



United States  
Environmental Protection Agency

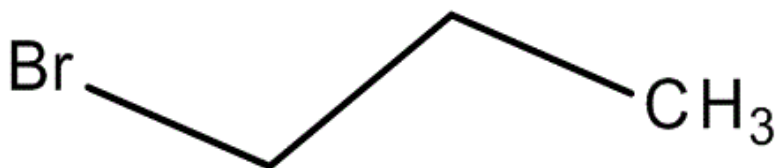
Office of Chemical Safety and  
Pollution Prevention

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

**CASRN: 106-94-5**

**Systematic Review Supplemental File:**

**Data Quality Evaluation of Human Health Hazard Studies –  
Epidemiologic Studies**



*July 2019, DRAFT*

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Study Citation: G. Ichihara, W. Li, E. Shibata, X. Ding, H. Wang, Y. Liang, S. Peng, S. Itohara, M. Kamijima, Q. Fan, Y. Zhang, E. Zhong, X. Wu, W. M. Valentine, Y. Takeuchi (2004). Neurologic abnormalities in workers of a 1-bromopropane factory Environmental Health Perspectives, 112(13,13), 1319-1325

Data Type: Jiangsu\_1-BP\_control workers\_distal latency-Neurological/Behavior

HERO ID: 1519100

Domain	Metric	Rating†	MWF*	Score	Comments††
<b>Domain 1: Study Participation</b>					
Metric 1:	Participant selection	High	× 0.4	0.4	Participants were female workers in 1-bromopropane (1-BP) production facilities in the Jiangsu Province of China. The 1-BP production process and inclusion/exclusion criteria were described in detail. Survey was conducted in 2001.
Metric 2:	Attrition	High	× 0.4	0.4	There was minimal attrition in the analysis sample. Four workers were excluded from some analyses due to inability to find age-matched controls.
Metric 3:	Comparison Group	High	× 0.2	0.2	Unexposed controls were age-matched and selected randomly from a cohort of female workers in a beer factory in the same city, with participants living in the same area. These workers were recruited during the same time frame. For neurobehavioral testing, outcome analysis, both age and education were matched for controls.
<b>Domain 2: Exposure Characterization</b>					
Metric 4:	Measurement of Exposure	High	× 0.4	0.4	Exposure to 1-BP was measured during an 8-hour work shift with a passive sampler (Sibata Scientific Technology Ltd., Tokyo, Japan) attached to each worker. The sampler was stored at 4 degrees C, and then analyzed using GC-MS (GCD system G1800A, Hewlett Packard). This represents a well-established method using a direct measurement of exposure.
Metric 5:	Exposure levels	Medium	× 0.2	0.4	The study evaluated both exposed workers at a 1-BP production facility and unexposed workers at a nearby facility. In addition, they also looked at levels of exposure and length of employment within the 1-BP factory workers. Exposure estimates for TWA for 8-hr shifts ranged from 0-49.19 ppm.
Metric 6:	Temporality	Medium	× 0.4	0.8	In this cross sectional study, the electrophysiological and neurobehavioral outcomes were assessed at the same time as sampling. Exposed workers had been at the factory for 27 +/- 31 months. Unclear if that temporality of outcome and exposure is appropriate.

Domain 3: Outcome Assessment

Continued on next page ...

Study Citation: G. Ichihara, W. Li, E. Shibata, X. Ding, H. Wang, Y. Liang, S. Peng, S. Itohara, M. Kamijima, Q. Fan, Y. Zhang, E. Zhong, X. Wu, W. M. Valentine, Y. Takeuchi (2004). Neurologic abnormalities in workers of a 1-bromopropane factory Environmental Health Perspectives, 112(13,13), 1319-1325  
 Data Type: Jiangsu\_1-BP\_control workers\_distal latency-Neurological/Behavior  
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Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	Vibration sensation examinations were conducted by one trained neurologist. Electrophysiological outcomes included distal latency and nerve conduction velocity. These measurements were recorded using a Neuropack evoked potential/electromyogram measurement system (model MEB5508; Nihon Kohden, Co., Tokyo, Japan). For neurobehavioral testing, the WHO sponsored Neurobehavioral Core Test Battery was used as well as the Profile of Mood States (POMS) questionnaire. A Gravicorder GS-30 stationometer (Anima Co., Tokyo, Japan) was used to measure postural balance and sway. Blinding is not discussed for both the vibration sensation assessments and the neurobehavioral testing, which may introduce bias into some results. Some of the clinical chemistry results are discussed, but not reported in a fashion that could be included in meta-analyses. Other results include full tabulation, including the number of pairs in the comparison.
Metric 8:	Reporting Bias	Low	× 0.333	1.0	
Domain 4: Potential Confounding/Variable Control					
Metric 9:	Covariate Adjustment	Medium	× 0.5	1	Control workers were age-matched, and in the neurobehavioral analyses workers were age- and education-matched. The study authors state that only one worker from each group was an alcohol drinker, and none of the workers were smokers or had diabetes. All workers were female. Length of employment differed strongly between the exposed (27 +/- 31 months) and unexposed (168 +/- 67 month), but was not adjusted for in the analysis..
Metric 10:	Covariate Characterization	Medium	× 0.25	0.5	There was no discussion of covariate collection, but it is assumed that this was conducted during the medical examination. There is no evidence to suggest this is an invalid method.

