~~ ⟶ Medium§		~~1.7~~	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "The maximum tolerated dose was not evaluated in this assay (OPP recommends testing at concentrations up to 1.5 times the maximum tolerated dose reported in the 2-year cancer bioassay). The sensitivity of the transgenic test system is also influenced by the duration of the post-exposure observation period. More specifically, the required manifestation time is directly related to the proliferation rate of the tissue in question. While a short manifestation time may be acceptable in rapidly dividing tissues (e.g. bone marrow or colon mucosa), a longer manifestation time may be necessary to get a maximum response in tissues with low mitotic rates. The significance of this negative result is uncertain in the absence of additional information on the mitotic index of the cells evaluated in this assay."

Table 32: **Animal toxicity evaluation results of Nepal et al 2019 for in vivo DNA binding and organ distribution**

Study Citation:	Nepal MR,Noh K,Shah S,Bist G,Lee ES,Jeong TC (2019). Identification of DNA and glutathione adducts in male Sprague-Dawley rats exposed to 1-Bromopropane Journal of Toxicology and Environmental Health, Part A: Current Issues, 82(8,8), 502-513
Data Type:	In vivo DNA binding and organ distribution for 1-BP
HERO ID:	6311554

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was identified as 1-bromopropane (1-BP).
	Metric 2:	Test Substance Source	High	× 1	1	The commercial source of the test substance was reported.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity of the test substance was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Appropriate concurrent negative controls (vehicle-treated animals) were included in the study design.
	Metric 5:	Positive Controls	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 6:	Randomized Allocation	High	× 1	1	Random allocation of animals to treatment groups was reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	The preparation of the test substance was adequately described and appropriate. Although the study design included a 3-day treatment, storage of the test substance between treatments was not reported.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was reported to be consistent across treatment groups.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	The exposure frequency and duration were reported and appropriate for this endpoint.
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	The dose spacing was appropriate. The number of exposure groups was somewhat lacking at two (500 and 1000 mg/kg), but was supplemented by the inclusion of two exposure durations (1 and 3 days).
	Metric 12:	Exposure Route and Method	High	× 1	1	The route and method of exposure were appropriate for the test substance.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	The species, strain, sex, age, starting body weight range, and commercial source was provided for the test animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Animal husbandry conditions were reported, appropriate, and consistent across treatment groups.

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Study Citation:	Nepal MR,Noh K,Shah S,Bist G,Lee ES,Jeong TC (2019). Identification of DNA and glutathione adducts in male Sprague-Dawley rats exposed to 1-Bromopropane Journal of Toxicology and Environmental Health, Part A: Current Issues, 82(8,8), 502-513
Data Type:	In vivo DNA binding and organ distribution for 1-BP
HERO ID:	6311554

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 15:	Number per Group	High	× 1	1	Each experimental condition was conducted with n = 5 rats.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology was appropriate for this endpoint.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	The outcome assessment methodology was consistent across treatment groups.
	Metric 18:	Sampling Adequacy	Low	× 1	3	It is unclear how many technical replicates per organ were utilized (may be single sample/tissue/animal).
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to this study design.
	Metric 20:	Negative Control Response	High	× 1	1	Although negative control data are not included in Table 2, it was specified in the text that no N7-propyl guanine adduct was detected in vehicle-treated animals.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	An approximation of initial body weight for all animals was reported (300 g). Food and water consumption were not reported, but this is not expected to have a significant impact on the results.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No attrition or adverse health outcomes were identified. It was indicated that all animals survived exposure without clinical signs of toxicity or adverse consequences with respect to body weight.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Data were appropriately analyzed by Student's t-test. Summary data (mean and standard deviation) are provided in Table 2 for each experimental condition and organ.
	Metric 24:	Reporting of Data	High	× 2	2	All data were reported adequately.
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study.

Table 33: **Animal toxicity evaluation results of Stelljes et al 2019 for 4-week inhalation study in transgenic mice on somatic mutation gene**

Study Citation:	Stelljes M,Young R,Weinberg J. (2019). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation: Support for a carcinogenic threshold Regulatory Toxicology and Pharmacology, 104 1-7
Data Type:	4-week somatic mutation gene inhalation study in transgenic mice
HERO ID:	6316280

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was clearly identified by name (1-bromopropane; 1-BP).
	Metric 2:	Test Substance Source	High	× 1	1	The test substance source/verification of the test substance was not reported. However, the commercial source of the test substance was reported in the corresponding full study report by Weinberg (2016).
	Metric 3:	Test Substance Purity	High	× 1	1	There was minor uncertainty with respect to the to test substance purity (not explicitly specified in the study report). However, this information was reported in the corresponding full study report by Weinberg (2016). The purity of the test substance was reported to be 99.99%.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	The study authors reported using an appropriate concurrent negative control group (i.e., a filtered air control group). Information from the study report suggests that all conditions except exposure to the test substance were equal across groups.
	Metric 5:	Positive Controls	High	× 1	1	A positive control was used (N-ethyl-N-nitrosourea or ENU). The positive control group was not concurrent (was from a different BioReliance study) and mice were exposed via oral gavage (rather than inhalation). However, guidelines for studies of this type indicate that positive control groups from previous studies can be used, and it is not necessary to use the same route of administration. The positive control used is known to induce mutations in the tissues of interest (lung, liver, and colon). In addition, the mutation frequency obtained for these animals were comparable to historical control observations.

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Study Citation:	Stelljes M,Young R,Weinberg J. (2019). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation: Support for a carcinogenic threshold Regulatory Toxicology and Pharmacology, 104 1-7
Data Type:	4-week somatic mutation gene inhalation study in transgenic mice
HERO ID:	6316280

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 6:	Randomized Allocation	High	× 1	1	The study report did not explicitly indicate the methods used to allocate animals to study groups (it was only stated that the study consisted of 4 groups of 7 female Big Blue mice per group). However, in the corresponding full study report by Weinberg (2016), it was reported that the animals were allocated using "a computerized randomization procedure based on body weight stratification in a block design."
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Test substance preparation details were reported in adequate detail. The methods and equipment used to generate test substance vapors were reported and were appropriate for the study type.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	Details of exposure administration were reported and were consistent across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target exposure concentrations (0, 62.5, 125, and 250 ppm) and analytical concentrations (0, 62.8, 125, and 258 ppm) were reported. The analytical method for measuring test substance concentrations (gas chromatography) was reported and appropriate for the study type. The standard deviation of the highest dose (258 ± 34.5 ppm) exceeded 10% of the target concentration, but this is not expected to have significantly impacted results.
	Metric 10:	Exposure Frequency and Duration	Low	× 1	3	The exposure frequency and duration of exposure were reported (i.e., 6 hours/day, 5 days/week, for 4 weeks; 20 exposures/animal). However, the OECD guideline for transgenic rodent somatic and germ cell gene mutation assays indicates that daily (7 days/week) 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”. Furthermore, this study used the same concentrations as the previous NTP carcinogenicity study, but the exposure duration was 4 weeks rather than 2 years; based on the negative results from 1-BP, there is uncertainty that the exposure duration was adequate.

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Study Citation:	Stelljes M,Young R,Weinberg J. (2019). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation: Support for a carcinogenic threshold Regulatory Toxicology and Pharmacology, 104 1-7
Data Type:	4-week somatic mutation gene inhalation study in transgenic mice
HERO ID:	6316280

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	The positive control induced a significant response following oral exposure to ENU (a potent alkylating agent). However, it is unclear that inhalation exposure to 1-BP was adequate to observe the intended response (as the duration of exposure was less than that evaluated in the NTP carcinogenicity assay).
	Metric 12:	Exposure Route and Method	High	× 1	1	Justification was provided with respect to the route of exposure. Inhalation was used because the same route was utilized by the NTP for carcinogenicity studies, as it was considered the relevant route of human occupational exposure. The use of whole-body inhalation chambers was considered appropriate for 1-BP vapors. Equipment was set to provide a minimum of 10 air changes per hour, which is considered adequate for this study type.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	Transgenic mice were appropriate to address the intended outcome of interest (in vivo genotoxicity). Although a rationale was provided (i.e., females developed more tumors than males, and females showed a significant exposure-response with respect to lung tumors in the NTP carcinogenicity study), the study utilized only female animals. The test animals were initially obtained from a commercial source (WIL Research, now Charles River Laboratories).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Husbandry conditions that were reported (e.g., housing of the animals) were the same for control and exposed animals. Although not all husbandry conditions were specified, this information was reported in the corresponding full study report by Weinberg (2016).
	Metric 15:	Number per Group	High	× 1	1	The study used 7 animals per exposure group (for evaluation of tissues from 6 animals per group with one "backup" replacement animal). The number of animals per group was considered appropriate for the study type and for the outcome analysis.
Domain 5: Outcome Assessment						

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Study Citation:	Stelljes M,Young R,Weinberg J. (2019). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation: Support for a carcinogenic threshold Regulatory Toxicology and Pharmacology, 104 1-7
Data Type:	4-week somatic mutation gene inhalation study in transgenic mice
HERO ID:	6316280

