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Environmental Protection Agency

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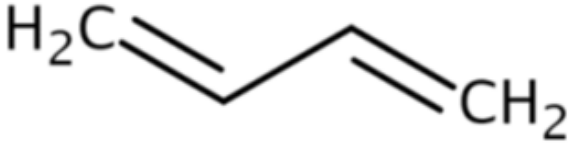
Office of Chemical Safety and
Pollution Prevention

Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for 1,3-Butadiene

Systematic Review Support Document for the Risk Evaluation

CASRN: 106-99-0



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This supplemental file contains information regarding the data extraction results conducted for references that (1) met PECO screening criteria, (2) passed further filtering, and (3) did not receive an overall quality determination of 'Uninformative'. For a detailed description on these criteria, see the *Risk Evaluation for 1,3-Butadiene – Systematic Review Protocol*. EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (also referred to as '2021 Draft Systematic Review Protocol'). Any updated steps in the systematic review process for data extraction since the publication of the 2021 Draft Systematic Review Protocol are described in the *Risk Evaluation for 1,3-Butadiene – Systematic Review Protocol*. EPA conducted data extraction based on author-reported descriptions and results; additional analyses (*e.g.*, statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file.

Human Health Hazard Animal Toxicity Extraction: The tables contain data extraction information for animal toxicology references. For 1,3-butadiene animal toxicology studies EPA instituted a unique data extraction form that extracted doses and points of departure for every endpoint assessed in the reference. Additionally, EPA indicated whether the findings are definitively adverse, dose-responsive, and either measured or nominal in order to better inform evidence integration and dose-response analysis. Studies that rated uninformative for dose-response are included in the data extraction summaries section, however endpoint extraction was not performed. For more details, see the *Risk Evaluation for 1,3-Butadiene – Systematic Review Protocol*.

Epidemiological Study Information Extraction: This table contains data extraction information for epidemiological references. The data extracted include the measured health effect or endpoints, the study population, the exposure measured, analysis methods, and a summary of the results. Each health outcome assessed in a reference is extracted separately, and as such, each reference may have more than one record in the data extraction tables, with each record categorized by health outcome.

The criteria for extracting data from 1,3-butadiene epidemiology studies were that the reference met PECO screening criteria and further filtering criteria, had an overall quality determination of High, Medium, or Low, and found statistically significant associations between 1,3-butadiene and an adverse health outcome. For additional data sources relevant for the risk evaluation that were received through public comments and/or recommended by SACC, an additional criteria for data extraction was that the reference was used for dose-response assessment in the risk evaluation. However, all studies were included in the evidence integration and considered for their contribution to the weight of scientific evidence in the human health hazard assessment.

For more details, see the *Risk Evaluation for 1,3-Butadiene – Systematic Review Protocol*.

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HERO ID	Reference	Page
Human Health Hazard Animal Toxicology		**8**
Endpoint Data Extraction		
Acute (less than or equal to 24 hr)		
5640580	Bucher, J. R., Melnick, R. L., Hildebrandt, P. K. (1993). Lack of carcinogenicity in mice exposed once to high concentrations of 1,3-butadiene. Journal of the National Cancer Institute 85(22):1866-1867.	**8**
62368	Shugaev, B. B. (1969). Concentrations of hydrocarbons in tissues as a measure of toxicity. Archives of Environmental and Occupational Health 18(6):878-882.	**8**
Short-term (>1-30 days)		
5663591	Adler I-D, Filser, J., Gonda, H., Schriever-Schwemmer, G. (1998). Dose response study for 1,3-butadiene-induced dominant lethal mutations and heritable translocations in germs cells of male mice. Mutation Research 397(1):85-92.	**9**
62354	Hackett, P. L., Brown, M. G., Clark, M. L., Evanoff, J. J., Rowe, S. E., McClanahan, B. J., Buschbom, R. L., Decker, J. R., Rommereim, R. L., Westerberg, R. B. (1988). Sperm-head morphology study in B6C3F1 mice following inhalation exposure to 1,3-butadiene.	**10**
1329207	Lee, J. H., Kang, H. S., Han, D. H. (2005). Ratios of N-(2,3,4-trihydroxybutyl) valine and N-(2-hydroxy-3-butenyl) valine formed hemoglobin adducts in female mice inhalation exposure with 1,3-butadiene. Toxicology and Industrial Health 21(1):15-20.	**11**
11273463	LRRI, (2005). [Redacted] 1,3-Butadiene: Whole-body inhalation exposure of rats and mice.	**11**
5553772	Pacchierotti, F., Tiveron, C., Ranaldi, R., Bassani, B., Cordelli, E., Leter, G., Spano, M. (1998). Reproductive toxicity of 1,3-butadiene in the mouse: Cytogenetic analysis of chromosome aberrations in first-cleavage embryos and flow cytometric evaluation of spermatogonial cell killing. Mutation Research 397(1):55-66.	**12**
5546732	Xiao, Y., Tates, A. D. (1995). Clastogenic effects of 1,3-butadiene and its metabolites 1,2-epoxybutene and 1,2,3,4-diepoxybutane in splenocytes and germ cells of rats and mice in vivo. Environmental and Molecular Mutagenesis 26(2):97-108.	**15**
Subchronic (>30-91 days)		
5663561	Anderson, D., Edwards, A. J., Brinkworth, M. H., Hughes, J. A. (1996). Male-mediated F1 effects in mice exposed to 1,3-butadiene. Toxicology 113(1-3):120-127.	**17**
5660612	Bevan, C., Stadler, J. C., Elliott, G. S., Frame, S. R., Baldwin, J. K., Leung, H. W., Moran, E., Panepinto, A. S. (1996). Subchronic toxicity of 4-vinylcyclohexene in rats and mice by inhalation exposure. Fundamental and Applied Toxicology 32(1):1-10.	**17**
5674659	BIBRA, (1996). Detection of dominant lethal mutations and foetal malformations in the offspring of male rats treated sub-chronically w/1,3-butadiene by inhalation w/cover letter dated 01/10/1997.	**23**
4934798	Brinkworth, M. H., Anderson, D., Hughes, J. A., Jackson, L. I., Yu, T. W., Nieschlag, E. (1998). Genetic effects of 1,3-butadiene on the mouse testis. Mutation Research 397(1):67-75.	**24**
94760	Crouch, C. N., Pullinger, D. H., Gaunt, I. F. (1979). Inhalation toxicity studies with 1,3-butadiene - 2 3 month toxicity study in rats. Journal of Occupational and Environmental Hygiene 40(9):796-802.	**25**
62366	Thurmond, L. M., Lauer, L. D., House, R. V., Stillman, W. S., Irons, R. D., Steinhagen, W. H., Dean, J. H. (1986). Effects of short-term inhalation exposure to 1,3-butadiene on murine immune functions. Toxicology and Applied Pharmacology 86(2):170-179.	**26**
Chronic (>91 days)		

5673742	Hazleton Laboratories, (1981). The toxicity and carcinogenicity of butadiene gas administered to rats by inhalation for approximately 24 months (volume I - IV) (final report) w-attachments and cover letter 081182.	**29**
62372	National Institutes of Health,, Department of Health and Human Services, (1984). Toxicology and carcinogenesis studies of 1,3-butadiene (CAS no. 106-99-0) in B6C3F1 mice (inhalation studies). 288:1-111.	**34**
1419645	NTP, (1993). NTP Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies). National Toxicology Program Technical Report Series 434:1-389.	**38**
Reproductive/Developmental		
1327602	Anderson, D., Hughes, J. A., Edwards, A. J., Brinkworth, M. H. (1998). A comparison of male-mediated effects in rats and mice exposed to 1,3-butadiene. Mutation Research 397(1):77-84.	**50**
62351	Battelle PNL, (1987). Inhalation developmental toxicology studies: Teratology study of 1,3-butadiene in mice.	**54**
94731	Battelle PNL, (1987). Inhalation developmental toxicology studies of 1,3-butadiene in the rat.	**55**
5665017	BIBRA, (1996). Initial submission: the detection of dominant lethal mutations and * in the offspring of male mice treated subchronically with butadiene by inhalation, w/cover letter dated 1/10/97.	**56**
62353	Hackett, P. L., Mast, T. J., Brown, M. G., Clark, M. L., Evanoff, J. J., Rowe, S. E., McClanahan, B. J., Buschbom, R. L., Decker, J. R., Rommereim, R. L., Westerberg, R. B. (1988). Dominant lethal study in CD-1 mice following inhalation exposure to 1,3-butadiene.	**57**
62371	Hazleton Labs, (1981). 1,3-Butadiene: Inhalation teratogenicity study in the rat (Final report).	**60**
10367501	WIL Research, (2003). An inhalation reproduction/developmental toxicity screening study of 1,3-butadiene in rats.	**61**

Data Extraction Summaries

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5663561	Anderson, D., Edwards, A. J., Brinkworth, M. H., Hughes, J. A. (1996). Male-mediated F1 effects in mice exposed to 1,3-butadiene. Toxicology 113(1-3):120-127.	**68**
4934798	Brinkworth, M. H., Anderson, D., Hughes, J. A., Jackson, L. I., Yu, T. W., Nieschlag, E. (1998). Genetic effects of 1,3-butadiene on the mouse testis. Mutation Research 397(1):67-75.	**68**
5640580	Bucher, J. R., Melnick, R. L., Hildebrandt, P. K. (1993). Lack of carcinogenicity in mice exposed once to high concentrations of 1,3-butadiene. Journal of the National Cancer Institute 85(22):1866-1867.	**68**
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94760	Crouch, C. N., Pullinger, D. H., Gaunt, I. F. (1979). Inhalation toxicity studies with 1,3-butadiene - 2 3 month toxicity study in rats. Journal of Occupational and Environmental Hygiene 40(9):796-802.	**75**
11273565	IBT Labs, (1977). Report to Tracor Jitco, Inc: Subchronic inhalation study with 1,3-butadiene (C50602) in B6C3F1 mice.	**75**
62366	Thurmond, L. M., Lauer, L. D., House, R. V., Stillman, W. S., Irons, R. D., Steinhagen, W. H., Dean, J. H. (1986). Effects of short-term inhalation exposure to 1,3-butadiene on murine immune functions. Toxicology and Applied Pharmacology 86(2):170-179.	**76**
Chronic (>91 days)		
5554646	Battelle PNL, (1982). Initial submission: Tracor Jitco inhalation carcinogenesis bioassay: Chronic study report in 1,3-butadiene in mice (final report) with attachments and cover letter dated 112191.	**78**
5673742	Hazleton Laboratories, (1981). The toxicity and carcinogenicity of butadiene gas administered to rats by inhalation for approximately 24 months (volume I - IV) (final report) w-attachments and cover letter 081182.	**79**
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646899 Cheng, H., Sathiakumar, N., Graff, J., Matthews, R., Delzell, E. (2007). 1,3-Butadiene and leukemia among synthetic rubber industry workers: Exposure-response relationships. Chemico-Biological Interactions 166(1-3):15-24. **88**

3011004 Danysh, H. E., Mitchell, L. E., Zhang, K., Scheurer, M. E., Lupo, P. J. (2015). Traffic-related air pollution and the incidence of childhood central nervous system tumors: Texas, 2001-2009. Pediatric Blood & Cancer 62(9):1572-1578. **91**

737524 Delzell, E., Macaluso, M., Sathiakumar, N., Matthews, R. (2001). Leukemia and exposure to 1,3-butadiene, styrene and dimethyldithiocarbamate among workers in the synthetic rubber industry. Chemico-Biological Interactions 135-136:515-534. **94**

737525 Delzell, E., Sathiakumar, N., Graff, J., Macaluso, M., Maldonado, G., Matthews, R., Health Effects Institute (2006). An updated study of mortality among North American synthetic rubber industry workers. Research Reports (Health Effects Institute) 62(132):1-63; discussion 65-74. **95**

51390 Delzell, E., Sathiakumar, N., Hovinga, M., Macaluso, M., Julian, J., Larson, R., Cole, P., Muir, F., D.C. (1996). A follow-up study of synthetic rubber workers. Toxicology 113(1-3):182-189. **97**

2453135 Ehrenstein, von, O. S., Aralis, H., Cockburn, M., Ritz, B. (2014). In utero exposure to toxic air pollutants and risk of childhood autism. Epidemiology 25(6):851-858. **98**

5684085 Ehrenstein, Von, O. S., Heck, J. E., Park, A. S., Cockburn, M., Escobedo, L., Ritz, B. (2016). In utero and early-life exposure to ambient air toxics and childhood brain tumors: a population-based case-control study in California, USA. Environmental Health Perspectives 124(7):1093-1099. **98**

2950774 Graff, J. J., Sathiakumar, N., Macaluso, M., Maldonado, G., Matthews, R., Delzell, E. (2009). The Effect of Uncertainty in Exposure Estimation on the Exposure-Response Relation between 1,3-Butadiene and Leukemia. International Journal of Environmental Research and Public Health 6(9):2436-2455. **99**

737523 Graff, J. J., Sathiakumar, N., Macaluso, M., Maldonado, G., Matthews, R., Delzell, E. (2005). Chemical exposures in the synthetic rubber industry and lymphohematopoietic cancer mortality. Journal of Occupational and Environmental Medicine 47(9):916-932. **99**

5641117 Hall, C., Heck, J. E., Ritz, B., Cockburn, M., Escobedo, L. A., Ehrenstein, von, O. S. (2019). Prenatal Exposure to Air Toxics and Malignant Germ Cell Tumors in Young Children. Journal of Occupational and Environmental Medicine 61(6):529-534. **101**

5586518 Hayes, R. B., Zhang, L., Yin, S., Swenberg, J. A., Xi, L., Wiencke, J., Bechtold, W. E., Yao, M., Rothman, N., Haas, R., O'Neill, J. P., Zhang, D., Wiemels, J., Dosemeci, M., Li, G., Smith, M. T. (2000). Genotoxic markers among butadiene polymer workers in China. Carcinogenesis 21(1):55-62. **102**

11438289 Heck, J. E., He, D., Wing, S. E., Ritz, B., Carey, C. D., Yang, J., Stram, D. O., Marchand, Le, L., Park, S. L., Cheng, I., Wu, A. H. (2024). Exposure to outdoor ambient air toxics and risk of breast cancer: The multiethnic cohort. International Journal of Hygiene and Environmental Health 259:114362. **103**

2345720 Heck, J. E., Park, A. S., Qiu, J., Cockburn, M., Ritz, B. (2014). Risk of leukemia in relation to exposure to ambient air toxics in pregnancy and early childhood. International Journal of Hygiene and Environmental Health 217(6):662-668. **104**

2369182 Heck, J. E., Park, A. S., Qiu, J., Cockburn, M., Ritz, B. (2013). Retinoblastoma and ambient exposure to air toxics in the perinatal period. Journal of Exposure Science and Environmental Epidemiology 25(2):182-186. **105**

5664525 IISRP, (2000). Support: Lymphohematopoietic cancer among workers exposed to 1,3-butadiene, styrene and dimethyldithiocarbamate in the synthetic rubber industry, with cover letter dated 012600. **106**

10192219 Sathiakumar, N., Bolaji, B. E., Brill, I., Chen, L., Tipre, M., Leader, M., Arora, T., Delzell, E. (2021). 1,3-Butadiene, styrene and lymphohaematopoietic cancers among North American synthetic rubber polymer workers: exposure-response analyses. Occupational and Environmental Medicine 78(12):859-868. **118**

9038746 Sathiakumar, N., Bolaji, B., Brill, I., Chen, L., Tipre, M., Leader, M., Arora, T., Delzell, E. (2021). 1,3-Butadiene, styrene and selected outcomes among synthetic rubber polymer workers: Updated exposure-response analyses. Chemico-Biological Interactions 347:109600. **119**

1600222	Sathiakumar, N., Brill, I., Delzell, E. (2009). 1,3-butadiene, styrene and lung cancer among synthetic rubber industry workers. Journal of Occupational and Environmental Medicine 51(11):1326-1332.	**121**
4659248	Sathiakumar, N., Brill, I., Leader, M., Delzell, E. (2015). 1,3-Butadiene, styrene and lymphohematopoietic cancer among male synthetic rubber industry workers–Preliminary exposure-response analyses. Chemico-Biological Interactions 241:40-49.	**122**
1330953	Sathiakumar, N., Delzell, E. (2009). A follow-up study of mortality among women in the North American synthetic rubber industry. Journal of Occupational and Environmental Medicine 51(11):1314-1325.	**124**
6592911	Sathiakumar, N., Tipre, M., Leader, M., Brill, I., Delzell, E. (2019). Mortality among men and women in the North American synthetic rubber industry, 1943 to 2009. Journal of Occupational and Environmental Medicine 61(11):887-897.	**127**
6544022	Sielken, (2007). Quantitative risk assessment of exposures to butadiene in European Union occupational settings based on the University of Alabama at Birmingham epidemiology study: acute myelogenous leukemia, chronic lymphocytic leukemia, and chronic myelogenous leukemia.	**130**
1798799	Sielken, R. L., Valdez-Flores, C. (2013). Quantitative risk assessment of exposures to butadiene in EU occupational settings based on the University of Alabama at Birmingham epidemiological study. Regulatory Toxicology and Pharmacology 65(2):214-225.	**132**
1940484	Sielken, R. L., Valdez-Flores, C. (2011). Butadiene cancer exposure-response modeling: based on workers in the styrene-butadiene-rubber industry: total leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, and chronic myelogenous leukemia. Regulatory Toxicology and Pharmacology 60(3):332-341.	**133**
1942871	Sielken, R. L., Valdez-Flores, C. (2001). Dose-response implications of the University of Alabama study of lymphohematopoietic cancer among workers exposed to 1,3-butadiene and styrene in the synthetic rubber industry. Chemico-Biological Interactions 135-136:637-651.	**135**
3358047	Symanski, E., Lewis, Tee, P. G., Chen, T. Y., Chan, W., Lai, D., Ma, X. (2016). Air toxics and early childhood acute lymphocytic leukemia in Texas, a population based case control study. Environmental Health: A Global Access Science Source 15(1):70.	**135**
5665016	UAB, (1995). Initial submission: Letter from intl inst syn rubber prod to USEPA RE prelim results in cohort mortality study of employees of 8 styrene butadiene rubber plants, dated 05/19/95.	**136**
6544020	UAB, (2007). A follow-up study of women in the synthetic rubber industry.	**146**
11531254	Valdez-Flores, C., Erraguntla, N., Budinsky, R., Cagen, S., Kirman, C. R. (2022). An updated lymphohematopoietic and bladder cancers risk evaluation for occupational and environmental exposures to 1,3-butadiene. Chemico-Biological Interactions 366:110077.	**150**
622776	Whitworth, K. W., Symanski, E., Coker, A. L. (2008). Childhood Lymphohematopoietic Cancer Incidence and Hazardous Air Pollutants in Southeast Texas, 1995–2004. Environmental Health Perspectives 116(11):1576-1580.	**151**
Metabolite: Monohydroxybutyl mercapturic acid (MHBMA), comprised of 1-hydroxy-2-(N-acetylcysteinyl)-3-butene and 1-(N-acetylcysteinyl)-2-hydroxy-3-butene		
1508766	Yuan, J. M., Gao, Y. T., Wang, R., Chen, M., Carmella, S. G., Hecht, S. S. (2012). Urinary levels of volatile organic carcinogen and toxicant biomarkers in relation to lung cancer development in smokers. Carcinogenesis 33(4):804-809.	**153**
Metabolite: mercapturic acid butanediol (M-1), hemoglobin N-(2,3,4-trihydroxybutyl)valine (THBVal) adducts		
5586518	Hayes, R. B., Zhang, L., Yin, S., Swenberg, J. A., Xi, L., Wiencke, J., Bechtold, W. E., Yao, M., Rothman, N., Haas, R., O'Neill, J. P., Zhang, D., Wiemels, J., Dosemeci, M., Li, G., Smith, M. T. (2000). Genotoxic markers among butadiene polymer workers in China. Carcinogenesis 21(1):55-62.	**154**
Metabolite: 3,4-dihydroxybutyl (DHBMA), 3-hydroxy-3-butenyl (MHBMA2).		
5660361	Pudrith, C., Dudley, W. N. (2019). Sensorineural hearing loss and volatile organic compound metabolites in urine. American Journal of Otolaryngology 40(3):409-412.	**155**

1,3-Butadiene- Parent compound - Acute (less than or equal to 24 hr)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Acute (less than or equal to 24 hr)-2	NOEL: 10000 ppm (in air, water, or food) LOEL: Not observed n= 60 Dose= 0, n= 60 Dose= 1000, n= 60 Dose= 5000, n= 60 Dose= 10000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Mortality: Survival Low	Bucher et al. 1993 5640580
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Acute (less than or equal to 24 hr)-2	NOEL: 5000 ppm (in air, water, or food) LOEL: 10000 ppm (in air, water, or food) n= 53 Dose= 0, n= 52 Dose= 1000, n= 53 Dose= 5000, n= 56 Dose= 10000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was nominal/estimated.	An increase in forestomach tumors were observed at the high dose only in males. These were approaching significance (p=.079) but are not believed to be treatment related/reliable.	Mortality: Incidence of lymphoma, hemangiosarcoma, alveolar-bronchiolar neoplasm in the lung, squamous cell neoplasm in the forestomach, acinar cell neoplasm in the mammary gland, granulosa cell neoplasm in the ovary, and hepatocellular neoplasm in the liver Low	Bucher et al. 1993 5640580
Mouse-Not specified-Unknown	Inhalation-Gas-Duration: Acute (less than or equal to 24 hr)-2	NOEL: Not observed LOEL: 270 mg chemical / L air Dose= 270, mg chemical / L air	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	The study text indicated that the concentrations in the exposure chamber were controlled by gas chromatography. The exposure concentrations and number of animals per group were not reported. An LD50 of 270 (95% CI 251 - 290) was reported for mice. This study also contains ADME data.	Mortality: LC50 Low	Shugaev 1969 62368
Rat-Not specified-Unknown	Inhalation-Gas-Duration: Acute (less than or equal to 24 hr)-2	NOEL: Not observed LOEL: 285 mg chemical / L air Dose= 285, mg chemical / L air	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The study text indicated that the concentrations in the exposure chamber were controlled by gas chromatography. The exposure concentrations and number of animals per group were not reported. An LD50 of 285(95% CI 219 - 370) was reported for rats. This study also contains ADME data.	Mortality: LC50 Low	Shugaev 1969 62368

* Overall Quality Determination

1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other (102/E1 X C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: 500 ppm (in air, water, or food) LOEL: Not observed n= 30 Dose= 0, n= 30 Dose= 130, n= 30 Dose= 500, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Exposed males were mated with 102/E1 x C3H/E1 females.	Reproductive/Developmental: Percentage of pregnant females, number implants/female, live implants/female, dead implants/female, and percentage of dead implants Medium	Adler et al. 1998 5663591
Mouse-Other (102/E1 X C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: 500 ppm (in air, water, or food) LOEL: Not observed n= 30 Dose= 0, n= 30 Dose= 130, n= 30 Dose= 500, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Exposed males were mated with 102/E1 x C3H/E1 females.	Dominant lethality Medium	Adler et al. 1998 5663591
Mouse-Other (102/E1 X C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: 500 ppm (in air, water, or food) LOEL: Not observed n= 30 Dose= 0, n= 30 Dose= 130, n= 30 Dose= 500, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Exposed males were mated with NMRI females.	Reproductive/Developmental: Percentage of pregnant females, number implants/female, and live implants/female Medium	Adler et al. 1998 5663591
Mouse-Other (102/E1 X C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: 130 ppm (in air, water, or food) LOEL: 500 ppm (in air, water, or food) n= 30 Dose= 0, n= 30 Dose= 130, n= 30 Dose= 500, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was nominal/estimated.	Exposed males were mated with NMRI females. Statistically significant increase in dead implants/female observed only at 1 week, corresponding to genotoxicity to developing sperm. No effects observed at later weeks indicating no effect on earlier stages of spermatogenesis.	Reproductive/Developmental: Increase in dead implants/female Medium	Adler et al. 1998 5663591
Mouse-Other (102/E1 X C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: 130 ppm (in air, water, or food) LOEL: 500 ppm (in air, water, or food) n= 30 Dose= 0, n= 30 Dose= 130, n= 30 Dose= 500, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was nominal/estimated.	Exposed males were mated with NMRI females. Statistically significant increase in dead implants/female observed only at 1 week, corresponding to genotoxicity to developing sperm. No effects observed at later weeks indicating no effect on earlier stages of spermatogenesis.	Positive for dominant lethality Medium	Adler et al. 1998 5663591
Mouse-Other (C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: 500 ppm (in air, water, or food) LOEL: Not observed n= 65 Dose= 0, n= 100 Dose= 500, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Reproductive/Developmental: Litter size at birth and at weaning Medium	Adler et al. 1998 5663591

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other (C3H/E1)-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-F0- premating-F0- premating (5)	NOEL: Not observed LOEL: 500 ppm (in air, water, or food) n= 434 Dose= 500, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was nominal/estimated.	Only one dose tested so a dose-response could not be determined.	Frequency of translocation carriers in F1 offspring Uninformative	Adler et al. 1998 5663591
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-6-5-day(s)	NOEL: 5000 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1000, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Decreased survival Medium	Hackett et al. 1988 62354
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-6-5-day(s)	NOEL: 5000 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1000, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Altered Body weights, body weight gain % Medium	Hackett et al. 1988 62354
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-6-5-day(s)	NOEL: 200 ppm (in air, water, or food) LOEL: 1000 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1000, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Even though sperm abnormalities were statistically significant, the biological significance is unclear because abnormalities were only increased 2% from controls.	Reproductive/Developmental: Decreased % of normal sperm and increased % of abnormal sperm Medium	Hackett et al. 1988 62354
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-6-5-day(s)	NOEL: 1000 ppm (in air, water, or food) LOEL: 5000 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1000, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effects ended within 30min of exposure cessation	Mortality: Pilorection, dyspnea Medium	Hackett et al. 1988 62354

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-ICR - [mouse]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-5-3-week(s)	NOEL: Not observed LOEL: 500 ppm (in air, water, or food) n= 15 Dose= 0, n= 15 Dose= 500, n= 15 Dose= 1000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Nutritional/Metabolic: Body weight Medium	Lee et al. 2005 1329207
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-4-week(s)	NOEL: 63.1 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 1.0, n= 20 Dose= 6.3, n= 20 Dose= 63.1, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Decreased survival Medium	LRRI 2005 11273463
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-4-week(s)	NOEL: 63.1 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 1.0, n= 20 Dose= 6.3, n= 20 Dose= 63.1, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Clinical signs of toxicity Medium	LRRI 2005 11273463
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-4-week(s)	NOEL: 63.1 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 1.0, n= 20 Dose= 6.3, n= 20 Dose= 63.1, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Decreased survival Medium	LRRI 2005 11273463
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-4-week(s)	NOEL: 63.1 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 1.0, n= 20 Dose= 6.3, n= 20 Dose= 63.1, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Clinical signs of toxicity Medium	LRRI 2005 11273463

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other ((102/E1 x C3H/E1)F1)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-F0- premating (5 days)	NOEL: 1300 ppm (in air, water, or food) LOEL: Not observed n= 28 Dose= 0, n= 8 Dose= 0, n= 28 Dose= 130, n= 24 Dose= 500, n= 28 Dose= 1300, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The exposure atmospheres were monitored at regular intervals (not further specified) for the test substance concentration. It was not indicated if the measured values were close to nominal, and it is presumed that the concentrations provided were nominal. The number of animals represents the number of exposed males per group as described in the study methods. Two experiments were conducted 2 years apart that measured the same endpoints; these experiments are combined here. Males were mated weekly for three weeks post-exposure (exposed and experiment 2 controls) or during weeks 2 and 3 post-exposure (controls experiment 1). There were no effects of exposure on the number of successful pairings.	Reproductive/Developmental: Percentage of mated females (successful pairings) Low	Pacchierotti et al. 1998 5553772

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other ((102/E1 x C3H/E1)F1)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-F0- premating (5 days)	NOEL: Not observed LOEL: 500 ppm (in air, water, or food) n= 80 Dose= 0, n= 29 Dose= 0, n= 134 Dose= 130, n= 107 Dose= 500, n= 134 Dose= 1300, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The exposure atmospheres were monitored at regular intervals (not further specified) for the test substance concentration. It was not indicated if the measured values were close to nominal, and it is presumed that the concentrations provided were nominal. The number of animals indicates the number of mated females per group spanning each weekly mating. Two experiments were conducted 2 years apart that measured the same endpoints; these experiments are combined here, but it is inappropriate to compare across experiments to determine a dose-response. There was a statistically significant increase in the number of unfertilized oocytes, compared to matched controls, in the 500 ppm group following the 3rd weekly mating (experiment 2). The control value was unusually high, and the total number of cells scored in the exposed group was low. No increases were observed at 1300 ppm in the first experiment, compared to matched controls. 500 ppm was the lowest concentration showing an effect; however, in experiment 1 no effects were observed at a higher concentration (1500 ppm). The effect may or may not be treatment-related, but an accurate NOAEL cannot be determined.	Reproductive/Developmental: % unfertilized metaphase II oocytes Low	Pacchierotti et al. 1998 5553772

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other ((102/E1 x C3H/E1)F1)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-F0- premating (5 days)	NOEL: Not observed LOEL: 130 ppm (in air, water, or food) n= 15 Dose= 0, n= 3 Dose= 0, n= 15 Dose= 130, n= 15 Dose= 500, n= 15 Dose= 1300, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The exposure atmospheres were monitored at regular intervals (not further specified) for the test substance concentration. It was not indicated if the measured values were close to nominal, and it is presumed that the concentrations provided were nominal. The number of animals reported is based on the following text "On the occasion of the first round of inhalation exposures, after the three-week mating period, 15 sham-exposed mice and 15 mice from each of the butadiene-exposed (130 and 1300 ppm) groups were killed at weekly intervals (on day 21, 28, and 35 after the end of exposure) for the flow cytometric analysis of testicular cell populations. Similarly, on the occasion of the second round of inhalations, 3 groups of 1 sham-exposed and 5 butadiene-exposed mice were killed on day 21, 28, and 35 after the end of the inhalation period." However, the text is a bit unclear and "n's" were not included in the data table.	Reproductive/Developmental: Testis weights; analysis of testicular cells (counts of early and mature spermatids, G1 and G2 spermatogonia, primary and secondary spermatocytes, testicular somatic cells, and tetraploid cells as well as evaluation of cytotoxicity. Low	Pacchierotti et al. 1998 5553772