Study Citation:	G. Ichihara, W. Li, E. Shibata, X. Ding, H. Wang, Y. Liang, S. Peng, S. Itohara, M. Kamijima, Q. Fan, Y. Zhang, E. Zhong, X. Wu, W. M. Valentine, Y. Takeuchi (2004). Neurologic abnormalities in workers of a 1-bromopropane factory Environmental Health Perspectives, 112(13,13), 1319-1325				
Data Type:	Jiangsu_1-BP_control workers_distal latency-Neurological/Behavior				
HERO ID:	1519100				
Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
	Metric 11: Co-exposure Confounding	Medium	× 0.25	0.5	The study authors state that 1-BP was the only substance produced at the factory at the time of the survey. The factory produced exclusively 2-BP prior to 1996, when 1-BP production started there. In 1999, the facility stopped all 2-BP production. Some workers may have been exposed to both, but this was addressed with a subsample of workers that were hired after the switch was made (1999). Four control workers reported prior exposure to other substances including ammonia and formalin. This is not expected to appreciably bias the results.
Domain 5: Analysis	Metric 12: Study Design and Methods	Medium	× 0.4	0.8	This study looks cross-sectionally at the prevalence of neurobehavioral deficits in two populations of workers (exposed/unexposed).
	Metric 13: Statistical power	Medium	× 0.2	0.4	There were sufficient number of pairs to detect an effect of 1-BP in the exposed population.
	Metric 14: Reproducibility of analyses	Medium	× 0.2	0.4	Cutpoints for length of employment and exposure level were described. Other details on the analysis were described in so that it could be reproduced.
	Metric 15: Statistical models	Medium	× 0.2	0.4	The choice of statistical tests to compare means was transparent. A t-test was applied for continuous variables, while the Wilcoxon and Fisher's test were used for menstruation outcome comparisons.
Domain 6: Other Considerations for Biomarker Selection and Measurement	Metric 16: Use of Biomarker of Exposure		NA	NA	
	Metric 17: Effect biomarker		NA	NA	
	Metric 18: Method Sensitivity		NA	NA	
	Metric 19: Biomarker stability		NA	NA	
	Metric 20: Sample contamination		NA	NA	
	Metric 21: Method requirements		NA	NA	
	Metric 22: Matrix adjustment		NA	NA	
Overall Quality Determination <sup>†</sup>		Medium		1.8	
Extracted		Yes			

Study Citation: G. Ichihara, W. Li, E. Shibata, X. Ding, H. Wang, Y. Liang, S. Peng, S. Itohara, M. Kamijima, Q. Fan, Y. Zhang, E. Zhong, X. Wu, W. M. Valentine, Y. Takeuchi (2004). Neurologic abnormalities in workers of a 1-bromopropane factory Environmental Health Perspectives, 112(13,13), 1319-1325  
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Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
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\* 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.

if any metric is Unacceptable

$$\text{Overall rating} = \begin{cases} 4 \\ \left\lfloor \frac{\sum_i (\text{Metric Score}_i \times \text{MWF}_i) / \sum_j \text{MWF}_j}{0.1} \right\rfloor & \text{(round to the nearest tenth) otherwise} \end{cases}$$

where High  $\geq 1$  to  $< 1.7$ ; Medium  $\geq 1.7$  to  $< 2.3$ ; Low  $\geq 2.3$  to  $\leq 3.0$ . 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