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	The positive control induced a significant response following oral exposure to ENU (a potent alkylating agent). However, it is unclear that inhalation exposure to 1-BP was adequate to observe the intended response (as the duration of exposure was less than that evaluated in the NTP carcinogenicity assay).
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	× 1	1	Details regarding sampling for the outcome of interest were provided in adequate detail. The report indicated that study evaluated at least 125,000 phage/tissue/animal (the standard for studies of this type). The individual animal was considered the experimental unit for analyses.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study type.
	Metric 20:	Negative Control Response	High	× 1	1	The biological responses of the negative control group were adequate. In general, filtered air control mutation frequencies were similar to historical control data for these tissue types. It was noted that DNA from one control animal was excluded from analysis because the mutant frequency in lung tissue was outside of the range for historical controls and was twice the upper 99% control limit and the previous maximum control frequency; the animal was considered an outlier and the replacement animal was used instead.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	High	× 2	2	No confounding variables with respect to test design and procedures were identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health effects unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were described in adequate detail and were considered appropriate for the study type/outcome of interest. The report indicated that, because the ratio of the total number of mutant phages to total phages screened was small (and likely not normally distributed), data for mutation frequency was subject to log10 transformation. The mutant frequency data met the criteria for parametric ANOVA (the statistical analysis used for this study).

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Study Citation:	Stelljes M,Young R,Weinberg J. (2019). A 28-day somatic gene mutation study of 1-bromopropane in female Big Blue® B6C3F1 mice via whole-body inhalation: Support for a carcinogenic threshold Regulatory Toxicology and Pharmacology, 104 1-7
Data Type:	4-week somatic mutation gene inhalation study in transgenic mice
HERO ID:	6316280

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 24: Reporting of Data	High	× 2	2	The mutation frequency for liver, lungs, and colon were reported for each exposure group (Figure 2). Note: the study indicated that other available data were numbers of plaque-forming units, mutants, mutation frequency, and packaging cycles in each tissue/animal (data not shown).
Overall Quality Determination‡		~~High~~ ⟶ Medium§		~~1.3~~	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Based on the data provided, it is unclear whether the protocol was adequate to address the intended outcome. The maximum tolerated dose (MTD) was not evaluated; it is recommended (by OPP) that concentrations up to 1.5 times the MTD reported in the 2-year carcinogenicity assay be tested. This study used the same exposure concentrations as the 2-year bioassay. In addition, the sensitivity of the test system (using a transgenic model) is associated with the duration of the post-exposure observation period."

Table 34: **In vitro evaluation results of Barber et al 1981 for bacterial reverse mutation**

Study Citation:	E. D. Barber, W. H. Donish, K. R. Mueller (1981). A procedure for the quantitative measurement of the mutagenicity of volatile liquids in the Ames salmonella/microsome assay Mutation Research: Genetic Toxicology, 90(1,1), 31-48
Data Type:	Bacterial reverse mutation for 1-BP
HERO ID:	200219

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was clearly identified as 1-bromopropane. A structure was also provided.
	Metric 2:	Test Substance Source	High	× 1	1	The commercial source of the test substance was reported (Eastman Organic Chemicals). A batch/lot number was not reported, but the chemical substance is not expected to vary in composition.
	Metric 3:	Test Substance Purity	High	× 1	1	The purity of 1-BP as per GLC was 99.85%.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls consisted of 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.
	Metric 5:	Positive Controls	High	× 2	2	Positive controls were used. It is noted that positive control substances were not volatile, and were (therefore) not subjected to a closed test system. 2-Aminoanthracene was the positive control with activation (all strains). Without activation, ICR-191 was used for S. typhimurium TA 98, methyl-N-nitro-N'-nitroguanidine was used for strains TA 100 and TA 1535, 9-aminoacridine was used for TA 1537, and picrolonic acid was used for TA 1538. Positive controls yielded positive responses.
	Metric 6:	Assay Procedures	High	× 1	1	In this study, a modified plate-incorporation test was conducted using a chemically inert, closed-system protocol. Assay methods were described in detail, including the system used and how the addition of 1-BP was handled.
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to this study type.
Domain 3: Exposure Characterization						

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Study Citation:	E. D. Barber, W. H. Donish, K. R. Mueller (1981). A procedure for the quantitative measurement of the mutagenicity of volatile liquids in the Ames salmonella/microsome assay Mutation Research: Genetic Toxicology, 90(1,1), 31-48
Data Type:	Bacterial reverse mutation for 1-BP
HERO ID:	200219

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Preparation and Storage of Test Substance	High	× 1	1	Owing to the volatility of the test substance, doses were confirmed. Plates containing only distilled water were included in the closed system 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 period and analyzed by GLC.
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was consistent across treatment groups.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Doses were reported without ambiguity. Measured 1-BP concentrations were 0, 1.1, 2.3, 4.9, 9.0, and/or 20.3 µmoles/plate.
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	The exposure duration was reported and appropriate. Plates were exposed for 48 hours at 37C. The 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 (without loss due to volatility).
	Metric 12:	Exposure Route and Method	Medium	× 1	2	The number of groups (at least 4 doses plus controls) was adequate for the study type; however, there was no indication of cytotoxicity at the highest tested concentration (Table 4).
	Metric 13:	Metabolic Activation	Medium	× 1	2	Aroclor-induced rat liver S9 was used. The source was reported (a manufacturer). Details regarding composition were not provided.
Domain 4: Test Model						
	Metric 14:	Test Model	High	× 2	2	The identity and donor source of the bacterial strains used here were identified, and these strains are routinely used for the outcome of interest.
	Metric 15:	Number per Group	High	× 1	1	Table 6 suggests that 5 replicates were used per group.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology is appropriate for the outcome of interest. The number of revertant colonies/plate was counted after 48 hours incubation. Revertant colonies were counted using a colony counter.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	The outcome assessment was consistent across treatment groups.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to this endpoint.

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Study Citation:	E. D. Barber, W. H. Donish, K. R. Mueller (1981). A procedure for the quantitative measurement of the mutagenicity of volatile liquids in the Ames salmonella/microsome assay Mutation Research: Genetic Toxicology, 90(1,1), 31-48
Data Type:	Bacterial reverse mutation for 1-BP
HERO ID:	200219

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study design.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	High	× 2	2	No differences among treatment group parameters were identified.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	Low	× 1	3	Data on outcome differences unrelated to exposure were not reported for each study group.
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	High	× 1	1	Increased revertants/plate compared to controls was evaluated using statistical analysis (Student's t-test). Statistics were used to determine the minimum vapor concentration that significantly increased the number of revertant colonies.
	Metric 23:	Data Interpretation	High	× 2	2	Evaluation criteria (number of colonies) were reported. The criteria for a positive result was increased revertants/plate compared to controls (analyzed statistically).
	Metric 24:	Cytotoxicity Data	Medium	× 1	2	Cytotoxicity was described as absence of a background lawn. Further details were not provided.
	Metric 25:	Reporting of Data	Medium	× 2	4	Average spontaneous reversion rates from negative controls were reported (and were reportedly in agreement with those found by an interlaboratory survey by de Serres and Shelby [1979] and those presented by Ames [1975]). Raw data (i.e., individual plate counts) were not provided. Negative data were reported qualitatively (no revertants/plate data for strains S. typhmurium strains TA 1537 and TA 1538 in which mutagenicity was not observed). Standard deviations for mean numbers of revertants/plate (except positive and negative controls) were not reported. No historical control data was provided.
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study.

Table 35: **In vitro evaluation results of Hasspieler et al 2006 for DNA SSBs and repair**

Study Citation:	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 Toxicology and Industrial Health, 22(7,7), 301-315
Data Type:	DNA SSBs and repair for 1-BP
HERO ID:	478653

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance (1-BP and stabilized 1-BP) was identified by name, CASRN, and structural formula.
	Metric 2:	Test Substance Source	High	× 1	1	The test substance source (manufacturer) was reported. The specific trade name for the stabilized 1-BP formulation was used (as it was noted that different stabilizing formulations have different components).
	Metric 3:	Test Substance Purity	Low	× 1	3	The test substance purity/grade was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Medium	× 2	4	The study authors reported using negative (solvent-only) controls. The study indicated that DMSO and acetone were used; however, the solvent used for 1-BP was not explicitly specified.
	Metric 5:	Positive Controls	High	× 2	2	The study authors reported using a positive control for the DNA damage and repair assays (4-nitroquinoline N-oxide).
	Metric 6:	Assay Procedures	Medium	× 1	2	Assay methods/procedures were described, but specific details were not reported (e.g., volumes). It was indicated that the procedure used for analyzing DNA SSB assay was a modification of a procedure cited to another publication (Hasspieler et al. 1995).
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 3: Exposure Characterization						
	Metric 8:	Preparation and Storage of Test Substance	Medium	× 1	2	It was indicated that the test substance was dissolved in solvent. Storage was not reported (but it not expected to impact the study results given the short-term nature of the experiments).
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure administration appeared to be consistent across study groups.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	A range of doses tested was reported (25 to 500 ppm). Individual doses of 1-BP can be estimated from data presented in Figure 4.