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other ((102/E1 x C3H/E1)F1)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-F0- premating (5 days)	NOEL: 130 ppm (in air, water, or food) LOEL: 500 ppm (in air, water, or food) n= 15 Dose= 0, n= 3 Dose= 0, n= 15 Dose= 130, n= 15 Dose= 500, n= 15 Dose= 1300, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The exposure atmospheres were monitored at regular intervals (not further specified) for the test substance concentration. It was not indicated if the measured values were close to nominal, and it is presumed that the concentrations provided were nominal. The number of animals reported is based on the following text "On the occasion of the first round of inhalation exposures, after the three-week mating period, 15 sham-exposed mice and 15 mice from each of the butadiene-exposed (130 and 1300 ppm) groups were killed at weekly intervals (on day 21, 28, and 35 after the end of exposure) for the flow cytometric analysis of testicular cell populations. Similarly, on the occasion of the second round of inhalations, 3 groups of 1 sham-exposed and 5 butadiene-exposed mice were killed on day 21, 28, and 35 after the end of the inhalation period." However, the text is a bit unclear and "n's" were not included in the data table.	Reproductive/Developmental: sperm chromatin structure assay Low	Pacchierotti et al. 1998 5553772
Mouse-Other (F1 (102 x C3H) hybrid)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-5-6-5-day(s)	NOEL: Not observed LOEL: 500 ppm (in air, water, or food) n= 5 Dose= 0, n= 5 Dose= 500, n= 5 Dose= 1300, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	No histopathological evaluations of the reproductive organs were conducted, but ratio of Golgi in developing stages of spermatogenesis provide indications of toxicity. The mechanistic findings indicated evidence of cytotoxicity and genotoxicity in male germ cells. There is some dose-response for Golgi ratio but numbers are variable, and relative testis weight is not dose-responsive.	Reproductive/Developmental: Decreased testis weights (absolute and relative to body weight) and decreased G/G+C ratio Low	Xiao et al. 1995 5546732

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-Other (F1 (102 x C3H) hybrid)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-5-6-5-day(s)	NOEL: 500 ppm (in air, water, or food) LOEL: 1300 ppm (in air, water, or food) n= 6 Dose= 0, n= 5 Dose= 200, n= 5 Dose= 500, n= 5 Dose= 1300, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	No histopathological evaluations of the reproductive organs were conducted, but ratio of Golgi in developing stages of spermatogenesis provide indications of toxicity. The mechanistic findings indicated evidence of cytotoxicity and genotoxicity in male germ cells. There is some dose-response for Golgi ratio but numbers are variable, and relative testis weight is not dose-responsive.	Reproductive/Developmental: Decreased testis weights (absolute and relative to body weight) and decreased G/G+C ratio Low	Xiao et al. 1995 5546732
Mouse-Other (F1 (102 x C3H) hybrid)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-5-6-5-day(s)	NOEL: 1300 ppm (in air, water, or food) LOEL: Not observed n= 5 Dose= 0, n= 5 Dose= 500, n= 5 Dose= 1300, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Nutritional/Metabolic: Body weight Low	Xiao et al. 1995 5546732
Mouse-Other (F1 (102 x C3H) hybrid)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-5-6-5-day(s)	NOEL: 1300 ppm (in air, water, or food) LOEL: Not observed n= 6 Dose= 0, n= 5 Dose= 200, n= 5 Dose= 500, n= 5 Dose= 1300, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Nutritional/Metabolic: Body weight Low	Xiao et al. 1995 5546732
Mouse-Other (F1 (102 x C3H) hybrid)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-5-6-5-day(s)	NOEL: Not observed LOEL: 500 ppm (in air, water, or food) n= 5 Dose= 0, n= 5 Dose= 500, n= 5 Dose= 1300, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Absence of a dose response was considered by the study authors to be related to cytotoxicity at the highest concentration.	Reproductive/Developmental: Genotoxicity (increased micronuclei formation in early spermatids) Low	Xiao et al. 1995 5546732
Mouse-Other (F1 (102 x C3H) hybrid)-Male	Inhalation-Gas-Duration: Short-term (>1-30 days)-5-6-5-day(s)	NOEL: Not observed LOEL: 200 ppm (in air, water, or food) n= 6 Dose= 0, n= 5 Dose= 200, n= 5 Dose= 500, n= 5 Dose= 1300, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Absence of a dose response was considered by the study authors to be related to cytotoxicity at the highest concentration.	Reproductive/Developmental: Genotoxicity (increased micronuclei formation in early spermatids) Low	Xiao et al. 1995 5546732

* Overall Quality Determination

1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10 weeks)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 25 Dose= 0, n= 25 Dose= 12.5, n= 48 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	The N indicates the number of males per group. The Ns for females are 41, 45, and 74, respectively. No effects were observed for these endpoints.	Reproductive/Developmental: % mated (males); % females pregnant Medium	Anderson et al. 1996 5663561
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 1250 ppm (in air, water, or food) n= 23 Dose= 0, n= 24 Dose= 12.5, n= 38 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Reproductive/Developmental: Implantations, early deaths. Medium	Anderson et al. 1996 5663561
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10 weeks)	NOEL: Not observed LOEL: 12.5 ppm (in air, water, or food) n= 23 Dose= 0, n= 24 Dose= 12.5, n= 38 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was nominal/estimated.	The test substance was positive for dominant lethality	Reproductive/Developmental: Dominant lethality Medium	Anderson et al. 1996 5663561
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10 weeks)	NOEL: Not observed LOEL: 12.5 ppm (in air, water, or food) n= 23 Dose= 0, n= 24 Dose= 12.5, n= 38 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was nominal/estimated.	No endpoint comments identified.	Reproductive/Developmental: late deaths., late deaths including dead fetuses, and abnormal fetuses. Medium	Anderson et al. 1996 5663561
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Mortality Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Two animals died, but the authors indicated the deaths were not exposure related.	Mortality: Mortality Medium	Bevan et al. 1996 5660612

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Body weights, food consumption Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Body weights, food consumption Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Hematology, spleen weight, gross necropsy, histopathology (bone marrow (sternal and femoral), mesenteric and mandibular lymph nodes, spleen, thymus) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: Not observed LOEL: 980 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Significant hematological changes consistent with macrocytic anemia, significant decrease in relative spleen wt, and low incidence of splenic lymphoid atrophy.	Mortality: Hematology (RBC, hemoglobin, hematocrit, reticulocytes, MCV, MCH, MCHC, platelets, lymphocytes), spleen weight, histopathology (spleen) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	There was a significant 8% increase in relative liver weight only in a single-sex and in the absence of supportive changes (e.g., clinical chemistry or histopathology). This is likely not a treatment-related effect.	Mortality: Clinical chemistry (ALP, ALT, ASP, total protein, albumin, globulin, cholesterol, glucose, total bilirubin), liver weights, gross necropsy, histopathology Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	There was a significant 8% increase in relative liver weight only in a single-sex and in the absence of supportive changes (e.g., clinical chemistry or histopathology). This is likely not a treatment-related effect.	Mortality: Clinical chemistry (ALP, ALT, ASP, total protein, albumin, globulin, cholesterol, glucose, total bilirubin), liver weights, gross necropsy, histopathology Medium	Bevan et al. 1996 5660612

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: Not observed LOEL: 980 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	There was a significant 12% increase in relative kidney weights in males only in the absence of body weight changes and in conjunction with 2/10 males showing hyaline droplets. It is presumed that there were no changes in absolute kidney weights, but quantitative results for absolute organ weights were not provided. The authors dismissed these results indicating that hyaline droplets were a normal feature of rats of this strain and age, and do not represent an adverse effect, but it is still possible that these changes are exposure-related.	Mortality: Organ weight, histopathology Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: 0 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No effects observed	Mortality: gross necropsy, histopathology (bone marrow (sternal and femoral), mesenteric and mandibular lymph nodes, thymus) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Serum chemistry (BUN, creatinine, electrolytes), urinalysis, gross necropsy, Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Serum chemistry (BUN, creatinine, electrolytes), gross necropsy, Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Heart weight, gross necropsy, histopathology (aorta, heart) Medium	Bevan et al. 1996 5660612

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Heart weight, gross necropsy, histopathology (aorta, heart) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Adrenal weights (rats only), gross necropsy, histopathology (pancreas, pituitary, adrenal glands) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Endocrine: gross necropsy, histopathology (pancreas, pituitary, adrenal glands) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Testes, ovary (rats only); gross necropsy, histopathology (prostate, testes, epididymides, seminal vesicles, mammary gland, ovaries, uterus, vagina) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: Not observed LOEL: 980 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	significant decreases in absolute (34%) and relative (36%) testes weight, slight testicular atrophy, ovarian atrophy	Mortality: Testes weight; histopathology (testes, ovary) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: gross necropsy, histopathology (prostate, epididymides, seminal vesicles, mammary gland, uterus, vagina) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Brain weight, gross pathology, histopathology (brain, spinal cord, sciatic nerve) Medium	Bevan et al. 1996 5660612

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Brain weight, gross pathology, histopathology (brain, spinal cord, sciatic nerve) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross necropsy; histopathology (salivary glands, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum. Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross necropsy; histopathology (salivary glands, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, gallbladder Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross pathology; histopathology (thyroid, parathyroid) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross pathology; histopathology (thyroid, parathyroid) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross necropsy, histopathology (trachea, lungs, nose, larynx, pharynx) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross necropsy, histopathology (trachea, lungs, nose, larynx, pharynx) Medium	Bevan et al. 1996 5660612

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross pathology; histopathology (eyes (retinas evaluated separately), exorbital lacrimal glands, Hardarian glands, Zymbal's glands) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross pathology; histopathology (eyes (retinas evaluated separately), exorbital lacrimal glands, Hardarian glands, Zymbal's glands) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross necropsy; histopathology (skeletal muscle, sternum, femur/knee joint) Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross necropsy; histopathology (skeletal muscle, sternum, femur/knee joint) Medium	Bevan et al. 1996 5660612
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross pathology, histopathology Medium	Bevan et al. 1996 5660612
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-5-13-week(s)	NOEL: 980 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 980, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Gross pathology, histopathology Medium	Bevan et al. 1996 5660612

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10-weeks)	NOEL: Not observed LOEL: 65 ppm (in air, water, or food) n= 50 Dose= 0, n= 25 Dose= 0, n= 25 Dose= 65, n= 25 Dose= 400, n= 25 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The atmospheres were analytically monitored continuously. The number of animals indicates the number of males in each group. Each male was mated to two females; the N for females is 100, 50, 50, 50, and 50. There were no treatment-related effects on mortality. One male died at the 65 ppm group but this is not considered relevant as there were no deaths in any other group.	Mortality: Mortality High	BIBRA 1996 5674659
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10-weeks)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 25 Dose= 0, n= 25 Dose= 65, n= 25 Dose= 400, n= 25 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The atmospheres were analytically monitored continuously. The number of animals indicates the number of males in each group. There were no treatment-related effects on male body weights.	Nutritional/Metabolic: Male body weights. Medium	BIBRA 1996 5674659
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10-weeks)	NOEL: Not observed LOEL: 65 ppm (in air, water, or food) n= 100 Dose= 0, n= 50 Dose= 0, n= 48 Dose= 65, n= 50 Dose= 400, n= 50 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The atmospheres were analytically monitored continuously. The number of animals indicates the number of pregnant females in each group. The number of males mated was 50, 15, 24, 25, and 25, respectively. There were no consistent treatment-related reproductive effects. There was a statistically significant decrease in the number of implantation sites at the lowest dose but this was not the case for any other dose groups or effects. The highest dose group is suggestive of a trend that may have been apparent at a higher dose but this is unknown.	Reproductive/Developmental: Mating frequency, pregnancy rate, period of coition, number of corpora lutea, number of live and dead implantations, post-implantation loss (early and late deaths, dead fetuses), fetal malformations. Medium	BIBRA 1996 5674659

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-1-F0- premating (10-weeks)	NOEL: Not observed LOEL: 65 ppm (in air, water, or food) n= 100 Dose= 0, n= 50 Dose= 0, n= 48 Dose= 65, n= 50 Dose= 400, n= 50 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The atmospheres were analytically monitored continuously. The number of animals indicates the number of pregnant females in each group. The number of males mated was 50, 15, 24, 25, and 25, respectively. The test substance was negative for dominant lethality. There was a statistically significant decrease in the number of implantation sites at the lowest dose but this was not the case for any other dose groups or effects. The highest dose group is suggestive of a trend that may have been apparent at a higher dose but this is unknown.	Number of corpora lutea, number of live and dead implantations, post-implantation loss (early and late deaths, dead fetuses), fetal malformations. Uninformative	BIBRA 1996 5674659
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-F0- premating (10 weeks)	NOEL: 125 ppm (in air, water, or food) LOEL: Not observed n= 30 Dose= 0, n= 30 Dose= 12.5, n= 30 Dose= 125, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Concentrations were monitored continuously and were considered acceptable if kept within 15% of the required concentration; however, the reported concentrations may be nominal. The text qualitatively stated that all animals gained weight normally based on comparisons of body weights.	Nutritional/Metabolic: Parental male body weights Medium	Brinkworth et al. 1998 4934798
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-F0- premating (10 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 125 ppm (in air, water, or food) n= 30 Dose= 0, n= 30 Dose= 12.5, n= 30 Dose= 125, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Concentrations were monitored continuously and were considered acceptable if kept within 15% of the required concentration; however, the reported concentrations may be nominal. There was a dose-related increase in the period to coition. The adversity of this effect is unclear, there were no other reproductive effects observed.	Nutritional/Metabolic: Time to coition Medium	Brinkworth et al. 1998 4934798
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-F0- premating (10 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 125 ppm (in air, water, or food) n= 44 Dose= 0, n= 38 Dose= 12.5, n= 47 Dose= 125, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Concentrations were monitored continuously and were considered acceptable if kept within 15% of the required concentration; however, the reported concentrations may be nominal. The number of animals reported represents the number of fertile females examined. The number total numbers of implantations were 576, 502, and 602, respectively. There was a significant increase in early fetal deaths.	Nutritional/Metabolic: Early fetal deaths Medium	Brinkworth et al. 1998 4934798

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-F0- premating (10 weeks)	NOEL: 125 ppm (in air, water, or food) LOEL: Not observed n= 25 Dose= 0, n= 25 Dose= 12.5, n= 25 Dose= 125, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Concentrations were monitored continuously and were considered acceptable if kept within 15% of the required concentration; however, the reported concentrations may be nominal. The number of animals reported represents the number of males/group mated. The N for the number of females pregnant is 50, 50, and 50 and the N for the total number of implants, late deaths, dead fetuses, and number of fetuses with malformations is 44, 38, and 46-47, respectively.	Nutritional/Metabolic: Proportion of males siring litters (number of males fertile); % of number paired; number of females pregnant, total number of implants, number of late deaths and dead fetuses), number of living fetuses with malformations. Medium	Brinkworth et al. 1998 4934798
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 17,600 mg/m^3 LOEL: Not observed n= 80 Dose= 0, n= 80 Dose= 2,200, n= 80 Dose= 4,400, n= 80 Dose= 8,800, n= 80 Dose= 17,600, mg/m^3	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The text indicated that the exposure atmospheres were monitored. The observed effects were not dose-related.	Nutritional/Metabolic: Body weight, body weight gain, food consumption Medium	Crouch et al. 1979 94760
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 17,600 mg/m^3 LOEL: Not observed n= 80 Dose= 0, n= 80 Dose= 2,200, n= 80 Dose= 4,400, n= 80 Dose= 8,800, n= 80 Dose= 17,600, mg/m^3	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The text indicated that the exposure atmospheres were monitored. It is unclear if the concentrations provided are measured or nominal. The number of animals is the number of animals exposed per group. The number of animals for each endpoint varies from 20-40 (10-20/sex) per collection timepoint. For all of the endpoints shown, no effects were observed.	Gastrointestinal: Gross necropsy, histopathology (caecum, colon, esophagus, rectum, salivary glands, small intestine, stomach) Medium	Crouch et al. 1979 94760
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 17,600 mg/m^3 LOEL: Not observed n= 80 Dose= 0, n= 80 Dose= 2,200, n= 80 Dose= 4,400, n= 80 Dose= 8,800, n= 80 Dose= 17,600, mg/m^3	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The text indicated that the exposure atmospheres were monitored. It is unclear if the concentrations provided are measured or nominal. The number of animals is the number of animals exposed per group. The number of animals for each endpoint varies from 20-40 (10-20/sex) per collection timepoint. For all of the endpoints shown, no effects were observed.	Gastrointestinal: Gross necropsy, histopathology (sternum, turbinate bones, femur, diaphragm) Medium	Crouch et al. 1979 94760

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 17,600 mg/m^3 LOEL: Not observed n= 80 Dose= 0, n= 80 Dose= 2,200, n= 80 Dose= 4,400, n= 80 Dose= 8,800, n= 80 Dose= 17,600, mg/m^3	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The text indicated that the exposure atmospheres were monitored. It is unclear if the concentrations provided are measured or nominal. The number of animals is the number of animals exposed per group. The number of animals for each endpoint varies from 20-40 (10-20/sex) per collection timepoint. For all of the endpoints shown, no effects were observed.	Gastrointestinal: Gross necropsy, histopathology (ears, eyes, optic nerve, harderian gland) Medium	Crouch et al. 1979 94760
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 17,600 mg/m^3 LOEL: Not observed n= 80 Dose= 0, n= 80 Dose= 2,200, n= 80 Dose= 4,400, n= 80 Dose= 8,800, n= 80 Dose= 17,600, mg/m^3	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The text indicated that the exposure atmospheres were monitored. It is unclear if the concentrations provided are measured or nominal. The number of animals is the number of animals exposed per group. The number of animals for each endpoint varies from 20-40 (10-20/sex) per collection timepoint. For all of the endpoints shown, no effects were observed.	Gastrointestinal: Gross necropsy, histopathology (skin) Medium	Crouch et al. 1979 94760
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-12-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 5 Dose= 0, n= 5 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Body weights were measured from 5-6 animals per group. The concentration in the exposure chamber was monitored continuously; however, it is unclear if the reported concentration represents the measured value. The methods state that body weights were measured at the time of sacrifice (i.e., at 6, 12, or 24 weeks), and the text qualitatively stated that there were no significant effects on body weights of exposed animals, compared to controls. Quantitative data were only provided for the 6 -week exposure duration.	Nutritional/Metabolic: Body weights Low	Thurmond et al. 1986 62366

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Gas-Duration: Chronic (>90 days)-5-6-24-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 5 Dose= 0, n= 5 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Body weights were measured from 5-6 animals per group at the 6-week sacrifice. The number of animals per group for each exposure duration was not specified, and it is unknown if measurements were taken from the same number of animals following chronic (24-week) exposure. The concentration in the exposure chamber was monitored continuously; however, it is unclear if the reported concentration represents the measured value. The methods state that body weights were measured at the time of sacrifice (i.e., at 6, 12, or 24 weeks), and the text qualitatively stated that there were no significant effects on body weights of exposed animals, compared to controls. Quantitative data were only provided for the 6-week exposure duration.	Nutritional/Metabolic: Body weights Low	Thurmond et al. 1986 62366
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)-5-6-12-week(s)	NOEL: Not observed LOEL: 1250 ppm (in air, water, or food) n= 5 Dose= 0, n= 5 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The number of animals assayed for each endpoint is not reported in several cases, but when reported, the ranges were from 5-6 animals. The concentration in the exposure chamber was monitored continuously; however, it is unclear if the reported concentration represents the measured value. The methods do not clearly describe which endpoints were evaluated for which exposure durations. It is evident from the data tables that some endpoints were tested at 6 weeks only. Although several endpoints showed statistically significant changes relative to controls, the study authors stated that the test substance does not exert any functional immunomodulatory effects on cells, but may affect hematopoietic or lymphoid precursor cells. The authors concluded that there were no important immunological effects. Therefore, the adversity is unclear.	Immune/Hematological: Spleen weight, humoral immunity (PFC response), cell-mediated immunity (mitogen stimulated lymphocyte proliferation assay, mixed lymphocyte response), spleen cellularity, spleen surface markers/immunolabeling, splenic cytotoxicity, spontaneous NK cytotoxicity. Low	Thurmond et al. 1986 62366

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Gas-Duration: Subchronic (>30-90 days)- 5-6-12-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 5 Dose= 0, n= 5 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The number of animals assayed for each endpoint is not reported in several cases, but when reported, the ranges were from 5-6 animals. The concentration in the exposure chamber was monitored continuously; however, it is unclear if the reported concentration represents the measured value. The methods do not clearly describe which endpoints were evaluated for which exposure durations. It is evident from the data tables that some endpoints were tested at 6 weeks only. No effects on thymus weight were observed.	Immune/Hematological: Thymus weight Low	Thurmond et al. 1986 62366

* Overall Quality Determination

1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	High mortality observed in controls, meaning no NOAEL could be determined.	Mortality: Decreased Survival Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 1000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Decreased body weight gain was only observed during weeks 0-12	Mortality: Decreased body weight gain Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 1000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	Effect on spleen weight only observed in males	Mortality: higher mean hemoglobin values, increased WBC, lymphocytes and reticulocytes, decreased spleen weight. Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 1000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	BUN was increased in males, but decreased in females. Authors did not consider these changes to be toxicologically relevant. Liver weights were only elevated in males.	Mortality: Altered BUN, increased liver weight Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 1000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	pH effect observed in males only, specific gravity effect observed in females	Mortality: Increased urine, decreased specific gravity of urine, decreased pH Medium	Hazleton Laboratories 1981 5673742

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 1000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	Effects were observed from weeks 53-76 of the study, but not on week 78. Brain weight effects only observed in females	Neurological/Behavioral: Decreased time spent on rotarod, decreased brain weights Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 1000 ppm (in air, water, or food) LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect observed only in males.	Mortality: Increased heart weight Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 1000 ppm (in air, water, or food) LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect observed only in males.	Mortality: Increased kidney weights Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 1000 ppm (in air, water, or food) LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect observed only in males.	Mortality: Increased lung weights Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Pneumonitis observed only in females, alveolar epithelialization only observed in males. 1000 ppm group not examined.	Mortality: Minor focal pneumonitis, alveolar epithelialization Medium	Hazleton Laboratories 1981 5673742

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect observed only in males, 1000 ppm group not examined.	Mortality: Spleen congestion Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect observed only in males, 1000 ppm group not examined.	Mortality: Liver Angiectasis Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 8000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect observed only in males, 1000 ppm group not examined.	Mortality: Nephropathy Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: Not observed LOEL: 1000 ppm (in air, water, or food) n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Significantly increased incidence of mammary tumors, thyroid follicular tumors, Zymbal gland sarcoma and uterine stromal sarcoma in females and Leydig cell tumors in males High	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: All other measured tumors High	Hazleton Laboratories 1981 5673742

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1,3-Butadiene- Parent compound - Chronic (>91 days)						
Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: All other end-points Medium	Hazleton Laborato-ries 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Neurological/Behavioral: All other endpoints Medium	Hazleton Laborato-ries 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: All other end-points Medium	Hazleton Laborato-ries 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: All other end-points Medium	Hazleton Laborato-ries 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: All other end-points Medium	Hazleton Laborato-ries 1981 5673742

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1,3-Butadiene- Parent compound - Chronic (>91 days)						
Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742

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1,3-Butadiene- Parent compound - Chronic (>91 days)						
Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Rat-Other (CD)-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-111-week(s)	NOEL: 8000 ppm (in air, water, or food) LOEL: Not observed n= 110 Dose= 0, n= 110 Dose= 1000, n= 110 Dose= 8000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Musculoskeletal: All other endpoints Medium	Hazleton Laboratories 1981 5673742
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Decreased survival High	National Institutes of Health 1984 62372

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Increased incidences of neoplasms at multiple sites (heart, hematopoietic system, liver, lung/respiratory tract, forestomach, mammary gland, ovary) High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 625 ppm (in air, water, or food) LOEL: 1250 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Increased incidence of non-neoplastic lesions in the nasal cavity including chronic inflammation, fibrosis, cartilaginous metaplasia, osseous metaplasia, and atrophy of the sensory epithelium High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Increased incidence of liver necrosis High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	Atrophy demonstrated a flat dose-response at the two doses, but this may because over 85% of mice were affected at the lowest dose.	Mortality: Increased incidence of testicular or ovarian atrophy; involution of uterus High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Increased incidence of epithelial hyperplasia in the forestomach High	National Institutes of Health 1984 62372

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Inflammation/abcesses High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	Increase of 13% observed in males at both doses, only 2-4% in females.	Mortality: bone marrow atrophy High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: No effects observed High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Inflammation, degeneration, hyperplasia High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 625 ppm (in air, water, or food) LOEL: 1250 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Effect only observed in males, no effects seen in control or low dose but 50% at highest dose.	Mortality: Olfactory epithelium atrophy High	National Institutes of Health 1984 62372

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Ectopia, cysts, inflammation High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Hyperplasia, cysts High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Hemorrhage, mineralization, inflammation High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: Not observed LOEL: 625 ppm (in air, water, or food) n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Response is more dose-responsive in females; response was decreased in the highest dose in males.	Mortality: Pre-neoplastic endothelial hyperplasia High	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Clinical signs of toxicity High	National Institutes of Health 1984 62372

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-60-week(s)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 100 Dose= 0, n= 100 Dose= 625, n= 100 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Due to higher starting body weight in dosed animals, body weight changes are difficult to interpret.	Nutritional/Metabolic: Decreased body weight/body weight gain Low	National Institutes of Health 1984 62372
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 6.21 ppm (in air, water, or food) LOEL: 19.8 ppm (in air, water, or food) n= 70 Dose= 0, n= 70 Dose= 6.21, n= 70 Dose= 19.8, n= 70 Dose= 61.4, n= 70 Dose= 199, n= 90 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Reported concentrations are target concentrations. Data on measured concentrations are also reported.	Mortality: Survival High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Body weights High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: Not observed LOEL: 6.21 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Malignant lymphoma; harderian gland adenoma, hepatocellular adenoma and carcinoma, alveolar bronchiolar adenoma and carcinoma; mammary gland carcinoma, adenoacanthoma, and malignant mixed tumor; lymphocytic lymphomas High	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 19.8 ppm (in air, water, or food) LOEL: 61.4 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	POD is for the effect in males. The same effect was observed in females at 199 ppm.	Cancer/Carcinogenesis: Decreased erythrocyte counts, hemoglobin concentration and packed red cell volume High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 61.4 ppm (in air, water, or food) LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	POD for spleen weights are based on effects in females.	Cancer/Carcinogenesis: Decreased neutrophils and lymphocytes. Increased Howell-Jolly bodies and absolute spleen weights. High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 199 ppm (in air, water, or food) LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The effect in platelets was only observed in males. The effect on thymus weights were only observed in females.	Cancer/Carcinogenesis: Increased mean erythrocyte volumes, platelets and erythroblasts with multilobed nuclei. Decreased absolute and relative thymus weights. Bone marrow atrophy. High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 19.8 ppm (in air, water, or food) LOEL: 61.4 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	POD for liver weights is based on observations in females.	Cancer/Carcinogenesis: Increased absolute liver weights. High	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 61.4 ppm (in air, water, or food) LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased lactate dehydrogenase. High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 61.4 ppm (in air, water, or food) LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	POD based on effects observed in females.	Cancer/Carcinogenesis: Increased absolute heart weights. High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 19.8 ppm (in air, water, or food) LOEL: 61.4 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Decreased testis weights were observed at a later time point in the study at 199 ppm.	Cancer/Carcinogenesis: Increased absolute testis weights High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 199 ppm (in air, water, or food) LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	POD based on effects observed in females.	Cancer/Carcinogenesis: Increased absolute kidney weights High	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 199 ppm (in air, water, or food) LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	POD based on effects observed in males.	Cancer/Carcinogenesis: Increased absolute and relative lung weights High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology/brain organ weights High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: Not observed LOEL: 6.21 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Harderian gland hyperplasia High	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 61.4 ppm (in air, water, or food) LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	POD based on effects observed in females.	Cancer/Carcinogenesis: Forestomach epithelium hyperplasia High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: Not observed LOEL: 6.21 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	POD based on effects observed in males.	Cancer/Carcinogenesis: Alveolar epithelium hyperplasia High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 19.8 ppm (in air, water, or food) LOEL: 61.4 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Ovarian angiectasis High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 61.4 ppm (in air, water, or food) LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Uterus atrophy High	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 199 ppm (in air, water, or food) LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Endothelial hyperplasia and mineralization High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 6.21 ppm (in air, water, or food) LOEL: 19.8 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	POD for forestomach neoplasms based on effects observed in females.	Cancer/Carcinogenesis: Histiocytic sarcoma, heart hemangiosarcoma, forestomach squamous cell papilloma or squamous cell carcinoma, kidney renal tubule adenoma High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: All other neoplasms with no incidence or highly inconsistent dose-response. High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-52-week(s)	NOEL: Not observed LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Decreased survival Medium	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-52-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Body weight changes Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-52-week(s)	NOEL: Not observed LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of malignant lymphoma, histiocytic sarcoma, cardiac hemangiosarcoma, alveolar/bronchial adenoma and carcinoma Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-52-week(s)	NOEL: 199 ppm (in air, water, or food) LOEL: 312 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of forestomach squamous cell papilloma and carcinoma and preputial gland adenoma and carcinoma Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-52-week(s)	NOEL: 312 ppm (in air, water, or food) LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Zymbal's gland carcinoma and adenomas, glioma and neuroblastoma Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-52-week(s)	NOEL: Not observed LOEL: 199 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of myocardial mineralization Medium	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: Not observed LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Decreased survival. Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Body weight changes Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: Not observed LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of neoplastic lesions: malignant lymphoma, histiocytic sarcoma, harderian gland adenoma, alveolar/bronchial adenom-Increa and carcinoma, hepatocellular adenoma, and forestomach squamous cell papilloma and carcinoma, renal tubule adenoma, Zymbal's gland carcinoma and adenomas, glioma and neuroblastoma, preputial gland adenoma and carcinoma Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: Not observed LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of harderian gland hyperplasia Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: Not observed LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of renal tubule epithelium hyperplasia Medium	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: Not observed LOEL: 619 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Increased incidence of myocardial mineralization Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology for spleen, thymus, lymph nodes Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology for spleen, thymus, lymph nodes High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)						
Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)- 5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)- 5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)- 5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)- 5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)- 5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)- 5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology Medium	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s)	NOEL: 619 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 199, n= 50 Dose= 312, n= 50 Dose= 619, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Histopathology High	NTP 1993 1419645
Mouse-B6C3F1 - [mouse]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-103-week(s)	NOEL: Not observed LOEL: 6.21 ppm (in air, water, or food) n= 50 Dose= 0, n= 50 Dose= 6.21, n= 50 Dose= 19.8, n= 50 Dose= 61.4, n= 50 Dose= 199, n= 70 Dose= 619, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Cancer/Carcinogenesis: Testicular atrophy (males), ovarian atrophy (females) High	NTP 1993 1419645