Study Citation: Li, W., Shibata, E., Zhou, Z., Ichihara, S., Wang, H., Wang, Q., Li, J., Zhang, L., Wakai, K., Takeuchi, Y., Ding, X., Ichihara, G. (2010). Dose-dependent neurologic abnormalities in workers exposed to 1-bromopropane Journal of Occupational and Environmental Medicine, 52(8), 769-777

Data Type: 1-BP Factories in China\_cumulative exposure\_neurobehavioral test-Neurological/Behavior  
 HERO ID: 1519103

Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
Domain 1: Study Participation					
Metric 1:	Participant selection	Low	× 0.4	1.2	Authors report that 87 female and 29 male workers at 3 1-BP factories (in Yixing city, Jiangsu Province in 2001 and 2004; in Yancheng city, Jiangsu Province in 2003; and in Weifang city, Shandong Province in 2005) were included in this study. It is not reported why these provinces or factories were selected, or if they are the only three factories of their kind. Sex-, age- (within 3 years), and region-matched control workers were randomly recruited from a beer factory in 2001, a refrigeration equipment factory in 2003, a knitting workshop in 2004, and a steel operation factory in 2005, but the authors do not describe why these specific locations were selected. The authors did not describe the recruitment process, and it is not clear whether the same workers included in the Ichihara et al 2004 study were recruited for this study.
Metric 2:	Attrition	Medium	× 0.4	0.8	The study explained that only the data of 60 female and 26 male exposed workers (out of 87 female workers and 29 male workers) could be used in the analysis because: data of 6 other females examined in 2001 could not be used because the period of exposure was <1 month; data of other females examined in 2001 and one male worker in Yancheng in 2003 could not be used because the period of exposure or exposure level was unknown; and age-matched controls could not be recruited for one male worker in Yixing in 2003, one female worker in Yixing in 2004, and 4 females and 1 male in Weifang in 2005.

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Study Citation: Li, W., Shibata, E., Zhou, Z., Ichihara, S., Wang, H., Wang, Q., Li, J., Zhang, L., Wakai, K., Takeuchi, Y., Ding, X., Ichihara, G. (2010). Dose-dependent neurologic abnormalities in workers exposed to 1-bromopropane Journal of Occupational and Environmental Medicine, 52(8), 769-777

Data Type: 1-BP Factories in China\_cumulative exposure\_neurobehavioral test-Neurological/Behavior  
 HERO ID: 1519103

Domain	Metric	Rating†	MWF*	Score	Comments††
Metric 3:	Comparison Group	Low	× 0.2	0.6	Control workers were randomly selected from a beer factory in 2001, a refrigeration equipment factory in 2003, a knitting workshop in 2004, and a steel operation factory in 2005. The controls were matched based on sex, age (within 3 years), and region. Further differences were considered in the statistical analysis including alcohol consumption and height and body weight. However, minimal details were provided on selection methods for the participants or why different factories were used for the different years. A table of characteristics was provided, but only included a few parameters. Therefore, there is only indirect evidence that the groups were similar. Ambient exposure levels varied by job and by plant and were collected in different years for each plant. For example, the ambient concentrations of aceraw product collection were more than 3 times higher at the Yancheng plant (analyzed in 2003) than at the Yixing plant. Exposure was measured only once for some of the female employees over 8- or 12-hour work shifts but TWA exposure concentrations to 1-BP were reported. TWAs were used to assign exposure groups, based on either 1 or 2 samples only. The median exposure level of the high exposure groups for females was 22.58 ppm but the range was 15.28-106.4 ppm, indicating that some of the workers were exposed to levels much higher than the lowest exposed workers in that group.

Domain 2: Exposure Characterization

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Study Citation: Li, W., Shibata, E., Zhou, Z., Ichihara, S., Wang, H., Wang, Q., Li, J., Zhang, L., Wakai, K., Takeuchi, Y., Ding, X., Ichihara, G. (2010). Dose-dependent neurologic abnormalities in workers exposed to 1-bromopropane Journal of Occupational and Environmental Medicine, 52(8), 769-777

Data Type: 1-BP Factories in China\_cumulative exposure\_neurobehavioral test-Neurological/Behavior  
 HERO ID: 1519103

Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
Metric 4:	Measurement of Exposure	Medium	× 0.4	0.8	Individual exposure during a work shift was assessed using a passive sampler that was attached to each worker during one 8- or 12-hour shift. Analysis was carried out using gas chromatography-mass spectrometry. Assessment of individual exposure was conducted twice for 2 shifts, except that it was conducted only once for each 5 female workers in Yixing in 2001 and 2 female workers in Yancheng in 2003 and 3 times for one female worker in Yancheng in 2003. Cumulative exposure was the product of exposure level (based on the individual TWA concentration) and period of exposure (in months). The cumulative exposure measures were based on only 1-3- day measurements of individual exposure levels.
Metric 5:	Exposure levels	Low	× 0.2	0.6	The range and distribution of exposure is adequate to develop an exposure-response relationship. The study used a continuous measure of exposure based on cumulative exposure (time-weighted-average x months of exposure) in the analysis.
Metric 6:	Temporality	Low	× 0.4	1.2	Exposed factory workers were exposed for approximately 3-4 years, on average, before outcome assessment so temporality is established. However, it is unclear if the exposure fell within the relevant windows for all outcomes. Controls were recruited in different years from different plants.

Domain 3: Outcome Assessment

Study Citation: Li, W., Shibata, E., Zhou, Z., Ichihara, S., Wang, H., Wang, Q., Li, J., Zhang, L., Wakai, K., Takeuchi, Y., Ding, X., Ichihara, G. (2010). Dose-dependent neurologic abnormalities in workers exposed to 1-bromopropane Journal of Occupational and Environmental Medicine, 52(8), 769-777

Data Type: 1-BP Factories in China\_cumulative exposure\_neurobehavioral test-Neurological/Behavior

HERO ID: 1519103

Domain	Metric	Rating†	MWF*	Score	Comments††
Metric 7:	Outcome measurement or characterization	Low	× 0.667	2	The neurobehavioral tests were conducted on the basis of the Chinese edition of the WHO Neurobehavioral Core Test Battery by trained Chinese researchers. The electrophysiological tests, including nerve conduction velocity, DL, F-wave conduction velocity sensory nerve conduction velocity, and F-wave studies were conducted using standard techniques. Description was provided in detail. Individual skin temperatures should have been taken at the site of the test (on the foot) based on standard methods (results are affected by body temperature on the foot). As acknowledged in the report by the study authors, vibration sense is inherently imprecise (based on the sensitivity of the subject relative to the examiner). Evidence of a high degree of variability was shown in the large standard deviations reported for vibration sense in females.
Metric 8:	Reporting Bias	Medium	× 0.333	0.67	The authors only presented the results with significant trend with exposure in the tables. The authors state that the other results are not significant but they do not present the non-significant results. Vibration sense can be influenced by BMI, but it was not reported or controlled in the study.

Domain 4: Potential Countounding/Variable Control	Metric 9: Covariate Adjustment	Medium	× 0.5	1	The controls were matched based on sex, age (within 3 years), and region. Further differences were adjusted for in the statistical analysis. Since all the subjects were factory workers, it can be assumed that they had similar socioeconomic status. Vibration sense can be influenced by BMI, but it was not reported or controlled in the study.
Metric 10: Covariate Characterization		Medium	× 0.25	0.5	Potential confounders were assessed using a questionnaire that was filled out by investigators from the local CDC who could communicate with the workers in their own dialect. However, the authors don't report that the questionnaire was validated.

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Data Type:	1-BP Factories in China_cumulative exposure_neurobehavioral test-Neurological/Behavior				
HERO ID:	1519103				
Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
	Metric 11: Co-exposure Confounding	Medium	× 0.25	0.5	There were data presented on one female worker who reported handling 2-BP and several male controls and male workers who reported using other chemicals. The exposure period for these workers was adjusted for these workers. Controls all came from different factories. It is unlikely there was differential co-exposure across groups that would have biased the results.
Domain 5: Analysis					
	Metric 12: Study Design and Methods	Medium	× 0.4	0.8	The study design (cross-sectional) was appropriate to assess the effects of 1-BP exposure on various health effects and the statistical method (regression analysis) was appropriate. Although the study was cross-sectional in nature, cumulative exposures were assessed.
	Metric 13: Statistical power	Medium	× 0.2	0.4	The number of participants (60 female and 26 male workers and same number of controls) was sufficient to detect an effect.
	Metric 14: Reproducibility of analyses	Medium	× 0.2	0.4	The description of the statistical methods is sufficient to reproduce the ANCOVA regression models and the adjustment factors were included in the footnotes to Table 7.
	Metric 15: Statistical models	Medium	× 0.2	0.4	The adjustment factors included in the ANCOVA model were determined by ANOVA models and model assumptions were met.
Domain 6: Other Considerations for Biomarker Selection and Measurement					
	Metric 16: Use of Biomarker of Exposure		NA	NA	
	Metric 17: Effect biomarker		NA	NA	
	Metric 18: Method Sensitivity		NA	NA	
	Metric 19: Biomarker stability		NA	NA	
	Metric 20: Sample contamination		NA	NA	
	Metric 21: Method requirements		NA	NA	
	Metric 22: Matrix adjustment		NA	NA	
Overall Quality Determination <sup>†</sup>		Low		2.4	
Extracted		Yes			
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\* 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.