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Study Citation:	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 Toxicology and Industrial Health, 22(7,7), 301-315
Data Type:	DNA SSBs and repair for 1-BP
HERO ID:	478653

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 11:	Number of Exposure Groups and Concentration Spacing	Low	× 2	6	The exposure duration for other assays performed in the study were up to 24 hours (cytotoxicity) or 24 hours (EROD bioassay). Descriptions of the genotoxicity assays (DNA SSB and repair assays) reported treatments "for a given period of time," and reference information described above for other assay types. The duration of exposure for the genotoxicity assays was not explicitly specified (DNA SSB duration may be included in a cited publication and/or 24 hours may be presumed). Based on positive results (e.g., for the positive control), the exposure duration was presumably adequate for the outcome of interest.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	The number of exposure groups was reported (i.e., can be determined for 1-BP based on the data presented in Figure 4). A rationale for dose selection was suggested (similar to expected tissue concentrations). The doses for stabilized 1-BP were presumably the same as those used for 1-BP.
	Metric 13:	Metabolic Activation	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 4: Test Model						
	Metric 14:	Test Model	Medium	× 2	4	The test model (human HepG2 cells) was reported and is routinely used for toxicity studies. The source of the cell line was specified, but few details were provided.
	Metric 15:	Number per Group	High	× 1	1	The legend for Figure 4 indicates that four replicates were used for 1-BP (and presumably for stabilized 1-BP).
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Outcome assessment methods were described and appeared appropriate for the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcome assessments appeared to be consistent across study groups.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to the study type.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Test design or procedural confounding variables were not reported.

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Study Citation:	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 Toxicology and Industrial Health, 22(7,7), 301-315
Data Type:	DNA SSBs and repair for 1-BP
HERO ID:	478653

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	Medium	× 1	2	No confounding variables in health outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	Medium	× 1	2	Data were shown for 1-BP in Figure 4 as means +/- standard error for 4 replicates (this statement presumably pertains to all of the assays). It was indicated that statistical analyses were performed (threshold $p < 0.05$); however, details of tests conducted were not provided. Qualitative results (i.e., positive or negative based on statistical significance) were reported for stabilized 1-BP (qualitative results were the same for both forms of 1-BP).
	Metric 23:	Data Interpretation	High	× 2	2	Based on information provided in Table 2, a test was scored as positive when percent change in activity was statistically significantly different from the negative control.
	Metric 24:	Cytotoxicity Data	High	× 1	1	Cytotoxicity methods were described; these methods (neutral red uptake assay) are commonly used. Results were provided quantitatively for 1-BP (and qualitatively for stabilized 1-BP).
	Metric 25:	Reporting of Data	High	× 2	2	Data for all 1-BP exposure groups were presented graphically. Data for 1-BP and stabilized 1-BP were summarized in Table 2.
Overall Quality Determination‡			High		1.6	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 36: **In vitro evaluation results of NTP 2011 for bacterial reverse mutation**

Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	Bacterial reverse mutation for 1-BP
HERO ID:	1737813

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was identified by name and CASRN.
	Metric 2:	Test Substance Source	High	× 1	1	The commercial source of the test substance was reported; a lot number was also provided.
	Metric 3:	Test Substance Purity	High	× 1	1	The overall purity of the lot utilized for this study was determined to be approximately 99% via gas chromatography.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Appropriate concurrent negative controls (buffer) were used.
	Metric 5:	Positive Controls	High	× 2	2	Appropriate concurrent positive controls for each bacterial strain with and without metabolic activation were included.
	Metric 6:	Assay Procedures	Medium	× 1	2	Assay procedures were partially described and partially cited to other publications (e.g., Zieger et al. 1992).
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to the study design.
Domain 3: Exposure Characterization						
	Metric 8:	Preparation and Storage of Test Substance	Low	× 1	3	The test substance was reportedly sent as an aliquot one of the laboratories that conducted the study (no further details provided). Test substance preparation was reported (i.e., added to buffer) in tubes; it is not clear if tubes were sealed to account for the volatility of the test substance. Test substance storage was not reported; however, this omission is unlikely to affect the study results (single-dose administration).
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure was consistent across treatment groups in each experiment.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Doses were reported without ambiguity.
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	The exposure duration was reported and appropriate.

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Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	Bacterial reverse mutation for 1-BP
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 12:	Exposure Route and Method	High	× 1	1	The number of exposure groups (at least 5 concentrations plus control) and dose spacing was appropriate. The study indicated that the high-dose was selected by toxicity or the limit dose of 10,000 ug/plate (when only slight toxicity was observed).
	Metric 13:	Metabolic Activation	High	× 1	1	The use of induced rat and hamster liver S9 was reported. The percentage of S9 utilized was reported for assays performed at each laboratory (SITEK Research Laboratories and BioReliance Corporation).
Domain 4: Test Model						
	Metric 14:	Test Model	Medium	× 2	4	The bacterial strains used are routinely used for this endpoint. The source of these strains was not reported, but more detailed methods were cited to other publications, and this is not expected to have impacted the results.
	Metric 15:	Number per Group	High	× 1	1	Each experimental condition was conducted in triplicate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology was appropriate for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	The outcome was consistently assessed across treatment groups in each experiment.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to this study design.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to this study design.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	High	× 2	2	No confounding variables were identified in each independent experiment.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	Medium	× 1	2	The authors reported that some replicates experienced disproportionate outcomes unrelated to exposure (i.e., contamination), but data from the remaining exposure replicates or groups were valid and is unlikely to have a substantial impact on results
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	High	× 1	1	No statistical analysis was conducted (and not requires by study type). Independent statistical analysis could possibly be completed using the provided mean and standard error (and n = 3) in Table E1.

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Study Citation:	NTP (2011). 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) GRA and I(GRA and I,GRA and I), 195
Data Type:	Bacterial reverse mutation for 1-BP
HERO ID:	1737813

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 23:	Data Interpretation	High	× 2	2	A positive response was clearly defined as a reproducible, dose-related increase in revertants . An equivocal response was defined as an increase in revertants that was not dose-related, reproducible, or not of sufficient magnitude. A negative response was defined as no increase in revertants. There was no minimum fold-change for a positive response (but usually greater than 2-fold).
	Metric 24:	Cytotoxicity Data	Low	× 1	3	Cytotoxicity endpoints were defined, but the methods of measurements were not fully described or reported; however, toxicity was accounted for in the study (i.e., toxicity was noted at some of the higher doses).
	Metric 25:	Reporting of Data	High	× 2	2	Data were adequately reported.
Overall Quality Determination‡			High		1.3	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 37: **In vitro evaluation results of Elf Atochem S.A. 1996 for gene mutation in mammalian cells**

Study Citation:	Elf Atochem S.A. (1996). In vitro mammalian cell gene mutation test in L5178y TK+/- mouse lymphoma cell of n-propyl bromide. Study no. 13293.					
Data Type:	Gene mutation in mammalian cells					
HERO ID:	3045017					
Domain		Metric	Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The chemical substance was identified by name and CASRN.
	Metric 2:	Test Substance Source	High	× 1	1	The source of the test substance was reported (Elf Atochem). Details including a description of the chemical substance and batch labeling were reported. An analytical certificate characterizing the test substance was also provided.
	Metric 3:	Test Substance Purity	High	× 1	1	The test substance purity was reported (99.3%). Purity was such that any observed effects were likely due to the test substance itself.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	The study authors reported using a vehicle-only (DMSO) control group for which conditions were the same except exposure to 1-BP.
	Metric 5:	Positive Controls	High	× 2	2	Positive controls were used concurrently and responded apropriately (i.e., higher mutation frequency than vehicle controls and within the range of historical control data). Methylmethane sulfonate was used in the presence of activation and cyclophosphamide was used in the absence of activation. The report indicates that acceptance criteria were met (although it appears that mutation frequency for positive controls in the second experiment without activation exceeded the maximum mutation frequency provided for historical controls).
	Metric 6:	Assay Procedures	High	× 1	1	The study authors described the methods and procedures used in the conduction of the experiments in detail, and they were applicable to the study type. The types of information that was reported included test conditions, cell density, culture media, incubation temperature, and slide preparation.
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 3: Exposure Characterization						

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Study Citation: Elf Atochem S.A. (1996). In vitro mammalian cell gene mutation test in L5178y TK+/- mouse lymphoma cell of n-propyl bromide. Study no. 13293.
Data Type: Gene mutation in mammalian cells
HERO ID: 3045017