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID

* Overall Quality Determination

1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 130 ppm (in air, water, or food) LOEL: Not observed n= 25 Dose= 0, n= 24 Dose= 12.5, n= 23 Dose= 65, n= 24 Dose= 130, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 10 to 678 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. No details on the endpoint (body weight measurements) were provided. A qualitative statement in the text indicated that no treatment-related effects on the body weights of surviving animals were observed. The frequency of body weight measurements is not specified. Some animals died during exposure due to injuries sustained thus the ”n” changed from 25 per group to 25, 24, 23, and 24 males in the control, low, mid, and high-exposure groups, respectively, at the end of the exposure period.	Reproductive/Developmental: Parental body weights Medium	Anderson 1998 1327602
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (10 weeks)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 25 Dose= 0, n= 24 Dose= 65, n= 25 Dose= 400, n= 25 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 1 to 437 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. No details on the endpoint (body weight measurements) were provided. A qualitative statement in the text indicated that no treatment-related effects on the body weights of surviving animals were observed. Two control groups were included, a room control (n =50) and a clear air control (n = 25). One animal in the 65 ppm group died, the time of death wasn’t specified.	Reproductive/Developmental: Parental body weights Medium	Anderson 1998 1327602

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 130 ppm (in air, water, or food) LOEL: Not observed n= 25 Dose= 0, n= 25 Dose= 12.5, n= 25 Dose= 65, n= 25 Dose= 130, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 10 to 678 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. Some animals died during exposure due to injuries.	Reproductive/Developmental: parental death Medium	Anderson 1998 1327602
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (10 weeks)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 25 Dose= 0, n= 24 Dose= 65, n= 25 Dose= 400, n= 25 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 1 to 437 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. One death due to unknown causes was reported.	Reproductive/Developmental: Parental body weights Medium	Anderson 1998 1327602
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 65 ppm (in air, water, or food) n= 46 Dose= 0, n= 44 Dose= 12.5, n= 45 Dose= 65, n= 47 Dose= 130, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 10 to 678 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The number of animals indicates the number of pregnant females per group that were sacrificed and examined. The number of implantations that were used to determine the numbers of early deaths were 572, 528, 559, and 562, in the control, low, mid, and high exposure groups, respectively. TA significant increase in early deaths was observed at 65 and 130 ppm; but the increase did not show a clear dose-response.	Reproductive/Developmental: Early deaths Medium	Anderson 1998 1327602

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (10 weeks)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 92 Dose= 0, n= 46 Dose= 0, n= 45 Dose= 65, n= 44 Dose= 400, n= 46 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 1 to 437 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The animal numbers represent the number of pregnant females that were sacrificed and analyzed. No statistically significant effects were observed in the endpoints listed.	Reproductive/Developmental: Mating frequency, % pregnant, number of live fetuses, number of post-implantation loss including early and late resorptions, number of fetuses with gross malformations, cytogenic analysis of fetal livers Medium	Anderson 1998 1327602
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (10 weeks)	NOEL: Not observed LOEL: 65 ppm (in air, water, or food) n= 92 Dose= 0, n= 46 Dose= 0, n= 45 Dose= 65, n= 44 Dose= 400, n= 46 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 1 to 437 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The animal numbers represent the number of pregnant females that were sacrificed and analyzed. The numbers of implantations were 1370, 695, 627, 650, and 655, respectively.	Reproductive/Developmental: Implantations Medium	Anderson 1998 1327602
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 130 ppm (in air, water, or food) LOEL: Not observed n= 46 Dose= 0, n= 44 Dose= 12.5, n= 45 Dose= 65, n= 47 Dose= 130, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 10 to 678 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The number of animals indicates the number of pregnant females per group that were sacrificed and examined. No statistically significant effects were observed for the endpoints noted.	Reproductive/Developmental: Mating frequency, % pregnant, number of live fetuses, number of post-implantation loss (late resorptions), number of fetuses with gross malformations, cytogenic analysis of fetal livers Medium	Anderson 1998 1327602

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 65 ppm (in air, water, or food) n= 46 Dose= 0, n= 44 Dose= 12.5, n= 45 Dose= 65, n= 47 Dose= 130, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 10 to 678 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The number of animals indicates the number of pregnant females per group that were sacrificed and examined. Early deaths indicate the potential for dominant lethal effects; however, a clear dose response was not observed.	Reproductive/Developmental: Dominant lethality Medium	Anderson 1998 1327602
Rat-Sprague-Dawley - [rat]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (10 weeks)	NOEL: 1250 ppm (in air, water, or food) LOEL: Not observed n= 92 Dose= 0, n= 46 Dose= 0, n= 45 Dose= 65, n= 44 Dose= 400, n= 46 Dose= 1250, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 1 to 437 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The animal numbers represent the number of pregnant females that were sacrificed and analyzed. The numbers of implantations were 1370, 695, 627, 650, and 655, respectively.	Reproductive/Developmental: Dominant lethality Medium	Anderson 1998 1327602
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (10 weeks)	NOEL: Not observed LOEL: 12.5 ppm (in air, water, or food) n= 46 Dose= 0, n= 44 Dose= 0, n= 45 Dose= 12.5, n= 47 Dose= 65, Dose= 130, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was nominal/estimated.	Atmospheres were analyzed for dimer concentrations, which ranged from 1 to 437 ppm; no further information on analytical measurements of atmosphere concentrations was provided. It is assumed the concentrations reported are nominal, but this is unclear. The animal numbers represent the number of pregnant females that were sacrificed and analyzed. The numbers of implantations were 1370, 695, 627, 650, and 655, respectively.	Reproductive/Developmental: Implantations Medium	Anderson 1998 1327602

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: 199.8 ppm (in air, water, or food) LOEL: 1,000 ppm (in air, water, or food) n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Decreased body weights	Nutritional/Metabolic: Maternal body weights (GD 18), extra-gestational weight Medium	Battelle PNL 1987 62351
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: 1,000 ppm (in air, water, or food) LOEL: Not observed n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No significant signs of toxicity were described (data were qualitatively described in the text)	Clinical signs Medium	Battelle PNL 1987 62351
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: 199.8 ppm (in air, water, or food) LOEL: 1,000 ppm (in air, water, or food) n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Decreased gravid uterine weight	Reproductive/Developmental: Gravid uterine weight; reduced ossification, abnormal sternebrae Medium	Battelle PNL 1987 62351
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: 39.9 ppm (in air, water, or food) LOEL: 199.8 ppm (in air, water, or food) n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Decreased body weights	Nutritional/Metabolic: Extragestational weight gain; body weight gain (GD 11-16) Medium	Battelle PNL 1987 62351
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: 1,000 ppm (in air, water, or food) LOEL: Not observed n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No observed effects.	Reproductive/Developmental: % pregnant, litters with live fetuses, implantations/dam, total resorptions/litter, live/dead fetuses/litter, sex ratio, malformations, lens opacity. Medium	Battelle PNL 1987 62351

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: 39.9 ppm (in air, water, or food) LOEL: 199.8 ppm (in air, water, or food) n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Decreased body weights; decreased placental weight	Reproductive/Developmental: Placental weight (total, and males); fetal body weights (males + females, and females); variations (increased incidences of supernumerary ribs/extra rudimentary ribs) Medium	Battelle PNL 1987 62351
Mouse-CD-1 - [mouse]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD6-15)	NOEL: Not observed LOEL: 39.9 ppm (in air, water, or food) n= 18 Dose= 0, n= 19 Dose= 39.9, n= 21 Dose= 199.8, n= 20 Dose= 1,000, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Decreased male fetal body weights	Reproductive/Developmental: Male fetal body weight Medium	Battelle PNL 1987 62351
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-F0 - gestation (GD 6-15)	NOEL: 1005 ppm (in air, water, or food) LOEL: Not observed n= 28 Dose= 0, n= 24 Dose= 40.1, n= 26 Dose= 199.8, n= 27 Dose= 1005, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No maternal deaths were observed.	Mortality: Maternal mortality High	Battelle PNL 1987 94731
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-F0 - gestation (GD 6-15)	NOEL: 199.8 ppm (in air, water, or food) LOEL: 1005 ppm (in air, water, or food) n= 28 Dose= 0, n= 24 Dose= 40.1, n= 26 Dose= 199.8, n= 27 Dose= 1005, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Significant decrease in body weight gain from GD 6-11 and in extragestational weight gain in the absence of changes to animal body weights.	Mortality: Weight gain (during gestation), Extragestational weight gain High	Battelle PNL 1987 94731

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-F0 - gestation (GD 6-15)	NOEL: 1005 ppm (in air, water, or food) LOEL: Not observed n= 28 Dose= 0, n= 24 Dose= 40.1, n= 26 Dose= 199.8, n= 27 Dose= 1005, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No treatment-related effects in any of the endpoints listed. An increase in the incidence of reduced sternebral ossification was observed, but only when the analysis was based on the number of affected fetuses. There was no significance when examinations were based on the number of affected litter. The effect was not considered to be treatment-related.	Reproductive/Developmental: Weight of gravid uterus, number of implantation sites, intrauterine mortality, placental weights, fetal observations (body weights, sex, lens opacity, examination of eyes, gross, visceral, and skeletal examinations) Medium	Battelle PNL 1987 94731
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 130 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 12.5, n= 50 Dose= 65, n= 50 Dose= 130, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	There were 50 males per group. The number of females paired with males was 50, 48, 46, and 48, respectively. A few males died due to injury. No female deaths were described.	Mortality: Mortality in parental animals Medium	BIBRA 1996 5665017
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 65 ppm (in air, water, or food) n= 46 Dose= 0, n= 44 Dose= 12.5, n= 45 Dose= 65, n= 47 Dose= 130, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The animal numbers indicates the number of pregnant females. The number of early deaths increased in a dose-related manner.	Reproductive/Developmental: Early fetal deaths Medium	BIBRA 1996 5665017
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 130 ppm (in air, water, or food) LOEL: Not observed n= 50 Dose= 0, n= 50 Dose= 12.5, n= 50 Dose= 65, n= 50 Dose= 130, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	There were 50 males per group. The number of females paired with males was 50, 48, 46, and 48, respectively. A few males died due to injury. No treatment-related effects on body weights were observed.	Nutritional/Metabolic: Mortality in parental animals Uninformative	BIBRA 1996 5665017

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 130 ppm (in air, water, or food) LOEL: Not observed n= 46 Dose= 0, n= 44 Dose= 12.5, n= 45 Dose= 65, n= 47 Dose= 130, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The animal numbers indicates the number of pregnant females. No effects on these reproductive endpoints were observed. Note: fetal body weight data were not reported, and skeletal malformation data were not statistically analyzed. Data for these endpoints are not included in this extraction form.	Reproductive/Developmental: Mating frequency, pregnancy rate, period of coition, number of corpora lutea, number of live and dead implantations, late deaths, dead fetuses, fetal sex, fetal abnormalities. Medium	BIBRA 1996 5665017
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0- premating (4 weeks)	NOEL: 12.5 ppm (in air, water, or food) LOEL: 65 ppm (in air, water, or food) n= 46 Dose= 0, n= 44 Dose= 12.5, n= 45 Dose= 65, n= 47 Dose= 130, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The animal numbers indicates the number of pregnant females. The number of early deaths increased in a dose-related manner indicating that the test substance was positive for dominant lethality.	Reproductive/Developmental: Dominant lethality Medium	BIBRA 1996 5665017
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: Not observed LOEL: 1010 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1010, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	One animal in the 1,1010 ppm group died due to dehydration. One control animal died due to an accident.	Mortality: Mortality Medium	Hackett 1988 62353
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: 1010 ppm (in air, water, or food) LOEL: 5000 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1010, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is an ambiguous dose response relationship or trend. The exposure was measured.	Males exposed to 5,000 ppm showed transient signs of piloerection and dyspnea for up to 30 minutes following exposure. The number of males was not specified. It is unclear if increased incidences were statistically significant.	Mortality: Clinical signs (piloerection, dyspnea) Medium	Hackett 1988 62353
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: 5000 ppm (in air, water, or food) LOEL: Not observed n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1010, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No significant effects on body weight or body weight gain were observed.	Mortality: Body weight and body weight gain Medium	Hackett 1988 62353

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: 5000 ppm (in air, water, or food) LOEL: Not observed n= 40 Dose= 0, n= 40 Dose= 200, n= 38 Dose= 1010, n= 38 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The number of animals represents the maximum number of females mated/group weekly over 8 weeks. Each week, the remaining males were mated to two naïve females. There was a significant amount of variation in the pregnancy rates within groups, across weeks. In controls, the % of pregnant females ranged from 90 to 98%. No significant differences within weeks and across exposure groups were noted.The number of males per group was 20; there were no effects on male fertility.	Reproductive/Developmental: % females pregnant; % male fertility Medium	Hackett 1988 62353
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: 5000 ppm (in air, water, or food) LOEL: Not observed n= 40 Dose= 0, n= 40 Dose= 200, n= 38 Dose= 1010, n= 38 Dose= 5000, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The number of animals represents the maximum number of females mated/group weekly over 8 weeks. Each week, the remaining males were mated to two naïve females. The range of females pregnant per week/group was: 35-39, 35-40, 33-38, and 34-38, in the 0, 200, 1010, and 5000 ppm groups, respectively. Significant decreases in the number of implantations/pregnancies were observed at 1,010 ppm following post-exposure mating weeks 1 and 8. No changes were observed at 200 or 5,000 ppm. The effect was not clearly treatment-related.There were no effects on late resorptions.	Reproductive/Developmental: number of implantations/pregnancy; late resorptions Medium	Hackett 1988 62353

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: Not observed LOEL: 200 ppm (in air, water, or food) n= 40 Dose= 0, n= 40 Dose= 200, n= 38 Dose= 1010, n= 38 Dose= 5000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The number of animals represents the maximum number of females mated/group weekly over 8 weeks. Each week, the remaining males were mated to two naïve females. The range of females pregnant per week/group was: 35-39, 35-40, 33-38, and 34-38, in the 0, 200, 1010, and 5000 ppm groups, respectively. Significant increases in early and total resorptions occurred at 1,010 ppm only during mating week 1, and at 200 and 1,010 ppm (but not at 5,000 ppm) during mating week 2. An increase in % dead implantations occurred during week 1 at 1,010 ppm only; during week 4 there was a decrease in % dead implantations, compared with controls.	Reproductive/Developmental: Early and total resorptions; dead implantations/total implantations Medium	Hackett 1988 62353
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: Not observed LOEL: 200 ppm (in air, water, or food) n= 40 Dose= 0, n= 40 Dose= 200, n= 38 Dose= 1010, n= 38 Dose= 5000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	The number of animals represents the maximum number of females mated/group weekly over 8 weeks. Each week, the remaining males were mated to two naïve females. The range of females pregnant per week/group was: 35-39, 35-40, 33-38, and 34-38, in the 0, 200, 1010, and 5000 ppm groups, respectively. The percentage of females with $\geq$2 intrauterine deaths was significantly increased in all exposure groups, compared to controls after mating week 2 (the effect was not exposure concentration-related), and at 200 and 5,000 ppm after mating week 4.	Reproductive/Developmental: % females with $\geq$ 2 intrauterine deaths Medium	Hackett 1988 62353

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Mouse-CD-1 - [mouse]-Male	Inhalation-Gas-Duration: Reproductive/Developmental-F0- premating (5 days)	NOEL: Not observed LOEL: 200 ppm (in air, water, or food) n= 20 Dose= 0, n= 20 Dose= 200, n= 20 Dose= 1010, n= 20 Dose= 5000, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Dominant lethality was assessed based on multiple reproductive parameters, some of which were observed in all exposure groups. The effects observed did not exhibit a clear dose-response relationship and the study authors did not specify whether they considered the test material was positive for eliciting dominant lethality. Based on the timing of the observed effects (soon after exposure), the authors speculated that more mature spermatozoa and spermatids were altered by exposure to 1,3-butadiene.	Reproductive/Developmental: Dominant lethality Medium	Hackett 1988 62353
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	NOEL: 7647 ppm (in air, water, or food) LOEL: Not observed n= 40 Dose= 2.8, n= 24 Dose= 202, n= 24 Dose= 990, n= 24 Dose= 7647, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No endpoint comments identified.	Mortality: Mortality and morbidity (dams) Medium	Hazleton Labs 1981 62371
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	NOEL: 7647 ppm (in air, water, or food) LOEL: Not observed n= 40 Dose= 2.8, n= 24 Dose= 202, n= 24 Dose= 990, n= 24 Dose= 7647, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No effect on dam body weights	Mortality: Dam body weights Medium	Hazleton Labs 1981 62371
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	NOEL: Not observed LOEL: 202 ppm (in air, water, or food) n= 40 Dose= 2.8, n= 24 Dose= 202, n= 24 Dose= 990, n= 24 Dose= 7647, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	No effect on dam body weights	Mortality: Dam body weight gain Medium	Hazleton Labs 1981 62371

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	NOEL: 7647 ppm (in air, water, or food) LOEL: Not observed n= 36 Dose= 2.8, n= 22 Dose= 202, n= 24 Dose= 990, n= 23 Dose= 7647, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The N indicates the number of pregnant dams. There were no statistically significant effects for the endpoints selected.	Mortality: Gravid uterine weights, numbers of corpora lutea, implantations (along with positions), live fetuses, early and late deaths, Medium	Hazleton Labs 1981 62371
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	NOEL: 990 ppm (in air, water, or food) LOEL: 7647 ppm (in air, water, or food) n= 36 Dose= 2.8, n= 22 Dose= 202, n= 24 Dose= 990, n= 23 Dose= 7647, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The N indicates the number of pregnant dams. There was a clear dose-response relationship for crown/rump length, but not for fetal weight.	Mortality: live fetal body weights, crown/rump length Medium	Hazleton Labs 1981 62371
Rat-Sprague-Dawley - [rat]-Female	Inhalation-Gas-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	NOEL: 202 ppm (in air, water, or food) LOEL: 990 ppm (in air, water, or food) n= 36 Dose= 2.8, n= 22 Dose= 202, n= 24 Dose= 990, n= 23 Dose= 7647, ppm (in air, water, or food)	These health effect(s) support an ambiguous effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	The N indicates the number of pregnant dams. There was a clear dose-response relationship for the percentage of fetuses showing major skeletal defects (fused/malformed ribs), but not for the number of fetuses showing minor external and visceral defects. Statistical significance was not determined and identifying the true LOEL is difficult.	Mortality: external, visceral, and skeletal examinations Medium	Hazleton Labs 1981 62371
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 301 ppm (in air, water, or food) LOEL: 1507 ppm (in air, water, or food) n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Statistically significant reduction in males only, and transient.	Nutritional/Metabolic: Nutritional/metabolic (decreased body weight/body weight gain in F0 animals) High	WIL Research 2003 10367501

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 301 ppm (in air, water, or food) LOEL: 1507 ppm (in air, water, or food) n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Clinical signs at 1507 ppm animals transient (i.e., observed only at the 1-hour post-exposure examination). Some perinasal staining at 300 ppm but not considered adverse/relevant.	Neurological/Behavioral: Other-clinical signs (chromodacryorrhea, chromorhinorrhea, and salivation in F0 animals) High	WIL Research 2003 10367501
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 301 ppm (in air, water, or food) LOEL: 1507 ppm (in air, water, or food) n= 18 Dose= 0, n= 24 Dose= 301, n= 20 Dose= 1507, n= 22 Dose= 6006, ppm (in air, water, or food)	These health effect(s) support an adverse effect on the organ system. There is a clear dose response relationship or trend. The exposure was measured.	Females more strongly impacted.	Nutritional/Metabolic: Nutritional/metabolic (decreased body weight/body weight gain in F1 animals) High	WIL Research 2003 10367501

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 12 Dose= 0, n= 12 Dose= 301, n= 12 Dose= 1507, n= 12 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	Exposure was maternal and in utero. No effects seen on any developmental or reproductive parameters (besides fetal weight). One male-female pair did not produce a litter at 6000 ppm but this is not considered adverse as it was not statistically significant.	Reproductive/Developmental: Mating index, fertility index, male/female reproductive organ histopathology and organ weights, sperm parameters, offspring clinical observations and malformations, litter size/live vs stillborn pups Medium	WIL Research 2003 10367501
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Animal Species, Strain, Sex	Exposure Route and Exposure Duration	NOEL, LOEL, and Dose/ Concentration(s)	Dose-Response/ Adversity	Comments	Target Organ/System and OQD*	Citation and HERO ID
Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (14 Days)-F0- mating (During 14-day mating period)-F0 - gestation (Throughout gestation until GD 20)-F0-lactation (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)-F0-premating (14 Days)-F0-mating (From LD 5 until the day prior to euthanasia for a total of 60 to 70 days of exposure)-F1- post-natal (PND 21-27 or 28-34)	NOEL: 6006 ppm (in air, water, or food) LOEL: Not observed n= 24 Dose= 0, n= 24 Dose= 301, n= 24 Dose= 1507, n= 24 Dose= 6006, ppm (in air, water, or food)	These health effect(s) do not support an adverse effect on the organ system. There is not a clear dose response relationship or trend. The exposure was measured.	No systemic effects other than body weight and some clinical signs observed in F0 animals	Neurological/Behavioral: This applies to all other clinical effects including neurological, respiratory, mortality, immune/hematological, gastrointestinal, and ocular High	WIL Research 2003 10367501

* Overall Quality Determination

1,3-Butadiene- Parent compound - Acute (less than or equal to 24 hr)

Summary	HERO ID and Citation
In an acute dominant lethality study, male CD-1 nice (25/control and low exposure group, 50/high exposure group) were exposed, whole body, to 1,3-butadiene gas at 0, 1,250 or 6,250 ppm for 6 hours. Five days after exposure, males were co-housed (1:2) with virgin females for 1 week. One mated female/group was killed on GD 17, and the other was allowed to deliver. F1 litters from the control and high-exposure groups only were maintained for 37 weeks. Uterine contents of the sacrificed female were examined for the number of live fetuses and post-implantation deaths. The fetuses were examined for gross malformations including runts. Skeletal examinations were performed on any malformed fetuses and on randomly selected normal littermates. The livers were karyotyped. Body weights were purportedly measured, but no further details on which animals were weighed and when were provided. No changes in body weights were observed in surviving animals (data not shown). A significant reduction in the mean number of implants per female was observed in the 1,250 ppm group, but not in the 6,250 ppm group. No increases in post-implantation losses or fetal abnormalities were observed. Karyotypes were normal. There were no differences in tumor incidences between control and exposed F1 animals (data not shown). The authors reported that the test substance did not elicit a dominant lethal effect. The study design was not appropriate to derive toxicity values for reproductive endpoints or to access carcinogenicity. Therefore, no NOAEC or LOAEC values were identified.	5663561 Anderson, D., Edwards, A. J., Brinkworth, M. H., Hughes, J. A. (1996). Male-mediated F1 effects in mice exposed to 1,3-butadiene. Toxicology 113(1-3):120-127.
In non-guideline genotoxicity tests, male CD-1 mice (5/group) were exposed, via whole body inhalation, to 1,3-butadiene (purity not) gas (presumed) at 0, 12.5, 125 ppm for 6 hrs/day, 5 days/week for 10 weeks. Males were monitored for clinical signs and body weights were measured prior to and at the end of the exposure period. 5 males/group were used for DNA damage repair (Comet) and UDS assays. At the end of exposure, one testis was removed and used for the Comet assay. The remaining testis was injected with tritiated thymidine, and animals were killed after 17 days. Radioactivity was determined, in duplicate, from 10^4 sperm.No mortality but data from only 4 low-exposure animals were reported for both assays, and the sample size for the UDS results was n = 4 for all groups. The comet assay showed a significant increase in DNA damage in both haploid and polyploid cells at 125 ppm. For the UDS assay, 100 - 1000-fold fewer sperm were recovered than expected. However, it is unclear if this was the case only for mice exposed for 10 weeks (evaluated separately), or those that were acutely exposed. Total sperm counts were not provided. Due to high inter-animal variability, no increases in tritiated thymidine counts reached statistical significance. No author-reported toxicity values were provided. Although a positive response was observed in the comet assay at 125 ppm, this assay is not appropriate for determining DNA strand breaks in sperm cells (OECD TG 489); therefore, a determination of genotoxicity cannot be concluded for this study.	4934798 Brinkworth, M. H., Anderson, D., Hughes, J. A., Jackson, L. I., Yu, T. W., Nieschlag, E. (1998). Genetic effects of 1,3-butadiene on the mouse testis. Mutation Research 397(1):67-75.
In this study, the authors seek to assess the carcinogenicity of 1,3-butadiene following a single, short high-exposure situation. They do this by acquiring male and female B6C3F1 mice (60/sex/group) and exposing them via inhalation to various concentrations (0, 1000, 5000, and 10000 ppm) of 1,3- butadiene for a single 2-hour period. The mice were then held for 2 years (during this 2 year period, body weights were presumably measured, but the authors do not provide any details as to how this was done), at which time they were killed and tissues and organs examined microscopically). The authors found that exposure to 1,3-butadiene in these conditions did not impact survival at 2 years, body weight throughout the 2 year experiment, or tumor incidence at 2 years.	5640580 Bucher, J. R., Melnick, R. L., Hildebrandt, P. K. (1993). Lack of carcinogenicity in mice exposed once to high concentrations of 1,3-butadiene. Journal of the National Cancer Institute 85(22):1866-1867.
In an acute lethality study reporting minimal details, rats (strain, sex, and number per group not specified), were exposed, whole body, to gaseous butadiene at unspecified concentrations for 4 hours. Animals were exposed in a dynamic chamber and the concentrations were controlled by gas chromatography. The duration of animal observation was not specified. Lethality values were reported. It is unclear if animals were assessed for other endpoints. The LD50 was 285 (95% CI219 - 370) mg/L. The LC16 was 175 mg/L and the LC84 was 460 mg/L.	62368 Shugaev, B. B. (1969). Concentrations of hydrocarbons in tissues as a measure of toxicity. Archives of Environmental and Occupational Health 18(6):878-882.
In an acute lethality study reporting minimal details, mice (strain, sex, and number per group not specified), were exposed, whole body, to gaseous butadiene at unspecified concentrations for 4 hours. Animals were exposed in a dynamic chamber and the concentrations were controlled by gas chromatography. The duration of animal observation was not specified. Lethality values were reported. It is unclear if animals were assessed for other endpoints. The LD50 was 270 (95% CI 251 - 290) mg/L. The LC16 was 203 mg/L and the LC84 was 375 mg/L.	62368 Shugaev, B. B. (1969). Concentrations of hydrocarbons in tissues as a measure of toxicity. Archives of Environmental and Occupational Health 18(6):878-882.