if any metric is Unacceptable

$$\text{Overall rating} = \begin{cases} 4 \\ \left\lfloor \frac{\sum_i (\text{Metric Score}_i \times \text{MWF}_i)}{\sum_j \text{MWF}_j} \right\rfloor_{0,1} \end{cases} \quad (\text{round to the nearest tenth) otherwise}$$

where High  $\geq 1$  to  $< 1.7$ ; Medium  $\geq 1.7$  to  $< 2.3$ ; Low  $\geq 2.3$  to  $\leq 3.0$ . 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

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 1 01-014  
 Data Type: Cross-sectional\_Occupational\_NC\_NIOSH\_cohort\_1-BP\_DNADamage\_air\_quartiles-Other (please specify below)  
 HERO ID: 3974874

Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
Domain 1: Study Participation					
Metric 1:	Participant selection	Medium	× 0.4	0.8	A subset of 64 occupationally exposed workers (18 males, 46 females) originally evaluated in a NIOS Health Hazard Evaluation were used for this study. Workers were assessed in 2001 and worked at 2 facilities where 1-bromopropane (1-BP) was a solvent vehicle for spray adhesives: Marx Industries Inc., Sawmills, NC and STN Cushion Company, Thomasville, NC. It is unclear what fraction of the original NIOSH study participants chose to join this more in depth study and if any bias was introduced with that selection process.
Metric 2:	Attrition	Low	× 0.4	1.2	No attrition is discussed. Study participants are a subset of the NIOSH study who were interested in participating. Not all subjects participated in the personal air monitoring (50/64) and results in Table 5 are reported for 48-60 participants.. In cases of missing exposure data, subjects were assigned to quartiles based on the single measurements available.
Metric 3:	Comparison Group	Low	× 0.2	0.6	Rather than using population controls, workers at the same factories were considered exposed or unexposed based on job title. The NIOSH assessment found that sprayers had high 1-BP exposure (exposed) and non-sprayers had relatively low 1-BP exposure. Thus, 19 sprayers served as the exposed population and 45 non-sprayers served as controls. Sprayers at Facility A had exposures an order of magnitude higher than sprayers at Facility B and the 6 sprayers at Facility B were all female.