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Preparation and Storage of Test Substance	Low	× 1	3	The study indicates that the test substance was dissolved in DMSO immediately before use. The analytical certificate indicates that 1-BP is soluble in DMSO and specifies storage conditions. It was unclear whether the volatility of the test substance was accounted for in the treatment methods.
	Metric 9:	Consistency of Exposure Administration	Medium	× 1	2	Exposures were consistently administered across study groups. Although parts of the study were conducted at different times (e.g., first mutagenicity assay with activation and without activation conducted on different days), this change is not expected to substantially impact the study results.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Exposure concentrations were reported without ambiguity.
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	The exposure period was reported (3 hours) and appropriate for the study type.
	Metric 12:	Exposure Route and Method	High	× 1	1	The number of exposure groups/concentration spacing was justified by the study authors (i.e., based on guideline recommendations and cytotoxicity results).
	Metric 13:	Metabolic Activation	High	× 1	1	The study authors reported that exposures were conducted in the presence and absence of metabolic activation. The type/source of activation was reported (rat liver S9 purchased from Moltox), its composition, and its concentration in the final volume was explicitly specified (2%).
Domain 4: Test Model						
	Metric 14:	Test Model	High	× 2	2	The test model (L5178Y cells) and descriptive information was provided. The source of the cells (originally obtained from ATCC and supplied by Dr. Oudelkhim-Diot) was reported. The study indicated that the test model used is an established cell line recommended by international guidelines for this study type.
	Metric 15:	Number per Group	High	× 1	1	The study indicates that there were two cultures per dose level tested with and without activation. In addition, controls were included using at least duplicate cultures. For cytotoxicity and viability, cells were seeded at two plates/dose level, and for mutagenicity, four plates/dose level.
Domain 5: Outcome Assessment						

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Study Citation:	Elf Atochem S.A. (1996). In vitro mammalian cell gene mutation test in L5178y TK+/- mouse lymphoma cell of n-propyl bromide. Study no. 13293.
Data Type:	Gene mutation in mammalian cells
HERO ID:	3045017

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology addressed the outcome of interest/was sensitive to the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Information in the study indicates that outcome assessments were conducted using the same protocol across groups and at the same time point after initial exposure.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to the study type.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	High	× 2	2	No differences among treatment group parameters were reported.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	High	× 1	1	No confounding variables were reported.
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	Low	× 1	3	Calculation methods were described (i.e., how to calculate cloning efficiency after treatment and expression periods, cloning efficiency in selective medium, survival relative to controls after treatment and expression periods, and relative mutant frequency). Although the study reported a "significant" increase in mutation frequency, it does not appear that statistical analyses were performed (or required). Raw or summary data were not provided in the study report; it is indicated that these data were stored in archives.
	Metric 23:	Data Interpretation	High	× 2	2	The study authors clearly reported their evaluation criteria: a reproducible, 2-fold increase in mutant frequency compared to controls, at any dose and/or evidence of a dose-response relationship was considered a positive result. Other factors that were considered were historical control data and biological relevance. These criteria are consistent with established practices.
	Metric 24:	Cytotoxicity Data	High	× 1	1	The study authors defined cytotoxicity endpoints clearly and outlined the methods used to measure cytotoxicity. A preliminary toxicity test was conducted.

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Study Citation:	Elf Atochem S.A. (1996). In vitro mammalian cell gene mutation test in L5178y TK+/- mouse lymphoma cell of n-propyl bromide. Study no. 13293.
Data Type:	Gene mutation in mammalian cells
HERO ID:	3045017

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 25: Reporting of Data	Medium	× 2	4	Data for exposure-related findings were reported for all outcomes by exposure group. Standard deviations were not reported.
Overall Quality Determination‡		High		1.2	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 38: **In vitro evaluation results of Thapa et al 2016 for DNA binding assay**

Study Citation:	P. Thapa, E. K. Kim, M. R. Nepal, K. S. Jeong, M. J. Kang, K. Noh, S. Lee, H. G. Jeong, J. H. Lee, T. C. Jeong, E. S. Lee (2016). Identification of a N7-guanine adduct of 1-bromopropane in calf thymus DNA by mass spectrometry Molecular and Cellular Toxicology, 12(1,1), 7-14
Data Type:	DNA binding assay for 1-BP
HERO ID:	3554778

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was identified as 1-bromopropane.
	Metric 2:	Test Substance Source	High	× 1	1	The commercial source of the test substance was reported. Although a batch/lot number was not provided, the test substance is not expected to vary in composition.
	Metric 3:	Test Substance Purity	High	× 1	1	The purity of the test substance was reported (99%).
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Not Rated	NA	NA	Use of a negative control was not necessary given the study design. 9-Methyl adenine was used as an internal standard in experiments evaluating the incorporation of 1-BP with calf thymus DNA.
	Metric 5:	Positive Controls	Not Rated	NA	NA	This metric is not applicable to the study design. Adduct production was proportional to the amount of 1-BP added (indicative of the efficacy of the assay).
	Metric 6:	Assay Procedures	High	× 1	1	Assay procedures were described adequately and were appropriate for the endpoint of interest.
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to this study type.
Domain 3: Exposure Characterization						
	Metric 8:	Preparation and Storage of Test Substance	Medium	× 1	2	The preparation of the test substance was adequately described and appropriate. It was not explicitly indicated how the methods used accounted for the volatility of the test substance (e.g., incubation in sealed containers).
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was reported to be consistent among treatment groups.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Doses were reported adequately. The doses were not explicitly stated, but could be determined by estimation from Figure 6B.
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	Exposure duration was appropriate for the outcome of interest.

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Study Citation:	P. Thapa, E. K. Kim, M. R. Nepal, K. S. Jeong, M. J. Kang, K. Noh, S. Lee, H. G. Jeong, J. H. Lee, T. C. Jeong, E. S. Lee (2016). Identification of a N7-guanine adduct of 1-bromopropane in calf thymus DNA by mass spectrometry Molecular and Cellular Toxicology, 12(1,1), 7-14
Data Type:	DNA binding assay for 1-BP
HERO ID:	3554778

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 12:	Exposure Route and Method	High	× 1	1	The number of exposure groups (approximately 8) and dose spacing were reported and appropriate for the outcome of interest. The doses selected permitted an analysis of the dose-relatedness of the response.
	Metric 13:	Metabolic Activation	Not Rated	NA	NA	This metric is not applicable to the study design. The study evaluated the ability of 1-BP to react with DNA without the support of enzymes.
Domain 4: Test Model						
	Metric 14:	Test Model	Medium	× 2	4	The test model, calf thymus DNA, was reported and appropriate for the outcome of interest. Limited details were provided, but this is unlikely to have a substantial impact on results, as the calf thymus DNA was obtained from a commercial source.
	Metric 15:	Number per Group	High	× 1	1	The dose-dependent production of N7-propyl guanine from calf thymus DNA and 1-BP was conducted in triplicate for each dose of 1-BP.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology was appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	The outcome was assessed consistently across all treatment groups.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study design.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	High	× 2	2	No confounding variables in the study design were reported.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	High	× 1	1	No confounding variables for outcomes unrelated to exposure were reported. The study authors provided data validating the detecting of a peak corresponding to the adduct of interest (with 1-BP and without; using a synthesized reference standard).
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 23:	Data Interpretation	High	× 2	2	Detection of the N7-propyl guanine adduct was considered a positive response. It is inferred from the text that the authors also considered the dose-relatedness of the response.

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Study Citation:	P. Thapa, E. K. Kim, M. R. Nepal, K. S. Jeong, M. J. Kang, K. Noh, S. Lee, H. G. Jeong, J. H. Lee, T. C. Jeong, E. S. Lee (2016). Identification of a N7-guanine adduct of 1-bromopropane in calf thymus DNA by mass spectrometry Molecular and Cellular Toxicology, 12(1,1), 7-14
Data Type:	DNA binding assay for 1-BP
HERO ID:	3554778

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 24: Cytotoxicity Data	Not Rated	NA	NA	This metric is not applicable to the study design, as no cells were utilized.
	Metric 25: Reporting of Data	High	× 2	2	Data were shown by exposure group.
Overall Quality Determination‡		High		1.1	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 39: **In vitro evaluation of Toraason et al 2006 for DNA damage**

Study Citation:	M. Toraason, D. W. Lynch, D. G. DeBord, N. Singh, E. Kreig, M. A. Butler, C. A. Toennis, J. Nemhauser (2006). DNA damage in leukocytes of workers occupationally exposed to 1-bromopropane Mutation Research: Genetic Toxicology and Environmental Mutagenesis, 603(1,1), 1-14
Data Type:	DNA damage for 1-BP
HERO ID:	3974874

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was identified by name (1-bromopropane) and CASRN (106-94-5).
	Metric 2:	Test Substance Source	High	× 1	1	The test substance source was reported (Sigma-Aldrich). Although a batch/lot number was not provided, the test substance is not expected to vary in composition.
	Metric 3:	Test Substance Purity	Low	× 1	3	The purity of the test substance was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	The study authors reported using a concurrent negative (vehicle-only) control.
	Metric 5:	Positive Controls	Low	× 2	6	A concurrent positive control was used (radiation; not a chemical substance as typically used). Data were not shown. The study indicated that x-rays increased the tail moment above controls by 50% to 150%.
	Metric 6:	Assay Procedures	Medium	× 1	2	Assay procedures were briefly described and cited to also another publication (Singh et al. 2002).
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 3: Exposure Characterization						
	Metric 8:	Preparation and Storage of Test Substance	Medium	× 1	2	The test substance was prepared in DMSO. Storage was not reported (but was not expected to impact the study results).
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was consistent across study groups.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Concentrations were reported without ambiguity (0, 0.01, 0.1, and /or 1 mM).
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	The exposure duration was reported (8 hours for dose-response assay and 1, 2, 4, or 8 hours for temporal response assay) and generally considered adequate for the study (about 3 to 6 hours recommended by study type; however, positive results were obtained).