1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Summary	HERO ID and Citation
In a dominant lethality study, male 102/E1 X C3H/E1 mice (30/group) were exposed to 0, 130, or 500 ppm of 1,3-butadiene 6 hours/day for 5 days. Four hours after exposure, one male was mated with 2 untreated females, one hybrid (102/E1 X C3H/E1) and one outcross NMRI female. This was done because the NMRI females have a higher implantation rate (15-16 implants/female) than the hybrid (10-11 implants/female) and the authors thought they may be able to detect small dominant lethal effects easier. Once a vaginal plug was observed, females were removed and replaced with a new female. Mating continued for 4 weeks. Twenty-nine to thirty females/group were mated per week.At gestation day 14-16, females were sacrificed. Endpoints evaluated included the number of pregnant females, and number of total implants, live and dead implants. Data were separated by weeks post exposure (i.e. females impregnated 1, 2, 3 or 4 weeks after exposure ended were evaluated as separate groups). Dominant lethality was calculated using the following equation : %DL = [1- (live implants per female in the experimental group / live implants per female in the control group)] X 100.These results are for the female 102/E1 x C3H/E1 females. No significant difference in the percentage of pregnant females was seen compared to control. The number implants/female, live implants/female, and percentage of dead implants were similar to control group at each week. No significant difference in dead implants/female was seen compared to compared to control at any week. Study authors consider both concentrations to be negative for dominant lethal effects.	5663591 Adler I-D, Filser, J., Gonda, H., Schriever-Schwemmer, G. (1998). Dose response study for 1,3-butadiene-induced dominant lethal mutations and heritable translocations in germs cells of male mice. Mutation Research 397(1):85-92.
In a dominant lethality study, male 102/E1 X C3H/E1 mice (30/group) were exposed to 0, 130, or 500 ppm of 1,3-butadiene 6 hours/day for 5 days. Four hours after exposure, one male was mated with 2 untreated females, one hybrid (102/E1 X C3H/E1) and one outcross NMRI female. This was done because the NMRI females have a higher implantation rate (15-16 implants/female) than the hybrid (10-11 implants/female) and the authors thought they may be able to detect small dominant lethal effects easier. Once a vaginal plug was observed, females were removed and replaced with a new female. Mating continued for 4 weeks. Twenty-nine to thirty females/group were mated per week.At gestation day 14-16, females were sacrificed. Endpoints evaluated included the number of pregnant females, and number of total implants, live and dead implants. Data were separated by weeks post exposure (i.e. females impregnated 1, 2, 3 or 4 weeks after exposure ended were evaluated as separate groups). Dominant lethality was calculated using the following equation : %DL = [1- (live implants per female in the experimental group / live implants per female in the control group)] X 100.These are the results for the NMRI females. No significant difference in the percentage of pregnant females was seen compared to control. The number implants/female, live implants/female, and percentage of dead implants were similar to control group at each week. A significant increase in dead implants/female was seen at 500 ppm mated during the first week post-exposure compared to control. No significant increase in dead implants/female was seen in mating week 2-4 compared to control at 500 ppm. Dominant lethality was considered positive by study authors in males mated one week after exposure to 500 ppm ended.	5663591 Adler I-D, Filser, J., Gonda, H., Schriever-Schwemmer, G. (1998). Dose response study for 1,3-butadiene-induced dominant lethal mutations and heritable translocations in germs cells of male mice. Mutation Research 397(1):85-92.
In a heritable translocation assay, male C3H/E1 mice (50/group) were exposed to 500 ppm of 1,3-butadiene 6 hours/day for 5 days. Males were mated 4 hours after exposure ended up to 7 days to untreated 102/E1 females in a 1:2 ratio (time point and dose shown to be sensitive for dominant lethal mutations). A control group of 65 males mated with 65 females was included. Pregnant females were allowed to deliver naturally. Litters were counted and sexed at birth and weaned at 3 weeks of age. This experiment was repeated in order to generate more progeny. At 10-12 weeks F1 male and females were mated; up to 3 litters were observed before pairs with reduced or no litters were separated. Confirmation of translocation suspect F1 males and females was performed by further mating with naive mice and cytogenetic confirmation. No significant differences in litter size at birth or at weaning were seen compared to control. Sex ratio was not reported. A significant increase in translocation carriers were seen in F1 offspring. Five out of 434 F1 offspring were found to be translocation carriers (1.15% compared to 0.05% in historical control). A NOAEL of 500 ppm was determined for reproductive effects. Positive for genotoxicity (increased frequency of translocation carriers).	5663591 Adler I-D, Filser, J., Gonda, H., Schriever-Schwemmer, G. (1998). Dose response study for 1,3-butadiene-induced dominant lethal mutations and heritable translocations in germs cells of male mice. Mutation Research 397(1):85-92.
Male B6C3F1 mice (20/group) were exposed to 0, 200, 1000 or 5000 ppm of 1,3-butadiene via whole body inhalation for 6 hours/day for 5 days. A separate group of 14 mice were exposed to 167 mg/kg of ethyl methanesulfonate (EMS) via intraperitoneal injection each day for 5 days as a positive control. Animals were then maintained without exposure for a 5-week period, after which they were sacrificed. During this 5-week period, animals were monitored for mortality and clinical signs of toxicity, and body weights were measured weekly. After sacrifice, the male reproductive tract was examined for gross lesions and a sperm suspension was isolated to evaluate sperm morphology. Prior to the experiment, animals were allowed 5-weeks of isolation, during which 5 mice were euthanized to check for parasites and pathogens via histopathology of several different tissues. These tissues were not considered target organs as the tissues were taken before exposure commenced. No animals died over the course of the study. Clinical signs that included pilorection and dyspnea were observed at 5000 ppm. No significant differences in absolute body weights nor body weight gain % in animals exposed to 1,3-butadiene were observed during the study. Decreased body weight gain % was observed in the EMS positive control group. Significantly decreased % of normal sperm and increased % of abnormal sperm was observed at $\geq$1000 ppm. A linear trend for increased incidence of blunt hook, banana and amorphous types of abnormal sperm were observed in 1,3-butadiene exposed animals. These measures were slightly elevated compared to controls at 200 ppm (without reaching clear statistical significance). No differences in sperm morphology were detected in the EMS positive control group. There were no significant differences in distribution of sperm abnormalities in animals exposed to different concentrations of 1,3-butadiene. A NOAEL of 200 ppm and LOAEL of 1000 ppm were identified for reproductive/developmental effects based on decreased % of normal sperm and increased % of abnormal sperm.	62354 Hackett, P. L., Brown, M. G., Clark, M. L., Evanoff, J. J., Rowe, S. E., McClanahan, B. J., Buschbom, R. L., Decker, J. R., Rommereim, R. L., Westerberg, R. B. (1988). Sperm-head morphology study in B6C3F1 mice following inhalation exposure to 1,3-butadiene.

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Summary	HERO ID and Citation
Female ICR mice (15/group) were exposed to 0, 500, or 1000 ppm of 1,3-butadiene via whole-body inhalation 5 hours/day, 5 days a week for 3 weeks. Body weights were measure 3 times a week. Interim sacrifices (5/group) were made after 1 and 2 weeks of exposure. Blood was collected for analysis of hemoglobin adducts (HB Val and THB Val adducts). Body weights in the 500-ppm group were significantly decreased (9, 10, 11, 10, and 8%) at days 9, 11, 14, 16, and 18, respectively compared to control. At 1000 ppm, body weights were significantly decreased (9, 10, 11, 11, 14, 15, 14, and 14%) at days 4, 7, 9, 11, 14, 16, and 18, respectively compared to control. Hemoglobin adducts increased with time and dose suggesting these may be valid biomarkers for biological monitoring of exposure. A LOAEL of 500 ppm was determined based on decreased body weight.	1329207 Lee, J. H., Kang, H. S., Han, D. H. (2005). Ratios of N-(2,3,4-trihydroxybutyl) valine and N-(2-hydroxy-3-butenyl) valine formed hemoglobin adducts in female mice inhalation exposure with 1,3-butadiene. Toxicology and Industrial Health 21(1):15-20.
Ten-week-old Sprague-Dawley rats were exposed to 0, 1.0, 6.3, or 63.1 ppm of 1,3-butadiene 6 hours/day, 5 days/week for 4 weeks. The study reports 160 animals will be used for exposure. It is unclear if this is 160/sex (40/sex/group) or 160 total animals (20/sex/group). Endpoints evaluated included mortality, clinical signs, and body weights. Blood and tissues (liver, spleen, kidneys, lungs, brain) were collected and sent to a third party to determine DNA and hemoglobin adduct levels. No morbidity or mortality were observed (data not shown). No abnormal clinical signs were observed (data not shown). Study only reports initial body weight data.	11273463 LRRI, (2005). [Redacted] 1,3-Butadiene: Whole-body inhalation exposure of rats and mice.
Ten-week-old B6C3F1 mice were exposed to 0, 1.0, 6.3, or 63.1 ppm of 1,3-butadiene 6 hours/day, 5 days/week for 4 weeks. The study reports 160 animals will be used for exposure. It is unclear if this is 160/sex (40/sex/group) or 160 total animals (20/sex/group). Endpoints evaluated included mortality, clinical signs, and body weights. Blood and tissues (liver, spleen, kidneys, lungs, brain) were collected and sent to a third party to determine DNA and hemoglobin adduct levels. No morbidity or mortality were observed (data not shown). No abnormal clinical signs were observed (data not shown). Study only reports initial body weight data.	11273463 LRRI, (2005). [Redacted] 1,3-Butadiene: Whole-body inhalation exposure of rats and mice.
Male and female B6C3F1 mice (5/sex/group) were exposed to the test substance at a concentration of 0, 625, 1250, 2500, 5000, or 8000 ppm (nominal concentrations) for 6 hours/day, 5 days/week, for 2 weeks. Animals were observed daily for mortality and signs of moribundity and weighed on days 0, 5, 10, and 15. Necropsies were performed on all animals on study day 15. Gross lesions and selected tissues (skin, mandibular lymph node, mesenteric lymph node, spleen, thymus, mammary gland, seminal vesicles, prostate, testes, ovaries, uterus, thigh muscle, sternebrae, vertebrae, femur [including bone marrow], costochondral junction [rib], salivary gland, esophagus, stomach, gallbladder, duodenum, jejunum, ileum, colon, cecum, rectum, sciatic nerve, brain, spinal cord, eyes, nasal cavity, nasal turbinates, larynx, pharynx, trachea, lungs, bronchi, thyroid glands, parathyroids, pituitary gland, adrenal glands, pancreas, liver, kidneys, urinary bladder, and heart) were examined. No mortalities occurred during the study. Final mean body weights of animals in the 5000 and 8000 ppm exposure groups were decreased by 16 and 10%, respectively, in males and by 18% and 17%, respectively, in females, compared to controls. No test substance-related effects were observed at necropsy. A NOAEL was not reported by the study authors. The reviewer did not determine a NOAEL value because the study has an overall rating of Uninformative.	62372 National Institutes of Health,, Department of Health and Human Services, (1984). Toxicology and carcinogenesis studies of 1,3-butadiene (CAS no. 106-99-0) in B6C3F1 mice (inhalation studies). 288:1-111.
Male and female B6C3F1 mice (10/sex/group) were exposed to the test substance at a concentration of 0, 625, 1250, 2500, 5000, or 8000 ppm (nominal concentrations) for 6 hours/day, 5 days/week, for 14 weeks (64 exposures). Because four males in the 8000 ppm group were dead by day 4, additional groups of males (10/sex/group) were similarly exposed to 0 or 8000 ppm for 6 hours/day, 5 days/week, for 14 weeks (63 exposures) in a supplemental study. Animals were observed daily for mortality and signs of moribundity and weighed on day 0 and then once weekly. Necropsies were performed on all animals at the end of the study. Gross lesions and selected tissues (skin, mandibular lymph node, mesenteric lymph node, spleen, thymus, mammary gland, seminal vesicles, prostate, testes, ovaries, uterus, thigh muscle, sternebrae, vertebrae, femur [including bone marrow], costochondral junction [rib], salivary gland, esophagus, stomach, gallbladder, duodenum, jejunum, ileum, colon, cecum, rectum, sciatic nerve, brain, spinal cord, eyes, nasal cavity, nasal turbinates, larynx, pharynx, trachea, lungs, bronchi, thyroid glands, parathyroids, pituitary gland, adrenal glands, pancreas, liver, kidneys, urinary bladder, and heart) were examined. Histopathological examinations were performed on animals of the control and 8000 ppm groups, and on all animals that died during the study. For males, survival in the 0, 625, 1250, 2500, 5000, and 8000 ppm groups was 10/10, 9/10, 9/10, 9/10, 4/10, and 4/10, respectively. For females, survival in the 0, 625, 1250, 2500, 5000, and 8000 ppm groups was 10/10, 9/10, 10/10, 10/10, 9/10, and 9/10, respectively. In the supplemental study, survival in the 0 and 8000 ppm groups was 10/10 and 4/10, respectively. The deaths of one animal of each sex at 625 ppm were considered by the study authors to be accidental. Final mean body weights of males were decreased by 13%, 25%, and 36% at 2500, 5000, and 8000 ppm, respectively, compared to controls. Final mean body weights of females were decreased by 12% and 19% at 5000 and 8000 ppm, respectively, compared to controls. For males in the supplemental study, final mean body weight was decreased by 39% at 8000 ppm compared to controls. No compound-related necropsy or histopathologic effects were reported. A NOAEL was not reported by the study authors. The reviewer did not determine a NOAEL value because the study has an overall rating of Uninformative.	62372 National Institutes of Health,, Department of Health and Human Services, (1984). Toxicology and carcinogenesis studies of 1,3-butadiene (CAS no. 106-99-0) in B6C3F1 mice (inhalation studies). 288:1-111.

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Summary	HERO ID and Citation
In a non-guideline study, male 102/E1 x C3H/E1)F1 mice aged 10-12 weeks were exposed via whole-body inhalation to 1,3-butadiene, presumably as a gas, at concentrations of 0, 130, or 1,300 ppm (experiment 1; n = 28/group) or to concentrations of 0, or 500 ppm (experiment 2; n = 8/control group and 24/exposed group) for 6 hours per day, for 5 consecutive days. Experiments 1 and 2 were conducted approximately 2 years apart but the same protocol was used. Control animals were sham-exposed to air only. On the last day of exposure, mice were shipped to a separate facility and were mated over three weeks (1 male: 2 females) with untreated B6C3F1 females that had been injected with pregnant mare serum and human chorionic gonadotropin. Details of mating were poorly described. It appears that animals were allowed a 24-hour mating period; the frequency is less clear, possibly once a week for three weeks. The percentage of mated females and unfertilized metaphase II oocytes were recorded. Mated females were injected with colchicine to arrest zygotes at first cleavage metaphase and were sacrificed 5 hours post-injection. Zygotes were examined for chromosome aberrations (evaluated in a separate form). Testis weights and flow cytometric analysis of testicular cell populations were conducted on 15 male mice/group after mating, 21, 28, and 35 days after the last exposure. Cytotoxicity was determined. Epididymal sperm was harvested from 5/treatment group and a total of 7 controls (specific control groups not specified) 28 days post-exposure to examine spermatocytes for chromatin changes via a sperm chromatin structure assay (SCSA) (evaluated in a separate form). Additional mice 21 and 35 days post-exposure in the 500 ppm group were also analyzed for effects on spermatogenic stages. Experiment 1: No effects on copulation, percent of mated females, or oocyte fertilization were observed. Absolute testis weights were significantly decreased at 130 ppm (9%) 21 days after exposure with no changes 28 or 35 days after exposure. Testis weights in the 1,300 ppm group after 21, 28, and 35 days of exposure were decreased by 29%, 33% and 14%, respectively. A concentration-related decrease in the number of round spermatids was observed 21 days after the last exposure, but not at other time points; the decreases were significant at $\geq$130 ppm. At 1,300 ppm, the number of elongated spermatids was significantly decreased on the 28 and 35-day sacrifices. Experiment 2: No effects on copulation or the percent of mated females were observed. A significant increase in the percentage of unfertilized oocytes was observed after the third week of mating despite a high value also in the controls. The average number of zygotes per female (presumably in all groups, including controls) was also lower than expected which the authors attributed to a decreased effectiveness of the female hormone treatments. A possibility of wrongly diagnosed vaginal plugs was also noted. Absolute testis weights were significantly reduced by 24% 21 and 28 days after treatment. The number of round spermatids was decreased on day 21 and elongated spermatids were significantly decreased on day 28 days after treatment. Overall: An author reported LD50 of 752 ppm was identified for differentiating spermatogonia, based on the decrease of elongated spermatids 28 days post-exposure. A LOAEC of 130 ppm was determined for this review, based on a low magnitude decrease (9%) in absolute testis weights and a significant decrease in the number of round spermatids. A NOAEC was not identified.	5553772 Pacchierotti, F., Tiveron, C., Ranaldi, R., Bassani, B., Cordelli, E., Leter, G., Spano, M. (1998). Reproductive toxicity of 1,3-butadiene in the mouse: Cytogenetic analysis of chromosome aberrations in first-cleavage embryos and flow cytometric evaluation of spermatogonial cell killing. Mutation Research 397(1):55-66.
In a non-guideline study, male 102/E1 x C3H/E1)F1 mice aged 10-12 weeks were exposed via whole-body inhalation to 1,3-butadiene, presumably as a gas, at concentrations of 0, 130, or 1,300 ppm (experiment 1; n = 28/group) or to concentrations of 0, or 500 ppm (experiment 2; n = 8/control group and 24/exposed group) for 6 hours per day, for 5 consecutive days. Experiments 1 and 2 were conducted approximately 2 years apart but the same protocol was used. Control animals were sham-exposed to air only. On the last day of exposure, mice were shipped to a separate facility and were mated over three weeks (1:2) with untreated B6C3F1 females that had been injected with pregnant mare serum and human chorionic gonadotropin. Details of mating were poorly described. It appears that animals were allowed a 24-hour mating period; the frequency is less clear and may have been once a week for three weeks. The percentage of mated females and unfertilized metaphase II oocytes were recorded. Mated females were injected with colchicine to arrest zygotes at first cleavage metaphase and were sacrificed 5 hours post-injection. Zygotes (first cleavage embryos) were examined for chromosome aberrations (chromosome breaks and exchanges). Epididymal sperm was harvested from 5/treatment group and a total of 7 controls (specific control groups not specified) 28 days post-exposure to examine spermatocytes for chromatin changes via a sperm chromatin structure assay (SCSA) (acridine orange staining to identify double-stranded vs. single-stranded DNA). Experiment 1: There was a significant increase in the number of zygotes with chromosomal aberrations in the 1,300 ppm group after the first and second weeks of mating. When considering the results from the 500 ppm group (experiment 2), there was a significant dose-related trend. The aberrations were primarily chromosome breaks or exchanges. There was a significant increase in the number of sperm with single-stranded DNA and in the percentage of sperm outside the main population at 1,300 ppm, 28 days after exposure.Experiment 2: There was an increase in the number of zygotes with chromosomal aberrations after the first mating, but not after the 2nd or 3rd matings. The aberrations were primarily chromosome breaks or exchanges. When considering the results from the 1300 ppm group (experiment 1), there was a significant dose-related trend. Results from the SCSA assay showed a significant increase in the percentage of variant sperm outside of normally distributed values 35 days after exposure. Overall, the test substance was positive for inducing chromosome aberrations in zygotes and sperm.	5553772 Pacchierotti, F., Tiveron, C., Ranaldi, R., Bassani, B., Cordelli, E., Leter, G., Spano, M. (1998). Reproductive toxicity of 1,3-butadiene in the mouse: Cytogenetic analysis of chromosome aberrations in first-cleavage embryos and flow cytometric evaluation of spermatogonial cell killing. Mutation Research 397(1):55-66.

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1,3-Butadiene- Parent compound - Short-term (>1-30 days)

Summary	HERO ID and Citation
Experiment I. In a short-term inhalation study, male mice were exposed to the test substance for 6 hours/day, on 5 consecutive days at concentrations of 0, 500, and 1300 ppm. HERO ID 2448931 was cited in the reference for the inhalation study methodology. Exposure groups were evaluated for body weight, absolute and relative (to body weight) testis weights, ratio of Golgi phase cells to Golgi plus cap phase spermatids (calculated as G/G + C) as a measure of toxicity in germ cells, and genotoxicity (frequency of micronuclei in early spermatids). Animals were examined at 2 to 5 days following exposure for controls, and at 2, 5, 11, and 15 days post-exposure for the 500 and 1300 ppm groups. No significant effects were observed on body weight. Testis weights (absolute and relative) were significantly decreased at both concentrations at 11 and 15 days post-exposure, compared to the control group. Mechanistic findings included significant decreases in the ratio of Golgi phase cells to Golgi plus cap phase spermatids at both concentrations for most timepoints evaluated, compared to controls. The frequencies of micronuclei in early spermatids were significantly increased at both concentrations at 15 days post-exposure, compared to controls. The absence of a clear dose-response relationship for micronuclei formation was attributed by the study authors to cytotoxicity at the highest concentration. The LOEL (determined by the reviewer) was 500 ppm based on decreased testis weights (absolute and relative to body weight) and decreased ratio of Golgi phase cells to Golgi plus cap phase spermatids at the lowest concentration tested. The study was also positive for increased micronuclei formation in early spermatids.	5546732 Xiao, Y., Tates, A. D. (1995). Clastogenic effects of 1,3-butadiene and its metabolites 1,2-epoxybutene and 1,2,3,4-diepoxybutane in splenocytes and germ cells of rats and mice in vivo. Environmental and Molecular Mutagenesis 26(2):97-108.
Experiment II. In a short-term inhalation study, male mice were exposed to the test substance for 6 hours/day, on 5 consecutive days at concentrations of 0, 200, 500, and 1300 ppm. HERO ID 2448931 was cited in the reference for the inhalation study methodology. Exposure groups were evaluated for body weight, absolute and relative (to body weight) testis weights, ratio of Golgi phase cells to Golgi plus cap phase spermatids (calculated as G/G + C) as a measure of toxicity in germ cells, and genotoxicity (frequency of micronuclei in early spermatids). Animals were examined at 15 days post-exposure for the control and test substance-exposed groups. No significant effects were observed on body weight. Testis weights (absolute and relative) were significantly decreased at 1300 ppm, compared to the control group. Mechanistic findings included a significant decrease in the ratio of Golgi phase cells to Golgi plus cap phase spermatids at the 1300 ppm, compared to controls. The frequency of micronuclei in early spermatids was significantly increased at all test concentrations (200, 500, and 1300 ppm), compared to controls. The absence of a dose-response relationship (particularly for the highest concentration) for micronuclei formation was attributed by the study authors to cytotoxicity at the highest concentration. The LOEL (determined by the reviewer) was 200 ppm based on increased micronuclei formation in spermatids at 200 ppm; there were also decreased testis weights (absolute and relative to body weight) and decreased ratio of Golgi phase cells to Golgi plus cap phase spermatids at 1300 ppm.	5546732 Xiao, Y., Tates, A. D. (1995). Clastogenic effects of 1,3-butadiene and its metabolites 1,2-epoxybutene and 1,2,3,4-diepoxybutane in splenocytes and germ cells of rats and mice in vivo. Environmental and Molecular Mutagenesis 26(2):97-108.

1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Summary	HERO ID and Citation
In a dominant lethality study, male CD-1 nice (25/control and low exposure group, 50/high exposure group) were exposed, whole body, to 1,3-butadiene gas at 0, 12.5 or 1,250 ppm 6hrs/day 5 days/week for 10 weeks. One day after the last exposure, males were co-housed with females (1:2) for 1 week. One of the females was killed on GD 17, and the other was allowed to deliver. Uterine contents of the sacrificed female were examined for the number of live fetuses and post-implantation deaths. The fetuses were examined for gross malformations including runts. Skeletal examinations were performed on malformed fetuses and randomly selected normal littermates. The livers were karyotyped. Body weights were purportedly measured, but no further details on which animals were weighed and when. Delivered F1 offspring (control and high exposure group only) were maintained to 75 weeks. Animals were examined grossly for tumors; those observed were kept for histopathological examination (not performed in this study). Two males in the 1,200 ppm group died: one after week 5 and one after week 7 of exposure. No changes in body weights were observed in surviving animals (data not shown). The percentage of pregnant females was 82%, 90%, and 77% for the controls, 12.5 and 1,250 ppm groups, respectively. There was a significant decrease in the number of implantations and early deaths at 1,250 ppm. Late deaths and late deaths including dead fetuses (per implantation per pregnancy) were increased in both exposure groups, compared with controls. Controls had no pre-implantation deaths or any fetal abnormalities. The total number of abnormal fetuses in the low exposure group was reported to be 7/282 (3 incidences of exencephaly in one litter, 1 in another, two runts (separate litters), and 1 fetus with blood in the amniotic sac), although it was later reported in the text that the incidence was 2.29% (7/306; there were 306 implantations). At 1,200 ppm there were 3 fetal abnormalities out of 406 implantations (0.74%); one with hydrocephaly, and two different litters with one runt. The mean number of abnormal fetuses per implantation per pregnancy was reported to be statistically different from controls in both exposure groups; however, when considering the historical control data, (0.75%; 22/2969), it is unclear how the authors obtained significance for the high exposure group. Karyotyping results were normal.No author-provided toxicity values were reported. A reproductive/developmental LOAEC of 12.5 ppm was identified based on a significant increase in late fetal deaths and evidence of abnormal fetuses. A NOAEC was not determined. The test substance was positive for dominant lethality.	5663561 Anderson, D., Edwards, A. J., Brinkworth, M. H., Hughes, J. A. (1996). Male-mediated F1 effects in mice exposed to 1,3-butadiene. Toxicology 113(1-3):120-127.
In a study conducted according to U.S. EPA TG 40CFR 798.2450 B6C3F1/CrlBR mice (10/sex/group) were exposed to 1,3-butadiene gas at 0, or 1,000 ppm (target) via whole-body inhalation for 6 hrs/day, 5 days/week for 13 weeks (total of 65 exposures). Endpoints evaluated included mortality, clinical signs, body weight, body weight gain, food consumption, hematology, and clinical chemistry. Select organs were weighed (heart, lungs, liver, kidneys, spleen, testes, and brain) at gross necropsy, and microscopic analysis was conducted on >30 tissues. Test atmospheres were monitored using GC, and the mean measured concentration was 980 $\pm$ 16 ppm. Two mice (sex not specified) died; the authors did not attribute the deaths to exposure. The results of clinical observations were not reported. There were no significant effects on body weight or weight gain throughout the exposure period. There were no changes in food consumption. Red blood cell indices were significantly changed in both sexes. RBC counts, hemoglobin, and hematocrit were significantly reduced, compared with controls, and MCV, MCH, and MCHC (males only), were significantly increased. An increase in reticulocytes and lymphocytes was also observed in males and platelets were reduced in both sexes. Organ weight changes included significant decreases in absolute (34%) and relative (36%) testes weights in males, increases in absolute (data not shown) and relative (8%) liver weights in females, and a decrease in relative spleen (12%) weight in females. Testes weight changes corresponded with slight testicular atrophy in 10/10 (vs. 4/10 in controls) of the males examined. The testicular atrophy was described as being slight, primarily unilateral, and not associated with changes in sperm quality or quantity. 3/10 exposed females showed splenic lymphoid atrophy, and 6/10 exposed females also had incidences of ovarian atrophy, characterized as "a severe reduction of all developmental stages of ovarian follicles," compared to zero in controls. No histopathological changes to the liver were specified. A LOAEC of 980 ppm was identified based on hematological changes consistent with macrocytic anemia, and organ-specific toxicity to the testis, ovary, and spleen in exposed mice. A NOAEC was not identified.	5660612 Bevan, C., Stadler, J. C., Elliott, G. S., Frame, S. R., Baldwin, J. K., Leung, H. W., Moran, E., Panepinto, A. S. (1996). Subchronic toxicity of 4-vinylcyclohexene in rats and mice by inhalation exposure. Fundamental and Applied Toxicology 32(1):1-10.
In a study conducted according to U.S. EPA TG 40CFR 798.2450 Crl:CD BR (Sprague Dawley) rats (10/sex/group) were exposed to 1,3-butadiene gas at 0, or 1,000 ppm (target) via whole-body inhalation for 6 hrs/day, 5 days/week for 13 weeks (total of 65 exposures). Endpoints evaluated included mortality, clinical signs, body weight, body weight gain, food consumption, hematology, clinical chemistry, and urinalysis. Select organs were weighed (heart, lungs, liver, kidneys, adrenal glands, spleen testes, ovaries, and brain) at gross necropsy, and microscopic analysis was conducted on >30 tissues. Test atmospheres were monitored using GC, and the mean measured concentration was 980 $\pm$ 16 ppm.No mortality was observed. The results of clinical observations were not reported. There were no significant effects on body weight or weight gain throughout the exposure period. There were no changes in food consumption. No exposure-related hematological, clinical chemistry or urinalysis changes were observed (data not shown). Relative organ weight changes included significant increases in liver (8%) and kidney (12%) weights in male rats. Female organ weights were comparable to controls. No changes in absolute organ weights were observed (data not shown). The only histopathological changes included a non-statistically significant increase in hyaline droplets in 2/10 males. Hyaline droplets are a normal feature of male rats of this strain and age. It is unclear if the changes were related to alpha-2u-globulin.The authors reported a NOEC of 980 ppm based on the lack of clear exposure-related effects. Although the increase in relative kidney weights in males was >10% and potentially biologically relevant, there were no increases in absolute kidney weights and no kidney weight changes in females.	5660612 Bevan, C., Stadler, J. C., Elliott, G. S., Frame, S. R., Baldwin, J. K., Leung, H. W., Moran, E., Panepinto, A. S. (1996). Subchronic toxicity of 4-vinylcyclohexene in rats and mice by inhalation exposure. Fundamental and Applied Toxicology 32(1):1-10.

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Summary	HERO ID and Citation
In a dominant lethality study, male Sprague-Dawley rats (25/group) were exposed to butadiene gas (purity ≥99.7%) at 0 (air control), 65, 400, and 1250 ppm (0, 144, 885, 2,765 mg/m3) for 6hrs/day, 5 days/ week for 10 weeks. An additional group of room (untreated) control animals (n =50) was also included. Three days after the last exposure, males were mated to untreated females for up to 10 days. During exposure, males were monitored for mortality and any deviations from normal. Body weights were recorded weekly. Males were necropsied at the end of the mating period. Females were weighed, sacrificed on GD20, and were also subjected to gross necropsy.Reproductive behavior and pregnancy success were determined based on mating frequency, pregnancy rate, period of coition, number of corpora lutea, and implantation sites. Other endpoints included examinations for post-implantation losses (early and late deaths, or deaths including dead fetuses), fetal sex, weights of any live fetuses, and examinations for abnormalities and malformations. A single male in the 133 mg/m3 group died (cause unknown). Although the methods indicated that animals were observed during exposure, no observational results or gross necropsy results were reported. There were no treatment-related effects on male body weight or reproductive behavior. Female body weight results were not reported. There was a significant reduction in the number of implantations in the 65 ppm group, but not in the mid or high-exposure groups. All of the endpoints included in the dominant lethal assay were comparable across groups. Fetal sex results were not reported. The authors concluded that the test substance was negative for dominant lethality in the current study. A NOAEC of 1,250 ppm (2,765 mg/m3) was determined based on the lack of adverse effects. Exposure concentrations were converted from ppm to mg/m3 using the following formula: mg/m3 = (ppm x MW)/ 24.45, using a MW of 54.09.	5674659 BIBRA, (1996). Detection of dominant lethal mutations and foetal malformations in the offspring of male rats treated subchronically w/1,3-butadiene by inhalation w/cover letter dated 01/10/1997.
In a non-guideline dominant lethality test, male CD-1 mice (30/group) were exposed, via whole-body inhalation, to 1,3-butadiene (purity not reported) gas (presumed) at 0, 12.5, 125 ppm for 6 hrs/day, 5 days/week for 10 weeks. Males were monitored for clinical signs, and body weights were measured before and at the end of the exposure period. One day after the last exposure, 25 males/group were caged with two virgin females for a maximum of 7 days. The time to coition was recorded and the proportion of males siring litters and the number of females pregnant were determined. The females were sacrificed on GD17 and uterine content was examined for the number of implantation sites, the number of early and late deaths, and the number of live fetuses. Live fetuses were examined for gross malformations at necropsy. The remaining 5 males/group were used for DNA damage repair and UDS assays (evaluated separately), but sperm was extracted from the cauda epididymis and counted. All males appeared healthy and there were no exposure-related effects on body weights (data not shown). There was an exposure-concentration-related delay in the time to coition that became significant at 125 ppm. No differences in fertility were observed. There was a significant increase in early deaths in the high-exposure group, compared with controls. Incidences of late deaths and in dead fetuses were also higher in exposed animals, but the increases did not reach statistical significance. Several abnormalities were observed, but there were no statistically significant differences between the controls and the exposure groups. It was noted that sperm counts were 100-1,000 fold lower than what would normally be expected, but data for each group were not reported, and it is unclear if the observed effect was for animals in the exposure groups only.No author-reported toxicity values were provided. A NOAEC of 12.5 ppm (27.7 mg/m3) and an LOAEC of 125 ppm (277 mg/m3) were determined for this review based on an increase in early fetal deaths and a delay in the time to coition. The test substance was positive for dominant lethality.mg/m3 = ppm (MW) ÷ 24.45, using a MW of 54.0916g/mol	4934798 Brinkworth, M. H., Anderson, D., Hughes, J. A., Jackson, L. I., Yu, T. W., Nieschlag, E. (1998). Genetic effects of 1,3-butadiene on the mouse testis. Mutation Research 397(1):67-75.
In a non-guideline dominant lethality test, male CD-1 mice (30/group) were exposed, via whole body inhalation, to 1,3-butadiene (purity not) gas (presumed) at 0, 12.5, 125 ppm for 6 hrs/day, 5 days/week for 10 weeks. Males were monitored for clinical signs and body weights were measured prior to and at the end of the exposure period. 5 males/group were used for DNA damage repair (Comet) and UDS assays. At the end of exposure, one testis was removed and used for the Comet assay. The remaining testis was injected with tritiated thymidine, and animals were killed after 17 days. Radioactivity was determined, in duplicate, from 10^4 sperm.No mortality was reported, but the sample size was n = 4 for the UDS assay; no explanations were provided. No statistically significant increases in DNA damage (comet assay) or unscheduled DNA synthesis were observed in any exposure group. Due to high inter-animal variability, no increases in tritiated thymidine counts reached statistical significance. No author-reported toxicity values were provided. Although a positive response was observed in the comet assay at 125 ppm, this assay is not appropriate for determining DNA strand breaks in sperm cells (OECD TG 489); therefore, a determination of genotoxicity cannot be concluded for this study.	4934798 Brinkworth, M. H., Anderson, D., Hughes, J. A., Jackson, L. I., Yu, T. W., Nieschlag, E. (1998). Genetic effects of 1,3-butadiene on the mouse testis. Mutation Research 397(1):67-75.