Domain 2: Exposure Characterization

Metric 4:	Measurement of Exposure	High	× 0.4	0.4	Personal air monitoring collected samples from the breathing zone of 50 participants for 1-3 days. Samples were analyzed with GC-FID. An 8-hr time weighted average concentration was used for these assessments. In addition, a biomarker of exposure (Br) was assessed in blood and urine at the start and end of the work week. Estimated exposure from these methods was highly correlated, increasing confidence in the measurements.
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Study Citation:	M. Torason, 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 1 01-014				
Data Type:	Cross-sectional_Occupational_NC_NIOSH_cohort_1-BP_DNADamage_air_quartiles-Other (please specify below)				
HERO ID:	3974874				
Domain	Metric	Rating†	MWF*	Score	Comments††
Metric 5:	Exposure levels	Medium	× 0.2	0.4	With the use of personal air monitoring and biomarkers, exposure was described as a continuum with a wide range of exposure (8 hr TWA of 2-83 ppm). Sprayers at Facility A had exposures an order of magnitude higher than sprayers at Facility B. Non-sprayers have considerably lower exposure to 1-BP. Analysis included dichotomized exposure levels (non-sprayer, sprayer), continuous exposures and quartiles of exposure.
Metric 6:	Temporality	High	× 0.4	0.4	Blood samples were collected for analysis of DNA damage in leukocytes on the morning of the first workday (Monday) and on the afternoon of the last workday (Thursday) in the same week. Temporality is appropriate for this endpoint.
Domain 3: Outcome Assessment					
Metric 7:	Outcome measurement or characterization	Medium	× 0.667	1.33	DNA damage in leukocytes was the only outcome assessed in this study. Blood samples were collected at the beginning and end of work week. A comet assay was used to determine average number of DNA breaks in 100 leukocytes per sample.
Metric 8:	Reporting Bias	Medium	× 0.333	0.67	Study fully reports exposures by job title/facility, biomarkers for start and end of week, comet analysis results, correlations between exposure and the determined associations. Covariates are clearly stated for each analysis. Confidence intervals or standard deviation not included with analysis, but p values were.
Domain 4: Potential Confounding/Variabile Control					
Metric 9:	Covariate Adjustment	Low	× 0.5	1.5	Models were adjusted for gender, age, smoking status, facility and glutathione S-transferase (GST) polymorphisms. No adjustments were made for SES, which may vary with job description (and associated exposure).
Metric 10:	Covariate Characterization	Low	× 0.25	0.75	GST polymorphisms were assessed from blood samples. Source of other covariate information not stated.
Metric 11:	Co-exposure Confounding	Medium	× 0.25	0.5	No indication of other co-exposures of concern.
Domain 5: Analysis					

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HERO ID:	3974874				
Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
Metric 12:	Study Design and Methods	Medium	× 0.4	0.8	In this cross sectional study, participants working at facilities using 1-BP were assessed for DNA damage in leukocytes. Paired analyses and linear regression models were used to determine the relationships between biomarkers of 1-BP exposure and DNA damage.
Metric 13:	Statistical power	Medium	× 0.2	0.4	There was sufficient participation (64 subjects) to determine a significant effect.
Metric 14:	Reproducibility of analyses	Medium	× 0.2	0.4	Details on the multiple linear regression models used in the analysis of 1-BP and DNA damage are limited but include variables used, including covariates in adjusted models, transformations of continuous variables, use of quartiles of exposure and how missing values were dealt with.
Metric 15:	Statistical models	Medium	× 0.2	0.4	Multiple linear regression models were used to determine relationship between 1-BP exposure markers (air, urine, blood) and DNA damage assessed using comet assay. Exposure divided by quartile, as well as continuous (log base 10 transformed).
Domain 6: Other Considerations for Biomarker Selection and Measurement					
Metric 16:	Use of Biomarker of Exposure	High	× 0.143	0.14	Levels of Br in serum and urine were used as a biomarker for exposure. Samples were obtained at the start and end of the work week (Monday morning and Thursday afternoon). Authors report that Br is a metabolite of 1-BP with a low excretion rate, which makes it an ideal biomarker for exposure. Estimated exposure from these biomarkers was highly correlated to personal air monitoring, increasing confidence in the measurements.
Metric 17:	Effect biomarker	High	× 0.143	0.14	DNA breaks in leukocytes served as a metric for DNA damage. This was evaluated using the comet assay, a well-established method.
Metric 18:	Method Sensitivity	Medium	× 0.143	0.29	Limits of detection were not presented, but only 14 individuals were missing exposure biomarkers, indicating sufficient sensitivity.
Metric 19:	Biomarker stability	Medium	× 0.143	0.29	Storage history for samples described in detail, indicates that samples were shipped to lab on ice immediately and subsequently frozen. Exposure biomarkers not expected to degrade, but no stability assessment reported.

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HERO ID:	3974874				
Domain	Metric	Rating <sup>†</sup>	MWF*	Score	Comments <sup>††</sup>
Metric 20:	Sample contamination	Medium	× 0.143	0.29	No indication that contamination occurred, but no description of ways to the authors took steps to avoid contamination.
Metric 21:	Method requirements	Low	× 0.143	0.43	Details on exposure biomarker methods are not described in this study. Citation with details (Vaiseman et al 1986) was not freely available to review.
Metric 22:	Matrix adjustment	Low	× 0.143	0.43	Details on exposure biomarker methods are not described in this study. Citation with details (Vaiseman et al 1986) was not freely available to review. Adjustments for creatine would be important for this study.
Overall Quality Determination <sup>†</sup>					
Extracted					
Medium					
Yes					
2.1					

\* 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.

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

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