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Study Citation:	M. Toraason, D. W. Lynch, D. G. DeBord, N. Singh, E. Kreig, M. A. Butler, C. A. Toennis, J. Nemhauser (2006). DNA damage in leukocytes of workers occupationally exposed to 1-bromopropane Mutation Research: Genetic Toxicology and Environmental Mutagenesis, 603(1,1), 1-14
Data Type:	DNA damage for 1-BP
HERO ID:	3974874

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 12:	Exposure Route and Method	High	× 1	1	The number of exposure groups was reported (3 plus controls) and appropriate for the study type. The doses used were presumably based on previous studies for 2-BP (referenced in the discussion).
	Metric 13:	Metabolic Activation	Not Rated	NA	NA	The study authors did not conduct the assay in the presence of activation. The rationale provided was that 1-BP was shown to be equally mutagenic in the presence/absence of activation in Salmonella typhimurium (Barber et al. 1981).
Domain 4: Test Model						
	Metric 14:	Test Model	Medium	× 2	4	The test model used was reported with limited information (i.e., male, non-smoking individual); the cell type is commonly used for studies of this type.
	Metric 15:	Number per Group	High	× 1	1	The study indicated that experiments were conducted in triplicate (i.e., three cultures).
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment was reported and sensitive for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	× 1	2	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	× 2	2	The study authors reported analysis of 100 leukocytes per blood sample.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study type.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No confounding variables were reported in test design or procedures.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	Medium	× 1	2	No differences in health outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	High	× 1	1	Statistical methods were reported and appropriate for the study type.
	Metric 23:	Data Interpretation	High	× 2	2	The study indicated that a positive result was seen based on a statistically significantly increased tail moment. Although not explicitly discussed, the response was dose-related. The study evaluated the time-relatedness of the effect as well.

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Study Citation:	M. Toraason, D. W. Lynch, D. G. DeBord, N. Singh, E. Kreig, M. A. Butler, C. A. Toennis, J. Nemhauser (2006). DNA damage in leukocytes of workers occupationally exposed to 1-bromopropane Mutation Research: Genetic Toxicology and Environmental Mutagenesis, 603(1,1), 1-14
Data Type:	DNA damage for 1-BP
HERO ID:	3974874

Domain	Metric	Rating†	MWF⋆	Score	Comments††
	Metric 24: Cytotoxicity Data	Low	× 1	3	The study evaluated apoptosis (not cytotoxicity per se) at the doses used in the comet assay. Presumably, doses were selected based on previous studies, and the doses used permitted adequate numbers of cells to be analyzed.
	Metric 25: Reporting of Data	High	× 2	2	Data were reported for all exposure groups (means +/- standard deviations for three cultures).
Overall Quality Determination‡		High		1.5	
Extracted		Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 40: **In vitro evaluation results of BioReliance 2015 for bacterial reverse mutation**

Study Citation:	BioReliance (2015). Appendix III. Closed-System Ames Test on 1-Bromopropane Conducted at BioReliance and Sponsored by Albemarle Corporation FINAL REPORT
Data Type:	Bacterial reverse mutation
HERO ID:	5234603

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was clearly identified as 1-bromopropane (by name and CASRN).
	Metric 2:	Test Substance Source	High	× 1	1	The source of the test substance was reported (including lot number), and its identity was certified by manufacturer and/or verified by analytical methods.
	Metric 3:	Test Substance Purity	High	× 1	1	The purity of 1-BP (determined by the sponsor) was 99%.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included for each strain, with and without activation, and treated the same as treatment groups. Negative controls were exposed to vehicle only (ethanol) in preincubation tubes.
	Metric 5:	Positive Controls	Medium	× 2	4	Positive controls (plated concurrently) were used. Positive controls responded appropriately (> 3-fold increase in the number of revertants compared to respective vehicle controls). However, there were no vehicle controls for DMSO or water (i.e., the substances used to dilute the positive controls). Although substances used as positive controls were consistent with those routinely used for these strains, no volatile positive controls were utilized. These deficiencies are not expected to have substantially impacted results.
	Metric 6:	Assay Procedures	High	× 1	1	The study authors described the methods and procedures (e.g., test conditions, cell density, culture media, and volumes, pre- and post-incubation temperatures) used for the test in detail. The preincubation methodology used was attributed to Yahagi et al. (1977). However, the use of screw-capped tubes during preincubation (documented for the second confirmatory mutagenicity assay only) and minimal headspace (documented for dosing formulations) did not appear to be appropriate methods for testing 1-BP (i.e., a volatile test substance).
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to this study type.
Domain 3: Exposure Characterization						

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Study Citation:	BioReliance (2015). Appendix III. Closed-System Ames Test on 1-Bromopropane Conducted at BioReliance and Sponsored by Albemarle Corporation FINAL REPORT
Data Type:	Bacterial reverse mutation
HERO ID:	5234603

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 8:	Preparation and Storage of Test Substance	High	× 1	1	The study indicated that the test substance, dissolved in ethanol, was stable for at least 3.25 hours (i.e., longer than the preincubation period); dosing formulations were prepared immediately before use. However, available information suggested that physical-chemical properties of the test substance (i.e., its volatility) may substantially impact the study results. While samples of dosing formulations (vehicle-control, low-, and high-dose groups only) were similar to target levels (85-115% of target concentrations), 1-BP concentrations in preincubation tubes (repeat confirmatory assay) were well below target levels (4-37% and 2-5% of target concentrations at 0 and 90 minutes, respectively). Concentrations were not measured after plate incubation.
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was consistent across treatment groups.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Target concentrations were reported without ambiguity (0, 1.5, 5.0, 15, 50, 150, 500, 1500, and 5000 µg/plate in the initial toxicity-mutagenicity assay, and 0, 50, 150, 500, 1500, 2000, 3000, and 5000 µg/plate in the confirmatory mutagenicity assays). Analytical measurements of dosing formulations showed 1-BP concentrations were 85-115% of target concentrations.
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	The exposure duration was reported. Cultures were subjected to a 90 minute preincubation period; plates were incubated for 48 to 72 hours at 37C.
	Metric 12:	Exposure Route and Method	High	× 1	1	The number of exposure groups (> 5 in each assay) and concentration spacing were justified by the study authors (i.e., based on the initial toxicity-preliminary mutagenicity assay).
	Metric 13:	Metabolic Activation	High	× 1	1	Aroclor 1254-induced rat liver S9 was used. The method of preparation and concentration/volume in final culture were described.
Domain 4: Test Model						

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Study Citation:	BioReliance (2015). Appendix III. Closed-System Ames Test on 1-Bromopropane Conducted at BioReliance and Sponsored by Albemarle Corporation FINAL REPORT
Data Type:	Bacterial reverse mutation
HERO ID:	5234603

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Test Model	High	× 2	2	S. typhimurium strains TA 98, TA 100, TA 1535, TA 1537, and Escherichia coli WP2 uvrA were used. The test model was reported, obtained from a commercial source or laboratory-maintained culture (S. typhimurium strains from Dr. Ames Master cultures and E.coli from the National Collection of Industrial and Marine Bacteria in Aberdeen, Scotland), and is routinely used for the outcome of interest.
	Metric 15:	Number per Group	High	× 1	1	Duplicate or triplicate plating was used in the initial toxicity-mutagenicity and confirmatory mutagenicity assays.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	The outcome assessment methodology was appropriate for the outcome of interest (enumeration of revertant colonies after 48 to 72 hours incubation). However, it was unclear whether methods were sensitive for the outcome of interest. There was no evidence of mutagenicity for the test substance (or negative controls), and positive controls (while showing a positive response), were not volatile substances.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Numbers of revertant colonies were counted after 48-72 hours incubation. Plates not counted immediately were stored at 2 to 8C. This protocol was applied consistently across groups.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study design.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	High	× 2	2	No differences among treatment group parameters were reported.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	High	× 1	1	No confounding variables were reported.
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	High	× 1	1	Statistical methods were not performed (and not required), but data manipulation methods were appropriate. Data were provided for independent analyses.