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Summary	HERO ID and Citation
In a non-guideline dominant lethality test, male CD-1 mice (30/group) were exposed, via whole-body inhalation, to 1,3-butadiene (purity not reported) gas (presumed) at 0, 12.5, 125 ppm for 6 hrs/day, 5 days/week for 10 weeks. Males were monitored for clinical signs and body weights were measured before and at the end of the exposure period. One day after the last exposure, 25 males/group were caged with two virgin females for a maximum of 7 days. The time to coition was recorded and the proportion of males siring litters and the number of females pregnant were determined. The females were sacrificed on GD17 and uterine content was examined for the number of implantation sites, the number of early and late deaths, and the number of live fetuses. Live fetuses were examined for gross malformations at necropsy. The remaining 5 males/group were used for DNA damage repair and UDS assays (evaluated separately), but sperm was extracted from the cauda epididymis and counted. All males appeared healthy and had no exposure-related effects on body weights (data not shown). There was an exposure-concentration-related delay in the time to coition that became significant at 125 ppm. No differences in fertility were observed. There was a significant increase in early deaths in the high-exposure group, compared with controls. Incidences of late deaths and dead fetuses were also higher in exposed animals, but the increases did not reach statistical significance. Several abnormalities were observed, but there were no statistically significant differences between the controls and the exposure groups. It was noted that sperm counts were 100-1,000 fold lower than what would normally be expected, but data for each group were not reported, and it is unclear if the observed effect was for animals in the exposure groups only. The test substance was positive for eliciting dominant lethality.	4934798 Brinkworth, M. H., Anderson, D., Hughes, J. A., Jackson, L. I., Yu, T. W., Nieschlag, E. (1998). Genetic effects of 1,3-butadiene on the mouse testis. Mutation Research 397(1):67-75.
In a subchronic inhalation toxicity study, Sprague-Dawley rats (40/sex/group), were exposed to 1,3-butadiene gas, at nominal concentrations of 0, 2,200, 4,400, 8,800, and 17,600 mg/m3 (0, 1,000, 2,000, 4,000, and 8,000 ppm; v/v) for 6 hrs/day, 5 days/week for 13 weeks. Ten animals per sex were sacrificed after 2 and 6 weeks of exposure. Animals were monitored daily for mortality and clinical signs of toxicity. Body weights were measured weekly and food consumption was monitored continuously. Blood was collected one week prior to sacrifice for limited hematological and clinical chemistry analysis. At the end of the study, prothrombin time, erythrocyte cholinesterase, erythrocyte sulfhydryl groups, and erythrocyte reduced sulfhydryl groups were also measured. Urinalysis was conducted at the end of the study. Before the 13-week termination, neuromuscular function was assessed using a rotating cone test. Necropsies were performed on all animals. Brain cholinesterase activity was measured at weeks 2 and 6 (5/sex), and 13 (all remaining animals). Organ weights (adrenals, brain, gonads, heart, kidney, liver, lung, pituitary, spleen, and thyroid) were recorded and histopathology was conducted on >30 tissues in animals from the control and high exposure groups. Five animals died (group and cause of death not specified). Increases in salivation and reductions in grooming were noted in females after ~8 weeks. The significance was not specified, but the effect was reported to be dose-related. An unknown number of males showed similar signs after 10 weeks. Female body weights were increased at 2,200 and 8,800 mg/m3 at the end of the study and body weight gains (weeks 1-13) were significantly increased at 8,800 mg/m3. Slight reductions in male body weights were not statistically significant by the end of the study, and body weight gains were directionally inconsistent throughout the study. The magnitudes of change were not specified. No changes in food consumption were observed. Clinical chemistry measurements showed statistically significant decreases in the globulin fraction of plasma protein in both sexes after 6 weeks, but not at 13 weeks (exposure groups not specified). At the end of the study, glutamic pyruvic transaminase in males was decreased but was within normal limits. Erythrocyte cholinesterase activity in males was significantly increased at $\geq$ 2,200 mg/m3 at six weeks, and at $\geq$ 4,400 mg/m3 at 13 weeks. In females, similar increases were observed at $\geq$4,400 mg/m3 at 2, 6, and 13 weeks. The authors described the changes in males at 6 weeks as “highly significant” yet did not consider the changes to be an adverse effect of treatment. No other significant clinical chemistry, hematology, or urinalysis changes were observed. Brain cholinesterase activity was significantly decreased in males at 8,800 mg/m3 only at 6 and 13 weeks; no changes were observed in females. No consistent or concentration-related effects were observed during neuromuscular function tests. Significant organ weight changes were reported to be “scattered” and not treatment-related (data not shown). Lungs from all groups (including controls) showed pulmonary congestion at 6 and 13 weeks, and microscopic analysis indicated pneumonitis, infiltration of immune cells, and medial hypertrophy of arterioles. Histopathology in the trachea, larynx, nasal turbinates, and other tissues of treated animals was comparable to controls. The author reported NOAEC = 17,600 mg/m3 (8,000 ppm) based on the lack of untoward effects. The confidence in the results is reduced due to the inability to independently verify the reported results.	94760 Crouch, C. N., Pullinger, D. H., Gaunt, I. F. (1979). Inhalation toxicity studies with 1,3-butadiene - 2 3 month toxicity study in rats. Journal of Occupational and Environmental Hygiene 40(9):796-802.
B6C3F1 mice (10/sex/group) were exposed to 0, 609, 1240, 2445, 4934, or 7780 ppm of 1,3-butadiene 6 hours/day 13 weeks for a total of 64 days. The study does not report how many days/week animals were exposed. Endpoints evaluated included mortality, clinical signs, body weights, gross necrosis, and histopathology (on control, 7780 ppm group and any animals that died early). Increased mortality was seen in the 4934 and 7780 ppm exposed males compared to control. No increase in mortality was seen in females. The following mortality numbers were reported in males (0/10, 1/10, 1/10, 1/10, 6/10, and 6/10) and females (0/10, 1/10, 0/10, 0/10, 1/10, and 1/10) at 0, 609, 1240,2445, 4934, and 7780 ppm, respectively. Alopecia was observed the control mice and in the 609, 1240, and 7780 ppm groups (not significantly different). Males and females exposed to $\geq$ 4934 ppm were hypoactive and had rough coats; these effects were not observed in controls. Terminal body weights were significantly decreased in males (13, 25, and 36%) at 2445, 4934, and 7780 ppm, respectively and in females (12 and 19%) at 4934, and 7780 ppm, respectively. Change in body weight was also significantly decreased in males $\geq$2445 ppm and females at $\geq$4934 ppm from 0-7 week and in males $\geq$2445 ppm and females at 7780 ppm from 0-14 weeks. No compound-related gross or histopathological effects were observed compared to control.	11273565 IBT Labs, (1977). Report to Tracor Jitco, Inc: Subchronic inhalation study with 1,3-butadiene (C50602) in B6C3F1 mice.

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Summary	HERO ID and Citation
B6C3F1 mice (10/sex/group) were exposed to 0, or 7786 ppm of 1,3-butadiene 6 hours/day for 13 weeks for a total of 63 days. The study does not report how many days/week animals were exposed. Endpoints evaluated included mortality, clinical signs, body weights, gross necrosis, and histopathology. Mortality was significantly increased in the 7786-ppm group (6/10 died) compared to control (0/10 died). Alopecia was observed in one control mouse, but not in any other mice. Clinical signs observed more in the exposed group but not in the control included hypoactivity (7/10), ruffed fur (7/10), ataxia (2/10), necrotic penis (1/10), and oily fur (3/10). Body weights were significantly decreased >10 % from week 3 until the end of the study, with terminal body weights 38% lower than control. No compound-related gross or histopathological changes were observed.	11273565 IBT Labs, (1977). Report to Tracor Jitco, Inc: Subchronic inhalation study with 1,3-butadiene (C50602) in B6C3F1 mice.
In a study focused on examining immunomodulatory effects of exposure, groups of male B6C3F1 mice (number per group per time point not specified) were exposed whole-body to 1,3-butadiene (99.5% pure) at concentrations of 0 (filtered air control) or 1,250 ppm for 6 hours/day, 5 days/week for a total of 6, 12, or 24 weeks. No monitoring of animals during the exposure period was specified. Mortality was not assessed. At an unspecified time prior to sacrifice, animals (duration not specified) were immunized with sheep red blood cells and IgM antibody plaque-forming cell (PFC) responses were quantitated. At the time of sacrifice, body weights were recorded along with spleen and thymus weights (duration group not specified). These organs were histologically examined in animals exposed for 24 weeks only. Splenocytes were purified from the spleens of animals exposed for 6 or 12 weeks and were labelled using immunofluorescent antibodies for several cell surface markers. The antibody combinations were then examined using flow cytometry. Cell-mediated immune function was assessed by measuring splenocyte lymphoproliferative responses to mitogens in a microculture assay. Briefly, lymphocytes isolated from control and exposed mice that were pulsed with tritiated thymidine were cultured for 72 hours with a panel of mitogens and cell proliferation was monitored. Several other in vitro assays were conducted including: the measurement of lymphocyte proliferation and cytotoxicity to an alloantigen; assessment of T-cell-mediated cytotoxicity against a target cell; and measurements of spontaneous natural killer cell cytotoxicity.There were no effects on body weight following 6 weeks of exposure. Body weight data were not shown for the other exposure durations, although it is unclear whether this endpoint was measured in all groups. Following a 6-week exposure, there were no effects on absolute or relative thymus weights, or on absolute spleen weights. Relative spleen weights were significantly decreased (-20%), compared with controls (no organ weight data were reported for other durations). Spleen cellularity was significantly decreased by 29% and 11% at 6 and 12 weeks, respectively. The effect returned to normal by 18 weeks. No effects on bone marrow cellularity were observed. Histopathology at 24 weeks showed increases in splenic erythroid hyperplasia and extramedullary hematopoiesis (incidences and significance not reported). A minor decrease in cellularity in periarteriolar sheaths and lymphoid follicles was also noted. Thymuses had moderate decreases in the number of cortical lymphocytes (again, incidences and significance not reported).Analysis of splenocyte surface markers was suggestive of a significant decrease in the number of cytotoxic/suppressor T cells, but no changes in the percentage of helper T lymphocytes or in B cells. No effects on humoral immunity (assessed by the number of IgM antibody PFC per 10^6 splenocytes) were observed; however, the number of PFCs per spleen was significantly suppressed by 30%, which corresponded with the decreased splenic cellularity and weight. Spontaneous lymphocyte proliferation was significantly increased in the mitogen assay and in the mixed alloantigen cultures. Proliferative responses to the PHA mitogen were suppressed by 45% and 24% in the 6 and 12-week exposure groups, respectively. The authors noted that these results may not be biologically significant because there is only marginal evidence of a correlation between responses to mitogens and functional immune changes. At 12 weeks, responses of T-cells to Con A and LPS-induced B-lymphocyte proliferation were significantly suppressed. In vitro assays showed an 11% reduction in cytotoxic T-lymphocyte generation after 6 weeks, but no differences from controls after 12 weeks. No differences in targeted cell cytotoxicity were observed.Overall, the authors concluded that there was "no direct or persistent immunomodulatory effect on functional end-stage cells," and that there were no important exposure-related immunological defects observed. These statements are suggestive of a NOAEC of 1,250 ppm, based on the lack of clearly adverse immunological effects.	62366 Thurmond, L. M., Lauer, L. D., House, R. V., Stillman, W. S., Irons, R. D., Steinhagen, W. H., Dean, J. H. (1986). Effects of short-term inhalation exposure to 1,3-butadiene on murine immune functions. Toxicology and Applied Pharmacology 86(2):170-179.

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1,3-Butadiene- Parent compound - Subchronic (>30-91 days)

Summary	HERO ID and Citation
In a study focused on examining immunomodulatory effects of exposure, groups of male B6C3F1 mice (number per group per time point not specified) were exposed whole-body to 1,3-butadiene (99.5% pure) at concentrations of 0 (filtered air control) or 1,250 ppm for 6 hours/day, 5 days/week for a total of 6, 12, or 24 weeks. No monitoring of animals during the exposure period was specified. Mortality was not assessed. At an unspecified time prior to sacrifice, animals (duration not specified) were immunized with sheep red blood cells and IgM antibody plaque-forming cell (PFC) responses were quantitated. At the time of sacrifice, body weights were recorded along with spleen and thymus weights (duration group not specified). These organs were histologically examined in animals exposed for 24 weeks only. Splenocytes were purified from the spleens of animals exposed for 6 or 12 weeks and were labelled using immunofluorescent antibodies for several cell surface markers. The antibody combinations were then examined using flow cytometry. Cell-mediated immune function was assessed by measuring splenocyte lymphoproliferative responses to mitogens in a microculture assay. Briefly, lymphocytes isolated from control and exposed mice that were pulsed with tritiated thymidine were cultured for 72 hours with a panel of mitogens and cell proliferation was monitored. Several other in vitro assays were conducted including: the measurement of lymphocyte proliferation and cytotoxicity to an alloantigen; assessment of T-cell-mediated cytotoxicity against a target cell; and measurements of spontaneous natural killer cell cytotoxicity.There were no effects on body weight following 6 weeks of exposure. Body weight data were not shown for the other exposure durations, although it is unclear whether this endpoint was measured in all groups. Following a 6-week exposure, there were no effects on absolute or relative thymus weights, or on absolute spleen weights. Relative spleen weights were significantly decreased (-20%), compared with controls (no organ weight data were reported for other durations). Spleen cellularity was significantly decreased by 29% and 11% at 6 and 12 weeks, respectively. The effect returned to normal by 18 weeks. No effects on bone marrow cellularity were observed. Histopathology at 24 weeks showed increases in splenic erythroid hyperplasia and extramedullary hematopoiesis (incidences and significance not reported). A minor decrease in cellularity in periarteriolar sheaths and lymphoid follicles was also noted. Thymuses had moderate decreases in the number of cortical lymphocytes (again, incidences and significance not reported).Analysis of splenocyte surface markers was suggestive of a significant decrease in the number of cytotoxic/suppressor T cells, but no changes in the percentage of helper T lymphocytes or in B cells. No effects on humoral immunity (assessed by the number of IgM antibody PFC per 10^6 splenocytes) were observed; however, the number of PFCs per spleen was significantly suppressed by 30%, which corresponded with the decreased splenic cellularity and weight. Spontaneous lymphocyte proliferation was significantly increased in the mitogen assay and in the mixed alloantigen cultures. Proliferative responses to the PHA mitogen were suppressed by 45% and 24% in the 6 and 12-week exposure groups, respectively. The authors noted that these results may not be biologically significant because there is only marginal evidence of a correlation between responses to mitogens and functional immune changes. At 12 weeks, responses of T-cells to Con A and LPS-induced B-lymphocyte proliferation were significantly suppressed. In vitro assays showed an 11% reduction in cytotoxic T-lymphocyte generation after 6 weeks, but no differences from controls after 12 weeks. No differences in targeted cell cytotoxicity were observed.Overall, the authors concluded that there was "no direct or persistent immunomodulatory effect on functional end-stage cells," and that there were no important exposure-related immunological defects observed. These statements are suggestive of a NOAEC of 1,250 ppm, based on the lack of clearly adverse immunological effects.However, the only data reported for mice exposed for 24 weeks were insufficiently reported histopathology results. These data are insufficient for the determination of POD.	62366 Thurmond, L. M., Lauer, L. D., House, R. V., Stillman, W. S., Irons, R. D., Steinhagen, W. H., Dean, J. H. (1986). Effects of short-term inhalation exposure to 1,3-butadiene on murine immune functions. Toxicology and Applied Pharmacology 86(2):170-179.

1,3-Butadiene- Parent compound - Chronic (>91 days)

Summary	HERO ID and Citation
B6C3F1 mice (50/sex/group) were exposed to 0, 627, or 1236 ppm of 1,3-butadiene for 6 hours/day, 5 days/week for either 61 weeks (males) or 62 weeks (females). Endpoints evaluated included, mortality, clinical sign and body weight (weekly for the first 91 days, and monthly thereafter), gross necropsy, and histopathology on gross lesions and a complete panel of 31 tissue and organs. A significant increase in mortality was seen in males and females at ≥627 ppm compared to control (males 1/50, 37/50, 44/50; females: 4/50, 34/50, 19/50 in control, low and high dose groups, respectively). Alopecia was observed in all groups of mice including controls during the course of the study and was not considered compound related. Terminal body weights were not significantly different from control (determined by this Reviewer with data reported by study authors). The study states that incidence data for neoplastic and non-neoplastic lesion can be found in Tables 3C, 4C, 3D, and 4D, however these tables are not included in this copy and could not be reviewed. Non-neoplastic lesions observed included chronic inflammation of the nasal cavity in high dose males, ovarian and testicular atrophy in low and high dose males and females, and uterine involution in low and high dose females. In addition, increases in hyperplastic lesions of granulosa cells and ovarian epithelial cells were seen in exposed females, and increased incidence of alveolar epithelial hyperplasia in both sexes (occurring more often in exposed females than males). Neoplastic lesions observed include hemangiosarcoma of the heart, "with metastatic lesions primarily in the liver, lung, and some other locations" in both males and females in the low and high dose groups compared to control. The study also reports inflammation in the heart, which was considered an early or pre-neoplastic lesion of hemangiosarcoma. Increased incidences of malignant lymphomas were observed in both exposure groups, occurring more frequently in males than females. Increased incidence of alveolar/bronchiolar adenomas in low and high dose group males and high dose females, and alveolar bronchiolar carcinomas in high dose males and low and high dose females were seen compared to control. Incidences of forestomach squamous cell papillomas and squamous cell carcinomas were increased in exposed males and females, occurring predominantly in high dose females. Increased incidences of mammary carcinomas (adenosquamous and acinar cell) and ovarian tumors (granulosa cell tumors, tubular adenomas) were observed in low and high dose females compared to control. Preputial gland tumors and brain tumors were observed in male mice, however the authors not the significance of these tumors is unknown.	5554646 Battelle PNL, (1982). Initial submission: Tracor Jitco inhalation carcinogenesis bioassay: Chronic study report in 1,3-butadiene in mice (final report) with attachments and cover letter dated 112191.

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Summary	HERO ID and Citation
CD strain rats (110/sex/group) were exposed to 0, 1000 or 8000 ppm of 1,3-Butadiene for 6 hours/day, 5 days/week for 105 weeks for females or 111 weeks for males. Animals were monitored for mortality and clinical signs of toxicity daily, and body weights were measured every weekly. Endpoints assessed at the end of the exposure duration included hematology (mean cell volume (MCV), haemoglobin concentration (Hb), red cell count, white blood cell count (WBC), lymphocytes, platelets, reticulocytes, packed cell volume (PCV), mean cell haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC), blood serum chemistry (glucose, blood urea nitrogen (BUN), total protein, electrophoresis of total proteins, alkaline phosphatase, glutamic oxaloacetic transaminases, glutamate pyruvate transaminase), urinalysis (glucose, blood, urobilinogen, protein, ketones, pH, bile pigments, bile salts), organ weights (spleen, heart, brain, liver, testes, adrenal glands), gross pathology, histopathology (lymph nodes, spleen, thymus, bone marrow, brain, sciatic nerve, spinal cord, optic nerve, lungs, diaphragm, trachea, larynx, heart, aorta, mammary gland, epididymis, prostate, seminal vesicle, gonads, vagina, femur, sternum, turbinate bones, kidneys, urinary bladder, ears, skin, oesophagus, caecum, colon, tongue, salivary gland, small intestine, stomach, adipose tissue, adrenal glands, parathyroid, pituitary, thyroid, eyes, harderian gland) and identification of neoplastic lesions (tumors in tissues including: mammary, thyroid, uterus/vaginal stroma, Leydig cells, pancreatic exocrine and Zymbal gland). Gross pathology and histopathology were only performed for control and 8000 ppm animals. Additionally, transmission scanning electron microscopy was performed on liver tissue cross sections and 40 animals/sex/group were tested for neuromuscular function using a modified rotarod test. Significant mortality or sacrifice in extremis were observed in all study groups, and were mainly observed after week 79 of exposures. Mortality and in extremis sacrifice were observed in 109/220 controls, 118/220 1000 ppm animals and 144/220 8000 ppm. Statistical analysis on differences in the survival in each group described a statistically significant reduction in survival at 8000 ppm, but not at 1000 ppm. Significantly decreased weight gain was observed in both sexes at $\geq$1000 ppm during weeks 0-12, but this deficit was no longer observed at later time points. Observed hematological changes included: higher mean hemoglobin values, increased WBC, lymphocytes and reticulocytes, increased lymphocytes at $\geq$1000 ppm. Observed blood serum chemistry changes included: increased BUN in males, but decreased BUN in females at $\geq$1000 ppm, decreased glutamic oxaloacetate transaminase in males at 8000 ppm. Observed urinalysis changes included: increased urine and decreased specific gravity in females at $\geq$1000 ppm and decreased pH in males at $\geq$1000 ppm and in females at 8000 ppm. Differences in hematology, blood serum chemistry and urinalysis were not considered by the authors to be toxicologically significant due to the parameters still falling between normal ranges. Significantly decreased time spent on the rotarod were observed at $\geq$1000 ppm, particularly from weeks 53-76 of the study, but no significant differences were found on week 78. Terminal organ weight changes included: increased absolute and relative liver weights but decreased absolute and relative spleen weights in males and decreased absolute and relative brain weights in females at $\geq$1000 ppm and increased absolute and relative heart, kidney and lung weights in males at 8000 ppm. Some ultrastructural changes were observed in liver tissue via transmission electron microscopy but were not considered to be toxicologically relevant. Minor focal pneumonitis was observed in lung tissue via gross pathology in females at 8000 ppm. Non-tumor histological findings in animals exposed to 8000 ppm included: increased incidence of focal alveolar epithelialization, nephropathy, liver angiectasis and spleen congestion in males. Tumor findings included: significantly increased incidence of mammary tumors, thyroid follicular tumors, Zymbal gland sarcoma and uterine stromal sarcoma in females and Leydig cell tumors in males at $\geq$1000 ppm. A study wide LOAEL of 1000 ppm was determined based on decreased body weight gain, increased incidence of tumors in various tissues, altered hematological, blood serum chemistry and urinalysis parameters, increased liver weights, decreased rotarod performance and decreased brain weights.	5673742 Hazleton Laboratories, (1981). The toxicity and carcinogenicity of butadiene gas administered to rats by inhalation for approximately 24 months (volume I - IV) (final report) w-attachments and cover letter 081182.

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Summary	HERO ID and Citation
Male and female B6C3F1 mice (50/sex/group) were exposed to the test substance at a concentration of 0, 625, or 1250 ppm (nominal concentrations; analytical test substance average concentrations of 627 +/- 25 ppm and 1236 ppm +/- 41 ppm, respectively) for 6 hours/day, 5 days/week, for 60 weeks (males) or 61 weeks (females). The study was originally intended to last 103 weeks but was terminated after 60 weeks (males) or 61 weeks (females) due to low survival. Animals were observed twice daily for mortality and signs of moribundity. Clinical signs were recorded once per week. Individual animal weights were recorded once weekly for 12 weeks and then monthly thereafter. Complete necropsy and histopathological examinations were performed on selected tissues of all animals at the end of the study. Tissues examined included gross lesions, mandibular lymph node, mammary gland, sternebrae including marrow, thymus, trachea, lungs, bronchi, heart, thyroid glands, parathyroids, esophagus, stomach, colon, small intestine, liver, gallbladder, pancreas, spleen, kidneys, adrenal glands, urinary bladder. prostate, testes, ovaries, uterus, nasal cavity, nasal turbinates, brain, pituitary, pharynx, and eyes (if abnormal). Survival of male and female mice at both test concentrations (625 and 1250 ppm) was significantly reduced compared to the corresponding controls. Survival at study termination at 0, 625, and 1250 ppm was 49/50, 11/50, and 7/50, respectively, in males, and 46/50, 14/50, and 30/50, respectively, in females. No effects on body weight were observed. The study report (HERO ID 62372, p. 32) states that, due to an apparent inadequate randomization, initial weights in dosed males and females were 9-11% higher than those of controls ($p < 0.01$ by Mann-Whitney U test) and these approximate relationships were observed throughout most of the study. There were no specific clinical signs related to treatment other than those associated with tumor development and moribundity. Incidences of neoplasms and non-neoplastic lesions were observed in both sexes and at both test substance concentrations at multiple tissue sites. Hemangiosarcomas of the heart occurred at increased incidences in exposed males and females (0, 625, and 1250 ppm: 0/50, 16/49, and 7/49, respectively, in males; 0/50, 11/48, and 18/49, respectively, in females). Endothelial hyperplasia in the heart was also observed at increased incidence in exposed males and females (0, 625, and 1250 ppm: 0/50, 5/49, and 2/49, respectively, in males; 0/49, 5/48, and 8/49, respectively, in females). Malignant lymphomas were diagnosed as early as Week 20 and were observed at increased incidences in exposed males and females (0, 625, and 1250 ppm: 0/50, 23/50, and 29/50, respectively, in males; 1/50, 10/49, and 10/49, respectively, in females). Alveolar/bronchiolar adenomas and alveolar/bronchiolar carcinomas (both separately and combined) occurred at increased incidences in exposed males and females (combined incidences for 0, 625, and 1250 ppm groups: 2/50, 14/49, and 15/49, respectively, in males; 3/49, 12/48, and 23/49, respectively, in females). Acinar cell carcinomas of the mammary gland occurred at increased incidence in females at the highest test concentration (0, 625, and 1250 ppm: 0/50, 2/49, and 6/49, respectively). Incidences of granulosa cell tumors of the ovary were increased in exposed females (0, 625, and 1250 ppm: 0/49, 6/45, and 12/48, respectively). Incidences of hepatocellular adenomas or carcinomas (combined) were increased in females at the high concentration (0, 625, and 1250 ppm: 0/50, 2/47, and 5/49, respectively). Liver necrosis was observed at increased incidences in exposed males and females (0, 625, and 1250 ppm: 1/50, 8/49, and 8/49, respectively, in males; 6/50, 15/47, and 6/49, respectively, in females). Papillomas of the forestomach occurred in males at the low concentration and in females at both test concentrations (0, 625, and 1250 ppm: 0/49, 5/40, and 0/44, respectively, in males; 0/49, 4/42, and 10/49, respectively, in females). Forestomach squamous cell carcinomas occurred at low incidence in exposed males and females (0, 625, and 1250 ppm: 0/49, 2/40, and 1/44, respectively, in males; 0/49, 1/42, and 1/49, respectively, in females). Epithelial hyperplasia of the forestomach occurred at increased incidences in exposed males and females (0, 625, and 1250 ppm: 0/49, 5/40, and 7/44, respectively, in males; 0/49, 5/42, and 9/49, respectively, in females). No neoplastic lesions were observed in the nasal cavity at any concentration. Non-neoplastic lesions observed in the nasal cavity of mice at 1250 ppm included chronic inflammation (males: 35/50, females: 2/49), fibrosis (males: 35/50, females: 2/49), cartilaginous metaplasia (males: 16/50, females: 1/49), osseous metaplasia (males: 11/50, females: 2/49), and atrophy of the sensory epithelium (males only: 32/50); no non-neoplastic lesions of the nasal cavity were observed in control animals. Brain gliomas and Zymbal gland carcinomas (both considered rare tumors in untreated B6C3F1 mice according to the study authors thus may be related to treatment, i.e., see HERO IDs 62372 and 5665509) were found in exposed males (0, 625, and 1250 ppm: 0/50, 2/48, and 1/49, respectively, for brain gliomas; 0/50, 0/50, and 2/50, respectively, for Zymbal gland carcinomas). Incidences of testicular atrophy (0, 625, and 1250 ppm: 0/50, 19/49, and 11/48, respectively) or ovarian atrophy (0, 625, and 1250 ppm: 2/49, 40/45, and 40/48, respectively) were increased in exposed males and females. The study authors concluded that there was clear evidence of carcinogenicity in male and female B6C3F1 mice under the conditions of this study, as demonstrated by increased incidences and early induction of hemangiosarcomas of the heart, malignant lymphomas, alveolar/bronchiolar adenomas and carcinomas, and papillomas of the forestomach in both sexes; and of acinar cell carcinomas of the mammary gland, granuolosa cell tumors of the ovary, and hepatocellular adenomas and adenomas or carcinoma (combined) in females. Exposure to 1,3-butadiene was also associated with non-neoplastic lesions in the respiratory epithelium, liver, forestomach, and testicular or ovarian atrophy.	62372 National Institutes of Health,, Department of Health and Human Services, (1984). Toxicology and carcinogenesis studies of 1,3-butadiene (CAS no. 106-99-0) in B6C3F1 mice (inhalation studies). 288:1-111.