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Study Citation:	BioReliance (2015). Appendix III. Closed-System Ames Test on 1-Bromopropane Conducted at BioReliance and Sponsored by Albemarle Corporation FINAL REPORT
Data Type:	Bacterial reverse mutation
HERO ID:	5234603

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 23:	Data Interpretation	High	× 2	2	Evaluation criteria (number of colonies) were reported. The criteria for a positive result were as follows: dose-related increased numbers of revertants/plate in at least one strain over a minimum of two increasing concentrations of 1-BP; at least a 3-fold increase in revertants for S typhimurium strains TA 1535 and TA 1537 and at least 2-fold increases for all other strains. These criteria are consistent with standards/guidelines.
	Metric 24:	Cytotoxicity Data	High	× 1	1	Cytotoxicity was defined and methods of measurement were reported. The condition of the bacterial background lawn was evaluated for evidence of toxicity using a dissecting microscope. Toxicity was scored (using a scale described in the study) relative to the vehicle control.
	Metric 25:	Reporting of Data	High	× 2	2	Data for exposure-related findings were presented for all outcomes by exposure group.
Overall Quality Determination‡			~~High~~ ⟶ Medium§		~~1.2~~	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Most of the metrics conformed to standards/guidelines for this study type, and procedures were well-described. However, testing of volatile substances is a special case. Data from this study indicate that the methods used may have been inadequate to assess the mutagenic potential of 1-BP because: methods attributed to Yahagi et al. (1977) may not have been appropriate for testing, these methods may not have prevented loss to volatility (possibly inconsistent use of minimal headspace and screw-capped tubes; decreased analytical concentrations in prior to and after preincubation), and in the absence of any positive results (all 1-BP assays negative, and no volatile substances used as positive controls)."

Table 41: **In vitro evaluation results of Nepal et al 2019 for DNA binding assay**

Study Citation:	Nepal MR,Noh K,Shah S,Bist G,Lee ES,Jeong TC (2019). Identification of DNA and glutathione adducts in male Sprague-Dawley rats exposed to 1-Bromopropane Journal of Toxicology and Environmental Health, Part A: Current Issues, 82(8,8), 502-513
Data Type:	DNA binding assay for 1-BP
HERO ID:	6311554

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	The test substance was identified as 1-bromopropane (1-BP).
	Metric 2:	Test Substance Source	High	× 1	1	The commercial source of the test substance was reported.
	Metric 3:	Test Substance Purity	Low	× 1	3	Test substance purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	Not Rated	NA	NA	This metric is not applicable to the study design (measurement of the radiolabeled test substance is the outcome).
	Metric 5:	Positive Controls	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 6:	Assay Procedures	High	× 1	1	Assay procedures were described adequately and were appropriate for the endpoint of interest.
	Metric 7:	Standards for Tests	Not Rated	NA	NA	This metric is not applicable to this study type.
Domain 3: Exposure Characterization						
	Metric 8:	Preparation and Storage of Test Substance	High	× 1	1	The preparation and exposure conditions for the volatile test substance were adequately described. Storage conditions were not described, but this is appropriate given the study design (single-dose administration).
	Metric 9:	Consistency of Exposure Administration	High	× 1	1	Exposure administration was reported to be consistent among treatment groups.
	Metric 10:	Reporting of Doses/Concentrations	High	× 2	2	Concentrations were reported without ambiguity.
	Metric 11:	Number of Exposure Groups and Concentration Spacing	High	× 2	2	Exposure duration was appropriate for the outcome of interest.
	Metric 12:	Exposure Route and Method	Medium	× 1	2	The dose spacing was appropriate for the outcome of interest. The number of exposure groups was somewhat lacking at 2 concentrations of 1-BP.
	Metric 13:	Metabolic Activation	Low	× 1	3	The concentration of liver homogenate was reported. The source and method of preparation, including the treatment type (i.e. Aroclor or phenobarbital) and species treated, was not included.
Domain 4: Test Model						

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Study Citation:	Nepal MR,Noh K,Shah S,Bist G,Lee ES,Jeong TC (2019). Identification of DNA and glutathione adducts in male Sprague-Dawley rats exposed to 1-Bromopropane Journal of Toxicology and Environmental Health, Part A: Current Issues, 82(8,8), 502-513
Data Type:	DNA binding assay for 1-BP
HERO ID:	6311554

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Test Model	Medium	× 2	4	The test model, calf thymus DNA, was reported and appropriate for the outcome of interest. Limited details were provided, but this is unlikely to have a substantial impact on results, as the calf thymus DNA was obtained from a commercial source.
	Metric 15:	Number per Group	High	× 1	1	The dose-dependent production of N7-propyl guanine from calf thymus DNA and 1-BP was conducted in triplicate for each dose of 1-BP.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	The outcome assessment methodology was appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	The outcome was assessed consistently across all treatment groups.
	Metric 18:	Sampling Adequacy	Not Rated	NA	NA	This metric is not applicable to the study design.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	This metric is not applicable to the study design.
Domain 6: Confounding / Variable Control						
	Metric 20:	Confounding Variables in Test Design and Procedures	High	× 2	2	No confounding variables in the study design were identified.
	Metric 21:	Confounding Variables in Outcomes Unrelated to Exposure	Low	× 1	3	No confounding variables in outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 22:	Data Analysis	High	× 1	1	It does not appear that statistical analysis was conducted on the data to compare dose levels or presence of metabolic activation. Means and standard deviations could be estimated from Figure 2a and 2b to enable independent statistical analysis.
	Metric 23:	Data Interpretation	High	× 2	2	The data were interpreted appropriately.
	Metric 24:	Cytotoxicity Data	Not Rated	NA	NA	This metric is not applicable to the study design, as no cells were utilized.
	Metric 25:	Reporting of Data	High	× 2	2	All data were reported adequately.
Overall Quality Determination‡			High		1.3	
Extracted			Yes			

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Study Citation:	Nepal MR,Noh K,Shah S,Bist G,Lee ES,Jeong TC (2019). Identification of DNA and glutathione adducts in male Sprague-Dawley rats exposed to 1-Bromopropane Journal of Toxicology and Environmental Health, Part A: Current Issues, 82(8,8), 502-513
Data Type:	DNA binding assay for 1-BP
HERO ID:	6311554

Domain	Metric	Rating†	MWF⋆	Score	Comments††

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.
†† This metric met the criteria for high confidence as expected for this type of study

7 Developmental and Reproductive

Table 42: **Animal toxicity evaluation results of Saito-Suzuki et al 1982 for a dominant lethal mating experiment study on reproductive outcomes**

Study Citation:	Saito-Suzuki, R., Teramoto, S., Shirasu, Y. (1982). Dominant lethal studies in rats with 1,2-dibromo-3-chloropropane and its structurally related compounds Mutation Research: Genetic Toxicology, 101(4), 321-327					
Data Type:	Dominant lethal mating experiment					
HERO ID:	1737959					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Identity and structure of test substance were provided.
	Metric 2:	Test Substance Source	High	× 1	1	Commercial source indicated
	Metric 3:	Test Substance Purity	High	× 1	1	>98%
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Vehicle control
	Metric 5:	Positive Controls	High	× 1	1	DBCP was used as a positive control
	Metric 6:	Randomized Allocation	Low	× 1	3	The study did not report how animals were allocated into study groups
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Authors indicate test substances were dissolved in olive oil prior to use.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	Groups appear to be exposed in a consistent manner
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	A single dose is reported with no indication of a confirmation of the actual dose.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Daily gavage for 5 -days
	Metric 11:	Number of Exposure Groups and Dose Spacing	Low	× 1	3	A single dose was used (10% of the LD50); multiple doses (3) are recommended
	Metric 12:	Exposure Route and Method	High	× 1	1	Exposure route was acceptable
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	Acceptable
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	Animal husbandry was not reported
	Metric 15:	Number per Group	High	× 1	1	The number of treated animals/group was appropriate (n = 15)
Domain 5: Outcome Assessment						

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Study Citation:	Saito-Suzuki, R., Teramoto, S., Shirasu, Y. (1982). Dominant lethal studies in rats with 1,2-dibromo-3-chloropropane and its structurally related compounds Mutation Research: Genetic Toxicology, 101(4), 321-327
Data Type:	Dominant lethal mating experiment
HERO ID:	1737959

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	To determine if 1-BP induces DL mutations per se, the appropriate method would include exposures throughout spermatogenesis (e.g., 10 wks in the rat), w/ 5-7 treatments/wk) and one pairing at the end.
	Metric 17:	Consistency of Outcome Assessment	Low	× 1	3	Consistent between groups; however, OECD 478 TG recommends a total of 10 weekly matings post-treatment.
	Metric 18:	Sampling Adequacy	High	× 1	1	All pregnant mated females were sampled
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Not necessary
	Metric 20:	Negative Control Response	High	× 1	1	Control measurements were as expected; positive control gave expected positive results
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	It is unclear whether the number of pregnant females was sufficient to provide at least 400 implants as indicated in the OECD 478 TG.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No detailed information of the animals (health, initial body weights etc.) were provided for independent review
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	Low	× 1	3	OECD guideline 478 suggests statistical analysis should be done considering the male as the experimental unit, including the male as a test of variance.
	Metric 24:	Reporting of Data	Medium	× 2	4	Data was reported clearly; however, reporting of clinical signs should be included (OECD guideline 478)
Overall Quality Determination‡			Medium		1.8	
Extracted			No			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 43: **Animal toxicity evaluation results of WIL Research 2001 for a 2-generation inhalation reproductive study on reproductive outcomes**

Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats					
Data Type:						
HERO ID:	2990994					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	
	Metric 2:	Test Substance Source	High	× 1	1	Commercial source, manufacturer and lot numbers provided.
	Metric 3:	Test Substance Purity	High	× 1	1	At least 99.8% pure.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative control exposed to filtered air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls are not used for 2-gen repro. studies.
	Metric 6:	Randomized Allocation	High	× 1	1	Animals were allocated to study groups using a computerized randomization procedure.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	High	× 1	1	Preparation and storage conditions were described and exposure concentrations were measured by GC every 35 minutes during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	SO: Document identified (on p. 36) deviations in exposure methods that are unlikely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and mean analytical concentrations were reported; no information was provided for range or variance (CV).
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	3 treatment groups and negative control; dose spacing was adequate. (no justification provided).
	Metric 12:	Exposure Route and Method	High	× 1	1	Appropriate number of air changes/hr. No aerosol formation detected in exposure chambers.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	25/sex/group
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Methods were well- described and appropriate.

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Study Citation: WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats
Data Type:
HERO ID: 2990994

Domain		Metric	Rating†	MWF⋆	Score	Comments††
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Blinding of assessors was not reported; however, substantial impacts are not anticipated as most endpoints are objective.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No significant differences between study groups in initial bw and food consumption; body temperature and respiration rate were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were identified.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were clearly described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.3	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor
† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.
‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 44: **Animal toxicity evaluation results of WIL Research 2001 for a 2-generation inhalation developmental study on growth (early life) and development outcomes**

Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats					
Data Type:	2-generation inhalation study - developmental					
HERO ID:	2990994					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	
	Metric 2:	Test Substance Source	High	× 1	1	Manufacturer and lot no. provided.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity at at least 99.8%.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	negative controls exposed to filtered air.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not used for 2-gen repro. studies.
	Metric 6:	Randomized Allocation	Low	× 1	3	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Equipment and method used to generate vapor was not described. Storage conditions were described and exposure concentrations were measured by GC every 35 minutes during exposure.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	
	Metric 9:	Reporting of Doses/Concentrations	Medium	× 2	4	Target and mean analytical concentrations were reported; no information was provided for range or variance.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	
	Metric 11:	Number of Exposure Groups and Dose Spacing	High	× 1	1	3 treatment groups plus negative control; adequate spacing of concentrations.
	Metric 12:	Exposure Route and Method	High	× 1	1	Vapor suitable for volatile substance.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	High	× 2	2	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	
	Metric 15:	Number per Group	High	× 1	1	25/sex/group; litters culled to 8/group.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	High	× 2	2	Methods were well reported.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	
	Metric 18:	Sampling Adequacy	High	× 1	1	Litter as the experimental unit.

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Study Citation:	WIL Research (2001). An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats
Data Type:	2-generation inhalation study - developmental
HERO ID:	2990994

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 19:	Blinding of Assessors	Medium	× 1	2	Binding not reported but is not expected to have a substantial impact on results.
	Metric 20:	Negative Control Response	High	× 1	1	
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	High	× 2	2	Initial bw and food consumption were reported and appropriate.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were well-reported and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	
Overall Quality Determination‡			High		1.2	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 45: **Animal toxicity evaluation results of Brominated Solvents Consortium 2000 for a summary of a 2-generation study on growth (early life) and development outcomes**

Study Citation:	Brominated Solvents Consortium (2000). Initial submission: Letter from Brominated Solvents Consortium, results from ongoing 2-generation reproductive inhalation toxicity study in rats w/1-bromopropane, dated 3/15/00
Data Type:	Summary of 2-gen study
HERO ID:	4158094

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance was identified by name and CASRN.
	Metric 2:	Test Substance Source	Low	× 1	3	The source was not reported.
	Metric 3:	Test Substance Purity	Low	× 1	3	The purity was not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Concurrent negative controls were found.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation was not reported in the summary.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Unacceptable	× 1	4	Information on preparation and storage was not reported.
	Metric 8:	Consistency of Exposure Administration	Unacceptable	× 1	4	Details were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Nominal concentrations reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of groups and spacing were reported but not justified.
	Metric 12:	Exposure Route and Method	Unacceptable	× 1	4	No details were reported.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Low	× 2	6	The source, strain, initial body weight, and health status were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	No details were reported.
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group was appropriate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Unacceptable	× 2	8	No details were reported.
	Metric 17:	Consistency of Outcome Assessment	Unacceptable	× 1	4	No details were reported.
	Metric 18:	Sampling Adequacy	Low	× 1	3	No details were reported.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not applicable.
	Metric 20:	Negative Control Response	Unacceptable	× 1	4	Responses were not sufficiently reported.
Domain 6: Confounding / Variable Control						

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Study Citation:	Brominated Solvents Consortium (2000). Initial submission: Letter from Brominated Solvents Consortium, results from ongoing 2-generation reproductive inhalation toxicity study in rats w/1-bromopropane, dated 3/15/00
Data Type:	Summary of 2-gen study
HERO ID:	4158094

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No details were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	× 1	3	No details were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	Unacceptable	× 1	4	Data were not provided.
	Metric 24:	Reporting of Data	Low	× 2	6	Data reported for specific outcomes.
Overall Quality Determination‡			Unacceptable⋆⋆		2.8	
Extracted			No			

⋆⋆ Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 46: **Animal toxicity evaluation results of Bsoc 2001 for a summary of audited results from 2-generation study on growth (early life) and development outcomes**

Study Citation:	BSOC (Brominated Solvents Committee) (2001). Support: LTR from Brominated Solvents Comm to US EPA, follow-up submission from audited final report of 2-gen reproductive study in rats of inhaled 1-bromopropane exposure, dated 6/21/01
Data Type:	Summary of audited results from 2-gen study
HERO ID:	4158095

Domain	Metric		Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by name and CASRN.
	Metric 2:	Test Substance Source	Low	× 1	3	Source not identified.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation method not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Unacceptable	× 1	4	Information on preparation and storage not reported.
	Metric 8:	Consistency of Exposure Administration	Unacceptable	× 1	4	Details not reported.
	Metric 9:	Reporting of Doses/Concentrations	Unacceptable	× 2	8	Target concentrations only were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of groups and spacing were reported but not justified.
	Metric 12:	Exposure Route and Method	Unacceptable	× 1	4	No details were reported.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Low	× 2	6	The source, strain, initial body weight and health status were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	No details were reported.
	Metric 15:	Number per Group	Low	× 1	3	Number of F0 parental animals not reported, but number of F1 parental animals were reported.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Unacceptable	× 2	8	No details were reported.
	Metric 17:	Consistency of Outcome Assessment	Unacceptable	× 1	4	No details were reported.
	Metric 18:	Sampling Adequacy	Low	× 1	3	Limited details were reported.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not required.

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Study Citation:	BSOC (Brominated Solvents Committee) (2001). Support: LTR from Brominated Solvents Comm to US EPA, follow-up submission from audited final report of 2-gen reproductive study in rats of inhaled 1-bromopropane exposure, dated 6/21/01
Data Type:	Summary of audited results from 2-gen study
HERO ID:	4158095

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 20:	Negative Control Response	Low	× 1	3	Limited details on negative control responses were provided, only in comparison to treated animals and only in text.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	No details were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	× 1	3	No details were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	Unacceptable	× 1	4	No numerical data provided.
	Metric 24:	Reporting of Data	Low	× 2	6	Results described only in text.
Overall Quality Determination‡			Unacceptable⋆⋆		2.9	
Extracted			No			

⋆⋆ Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 47: **Animal toxicity evaluation results of Bsoc 1998 for a summary of range-finding reproductive/developmental toxicity study in 4158101 study on growth (early life) and development outcomes**

Study Citation:	BSOC (Brominated Solvents Committee) (1998). Initial submission: LTR from Brominated Solvents Committee to US EPA regarding range-finding developmental/reproductive toxicity study in rats via whole-body inhalation exposure with 1-bromopropane, with attachments & dated 12/23/98
Data Type:	Summary of range-finding repro/dev tox, full study in 4158101
HERO ID:	4158100

Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by name and CASRN.
	Metric 2:	Test Substance Source	Low	× 1	3	Source not identified.
	Metric 3:	Test Substance Purity	Low	× 1	3	Purity not reported.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation method was not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Unacceptable	× 1	4	No details were reported.
	Metric 8:	Consistency of Exposure Administration	Unacceptable	× 1	4	No details were reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	× 2	6	Concentrations reported, but unclear if target, nominal, or analytical.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of groups and spacing were reported but not justified.
	Metric 12:	Exposure Route and Method	Unacceptable	× 1	4	No details were reported.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Low	× 2	6	The source, strain, age, health status, and initial body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	× 1	3	No details were reported.
	Metric 15:	Number per Group	Medium	× 1	2	The number per group was taken from summary table.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Low	× 2	6	Incomplete reporting of outcome assessment methods. Endpoints not sufficient to determine developmental toxicity.
	Metric 17:	Consistency of Outcome Assessment	Low	× 1	3	No details were reported.

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Study Citation:	BSOC (Brominated Solvents Committee) (1998). Initial submission: LTR from Brominated Solvents Committee to US EPA regarding range-finding developmental/reproductive toxicity study in rats via whole-body inhalation exposure with 1-bromopropane, with attachments & dated 12/23/98
Data Type:	Summary of range-finding repro/dev tox, full study in 4158101
HERO ID:	4158100

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 18:	Sampling Adequacy	Low	× 1	3	Sampling for data presented in tables was appropriate, but not sensitive for developmental outcomes.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not required.
	Metric 20:	Negative Control Response	High	× 1	1	Negative responses for the reported data were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Parameters not reported to have been measured.
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	× 1	3	Data not reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	Low	× 1	3	Statistical methods were not described.
	Metric 24:	Reporting of Data	Low	× 2	6	All data not reported, but some summary tables were included.
Overall Quality Determination‡			Unacceptable⋆⋆		2.6	
Extracted			No			

⋆⋆ Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

Table 48: **Animal toxicity evaluation results of Bsoc 1999 for a range-finding developmental study on reproductive, and growth (early life), and development outcomes**

Study Citation:	BSOC (Brominated Solvents Committee) (1999). Support: Letter from Brominated Solvents Comm to USEPA reporting results from an unaudited draft report for definitive developmental study in rats with 1-bromopropane, dated 030999
Data Type:	Range-finding developmental
HERO ID:	4158101

Domain	Metric		Rating[†]	MWF[⋆]	Score	Comments[††]
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by name, certificate of analysis, and purity testing.
	Metric 2:	Test Substance Source	High	× 1	1	Manufacturer, supplier, lot number, and certificate of analysis.
	Metric 3:	Test Substance Purity	High	× 1	1	Purity (99.9%) determined by purity testing and was such that effects likely due to test substance.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	Negative controls were included.
	Metric 5:	Positive Controls	Not Rated	NA	NA	Positive controls were not required.
	Metric 6:	Randomized Allocation	Low	× 1	3	Authors reported use of randomization procedure based on GD 0 body weights provided by the sponsor. No randomization procedure for culling pups was provided.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	No information was provided other than 'stored at room temperature'.
	Metric 8:	Consistency of Exposure Administration	Low	× 1	3	The method and equipment used to generate the vapor were reported; however, the actual number of air changes per hour is not clear.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	The nominal, target, and analytical concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration were reported and justified.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Medium	× 1	2	The number of groups and spacing were determined by the sponsor.
	Metric 12:	Exposure Route and Method	Low	× 1	3	Number of air changes/hr not reported; particle size of test article is above the range recommended for pulmonary deposition in OECD 412 TG (< 2 µm)
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strain, sex, age, and initial body weight were reported. Health status was not reported.

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Study Citation:	BSOC (Brominated Solvents Committee) (1999). Support: Letter from Brominated Solvents Comm to USEPA reporting results from an unaudited draft report for definitive developmental study in rats with 1-bromopropane, dated 030999
Data Type:	Range-finding developmental
HERO ID:	4158101

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	The housing, food, water, lighting, temperature, humidity, and air changes were reported.
	Metric 15:	Number per Group	High	× 1	1	The number of animals per group was appropriate.
Domain 5: Outcome Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	× 2	4	Outcome assessment methodology did not include information on body temperature or respiration rate.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Outcomes were assessed consistently.
	Metric 18:	Sampling Adequacy	Medium	× 1	2	Limited information provided; however sampling was adequate.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Blinding not required.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	× 2	6	Respiratory rate was not reported to have been measured.
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	× 1	3	Early delivery was observed in two females and one female had full resorptions which authors stated were not related to exposure to the test substance.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were clearly described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	All data were reported.
Overall Quality Determination‡			~~High~~ ⟶ Medium§		~~1.7~~	
Extracted			Yes			

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High $=\geq 1$ to < 1.7; Medium $=\geq 1.7$ to < 2.3; Low $=\geq 2.3$ to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study

§ Evaluator's explanation for rating change: "Important details regarding the exposure chamber are missing."

Table 49: **Animal toxicity evaluation results of Yu et al 2008 for an oral development-dominant lethality, male reproductive study on growth (early life) and development, and reproductive outcomes**

Study Citation:	Yu, W. J., Kim, J. C., Chung, M. K. (2008). Lack of dominant lethality in mice following 1-bromopropane treatment Mutation Research: Genetic Toxicology and Environmental Mutagenesis, 652(1), 81-87					
Data Type:	Oral development-dominant lethality, male reproductive					
HERO ID:	1410098					
Domain		Metric	Rating†	MWF⋆	Score	Comments††
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	× 2	2	Test substance identified by name and CASRN.
	Metric 2:	Test Substance Source	High	× 1	1	The source and Batch number were reported.
	Metric 3:	Test Substance Purity	High	× 1	1	The reported purity (99%) was such that effects likely due to the test substance.
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	× 2	2	A vehicle control group was included.
	Metric 5:	Positive Controls	High	× 1	1	An appropriate positive control (cyclophosphamide monohydrate 40 mg/kg) was included.
	Metric 6:	Randomized Allocation	Low	× 1	3	Allocation method was not reported.
Domain 3: Exposure Characterization						
	Metric 7:	Preparation and Storage of Test Substance	Medium	× 1	2	Preparation of the test substance was described with limited details and stability and homogeneity of the suspension was not reported.
	Metric 8:	Consistency of Exposure Administration	High	× 1	1	Exposures were administered consistently.
	Metric 9:	Reporting of Doses/Concentrations	High	× 2	2	The doses were reported.
	Metric 10:	Exposure Frequency and Duration	High	× 1	1	Frequency and duration of dosing were reported.
	Metric 11:	Number of Exposure Groups and Dose Spacing	Low	× 1	3	The number of groups were inadequate. OECD 478 recommends at least three treated groups should be analyzed.
	Metric 12:	Exposure Route and Method	High	× 1	1	Exposure route and method were appropriate.
Domain 4: Test Organism						
	Metric 13:	Test Animal Characteristics	Medium	× 2	4	The source, species, strain, sex, age, and health status were reported; however, initial body weight was not reported. Although OECD guideline test recommends use of rats, mice are acceptable.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	× 1	1	Animal husbandry was appropriate and adequately reported.
	Metric 15:	Number per Group	High	× 1	1	Number of animals per group was adequate.
Domain 5: Outcome Assessment						

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Study Citation:	Yu, W. J., Kim, J. C., Chung, M. K. (2008). Lack of dominant lethality in mice following 1-bromopropane treatment Mutation Research: Genetic Toxicology and Environmental Mutagenesis, 652(1), 81-87
Data Type:	Oral development-dominant lethality, male reproductive
HERO ID:	1410098

Domain	Metric		Rating†	MWF⋆	Score	Comments††
	Metric 16:	Outcome Assessment Methodology	Unacceptable	× 2	8	Outcome assessment methodology was reported as mating mice over a 6-week period; however, the OECD 478 test guidelines recommend weekly mating over an 8-week period to ensure that all phases of male germ cell maturation are evaluated for dominant lethal induction.
	Metric 17:	Consistency of Outcome Assessment	High	× 1	1	Consistency of assessment was appropriate.
	Metric 18:	Sampling Adequacy	High	× 1	1	Sampling was adequate.
	Metric 19:	Blinding of Assessors	Not Rated	NA	NA	Assessors were not blinded to treatment group; however, no subjective endpoints were evaluated beyond clinical signs.
	Metric 20:	Negative Control Response	High	× 1	1	Negative control response was appropriate.
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	× 2	4	No confounding variables were reported; however, minor inconsistencies and uncertainties were noted in data reporting.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	× 1	1	No health outcomes unrelated to exposure were reported.
Domain 7: Data Presentation and Analysis						
	Metric 23:	Statistical Methods	High	× 1	1	Statistical methods were described and appropriate.
	Metric 24:	Reporting of Data	High	× 2	2	Data for all outcomes were reported.
Overall Quality Determination‡			Unacceptable⋆⋆		1.5	
Extracted			No			

⋆⋆ Consistent with our *Application of Systematic Review in TSCARisk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one or more of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.

⋆ MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left\lfloor \sum_i (\text{Metric Score}_i \times \text{MWF}_i) \,/\, \sum_j \text{MWF}_j \right\rceil_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases},$$

where High =≥ 1 to < 1.7; Medium =≥ 1.7 to < 2.3; Low =≥ 2.3 to ≤ 3.0. If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

†† This metric met the criteria for high confidence as expected for this type of study