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Summary	HERO ID and Citation
B6C3F1 mice (70-90/sex/group) were exposed to target concentrations of 0, 6.25, 20, 62.5, 200 or 625 ppm (measured concentrations of 6.21, 19.8, 61.4, 199 and 619 ppm) of 1,3-butadiene via inhalation for 6 hours/day, 5 days/week for up to 103 weeks. 10 animals/sex/group were used for interim evaluations. Animals were monitored daily for mortality and clinical signs of toxicity and body weights were measured weekly. Animals sacrificed during the interim evaluations were sacrificed early at 9 or 15 months of exposure. For both the 9- and 15-month interim groups, blood was collected (and analyzed for hematological parameters and blood serum chemistry), and the brain, heart, right kidney, liver, lungs, spleen, right testis and thymus were collected and weighed. Bone marrow was collected at the 15-month timepoint for determination of cellularity. All animals were necropsied at sacrifice, and all tissues were evaluated for gross lesions. Histopathology was performed for: gross lesions and tissue masses with regional lymph nodes, adrenal gland, brain, epididymis, esophagus, gallbladder, harderian gland, heart, kidney, large intestine (Cecum, colon, rectum), larynx, liver, lung, lymph node (bronchial, mediastinal, mandibular, mesenteric), mammary gland, nose, ovary, pancreas, parathyroid gland, pharynx, pituitary gland, prostate gland, salivary gland, seminal vesicle, small intestine (duodenum, jejunum, ileum), spleen, sternebrae (including marrow), stomach (forestomach and glandular), testis, thymus, thyroid gland, trachea, and uterus. Neoplastic and non-neoplastic lesions were identified in each evaluated tissue. Significantly increased mortality was observed at concentrations of 20 ppm and above and increased with dose. No females in the 200 and 625 ppm groups or males in the 625-ppm group survived to the end of the 103-week exposure period. No clinical observations independent of lesion development and moribundity were observed and there were no significant differences in body weights. At the 9-month interim evaluation hematological changes in males included: decreased erythrocyte counts, hemoglobin concentration and packed red cell volume at concentrations of 62.5 ppm and above, increased mean erythrocyte volume at 625 ppm, and leukopenia and lymphopenia at 200 and 625 ppm. Hematological changes in females included: decreased erythrocyte counts, hemoglobin concentrations and packed red cell volume at 200 or 625 ppm, macrocytosis and increased Howell-Jolly bodies and mean erythrocyte hemoglobin at 200 or 625 ppm and decreased neutrophils and lymphocytes at 200 or 625 ppm. No differences in blood serum chemistry were observed at 9 months. At 15 months, hematological changes in both sexes included: decreased mean erythrocyte counts, hemoglobin concentrations and significantly increased mean erythrocyte volumes and Howell-Jolly bodies at 625 ppm. Males additionally had significantly increased mean platelet values. Bone marrow smears indicated a left shift in the erythroid series of both sexes at 200 or 625 ppm and increase in erythroblasts with some megaloblastic characteristics and increased erythroblasts with a multilobed nucleus at 625 ppm. Blood serum chemistry changes included increased lactate dehydrogenase in both sexes at concentrations of 200 ppm and higher. Organ weight changes observed at 9 months included: increased absolute heart and kidney weights in females at 625 ppm, decreased absolute and relative thymus weights in females at 625 ppm, increased absolute liver weights in females at concentrations of 62.5 ppm and higher, increased absolute and relative liver weights in males at 625 ppm, and increased absolute testis weights in males at concentrations of 62.5 ppm and higher. Organ weight changes observed at 15 months included: increased absolute heart and spleen weights in females at concentrations of 200 ppm and higher, increased absolute and relative lung and spleen weights in males at 625 ppm, decreased absolute and relative testis weight in males at concentrations of 200 ppm and higher. At the end of the 2-year exposure period, increased incidence of neoplasms and non-neoplastic lesions throughout were observed at concentrations of 20 ppm and higher in males and at 6.25 ppm and higher in females. Neoplasms with significantly increased incidence included: malignant lymphoma, histiocytic sarcoma, cardiac hemangiosarcoma, harderian gland adenoma, alveolar/bronchial adenoma and carcinoma, mammary gland carcinoma, adenoacanthoma, and malignant mixed tumor in females only, as well as benign and malignant ovarian granulosa cell tumor and forestomach squamous cell papilloma and carcinoma. Some less common observed neoplasms included: intestinal and preputial carcinomas in males, renal tubule adenomas in in males and females, skin sarcomas in females and Zymbal's gland adenomas and carcinomas in females. Increased incidence of non-neoplastic lesions included: bone marrow atrophy, ovarian atrophy, angiectasis, germinal epithelial hyperplasia, myocardial mineralization and granulosa cell hyperplasia and mineralization, alveolar epithelial hyperplasia, and harderian gland hyperplasia. A study-wide LOAEL for cancer/carcinogenesis of 6.25 ppm for females and 20 ppm for males and a NOAEL of 6.25 ppm for males was determined based on neoplastic lesions. No NOAEL for neoplastic lesions in females was determined. A LOAEL for mortality of 20 ppm and NOAEL of 6.25 ppm in males and females was determined based on decreased survival.	1419645 NTP, (1993). NTP Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies). National Toxicology Program Technical Report Series 434:1-389.

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1,3-Butadiene- Parent compound - Chronic (>91 days)

Summary	HERO ID and Citation
Male B6C3F1 mice (50/group) were exposed to 1,3-Butadiene via inhalation for 6 hours/day, 5 days/week at varying durations at target concentrations of 0 ppm for 103 weeks, 200 ppm for 40 weeks, 312 ppm for 52 weeks or 625 ppm for 26 weeks (measured concentrations of 199 ppm, 312 ppm and 619 ppm). At the end of each exposure duration, animals were switched to the sham-air control exposure for the rest of the 103-week study duration and evaluated at 103 weeks. Animals were monitored daily for mortality and clinical signs of toxicity and body weights were measured weekly. Histopathology was performed for: gross lesions and tissue masses with regional lymph nodes, adrenal gland, brain, epididymis, esophagus, gallbladder, harderian gland, heart, kidney, large intestine (Cecum, colon, rectum), larynx, liver, lung, lymph node (bronchial, mediastinal, mandibular, mesenteric), mammary gland, nose, ovary, pancreas, parathyroid gland, pharynx, pituitary gland, prostate gland, salivary gland, seminal vesicle, small intestine (duodenum, jejunum, ileum), spleen, sternebrae (including marrow), stomach (forestomach and glandular), testis, thymus, thyroid gland, trachea, and uterus. Neoplastic and non-neoplastic lesions were identified in each evaluated tissue. Significantly decreased survival was observed at concentrations of 200 ppm and higher. No significant differences in body weights were observed. Significantly increased incidence of neoplastic lesions was observed at concentrations of 200 ppm and higher. Observed neoplastic lesions included: malignant lymphoma, histiocytic sarcoma, cardiac hemangiosarcoma, alveolar/bronchial adenoma and carcinoma, and forestomach squamous cell papilloma and carcinoma (only at $\geq$312 ppm), renal tubule adenoma, Zymbal's gland carcinoma and adenomas (at 625 ppm only), glioma and neuroblastoma (only at 625 ppm), preputial gland adenoma and carcinoma (only at $\geq$312 ppm). Observed non-neoplastic lesions included myocardial mineralization, focal hyperplasia of the harderian gland (with low frequency in each concentration group) and renal tubule epithelium focal hyperplasia (with low frequency in each concentration group). A LOAEL for cancer/carcinogenesis of 200 ppm was identified based on formation of neoplastic lesions. A LOAEL for mortality of 200 ppm was identified based on decreased survival. No NOAEL was determined.	1419645 NTP, (1993). NTP Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies). National Toxicology Program Technical Report Series 434:1-389.
Male B6C3F1 mice (50/group) were exposed to 1,3-Butadiene via inhalation for 6 hours/day, 5 days/week at varying durations at target concentrations of 0 ppm for 103 weeks or 625 ppm for 13 weeks (measured concentration of 619 ppm). At the end the 13-week exposure duration, animals were switched to the sham-air control exposure for the rest of the 103-week study duration and evaluated at 103 weeks. Animals were monitored daily for mortality and clinical signs of toxicity and body weights were measured weekly. Histopathology was performed for: gross lesions and tissue masses with regional lymph nodes, adrenal gland, brain, epididymis, esophagus, gallbladder, harderian gland, heart, kidney, large intestine (Cecum, colon, rectum), larynx, liver, lung, lymph node (bronchial, mediastinal, mandibular, mesenteric), mammary gland, nose, ovary, pancreas, parathyroid gland, pharynx, pituitary gland, prostate gland, salivary gland, seminal vesicle, small intestine (duodenum, jejunum, ileum), spleen, sternebrae (including marrow), stomach (forestomach and glandular), testis, thymus, thyroid gland, trachea, and uterus. Neoplastic and non-neoplastic lesions were identified in each evaluated tissue. Significantly decreased survival was observed at concentrations of 625 ppm. No significant differences in body weights were observed. Significantly increased incidence of neoplastic lesions was observed at 625 ppm. Observed neoplastic lesions included: malignant lymphoma, histiocytic sarcoma, harderian gland adenoma, alveolar/bronchial adenoma and carcinoma, hepatocellular adenoma, and forestomach squamous cell papilloma and carcinoma, renal tubule adenoma, Zymbal's gland carcinoma and adenomas, glioma and neuroblastoma, preputial gland adenoma and carcinoma. Observed non-neoplastic lesions included myocardial mineralization, focal hyperplasia of the harderian gland and renal tubule epithelium focal hyperplasia. A LOAEL for cancer/carcinogenesis of 625 ppm was identified based on formation of neoplastic lesions. A LOAEL for mortality of 625 ppm was identified based on decreased survival. No NOAEL was determined.	1419645 NTP, (1993). NTP Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies). National Toxicology Program Technical Report Series 434:1-389.

1,3-Butadiene- Parent compound - Reproductive/Developmental

Summary	HERO ID and Citation
In a modified dominant lethality test, male CD-1 mice (25/group) were exposed, whole body, to 1,3-butadiene (purity 99.73%) gas at 0, 12.5, 65, and 130 ppm for 6 hrs/day, 5 days/week for 4 weeks. Four days after the last exposure, each male cohabitated with two virgin females for up to one week. The body weights of parental animals were purportedly monitored (no additional details were provided). The females were sacrificed on GD17. Mating frequency and pregnancy frequency were observed. Uterine contents were examined for the number of implantation sites, the number of early and late deaths and the number of live fetuses. Presumably live fetuses were examined for gross malformations at necropsy, and select fetuses were subjected to skeletal examinations and cytogenic analysis of the livers. It is unclear whether the "selected" animals were only those showing gross changes. The study text mentioned "randomly selected normal litter mates" but 10, 2, 1, and 4 animals in the control, 12.5, 65, and 130 ppm groups, respectively, were referred to as "all selected fetuses."No effects on body weights (data not shown) or on mating or pregnancy frequencies were observed. The only statistically significant effect was an increase in early deaths at 65 (113% increase) and 130 (110% increase) ppm on a per implantation per pregnancy basis; however, there was not a clear dependence on exposure concentration. There were no differences in the number of implantations, or late deaths. There was a slight, increase in the number of fetuses considered to be runts (having a body weight of 75% or less than the mean weight of litter mates) at 130 ppm, but the effect was not statistically significant. No author-reported toxicity values were provided. A NOAEC of 12.5 ppm (27.7 mg/m3) and a LOAEC of 65 ppm (144 mg/m3) were determined for this review based on an increase in early fetal deaths in mice in a dominant lethality study. The test substance was positive for eliciting dominant lethality.Mg/m3 = ppm (MW) ÷ 24.45, using a MW of 54.0916g/mol	1327602 Anderson, D., Hughes, J. A., Edwards, A. J., Brinkworth, M. H. (1998). A comparison of male-mediated effects in rats and mice exposed to 1,3-butadiene. Mutation Research 397(1):77-84.
In a modified dominant lethality test, male Sprague Dawley rats (25/group) were exposed, whole body, to 1,3-butadiene (purity 99.5%) gas at 0 (air only control), 0 (room control), 65, 400, or 1,250 ppm for 6 hrs/day, 5 days/week for 10 weeks. An additional 50 rats were included that were held in free-standing cage racks in standard room air. These animals were not placed in inhalation chambers and were used as controls for possible stress effects resulting from being enclosed during exposure. Three days after the last exposure, each male was co-housed with two virgin females for up to 9 days. The body weights of parental animals were purportedly monitored (no additional details were provided). The females were sacrificed on GD19. Mating frequency and pregnancy frequency were recorded. Uterine contents were examined for the number of implantation sites, the number of early and late deaths and the number of live fetuses. Presumably, live fetuses were examined for gross malformations at necropsy. No effects on body weights or on mating frequencies were observed (data not shown). There were no statistically significant effects on fetal lethality or any of the reproductive endpoints measured. No author-reported toxicity values were provided, the NOAEC was 1,250 ppm (2,765 mg/m3), the highest concentration tested. The test substance was negative for dominant lethality in rats.Mg/m3 = ppm (MW) ÷ 24.45, using a MW of 54.0916g/mol	1327602 Anderson, D., Hughes, J. A., Edwards, A. J., Brinkworth, M. H. (1998). A comparison of male-mediated effects in rats and mice exposed to 1,3-butadiene. Mutation Research 397(1):77-84.
Pregnant Swiss CD-1 mice (31-33/group) were exposed to 1,3-butadiene gas at mean daily concentrations of 0, 39.9, 199.8, and 1,000 ppm (corresponding to target concentrations of 40, 200, or 1000 ppm), via whole body inhalation, for 6 hours/day from gestational day (GD) 6-15. Dams were monitored for mortality and clinical signs of toxicity twice per day during the exposure period. Maternal body weights were measured on GD 0, 6, 11, 16 and 18. Animals were sacrificed on GD 18 and were examined for lesions via gross necropsy; weights of gravid uterus and placenta, number of implantation sites, and intrauterine mortality were recorded. Fetuses were extracted and were sexed, weighed, and examined for gross, visceral, and skeletal abnormalities. Fetal lens opacity was recorded and eyes were examined microscopically.The percentage of dams that were actually pregnant was low; therefore, data are from only 18, 19, 21, and 20 dams in the 40, 200, and 1,000 ppm groups, respectively. Three dams in the 1,000 ppm group died; they showed signs of dehydration. Significantly decreased maternal body weights, extra gestational weight at sacrifice, and gravid uterine weights were observed at 1,000 ppm, compared with controls. Maternal weight gain, particularly from GD 11-16, and extra-gestational weight gain were decreased in a concentration-dependent manner and were statistically significant $\geq$200 ppm. Extra gestational weights as well as gravid uteri weights were significantly decreased at 1,000 ppm. No effects on the number of resorptions or on the percentages of resorptions per litter were observed. There was a decrease in early resorptions that was significant at 200 ppm, compared with controls, which was not considered to be adverse, whereas incidences of late resorptions were slightly elevated in exposed groups, but the increases were not statistically significant. Fetal body weights were decreased at $\geq$40 ppm for males and at $\geq$200 ppm for females. The was a concentration-related linear trend. Fetal placental weights were also decreased at $\geq$ 200 ppm for males and at 1,000 ppm for females. No differences in malformations were observed, though there were significantly increased incidences of fetal variations (supernumerary ribs at $\geq$ 200 ppm, and reduced ossification and abnormal sternebrae at 1,000 ppm). There was no lens opacity in fetal eyes.The study authors concluded that there was evidence of maternal toxicity at 200 ppm and higher and that there was no evidence of teratogenicity but some evidence of fetotoxicity was observed. No toxicity values were provided. A maternal NOAEC of 39.9 ppm and LOAEC of 199.9 ppm was determined for this review based on decreases in maternal weight gain both during the end of the exposure period and extra gestationally. A developmental LOAEC of 39.9 ppm was determined based on significant reductions in male fetal body weights at a non-maternally toxic concentration; A NOAEL was not determined.	62351 Battelle PNL, (1987). Inhalation developmental toxicology studies: Teratology study of 1,3-butadiene in mice.

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Summary	HERO ID and Citation
In a teratogenicity study, pregnant Sprague-Dawley rats (30/group) were exposed whole body to 1,3-butadiene gas at measured concentrations of 0 (filtered air), 40, 200, and 1,005 ppm, 6hrs/day from GDs 6-15. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days 0, 6, 11, 16, and 20. The animals were sacrificed on GD20 and necropsied. Gravid uterus weights were recorded along with placental weight, the number of implantation sites, intrauterine mortality (resorptions), and placental weights. Fetal observations included body weights and sex, and fetuses were subjected to gross, visceral, and skeletal examinations. Fetal lens opacity was also assessed and eyes were examined under a dissecting microscope.No dams died. No clinical signs of toxicity were observed in the 40 and 200 ppm groups. Results for the 1,005 ppm group were not reported. Body weight gain between GDs 6-11 and extragestational weight gain was slightly, but significantly decreased in the 1,005 ppm group, compared with controls, but there were no resulting effects on body weights in any group. Out of the 30 animals per group, 28, 24, 26, and 28 rats were pregnant in the 0, 40, 200, and 1,005 ppm groups, respectively. There were no exposure-related effects on the numbers of implantations, live or dead fetuses, or resorptions. One dam in the 1,005 ppm group had a single implantation. This dam was considered an outlier and was excluded from statistical analysis. Gravid uterine weights, fetal body weights, placental weights, and fetal sex ratios were all comparable to controls. Isolated incidences of malformations showed no treatment-related differences or trends. Skeletal examinations showed an increased incidence in fetuses in the 200 ppm group with reduced ossification of sternebrae, but incidences of this effect in the higher exposure group were comparable to controls. There were significantly fewer incidences of fetuses with reduced ossification in thoracic vertebrae compared with controls. When considered on a litter basis, there were no effects of treatment on reduced ossification (all anatomical sites). No effects on fetal eyes were observed.The author reported NOAEC was 1,005 ppm, based on the lack of teratogenic effects.	94731 Battelle PNL, (1987). Inhalation developmental toxicology studies of 1,3-butadiene in the rat.
In a dominant lethality study, male CD-1 mice (50/group) were exposed to butadiene gas (purity ≥99.7%) at 0 (air control), 12.5, 65, and 130 ppm (0, 27.8, 144, 288 mg/m3) for 6hrs/day, 5 days/ week for 4 weeks. Four days after the last exposure, approximately half of the surviving males were mated to two untreated females for approximately one week; the remaining males were sent to another laboratory for testing not described in this report. During exposure, males were monitored for mortality and any deviations from normal. Body weights were recorded weekly for males and 6, 10, 14, and 16 days after the start of mating in females. Males were disposed of at the end of mating without necropsy. Females were weighed, sacrificed on presumed GD17, and were subjected to gross necropsy and examination of uterine contents.Reproductive behavior and pregnancy success were determined based on mating frequency, pregnancy rate, period of coition, number of corpora lutea, and implantation sites. Other endpoints included examinations for post-implantation losses (early and late deaths, or deaths including dead fetuses), fetal sex, weights of any live fetuses, gross necropsy, and examinations for abnormalities (runts). Select fetuses that were identified as runts were processed for skeletal examinations along with an equal number of normal fetuses per group. Fetal livers were assessed for chromosome damage (i.e., karyotyping).During exposure, one male in the 12.5 and 130 ppm groups died, and two died in the 65 ppm group. These deaths were due to injury and were not related to exposure. Except for a significant decrease in male body weights on day 7 in the 130 ppm group, no changes in male body weights were observed. There were no effects on any measures of fertility or reproductive success. There were difficulties confirming pregnancy via a vaginal plug. Gestation day was estimated based on the body weight gain of the dams. Examination of dominant lethal endpoints showed a significant increase in early deaths at ≥65 ppm. There were no differences in late deaths or dead fetuses across groups. Examination for abnormal fetuses (runts) showed 2 runts in two litters in the control and 12.5 ppm groups, one runt in the 65 ppm group, and 6 runts in 5 litters in the 130 ppm group; however, the increase was not statistically significant. The number of fetuses examined for skeletal malformations was small and varied across groups, and the data were not amenable to statistical analysis. No chromosome damage was observed in the offspring of exposed male mice. The study authors concluded that the test substance was positive for dominant lethality based on the increase in early deaths and indicated the ”no effect” level was 12.5 ppm (27.8 mg/m3), suggesting a LOEL of 65 ppm (144 mg/m3) based on increased incidences of early fetal deaths. Exposure concentrations were converted from ppm to mg/m3 using the following formula: mg/m3 = (ppm x MW)/ 24.45, using a MW of 54.09.	5665017 BIBRA, (1996). Initial submission: the detection of dominant lethal mutations and * in the offspring of male mice treated subchronically with butadiene by inhalation, w/cover letter dated 1/10/97.

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Summary	HERO ID and Citation
In a dominant lethality study, male CD-1 mice (50/group) were exposed to butadiene gas (purity ≥99.7%) at 0 (air control), 12.5, 65, and 130 ppm (0, 27.8, 144, 288 mg/m3) for 6hrs/day, 5 days/ week for 4 weeks. Four days after the last exposure, approximately half of the surviving males were mated to two untreated females for approximately one week. the remaining males were sent to another laboratory for testing not described in this report. During exposure, males were monitored for mortality and any deviations from normal. Body weights were recorded weekly for males and 6, 10, 14, and 16 days after the start of mating in females. Males were disposed of at the end of mating without necropsy. Females were weighed, sacrificed on presumed GD17, and were subjected to gross necropsy and examination of uterine contents.Reproductive behavior and pregnancy success were determined based on mating frequency, pregnancy rate, period of coition, number of corpora lutea, and implantation sites. Other endpoints included examinations for post-implantation losses (early and late deaths, or deaths including dead fetuses), fetal sex, weights of any live fetuses, gross necropsy, and examinations for abnormalities (runts). Select fetuses that were identified as runts were processed for skeletal examinations along with an equal number of normal fetuses per group. Fetal livers from these animals were assessed for chromosome damage (i.e., karyotyping).During exposure, one male in the 12.5 and 130 ppm groups died, and two died in the 65 ppm group. These deaths were due to injury and were not related to exposure. Except for a significant decrease in male body weights on day 7 in the 130 ppm group, no changes in male body weights were observed. There were no effects on any measures of fertility or reproductive success. There were difficulties confirming pregnancy via a vaginal plug. Gestation day was estimated based on the body weight gain of the dams. Examination of dominant lethal endpoints showed a significant increase in early deaths at ≥65 ppm. There were no differences in late deaths or dead fetuses across groups. Examination for abnormal fetuses (runts) showed 2 runts in two litters in the control and 12.5 ppm groups, one runt in the 65 ppm group, and 6 runts in 5 litters in the 130 ppm group; however, the increase was not statistically significant. The number of fetuses examined for skeletal malformations was small and varied across groups, and the data were not amenable to statistical analysis. No chromosome damage was observed in the offspring of exposed male mice. The results indicate the test substance was negative for inducing chromosome damage in the F1 offspring of exposed parental males. Exposure concentrations were converted from ppm to mg/m3 using the following formula: mg/m3 = (ppm x MW)/ 24.45, using a MW of 54.09.	5665017 BIBRA, (1996). Initial submission: the detection of dominant lethal mutations and * in the offspring of male mice treated subchronically with butadiene by inhalation, w/cover letter dated 1/10/97.
In a dominant lethality study, male CD-1 mice (20/group) were exposed, whole body, to 1,3-butadiene gas at measured concentrations of 0, 200, 1010, or 5,000 ppm (target 200, 1,000 and 5,000 ppm) for 6 hours/day, for 5 consecutive days. After the last exposure, males were paired 1:2 with unexposed females for 1 week. Pairing with new females occurred weekly for a total of 8 weeks. Males were sacrificed after the last mating; all females were sacrificed 12 days after the last day of cohabitation. All animals were observed for mortality and clinical signs of toxicity. Male mice were weighed prior to the start of exposure and weekly thereafter. The reproductive status was assessed and the uteri from females were examined for the total number and position of implantations, and for early and late resorptions and live and dead fetuses. One control and one male in the 1,010 ppm group died due to an accident and dehydration, respectively. Males exposed to 5,000 ppm showed transient signs of piloerection and dyspnea for up to 30 minutes following exposure. No effects on body weight or weight gain were observed. There were no differences in the number of males that mated or in the number of pregnant females. Some significant differences in the number of live and total implantations were observed among the control animals across weeks. Additionally, implantation results in exposed animals, relative to controls, did not demonstrate a clear exposure-concentration-related response. Week 1 matings resulted in a significant increase in dead implantations per pregnancy (early and total resorptions) in the 1,010 ppm group, but not in the 5,000 ppm group. The percentage of dead implantations/total implantations was also significantly increased in the 1,010 ppm group only (12.27%), compared with controls (6.87%). Also, during week 1, the percentages of females with ≥2 intrauterine deaths was significantly higher in all exposure groups (38.6%, 42.11%, and 37.1%) at 200, 1,010, 5,000 ppm, respectively, compared with controls (13.5%). During week 2, significant increases in early and total resorptions occurred in the low and mid-exposure groups only. During week 4, the % dead implantations/total were significantly lower (not higher) in all treatment groups compared with controls, and controls had a significantly higher percentage of females with ≥ intrauterine deaths than those in the low and high exposure groups. In week 8, there was a slight, but significant decrease in the number of live implantations per pregnancy at 1,010 ppm. Lethality endpoints from weeks 3, 5, 6, and 7 were all comparable to controls.No toxicity values were identified by the study author. The authors acknowledge the lack of a clear concentration-response relationship in the lethality endpoints. However, because all three exposure groups showed a significant elevation in the percentage of females with ≥2 dead implantations following the first week of mating, the authors considered this evidence that 1,3-butadiene altered more mature spermatozoa and spermatids. The authors did not specify whether they considered the test material was positive for eliciting dominant lethality. Based on this observation, a LOAEC of 200 ppm was determined for this review based on an increased percentage of females with ≥ 2 intrauterine deaths.	62353 Hackett, P. L., Mast, T. J., Brown, M. G., Clark, M. L., Evanoff, J. J., Rowe, S. E., McClanahan, B. J., Buschbom, R. L., Decker, J. R., Rommereim, R. L., Westerberg, R. B. (1988). Dominant lethal study in CD-1 mice following inhalation exposure to 1,3-butadiene.

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Summary	HERO ID and Citation
In a teratology study, pregnant female Sprague-Dawley CD rats (40 controls, 24/exposure group) were exposed, whole body, to 1,3-butadiene gas at mean measured concentrations of 2.8 (control), 202, 990, and 7,647 ppm [corresponding to 0, 200, 1,000, or 8,000 ppm nominal] 6hrs/day from gestation days (GDs 6-15). A positive control group was administered 250 mg/kg acetylsalicylic acid via gavage during the same treatment period. Animals were monitored twice daily for mortality or moribundity, and once per day were subjected to detailed clinical examinations following the exposure period. Body weights were recorded every 3 days and before sacrifice on GD20. At sacrifice, dams were subjected to gross necropsy; gravid uterine weights were recorded along with the numbers of corpora lutea, implantations (along with positions), live fetuses, and early and late deaths. Litter weights, fetal body weights, and crown/rump length were measured in live fetuses. The sex ratio was recorded and external, visceral (2/3rd of fetuses), and head and skeletal (1/3rd of fetuses) examinations were performed. A re-examination of the skeletal defects was conducted.One animal in the 1,000 ppm group was killed moribund on GD19. The authors indicated the animals' condition was not related to exposure. There were no additional deaths or clinical changes related to exposure. Positive control animals exhibited signs of respiratory stress. No significant changes in dam body weights were observed, including no differences in terminal weights. However, the percent body weight gain (GD 6-15) was significantly decreased in all exposure groups, compared with controls. Weight loss was observed during the first three days of exposure (GD6-9) in the high exposure group. Weight gain from GD 0-20, decreasing in an exposure-concentration-related manner, was significant in the 7,647 ppm group only. When measurements were adjusted for gravid uterine weight, the decrease was significant at $\geq$990 ppm. Necropsy showed a few cases hydronephrosis in all groups, including controls. No effects on pregnancy incidence, gravid uterine weights, or numbers of corpora lutea or implantations. Non-statistically significant increases in incidences of early post-implantation losses occurred in all exposure groups and the authors attributed this to the initial body weights of the dams. Significant litter effects included a decrease in mean fetal (6%), but not litter weight, and a 5% reduction in crown-rump length at 7,647 ppm. The percentage of fetuses showing minor external or visceral defects (subcutaneous hemorrhagic areas and bilateral lens opacities) was higher than controls in all groups (16.9%, 23.8%, 24.4%, and 25.5% in the control, low, mid, and high-exposure groups, respectively), but was only statistically significant at 990 ppm. The percentage of fetuses showing major skeletal defects was significant (using the litter as the statistical unit), at $\geq$990 ppm, and the effect increased with exposure concentration. The most notable major defect included increasing incidences of wavy and/or fused ribs market (graded slight to severe) in exposed fetuses. The percentage of fetuses with variance was also significantly higher at 7,647 ppm, compared to controls. Some abnormalities were also observed (in the skull, spine, sternum, long bones, and ribs) in the high-exposure group, but the increased incidences did not reach statistical significance. The positive control gave the expected results in all of the endpoints assessed.The authors made special note that the animals in this study differed from historical controls. Even control animals were smaller (fetal weight and crown/rump length) than normal, and incidences of wavy ribs occurred in control animals (2 showing marked to severe, and 5 showing slight to moderate grade), which is extremely rare (only 1 incidence in 3,228 fetuses in historical controls). Therefore, there is uncertainty as to whether the increases in wavy ribs in the exposure groups reflect the increasing maternal toxicity (reduced weight gain) and the unusually small fetal sizes, rather than being indicative of a teratogenic response. The author reported the "no effect level" for teratogenicity was 990 ppm, indicating that any effects in the low and mid-exposure groups were not regarded as teratogenic responses.The effects at 7,647 ppm were regarded by the authors as a teratogenic response to exposure and, therefore, 7,647 ppm is considered a LOAEL. The authors did not report a toxicity value for maternal effects but described maternal toxicity in all exposure groups (reductions in body weight gain) suggesting a LOEL of 202 ppm. The reduction in body weight gain without an influence on animal body weights does not suggest an adverse effect on dams.	62371 Hazleton Labs, (1981). 1,3-Butadiene: Inhalation teratogenicity study in the rat (Final report).

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1,3-Butadiene- Parent compound - Reproductive/Developmental

Summary	HERO ID and Citation
In a reproductive/developmental screening test, male and female Sprague-Dawley rats (12/sex/group, total of 24 animals per group) were exposed to 1,3-butadiene (purity: 99.94%) via whole-body exposure at nominal concentrations of 0, 300, 1500, and 6000 ppm. The control group was exposed to clean, filtered air with no test substance. Analytically determined test substance concentrations were 301, 1507, and 6006 ppm for nominal concentrations of 300, 1500, and 6000 ppm, respectively. F0 males were exposed from 14 days prior to mating, through mating, and until scheduled euthanasia for 83-84 consecutive total days. F0 females were exposed from 14 days prior to mating, throughout mating until gestation day (GD) 20, and then from lactation day (LD) 5 until the day prior to euthanasia (60-70 total days). F0 females that did not deliver were exposed until one day prior to scheduled euthanasia (post-mating day 25). Selected F1 males and females (one male and one female from each litter, total number of F1 animals: 18, 24, 20, and 22 for the respective dose groups) were exposed to the same concentration as their parents for 7 consecutive days (either postnatal days [PND] 21-27 or 28-34). One male in the 6000-ppm exposure group died during Week 8. This death was considered by the study authors as likely due to complications resulting from the formation of urinary calculi (observed at necropsy) and not related to test substance exposure. All other animals survived until scheduled necropsy. Test substance-related clinical observations in F0 males and females included chromodacryorrhea, chromorhinorrhea, and salivation at 1500 and 6000 ppm. All clinical observations in 1500 ppm animals were transient (i.e., only evident at the 1-hour post-exposure examinations). At 300 ppm, only a few males and females had transiently observed perinasal staining at 1-hour post-exposure. F0 male and female mean body weights and body weight changes were significantly decreased at 1500 and/or 6000 ppm throughout the study, compared to the control group. The body weight effects were correlated with a transient decrease in food consumption (Week 0-1). Relative brain weight (relative to body weight) was significantly increased in F0 males at 6000 ppm and was considered to be the result of treatment-related body weight decrements at this concentration and not a direct effect of exposure. Absolute seminal vesicle (including coagulating glands and fluid) weights were slightly (not statistically significant) decreased at 1500 and 6000 ppm (~14% and ~15%, respectively), compared to the control group. A slight reduction in relative seminal vesicle weight (relative to body weight) was also observed (12% and 11%, respectively) but also did not attain statistical significance; a decrease in relative seminal vesicle weight (relative to brain weight) was observed at 1500 and 6000 ppm, which did attain statistical significance. As no histological correlates were observed for the seminal vesicle weight changes, these were attributed to biological variation and were not considered to be treatment related. There were no test substance-related effects on F0 animal mating behavior, conception, gestation, parturition, spermatogenic evaluations, macroscopic findings at necropsy, organ weight changes, or histopathology findings, or F1 offspring development from conception through weaning. An increased number of ejaculatory plugs was observed at all exposure levels compared to the control group, but the significance of this result is uncertain. There were two non-gravid females in the control group and one in the 6000 ppm group; the number of live litters on PND 0 was 10, 12, 12, and 11 for the 0, 300, 1500, and 6000 ppm exposure groups, respectively. The mean viable litter size at 6000 ppm was slightly decreased (-6%; not statistically significant) on PND 0, compared to the control group. Total litter loss occurred in one control female (by PND 16) and in two females at 1500 ppm (by PND 12 and 17, respectively). The occurrences of litter loss at 1500 ppm were not considered treatment related due to the absence of a dose-response relationship. In F1 offspring exposed from PND 21 to 27 or PND 28 to 34, test substance-related clinical observations were limited to infrequent occurrences of perioral and perinasal dried red material at 6000 ppm (one female exposed to 6000 ppm from PND 21-27; three males exposed to 6000 ppm from PND 28-34). F1 male and female body weights were decreased (>5%) throughout the exposure week at 1500 and 6000 ppm, compared to controls, with decreases at several time points attaining statistical significance. The NOAEC for F0 and F1 males and females for systemic toxicity was 301 ppm (nominal concentration: 300 ppm) based on decreases in body weight and body weight gain in F0 and F1 animals; the LOAEC was 1507 ppm (nominal concentration: 1500 ppm). The NOAEC for reproductive and developmental toxicity was 6000 ppm. [Note: HERO IDs 10367501 and 10192292 were considered for this review.]	10367501 WIL Research, (2003). An inhalation reproduction/developmental toxicity screening study of 1,3-butadiene in rats.

Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Immune/Hematological-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Mortality-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality. Outcome measure: Vital status databases and medical records	Occupational workers. Adults (18+), Older Adults (65+). US; Canada; Texas, Kentucky, Louisiana, Canada (unspecified). Male. Cohort (Retrosepctive). North American synthetic rubber industry workers employed for at least one year (N=16,579). Earliest date of hire 1944. Follow-up for vital status through 1988 (N=16,091).. 1944-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Cumulative occupational exposure estimates, mean of 30 years since initial hire.	Cox Proportional Hazards Model. Confounders adjusted for: Age, year of birth, race, DMDTC, years since hire and plant.	Lowest exposure concentration for a significant adverse health outcome response: NA. RR (95% CI) for cumulative BD ppm-years, reference = 0 ppm-years. 0: 1.00 >0–<12.1 ppm-years v. 0: 0.98 (0.37, 2.61) 12.1–<22.9 ppm-years v. 0: 1.67 (0.62, 4.50) 22.9–<38.8 ppm-years v. 0: 1.45 (0.53, 3.97) 38.8–<78.1 ppm-years v. 0: 0.83 (0.30, 2.32) 78.1–<184.6 ppm-years v. 0: 0.61 (0.21, 1.73) 184.6–<251.1 ppm-years v. 0: 1.77 (0.60, 5.24) 251.1–<318.5 ppm-years v. 0: 2.47 (0.82, 7.44) 318.5–<450.9 ppm-years v. 0: 1.96 (0.65, 5.87) 450.9–<829.6 ppm-years v. 0: 1.86 (0.62, 5.55) 829.6+ ppm-years v. 0: 2.56 (0.85, 7.66)RR (95% CI) for BD average intensity (ppm) 0: 1.00 >0–<4.8 ppm v. 0: 0.55 (0.20, 1.50) 4.8–<6.5 ppm v. 0: 1.47 (0.54, 4.03) 6.5–<8.2 ppm v. 0: 2.27 (0.85, 6.04) 8.2–<11.0 ppm v. 0: 1.69 (0.60, 4.79) 11.0–<15.0 ppm v. 0: 0.81 (0.27, 2.41) 15.0–<21.5 ppm v. 0: 1.32 (0.48, 3.65) 21.5–<28.4 ppm v. 0: 1.96 (0.70, 5.51) 28.4–<42.3 ppm v. 0: 1.46 (0.52, 4.13) 42.3–<51.6 ppm v. 0: 2.46 (0.86, 7.04) 51.6+ ppm v. 0: 1.43 (0.48, 4.24). Irregular associations for ppm-years and average intensity. There was a mixture of non-significant positive and non-significant association across all deciles. Results significant after age-adjustment; no significant results for BD cumulative exposure or intensity variables reported after multivariate adjustment..	Cheng et. al 2007 646899 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Immune/Hematological-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Mortality-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality. Outcome measure: Vital status databases and medical records	Occupational workers. Adults (18+), Older Adults (65+). US; Canada; Texas, Kentucky, Louisiana, Canada (unspecified). Male. Cohort (Retrosepctive). North American synthetic rubber industry workers employed for at least one year (N=16,579). Earliest date of hire 1944. Follow-up for vital status through 1988 (N=16,091).. 1944-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Cumulative occupational exposure estimates, mean of 30 years since initial hire.	Cox Proportional Hazards Model. Confounders adjusted for: Age, year of birth, race, DMDTC, years since hire and plant.	Lowest exposure concentration for a significant adverse health outcome response: NA. No significant associations. Nonsignificant positive association for the relationship between BD ppm-years and lymphoid neoplasm mortality. Null association for the relationship between BD average intensity and lymphoid neoplasm mortality..	Cheng et. al 2007 646899 Medium
Myeloid neoplasm mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Immune/Hematological-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Mortality-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality. Outcome measure: Vital status databases and medical records	Occupational workers. Adults (18+), Older Adults (65+). US; Canada; Texas, Kentucky, Louisiana, Canada (unspecified). Male. Cohort (Retrosepctive). North American synthetic rubber industry workers employed for at least one year (N=16,579). Earliest date of hire 1944. Follow-up for vital status through 1988 (N=16,091).. 1944-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Cumulative occupational exposure estimates, mean of 30 years since initial hire.	Cox Proportional Hazards Model. Confounders adjusted for: Age, year of birth, race, DMDTC, years since hire and plant.	Lowest exposure concentration for a significant adverse health outcome response: NA. No significant associations. Nonsignificant positive association for the relationship between both BD ppm-years BD average intensity and myeloid neoplasm mortality..	Cheng et. al 2007 646899 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Immune/Hematological-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality-Mortality-Leukemia mortality, lymphoid neoplasms mortality, myeloid neoplasms mortality. Outcome measure: Vital status databases and medical records	Occupational workers. Adults (18+), Older Adults (65+). US; Canada; Texas, Kentucky, Louisiana, Canada (unspecified). Male. Cohort (Retrosepctive). North American synthetic rubber industry workers employed for at least one year (N=16,579). Earliest date of hire 1944. Follow-up for vital status through 1988 (N=16,091).. 1944-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Cumulative occupational exposure estimates, mean of 30 years since initial hire.	Cox Proportional Hazards Model. Confounders adjusted for: Age, year of birth, race, DMDTC, years since hire and plant.	Lowest exposure concentration for a significant adverse health outcome response: continuous. Multivariate beta (SE), p-value for per unit increase in cumulative BD-ppm-years and leukemia mortality:-continuous untransformed BD ppm-years = 3.0×10^-4 (1.4×10^-4), p=0.04. -continuous square root transformed BD ppm-years = 2.5×10^-2 (1.1×10^-2), p=0.02. -continuous mean-scored deciles BD ppm-years = 5.8×10^-4 (2.7×10^-4), p=0.03. -continuous ln transformed BD ppm-years = 4.7×10^-2 (3.7×10^-2), p=0.21. Multivariate beta (SE), p-value for per unit increase in average BD intensity (ppm) and leukemia mortality:-continuous untransformed BD ppm-years = 5.6×10^-5 (2.4×10^-5), p=0.02. -continuous square root transformed BD ppm-years = 1.1×10^-2 (0.4×10^-2), p<0.01. -continuous mean-scored deciles BD ppm-years = 3.8×10^-3 (3.7×10^-3) p=0.40. -continuous ln transformed BD ppm-years = 6.1×10^-2 (4.5×10^-2), p=0.17.. Significant positive adjusted associations between cumulative occupational BD exposure (ppm-years) and leukemia mortality using continuous untransformed, square root transformed and continuous mean-scored decile variables. Association positive but not significant after adjustment using ln-transformed cumulative BD exposure variable. Significant positive adjusted association between average intensity of occupational BD exposure (ppm) and leukemia mortality using square root transformed variable. Association positive but not significant after adjustment using untransformed, ln-transformed and mean scored decile variables..	Cheng et. al 2007 646899 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
All central nervous system tumors	Health Effect: Neurological/Behavioral-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors-Cancer/Carcinogenesis-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors. Outcome measure: Texas Cancer Registry, all tumors classified under group III of the International Classification of Childhood Cancer, 3rd edition	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17). United States; Texas. Female, Male. Ecological. Children age <15 living in Texas with incident central nervous system tumors 2001-2009 (n=1,949) and the total Texas population age <15 in the year 2000 (n=5,797,483).. 2001-2009.	Outdoor air Exposure Route: Inhalation Unclear Exposure estimated for the year 2005 for all study subjects.	Poisson Regression. Confounders adjusted for: Race, sex, age category, area-level poverty.	Lowest exposure concentration for a significant adverse health outcome response: NA. IRR (95% CI):Medium vs. low: 1.10 (0.97, 1.25)Medium-high vs. low: 1.07 (0.94, 1.23)High vs. low: 0.97 (0.83, 1.11). No significant associations for all CNS tumors..	Danysh et. al 2015 3011004 Medium
Juvenile pilocytic astrocytoma (JPA)	Health Effect: Neurological/Behavioral-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors-Cancer/Carcinogenesis-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors. Outcome measure: Texas Cancer Registry, International Classification of Diseases for Oncology, 3rd edition code 9421	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17). United States; Texas. Female, Male. Ecological. Children age <15 living in Texas with incident juvenile pilocytic astrocytomas 2001-2009 (n=384) and the total Texas population age <15 in the year 2000 (n=5,797,483).. 2001-2009.	Outdoor air Exposure Route: Inhalation Unclear Exposure estimated for the year 2005 for all study subjects.	Poisson Regression. Confounders adjusted for: Race, sex, age category, area-level poverty.	Lowest exposure concentration for a significant adverse health outcome response: NA. IRR (95% CI):Medium vs. low: 1.11 (0.84, 1.47)Medium-high vs. low: 0.92 (0.68, 1.25)High vs. low: 0.92 (0.67, 1.27). No significant associations for juvenile pilotcytic astrocytomas..	Danysh et. al 2015 3011004 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Other astrocytomas	Health Effect: Neurological/Behavioral-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors-Cancer/Carcinogenesis-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors. Outcome measure: Texas Cancer Registry, International Classification of Childhood Cancer, 3rd edition group IIIb excluding juvenile pilocytic astrocytomas	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17). United States; Texas. Female, Male. Ecological. Children age <15 living in Texas with incident other astrocytomas 2001-2009 (n=372) and the total Texas population age <15 in the year 2000 (n=5,797,483).. 2001-2009.	Outdoor air Exposure Route: Inhalation Unclear Exposure estimated for the year 2005 for all study subjects.	Poisson Regression. Confounders adjusted for: Race, sex, age category, area-level poverty.	Lowest exposure concentration for a significant adverse health outcome response: 0.031-0.046 ug/m3. IRR (95% CI):Medium vs. low: 1.46 (1.05, 2.01)Medium-high vs. low: 1.69 (1.22, 2.33)High vs. low: 1.05 (0.73, 1.50). Significant positive associations were reported for medium vs. low and medium-high vs. low exposure for other astrocytomas. No significant association for high vs. low exposure..	Danysh et. al 2015 3011004 Medium
Ependymoma	Health Effect: Neurological/Behavioral-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors-Cancer/Carcinogenesis-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors. Outcome measure: Texas Cancer Registry, International Classification of Childhood Cancer, 3rd edition group IIIa.1	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17). United States; Texas. Female, Male. Ecological. Children age <15 living in Texas with incident ependymoma 2001-2009 (n=142) and the total Texas population age <15 in the year 2000 (n=5,797,483).. 2001-2009.	Outdoor air Exposure Route: Inhalation Unclear Exposure estimated for the year 2005 for all study subjects.	Poisson Regression. Confounders adjusted for: Race, sex, age category, area-level poverty.	Lowest exposure concentration for a significant adverse health outcome response: NA. IRR (95% CI):Medium vs. low: 0.85 (0.54, 1.35)Medium-high vs. low: 0.74 (0.46, 1.21)High vs. low: 0.94 (0.59, 1.51). No significant associations for ependymomas..	Danysh et. al 2015 3011004 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Medulloblastoma	Health Effect: Neurological/Behavioral-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors-Cancer/Carcinogenesis-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors. Outcome measure: Texas Cancer Registry, International Classification of Childhood Cancer, 3rd edition group IIIc.1	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17). United States; Texas. Female, Male. Ecological. Children age <15 living in Texas with incident medulloblastoma 2001-2009 (n=235) and the total Texas population age <15 in the year 2000 (n=5,797,483).. 2001-2009.	Outdoor air Exposure Route: Inhalation Unclear Exposure estimated for the year 2005 for all study subjects.	Poisson Regression. Confounders adjusted for: Race, sex, age category, area-level poverty.	Lowest exposure concentration for a significant adverse health outcome response: NA. IRR (95% CI):Medium vs. low: 0.98 (0.67, 1.42)Medium-high vs. low: 0.95 (0.64, 1.39)High vs. low: 1.09 (0.74, 1.60). No significant associations for medulloblastoma..	Danysh et. al 2015 3011004 Medium
Primitive neuroectodermal tumors	Health Effect: Neurological/Behavioral-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors-Cancer/Carcinogenesis-All central nervous system tumors, juvenile pilocytic astrocytoma, other astrocytomas, ependymoma, medulloblastoma, primitive neuroectodermal tumors. Outcome measure: Texas Cancer Registry, International Classification of Childhood Cancer, 3rd edition group IIIc.2	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17). United States; Texas. Female, Male. Ecological. Children age <15 living in Texas with incident primitive neuroectodermal tumors (PNET) 2001-2009 (n=47) and the total Texas population age <15 in the year 2000 (n=5,797,483).. 2001-2009.	Outdoor air Exposure Route: Inhalation Unclear Exposure estimated for the year 2005 for all study subjects.	Poisson Regression. Confounders adjusted for: Race, sex, age category, area-level poverty.	Lowest exposure concentration for a significant adverse health outcome response: NA. IRR (95% CI):Medium vs. low: 2.60 (0.94, 7.24)Medium-high vs. low: 2.76 (0.98, 7.72)High vs. low: 2.40 (0.83, 6.93). No significant associations for medulloblastoma..	Danysh et. al 2015 3011004 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
leukemia mortality	Health Effect: Cancer/Carcinogenesis-leukemia mortality-Mortality-leukemia mortality-Immune/Hematological-leukemia mortality. Outcome measure: Personnel, medical, and individual tracing records	Occupational workers. Adults (18+), Older Adults (65+). United States; Canada. Male. Cohort (Retrosepctive). Male workers from six synthetic rubber plants in the United States and Canada (Enrolled n = 13,130; Follow-up of 99% of study population). SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure measured in years prior to diagnosis (exact timing not specified)..	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=362.2 ppm-years. RR (95% CI) in single agent modelT1 vs. no exposure: 1.2 (0.5-3.0)T2 vs. no exposure: 2.0 (0.8-4.8) T3 vs. no exposure: 3.8 (1.6 - 9.1). Significant positive association reported for T4. T2 and T3 were positive but not significant (compared to no exposure). Results from multiple agent models were positive, non-singificant..	Delzell et. al 2001 737524 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia (Hodgkin's disease, multiple myeloma, all leukemia, non-Hodgkin's lymphoma)	Health Effect: Immune/Hematological-All lymphopoietic cancer (LHC) mortality. LHC mortality subtypes analyzed: leukemia (lymphocytic, myelogenous, other), non-Hodgkin's lymphoma, Hodgkins's disease, multiple myeloma,-Cancer/Carcinogenesis-All cancers mortality, all benign neoplasm mortality. Lymphopoietic cancer mortality (leukemia, Hodgkin's disease, non-Hodgkin's disease, multiple myeloma), buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, prostate cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, other cancer mortality.-Mortality-All lymphopoietic cancer (LHC) mortality. LHC mortality subtypes analyzed: leukemia (lymphocytic, myelogenous, other), non-Hodgkin's lymphoma, Hodgkins's disease, multiple myeloma mortality. Prostate cancer mortality. Buccal cavity and pharynx cancer mortality; esophageal cancer mortality; stomach cancer mortality; colorectal cancer mortality; pancreatic cancer mortality. Pancreatic cancer mortality. Bladder cancer mortality, kidney cancer mortality. Lung cancer mortality. Brain cancer mortality.. Outcome measure: ICD codes from death certificates	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). 17,924 male synthetic rubber workers. SBR Workers. 1944-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured at least one year prior to outcome.	Standardized Mortality Ratio (SMR). Confounders adjusted for: 0.	Lowest exposure concentration for a significant adverse health outcome response: No quantitative data. SMR (95%) for:All leukemia: 116 (91-147)Non-hodgkin's lymphoma: 100 (75-130)Multiple myeloma: 95 (62-140)Hodgkin's disease: 11 (58-195). No statistically significant results and no quantitative exposure data..	Delzell et. al 2006 737525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Bladder cancer	Health Effect: Cancer/Carcinogenesis-All cancers mortality, all benign neoplasm mortality. Lymphopoietic cancer mortality (leukemia, Hodgkin's disease, non-Hodgkin's disease, multiple myeloma), buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, prostate cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, other cancer mortality.-Mortality-All lymphopoietic cancer (LHC) mortality. LHC mortality subtypes analyzed: leukemia (lymphocytic, myelogenous, other), non-Hodgkin's lymphoma, Hodgkins's disease, multiple myeloma mortality. Prostate cancer mortality. Buccal cavity and pharynx cancer mortality; esophageal cancer mortality; stomach cancer mortality; colorectal cancer mortality; pancreatic cancer mortality. Pancreatic cancer mortality. Bladder cancer mortality, kidney cancer mortality. Lung cancer mortality. Brain cancer mortality.-Renal/Kidney-Bladder cancer mortality, kidney cancer mortality.. Outcome measure: ICD codes from death certificates	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). 17,924 male synthetic rubber workers. SBR Workers. 1944-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured at least one year prior to outcome.	Standardized Mortality Ratio (SMR). Confounders adjusted for: 0.	Lowest exposure concentration for a significant adverse health outcome response: No quantitative data. SMR (95%) for 1944-1998: 90 (64-125). No statistically significant results and no quantitative exposure data..	Delzell et. al 2006 737525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Immune/Hematological– Cancer mortality: All lymphopoietic cancer mortality. Leukemia mortality; leukemia subtype mortality [myelogenous leukemia (acute, chronic, unspecified), lymphocytic leukemia (acute, chronic unspecified), and unspecified leukemia (acute, chronic, unspecified)]; lymphosarcoma mortality; other lymphatic tissue cancer mortality. -Cancer incidence: Lymphopoietic cancer incidence (subtypes: Non-Hodgkins lymphoma, leukemia, multiple myeloma).-Cancer/Carcinogenesis-All cancers mortality, all benign neoplasm mortality. Lymphopoietic cancer mortality (leukemia, lymphosarcoma, other), central nervous system cancer mortality; prostate cancer mortality, buccal cavity and pharynx cancer mortality, digestive organ cancer mortality, esophageal cancer mortality, stomach cancer mortality, large intestine cancer mortality, rectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, bladder cancer mortality, kidney cancer mortality, lung cancer mortality, skin cancer mortality.-Mortality-Cancer mortality: all cancer mortality; all lymphopoietic cancer and subtype mortality (leukemia, leukemia subtypes, lymphosarcoma, other); central nervous system cancer mortality; prostate cancer mortality; buccal cavity and pharynx cancer mortality; digestive organ cancer mortality;	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). 15,649 male synthetic rubber workers employed at one of 8 plants for at least 1 year before 01/01/1992. SBR Workers. 1943-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) At work, prior to outcome assessment.	Standardized Mortality Ratio (SMR). Confounders adjusted for: Age, calendar-period, and race.	Lowest exposure concentration for a significant adverse health outcome response: 20-99 ppm-yrs (median=42.7). SMR (95% CI) for cumulative exposure to BD:0 vs. >0-19 ppm-yrs: 103 (56-172)0 vs. 20-99 ppm-yrs: 202 (120-320)0 vs. 100-199 ppm-yrs: 213 (85-438)0 vs. 200+ ppm-yrs: 331 (107-773). Significant positive associations were reported for the 20-99 ppm-yrs group and the 200+ ppm-yrs group..	Delzell et. al 1996 51390 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
autistic disorder	Health Effect: Neurological/Behavioral-Autistic disorder-Reproductive/Developmental-Autistic disorder. Outcome measure: Diagnostic and Statistical Manual of Mental Disorders code 299.00	General public, Patients in clinics, Pregnant people. Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17), Adults (18+). United States; Los Angeles County, California. Female, Male. Cohort (Retrosepctive). Cohort of children born in Los Angeles County, California 1995–2006, those whose mothers resided during pregnancy in a 5km buffer around air-toxics monitoring stations (n=148,722), including 768 autistic disorder cases and 147,954 non-cases.. Exposure assessment: 1995 - 2006; Outcome ascertainment: 1998 - 2009.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured during pregnancy.	Logistic Regression. Confounders adjusted for: birth year, maternal age, race/ethnicity, place of birth (US vs. non-US), education, parity, type of insurance, offspring sex.	Lowest exposure concentration for a significant adverse health outcome response: continuous. 1,3 -butadiene exposure in relation to autistic disorder:OR (95% CI): 1.59 (1.18, 2.15) for participants within 5 km of a monitorOR (95% CI): 1.70 (1.12–2.57) for participants within 3.5 km of a monitor1,3-Butadiene exposure in relation to autistic disorder among boysOR ((5% CI): 1.54 (1.11, 2.15)1,3 - butadiene exposure in relation to ”less impaired” expressive languageOR (95% CI): 2.25 (1.18–4.28). Significant positive associations were reported between 1,3-butadiene exposure and autistic disorder among all study participants within 3.5km and 5km of a monitor, among boys, and among those with less impaired expressive language. Results were not statistically significant among girls or among those with more impaired expressive language. Results were attenuated to non-significance in multi-pollutant models..	Ehrenstein et. al 2014 2453135 Medium
primitive neuroectodermal tumor	Health Effect: Neurological/Behavioral-primitive neuroectodermal tumor (PNET), medulloblastoma, astrocytoma-Cancer/Carcinogenesis-primitive neuroectodermal tumor (PNET), medulloblastoma, astrocytoma. Outcome measure: ICD-O Code 9473	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; California. Female, Male. Case-Control. Children younger than age 6 in California (n=183 cases, n = 30,569 controls). 1990-2007.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured prenatally and during first year of life.	Logistic Regression. Confounders adjusted for: Birth year, maternal race/ethnicity, maternal age and education, place of birth mother.	Lowest exposure concentration for a significant adverse health outcome response: Continuous (IQR=0.257 ppbV). OR (95% CI) per interquartile range increase for 1,3-butadiene exposure during pregnancy: 2.23 (1.28, 3.88)OR (95% CI) per interquartile range increase for 1,3-butadiene exposure during the first year of life: 3.15 (1.57, 6.32). Significant positive associations were reported per IQR increase in 1,3-butadiene for PNET when exposure was measured prenatally and during the first year of life. No significant results were reported for other brain tumors..	Ehrenstein et. al 2016 5684085 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Mortality-Leukemia mortality-Immune/Hematological-Leukemia mortality-Cancer/Carcinogenesis-Leukemia mortality. Outcome measure: Death certificated and medical records, based on ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). >16,000 male styrene-butadiene rubber workers employed for at least one year between 1943 and 1991 at 8 facilities in the US and Canada. SBR Workers. Employed: 1943-1991; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Adult occupational exposure, outcome was mortality 7 to 55 years later.	Poisson Regression. Confounders adjusted for: age, years since hire, and co-exposure to other agents (styrene and dimethyldithiocarbamate (DMDTC).	Lowest exposure concentration for a significant adverse health outcome response: 184.7–<425.0 ppm-years. RRs for increasing quartiles of 1,3 butadiene cumulative exposure in ppm-years, relative to none, in an uncertainty analysis of 1,000 datasets. The mean RRs (95% CI) in the main analysis vs. the median values in this study were:[1] >0–<33.7 ppm-years = 1.4 (0.7-3.1) vs mean RR of 1.5; [2] 33.7–<184.7 ppm-years 1.2 (0.6-2.7) vs. mean RR of 1.6; [3] 184.7–<425.0 ppm-years = 2.9 (1.4-6.4) vs. mean RR of 2.6, [4] 425.0+ ppm-years = 3.7 (1.7-8.0) vs. mean RR of 3.3,. Results support the validity of findings in Graff et al 2005 HEROID 737523 after accounting for uncertainty in exposure estimates..	Graff et. al 2009 2950774 Medium
Leukemia mortality	Health Effect: Immune/Hematological-Lymphohematopoietic cancer mortality-Cancer/Carcinogenesis-Lymphohematopoietic cancer mortality-Mortality-Lymphohematopoietic cancer mortality. Outcome measure: Death certificate cause of death codes	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Men working at six North American rubber plants (n=16,579). 1943-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated for each participant's entire working history at the included plants.	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: 184.7-<425.0 ppm-years (Q3). RR (95% CI) for Q1 vs. no exposure: 1.4 (0.7 - 3.1);RR (95% CI) for Q2 vs. no exposure: 1.2 (0.6 - 2.7);RR (95% CI) for Q3 vs. no exposure: 2.9 (1.4 - 6.4);RR (95% CI) for Q4 vs. no exposure: 3.7 (1.7 - 8.0). Significant positive associations for Q3 and Q4 of exposure distribution among exposed leukemia decedents versus no exposure (0 ppm-years). Results for Q1 and Q2 vs. no exposure positive but not significant.Table 3 also presents results for 1,3-butadiene peaks >100 ppm, which is a less well-defined exposure. Results are similar to cumulative exposure.Table 4 repeats associations shown in Table 3 additionally showing influence of adjusting for one vs. both co-exposures (styrene, dimethyldithiocarbamate)..	Graff et. al 2005 737523 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Immune/Hematological-Lymphohematopoietic cancer mortality-Cancer/Carcinogenesis-Lymphohematopoietic cancer mortality-Mortality-Lymphohematopoietic cancer mortality. Outcome measure: Death certificate cause of death codes	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Men working at six North American rubber plants (n=16,579). 1943-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated for each participant's entire working history at the included plants.	Poisson Regression. Confounders adjusted for: age, years since hire, styrene, dimethyldithiocarbamate (DMDTC).	Lowest exposure concentration for a significant adverse health outcome response: nan. RR (95% CI) for Q1 vs. no exposure: 1.4 (0.5 - 3.9);RR (95% CI) for Q2 vs. no exposure: 0.9 (0.3 - 2.6);RR (95% CI) for Q3 vs. no exposure: 2.1 (0.7 - 6.2);RR (95% CI) for Q4 vs. no exposure: 3.0 (1.0 - 9.2). Results from single pollutant model were attenuated to non-significance in this multi-pollutant mode. Results for Q1, Q3, and Q4 (vs. no exposure) were positive but not significant.Table 3 also presents results for 1,3-butadiene peaks >100 ppm, which is a less well defined exposure. Results are similar to cumulative exposure.Table 4 repeats associations shown in Table 3 additionally showing influence of adjusting for one vs. both co-exposures (styrene, dimethyldithiocarbamate)..	Graff et. al 2005 737523 Medium
Leukemia mortality	Health Effect: Immune/Hematological-Lymphohematopoietic cancer mortality-Cancer/Carcinogenesis-Lymphohematopoietic cancer mortality-Mortality-Lymphohematopoietic cancer mortality. Outcome measure: Death certificate cause of death codes	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Men working at six North American rubber plants (n=16,579). 1943-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated for each participant's entire working history at the included plants.	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >0-<16.3 ppm-years (Q1). RR (95% CI) for Q1 vs. no exposure: 2.6 (1.2 - 5.8);RR (95% CI) for Q2 vs. no exposure: 1.9 (0.9 - 4.2);RR (95% CI) for Q3 vs. no exposure: 4.0 (1.8 - 8.7);RR (95% CI) for Q4 vs. no exposure: 4.6 (2.1 - 10.1). Significant positive associations for Q1, Q3, and Q4 of exposure distribution among exposed leukemia decedents versus no exposure (0 ppm-years)..	Graff et. al 2005 737523 Medium
Leukemia mortality	Health Effect: Immune/Hematological-Lymphohematopoietic cancer mortality-Cancer/Carcinogenesis-Lymphohematopoietic cancer mortality-Mortality-Lymphohematopoietic cancer mortality. Outcome measure: Death certificate cause of death codes	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Men working at six North American rubber plants (n=16,579). 1943-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated for each participant's entire working history at the included plants.	Poisson Regression. Confounders adjusted for: age, years since hire, styrene, dimethyldithiocarbamate (DMDTC).	Lowest exposure concentration for a significant adverse health outcome response: >247.6 ppm-years (Q4). RR (95% CI) for Q1 vs. no exposure: 2.8 (1.0 - 7.7);RR (95% CI) for Q2 vs. no exposure: 1.7 (0.6 - 4.7);RR (95% CI) for Q3 vs. no exposure: 3.0 (1.0 - 8.5);RR (95% CI) for Q4 vs. no exposure: 3.7 (1.3 - 11.1). Significant positive associations for Q4 of exposure distribution among exposed leukemia decedents versus no exposure (0 ppm-years). Results generally attenuated compared to single agent model for exposures > 100 ppm..	Graff et. al 2005 737523 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Immune/Hematological-Lymphohematopoietic cancer mortality-Cancer/Carcinogenesis-Lymphohematopoietic cancer mortality-Mortality-Lymphohematopoietic cancer mortality. Outcome measure: Death certificate cause of death codes	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Men working at six North American rubber plants (n=16,579). 1943-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated for each participant's entire working history at the included plants.	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: 56.2-<124.7 ppm-years (Q3). RR (95% CI) for Q1 vs. no exposure: 1.8 (0.8 - 3.9);RR (95% CI) for Q2 vs. no exposure: 1.2 (0.5 - 2.5);RR (95% CI) for Q3 vs. no exposure: 2.9 (1.3 - 6.3);RR (95% CI) for Q4 vs. no exposure: 2.9 (1.4 - 6.4). Significant positive associations for Q3, and Q4 of exposure distribution among exposed leukemia decedents versus no exposure (0 ppm-years). Associations for Q1 and Q2 positive but not significant..	Graff et. al 2005 737523 Medium
Leukemia mortality	Health Effect: Immune/Hematological-Lymphohematopoietic cancer mortality-Cancer/Carcinogenesis-Lymphohematopoietic cancer mortality-Mortality-Lymphohematopoietic cancer mortality. Outcome measure: Death certificate cause of death codes	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Men working at six North American rubber plants (n=16,579). 1943-1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated for each participant's entire working history at the included plants.	Poisson Regression. Confounders adjusted for: age, years since hire, styrene, dimethyldithiocarbamate (DMDTC).	Lowest exposure concentration for a significant adverse health outcome response: nan. RR (95% CI) for Q1 vs. no exposure: 1.8 (0.7 - 5.0);RR (95% CI) for Q2 vs. no exposure: 0.8 (0.3 - 2.4);RR (95% CI) for Q3 vs. no exposure: 2.0 (0.7 - 5.9);RR (95% CI) for Q4 vs. no exposure: 2.0 (0.6 - 6.0). Results attenuated to non-significance compared to single agent model for exposure intensities <=100 ppm..	Graff et. al 2005 737523 Medium
all germ cell tumors	Health Effect: Cancer/Carcinogenesis-germ cell tumors (all germ cell tumors, yolk sac tumors, teratomas)-Reproductive/Developmental-germ cell tumors (all germ cell tumors, yolk sac tumors, teratomas). Outcome measure: California Cancer Registry records (International Classification of Childhood Cancer, Version 3 [ICCC-3] codes 101-105)	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; California. Female, Male. Case-Control. Pregnant women and their children in California (Enrolled n = 243 cases and n = 147,100 controls; used up to n = 18 cases and n = 13,362 controls in analys3s of all germ cell tumors). 1984-2013.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured during second trimester of pregnancy.	Logistic Regression. Confounders adjusted for: birth year, maternal age, maternal race, neighborhood-level socioeconomic status.	Lowest exposure concentration for a significant adverse health outcome response: continuous. OR (95% CI) for 1-IQR increase in second trimester exposure: 1.51 (1.01 - 2.26). Significant positive association for second trimester exposure. Non-significant inverse association for first trimester exposure, and non-significant positive association for entire pregnancy exposure..	Hall et. al 2019 5641117 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
yolk sac tumors	Health Effect: Cancer/Carcinogenesis-germ cell tumors (all germ cell tumors, yolk sac tumors, teratomas)-Reproductive/Developmental-germ cell tumors (all germ cell tumors, yolk sac tumors, teratomas). Outcome measure: California Cancer Registry records (International Classification of Diseases for Oncology, Version 3 [ICD-O-3] code 9071)	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; California. Female, Male. Case-Control. Pregnant women and their children in California (Enrolled n = 243 cases and n = 147,100 controls; used up to n = 10 cases and n = 21,770 controls in analyses of yolk sac tumors). 1984-2013.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured during second trimester of pregnancy.	Logistic Regression. Confounders adjusted for: birth year, maternal age, maternal race, neighborhood-level socioeconomic status.	Lowest exposure concentration for a significant adverse health outcome response: continuous. OR (95% CI) for a 1-IQR increase in exposure in the second trimester: 1.80 (1.02 - 3.16). Significant positive association for second trimester exposure. Non-significant positive association for entire pregnancy exposure and no association for first trimester exposure..	Hall et. al 2019 5641117 Medium
Lymphocyte number, lymphocyte percent of white blood cell count	Health Effect: Immune/Hematological-White blood cell count, granulocytes, lymphocytes, lymphocyte %, erythrocytes, platelets. Outcome measure: Blood sample collection	Occupational workers. Adults (18+). China; Yanshan. Female, Male. Cross-Sectional. 79 workers from polybutadiene rubber production facility (n = 41 exposed workers, n = 38 unexposed workers). NR.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure assigned based on work unit (exposed vs. unexposed).	Wilcoxon test. Confounders adjusted for: age, sex.	Lowest exposure concentration for a significant adverse health outcome response: Exposed. Median lymphocyte number = 1.8 in unexposed workers vs. 2.4 in exposed workers, p-value from Wilcoxon test = 0.002Median lymphocyte % = 28.4% in unexposed workers vs. 32.8% in exposed workers, p-value from Wilcoxon test = 0.005. Workers with jobs exposed to 1,3-butadiene had significantly higher lymphocyte number and lymphocyte percent of total white blood cell count than workers with jobs unexposed to 1,3-butadiene.	Hayes et. al 2000 5586518 Low
Lymphocyte number, lymphocyte percent of white blood cell count	Health Effect: Immune/Hematological-White blood cell count, granulocytes, lymphocytes, lymphocyte %, erythrocytes, platelets. Outcome measure: Blood sample collection	Occupational workers. Adults (18+). China; Yanshan. Female, Male. Cross-Sectional. 79 workers from polybutadiene rubber production facility (n = 41 exposed workers, n = 38 unexposed workers). NR.	Indoor air Exposure Route: Inhalation Acute (less than 24 hours) Exposure assessed in air samples collected at the breathing zone using personal samplers during a 6-hour shift.	Spearman correlation.	Lowest exposure concentration for a significant adverse health outcome response: continuous. Spearman correlation coefficient between 1,3-butadiene in air samples and lymphocyte number among exposed workers = 0.52 (p = 0.001)Spearman correlation coefficient between 1,3-butadience in air samples and lymphocyte % among exposed workers = 0.46 (p = 0.003). Significant positive correlation between 1,3-butadience in personal air samples and both lymphocyte number and lymphocyte percent of total white blood cell count among workers with jobs exposed to 1,3-butadiene..	Hayes et. al 2000 5586518 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Invasive breast cancer incidence	Health Effect: Cancer/Carcinogenesis-Breast cancer-Reproductive/Developmental-Breast cancer. Outcome measure: ICD codes C500-C509 reported to the state cancer registry	General public. Adults (18+). United States; California. Female. Cohort (Prospective). Large population-based cohort study of women residing in California (n=48,665) aged 45 to 75 years at baseline. Multiethnic Cohort (MEC). 1993-1996.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Monthly estimates were computed using data from NATA.	Cox Proportional Hazards Model. Confounders adjusted for: age at entry (as a strata variable, 5-year categories), race and ethnicity, BMI, family history of breast cancer, age at first live birth, age at menarche, number of children, menopausal status, hormone replacement therapy, physical activity, energy intake, alcohol use, smoking, education and neighborhood SES (baseline and current)..	Lowest exposure concentration for a significant adverse health outcome response: Continuous. All women: HR (95% CI): 1.18 (1.13, 1.23) per IQR increase. Significant positive associated was reported for a 5-year exposure lag in census tract 1,3-butadiene (per 1 IQR increase) and invasive breast cancer risk.	Heck et. al 2024 11438289 Medium
Invasive breast cancer incidence	Health Effect: Cancer/Carcinogenesis-Breast cancer-Reproductive/Developmental-Breast cancer. Outcome measure: ICD codes C500-C509 reported to the state cancer registry	General public. Adults (18+). United States; California. Female. Cohort (Prospective). Large population-based cohort study of women residing in California (n=48,665) aged 45 to 75 years at baseline. Multiethnic Cohort (MEC). 1993-1996.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Monthly estimates were computed using data from NATA.	Cox Proportional Hazards Model. Confounders adjusted for: age at entry (as a strata variable, 5-year categories), race and ethnicity, BMI, family history of breast cancer, age at first live birth, age at menarche, number of children, menopausal status, hormone replacement therapy, physical activity, energy intake, alcohol use, smoking, education and neighborhood SES (baseline and current)..	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Hormone receptor negative tumors: HR (95% CI): 1.24 (1.14-1.35) per IQR increase. Significant positive associated was reported for a 5-year exposure lag traffic-related 1,3-butadiene (per 1 IQR increase) and breast cancer risk, among hormone receptor negative tumors [status for both estrogen receptors (ER-) and progesterone receptors (PR-)].	Heck et. al 2024 11438289 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Invasive breast cancer incidence	Health Effect: Cancer/Carcinogenesis- Breast cancer- Reproductive/Developmental- Breast cancer. Outcome measure: ICD codes C500-C509 reported to the state cancer registry	General public. Adults (18+). United States; California. Female. Cohort (Prospective). Large population-based cohort study of women residing in California (n=48,665) aged 45 to 75 years at baseline. Multiethnic Cohort (MEC). 1993-1996.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Monthly estimates were computed using data from NATA.	Cox Proportional Hazards Model. Confounders adjusted for: age at entry (as a strata variable, 5-year categories), race and ethnicity, BMI, family history of breast cancer, age at first live birth, age at menarche, number of children, menopausal status, hormone replacement therapy, physical activity, energy intake, alcohol use, smoking, education and neighborhood SES (baseline and current)..	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Hormone receptor positive tumors: HR (95% CI): 1.17 (1.11, 1.23) per IQR increase. Significant positive associated was reported for a 5-year exposure lag traffic-related 1,3-butadiene (per 1 IQR increase) and breast cancer risk, among hormone receptor positive tumors [status for either estrogen receptors (ER+) or progesterone receptors (PR+)].	Heck et. al 2024 11438289 Medium
acute lymphoblastic leukemia (ALL)	Health Effect: Cancer/Carcinogenesis- Acute lymphoblastic leukemia (ALL)- Immune/Hematological- Acute lymphoblastic leukemia (ALL). Outcome measure: Medical records	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5). United States; California. Female, Male. Case-Control. Children with acute lymphoblastic leukemia (ALL) younger than age 6 who were listed in the California Cancer Registry between 1990 and 2007 and controls randomly selected from California birth certificates and frequency matched by year of birth (ALL cases= 66, controls= 2626).. Air Pollution and Childhood Cancer Study (APCC). 1990-2007.	Outdoor air Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure measured during pregnancy (1st trimester, 2nd trimester, 3rd trimester, and overall pregnancy) and during child's first year of life.	Logistic Regression. Confounders adjusted for: maternal race/ethnicity, birth year, parity, maternal birthplace, neighborhood socioeconomic index.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Third trimester OR (95% CI): 1.54 (1.19, 1.99)Entire pregnancy OR (95% CI): 1.76 (1.09, 2.86). Significant positive association between 1,3-butadiene exposure during the third trimester and during the entire pregnancy and ALL. Associations with exposure during the 1st and 2nd trimesters and during the child's first year of life not significant..	Heck et. al 2014 2345720 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
acute myeloid leukemia (AML)	Health Effect: Cancer/Carcinogenesis-Acute myeloid leukemia (AML)-Immune/Hematological-Acute myeloid leukemia (AML). Outcome measure: Medical records	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5). United States; California. Female, Male. Case-Control. Children with acute myeloid leukemia (AML) younger than age 6 who were listed in the California Cancer Registry between 1990 and 2007 and controls randomly selected from California birth certificates and frequency matched by year of birth (AML cases=41, controls=17,296).. Air Pollution and Childhood Cancer Study (APCC). 1990-2007.	Outdoor air Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure measured during pregnancy (1st trimester, 2nd trimester, 3rd trimester, and overall pregnancy) and during child's first year of life.	Logistic Regression. Confounders adjusted for: maternal race/ethnicity, birth year, parity, maternal birthplace, neighborhood socioeconomic index.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Child's first year of life OR (95% CI): 2.35 (1.02, 5.39). Significant positive association between 1,3-butadiene exposure during the child's first year of life and AML. Associations between prenatal exposures and AML not significant..	Heck et. al 2014 2345720 Medium
retinoblastoma development	Health Effect: Ocular/Sensory-Retinoblastoma-Cancer/Carcinogenesis-Retinoblastoma. Outcome measure: ICC code 050	Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; California. Female, Male. Case-Control. 30,704 children (103 cases, 30,601 controls). Air Pollution and Childhood Cancer (APCC) study. 1990-2007.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured during pregnancy and first year of life.	Logistic Regression. Confounders adjusted for: maternal race/ethnicity and nativity (White non-Hispanic, Hispanic and US born, Hispanic and foreign born, and other (o29, race/not specified), paternal age 30–34, 35þ), and year of birth, and socioeconomic status.	Lowest exposure concentration for a significant adverse health outcome response: continuous. Average pregnancy exposure:OR (95% CI): 1.59 (1.08, 2.35)Average first year of life exposure:OR (95% CI): 1.64 (0.89, 3.01). Retinoblastoma risk was found to be increased with pregnancy exposure to 1,3-butadiene..	Heck et. al 2013 2369182 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers Cohort. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=392.1 ppm-years. RR (95% CI) for:T1 vs. 0ppm: 1.2 (0.5 - 2.9)T2 vs. 0 ppm: 2.0 (0.8 - 4.7)T3 vs. 0 ppm: 4.1 (1.7 - 9.8). Significant positive associations reported for T3. T2 and T1 positive but not significant. All tertiles compared to 0 ppm exposure in models..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=10,249.0 total peaks >=100ppm. RR (95% CI) for:T1 vs. 0 ppm: 1.8 (0.8-4.1)T2 vs. 0 ppm: 1.8 (0.8-4.1)T3 vs. 0 ppm: 5.4 (2.4-12.1). Significant positive associations reported for T3. T2 and T1 positive but not significant. All tertiles compared to 0 ppm in models..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=315.1 ppm-years. RR (95% CI) with 5-year lagged exposure (single-pollutant model) for:T1 vs. 0 ppm: 1.2 (0.5-2.9)T2 vs. 0 ppm: 2.2 (0.9-5.4)T3 vs. 0 ppm: 3.8 (1.6-9.1). Significant positive associations reported for T3. T2 and T1 positive but not significant in single-pollutant model. All tertiles compared to 0 ppm in models. No statistically significant results for multi-pollutant model..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=313.8 ppm-years. RR (95% CI) with 10-year lagged exposure (single-pollutant model) for:T1 vs. 0 ppm: 1.4 (0.6-3.5)T2 vs. 0 ppm: 1.9 (0.8-4.6)T3 vs. 0 ppm: 4.6 (1.9-11.1). Significant positive associations reported for T3. T2 and T1 positive but not significant. All tertiles compared to 0 in models. No statistically significant results for multi-pollutant model..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=180.9 ppm-years. RR (95% CI) for exposure intensities >=100 ppm:T1 vs. 0ppm: 2.2 (0.5 - 9.5)T2 vs. 0 ppm: 3.0 (0.7 - 13.4)T3 vs. 0 ppm: 4.0 (1.0 - 20.0). T3, T2, and T1 positive but not significant. All tertiles compared to 0 in models. No statistically significant results for multi-pollutant model..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=114.4 ppm-years due to exposure intensities < 100ppm. RR (95% CI) for T3 vs. 0 ppm: 0.8 (0.2 - 4.3)RR (95% CI) for T2 vs. 0 ppm: 1.0 (0.2 - 5.2)RR (95% CI) for T1 vs. 0ppm: 0.5 (0.1 - 2.6). T3, T2, and T1 positive but not significant. All tertiles compared to 0 in models..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Chronic lymphocytic leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: None. RR (95% CI) for T2 vs. T1: 1.9 (0.6 - 5.7)RR (95% CI) for T3 vs. T1: 3.3 (1.0 - 10.3). T3 and T2 positive but not significant. T1 used as referent in this analysis..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Acute myelogenous or monocytic leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: None. RR (95% CI) for T2 vs. T1: 2.4 (0.8 - 7.3)RR (95% CI) for T3 vs. T1: 2.7 (0.7 - 10.8). T3 and T2 positive but not significant. T1 used as referent in this analysis..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Chronic myelogenous leukemia	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: None. RR (95% CI) for T2 vs. T1: 1.0 (0.2 - 3.7)RR (95% CI) for T3 vs. T1: 2.8 (0.8 - 9.6). T3 positive but not significant. T2 null. T1 used as referent in this analysis..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Other leukemias	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: >=392.1 ppm-years. RR (95% CI) for T2 vs. T1: 1.8 (0.4 - 8.3)RR (95% CI) for T3 vs. T1: 6.9 (1.8 - 26.1). Significant positive associations for T3. T2 positive but not significant. T1 used as referent in this analysis..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Non-Hodgkin's lymphoma	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: None. RR (95% CI) for:T1 vs. 0ppm: 1.5 (0.6 - 4.2)T2 vs. 0 ppm: 1.5 (0.5 - 4.5)T3 vs. 0 ppm: 2.4 (0.8 - 7.3). T3, T2, and T1 positive but not significant. All tertiles compared to 0 in models..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Multiple myeloma	Health Effect: Cancer/Carcinogenesis-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Immune/Hematological-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease)-Mortality-lymphohematopoietic cancer (leukemias, non-Hodgkin's lymphomas, multiple myelomas, Hodgkin's disease). Outcome measure: Personnel records, death certificates, and national databases (e.g., National Death Index, Social Security Administration Death Master File). ICD codes were used to identify causes of death.	Occupational workers. Adults (18+), Older Adults (65+). United States. Male. Cohort (Retrosepctive). 13,130 male workers from six synthetic rubber plants in the United States. SBR Workers. 1944-1991.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age, years since hire.	Lowest exposure concentration for a significant adverse health outcome response: None. RR (95% CI) for:T1 vs. 0ppm: 0.2 (0.0 - 1.7)T2 vs. 0 ppm: 0.9 (0.2 - 4.2)T3 vs. 0 ppm: 3.2 (0.8 - 13.5). T3 positive but not significant. Negative associations for T2 and T1 but not significant. All tertiles compared to 0 in models..	IISRP, 2000 5664525 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
all leukemia	Health Effect: Cancer/Carcinogenesis-Mortality from all leukemia, leukemia subtypes (lymphoid leukemia, myeloid leukemia, acute myeloid leukemia (AML)).Mortality from non-Hodgkin's lymphoma (NHL), multiple myeloma, and all B-cell malignancies (includes lymphoid leukemia, NHL and multiple myeloma).-Immune/Hematological-Mortality from all leukemia, leukemia subtypes (lymphoid leukemia, myeloid leukemia, acute myeloid leukemia (AML)).Mortality from non-Hodgkin's lymphoma (NHL), multiple myeloma, and all B-cell malignancies (includes lymphoid leukemia, NHL and multiple myeloma).. Outcome measure: Data linkage, ICD codes, medical records review (subset)	Occupational workers. Adults (18+), Older Adults (65+). United States; Canada; Kentucky, Louisiana, Texas, Ontario. Female, Male. Cohort (Retrosepctive). Styrene-butadiene rubber workers in North America (n= 21,087). Employment: any time from 1943 to 1991; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Occupationally exposed, median follow-up 40 years since first hire.	Cox Proportional Hazards Model. Confounders adjusted for: age at hire, calendar year of hire, sex, race, plant and payroll status (ever hourly paid or always salaried).	Lowest exposure concentration for a significant adverse health outcome response: 363.64-7741.41 ppm-years. RR (95% CI) for increasing cumulative 1,3 - butadiene exposure quartiles (based on case distribution) vs no exposure: Q1 vs 0: 1.04 (0.60 - 1.83) Q2 vs 0: 1.37 (0.76 - 2.46) Q3 vs 0: 1.60 (0.87 - 2.94) Q4 vs 0: 2.53 (1.37 - 4.67). Positive association between cumulative exposure to 1,3-butadiene and all leukemia. Statistically significant for the highest vs lowest quartile and using continuous exposure variables. Stronger association when limited to exposed person-time <=95th percentile..	Sathiakumar et. al 2021 10192219 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
lymphoid leukemia	Health Effect: Cancer/Carcinogenesis-Mortality from all leukemia, leukemia subtypes (lymphoid leukemia, myeloid leukemia, acute myeloid leukemia (AML)).Mortality from non-Hodgkin's lymphoma (NHL), multiple myeloma, and all B-cell malignancies (includes lymphoid leukemia, NHL and multiple myeloma).-Immune/Hematological-Mortality from all leukemia, leukemia subtypes (lymphoid leukemia, myeloid leukemia, acute myeloid leukemia (AML)).Mortality from non-Hodgkin's lymphoma (NHL), multiple myeloma, and all B-cell malignancies (includes lymphoid leukemia, NHL and multiple myeloma).. Outcome measure: Data linkage, ICD codes, medical records review (subset)	Occupational workers. Adults (18+), Older Adults (65+). United States; Canada; Kentucky, Louisiana, Texas, Ontario. Female, Male. Cohort (Retrosepctive). Styrene-butadiene rubber workers in North America (n= 21,087). Employment: any time from 1943 to 1991; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Occupationally exposed, median follow-up 40 years since first hire.	Cox Proportional Hazards Model. Confounders adjusted for: age at hire, calendar year of hire, sex, race, plant and payroll status (ever hourly paid or always salaried).	Lowest exposure concentration for a significant adverse health outcome response: 213.43 -<376.31 ppm-years. RR (95% CI) for increasing cumulative 1,3 - butadiene exposure quartiles (based on case distribution) vs no exposure: Q1 vs 0: 0.72 (0.29 - 1.78) Q2 vs 0: 0.85 (0.37 - 2.14) Q3 vs 0: 2.61 (1.02 - 6.67) Q4 vs 0: 1.95 (0.76 - 5.03). Positive association between cumulative exposure to 1,3-butadiene and lymphoid leukemia. Statistically significant for the third vs lowest quartile, positive but ns for the highest vs lowest quartile. Significant using continuous exposure variables. Stronger association when BD was limited to exposed person-time <=95th percentile..	Sathiakumar et. al 2021 10192219 Medium
COPD mortality	Health Effect: Lung/Respiratory-Non-cancer respiratory mortality: nonmalignant respiratory disease (NMRD), chronic obstructive pulmonary disease (COPD) and pneumonia-Mortality-Non-cancer respiratory mortality: nonmalignant respiratory disease (NMRD), chronic obstructive pulmonary disease (COPD) and pneumonia. Outcome measure: Death records	Occupational workers. Adults (18+), Older Adults (65+). United States; Canada; Kentucky, Louisiana, Texas; Ontario. Female, Male. Cohort (Retrosepctive). Synthetic rubber polymer workers (n=21,087). Enrollment: employed workers from 1943 - 1992; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated cumulatively for duration in job.	Cox Proportional Hazards Model. Confounders adjusted for: age at hire, year of hire, race, sex, plant and ever hourly status.	Lowest exposure concentration for a significant adverse health outcome response: continuous. Regression coefficient (95% CI) for continuous ppm-year butadiene trend of all person-time among men: 1.42x10^-4 ((0.16 - 2.66)x10-^4). Significant positive association reported for continuous all person-time exposure among men however trend for exposed person-time and exposed person-time trimmed to <=95th percentile of exposure were positive but not significant. Additionally, lag10 years (regression coefficient (95% CI): 1.49x10^-4 ((0.21-2.78)x10^4) and lag20 years (regression coefficient (95% CI): 1.65x10^-4 ((0.20-3.09)x10^4) models for trend observed significant positive associations..	Sathiakumar et. al 2021 9038746 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Bladder cancer mortality	Health Effect: Renal/Kidney-bladder cancer mortality-Cancer/Carcinogenesis-bladder cancer mortality-Mortality-bladder cancer mortality. Outcome measure: Death records	Occupational workers. Adults (18+), Older Adults (65+). United States; Canada; Kentucky, Louisiana, Texas; Ontario. Female, Male. Cohort (Retrosepctive). Synthetic rubber polymer workers (n=21,087). Enrollment: employed workers from 1943 - 1992; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated cumulatively for duration in job.	Cox Proportional Hazards Model. Confounders adjusted for: age at hire, year of hire, race, sex, plant and ever hourly status.	Lowest exposure concentration for a significant adverse health outcome response: >= 328.79 ppm-years. Rate ratio (95% CI) increasing ppm-years butadiene exposure quartiles vs. no exposure: Q4vs 0: 2.13 (1.03 - 4.41). Significant positive association reported for Q4; Q1, Q2, and Q3 vs. unexposed positive but not significant.Significant positive trend reported for all person-time and exposed person-time with categorical and continuous exposures, respectively. Trimmed exposed person-time <= 95th percentile positive but not significant for both categorical and continuous exposure estimates.Styrene co-exposure model observed significant positive trend for continuous and categorical exposures among those with >= 21 ppm-years of styrene exposure and positive but not significant for <21 ppm-years styrene exposure..	Sathiakumar et. al 2021 9038746 Medium
Lung cancer mortality	Health Effect: Lung/Respiratory-lung cancer mortality-Cancer/Carcinogenesis-lung cancer mortality-Mortality-lung cancer mortality. Outcome measure: Death records	Occupational workers. Adults (18+), Older Adults (65+). United States; Canada; Kentucky, Louisiana, Texas; Ontario. Female, Male. Cohort (Retrosepctive). Synthetic rubber polymer workers (n=21,087). Enrollment: employed workers from 1943 - 1992; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated cumulatively for duration in job.	Cox Proportional Hazards Model. Confounders adjusted for: age at hire, year of hire, race, sex, plant and ever hourly status.	Lowest exposure concentration for a significant adverse health outcome response: >0.00 - 1.93 ppm-years. Rate ratio (95% CI) increasing ppm-years butadiene exposure quartiles vs. no exposure among women: Q1vs 0: 2.47 (1.37 - 4.43) Q2 vs. 0: 1.94 (1.08 - 3.47) Q3 vs. 0: 1.90 (1.03 - 3.51). Among women only. Significant positive associations reported for Q1, Q2, and Q3 vs. unexposed; Q4 vs. unexposed positive but not significant. Trend analyses for all person-time, exposed person-time, and trimmed exposed person-time <= 95th percentile of exposure reported no association for categorical and continuous exposures.	Sathiakumar et. al 2021 9038746 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lung cancer mortality	Health Effect: Lung/Respiratory-Lung cancer mortality-Cancer/Carcinogenesis-Lung cancer mortality-Mortality-Lung cancer mortality. Outcome measure: Linkage to vital records	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female, Male. Cohort (Retrosepctive). The study included 20,059 rubber industry workers (4101 women and 15,958 men) employed at 8 styrene-butadiene plants in the US and Canda.. Women hired: 1943-1991; Follow-up: 2002 , Men hired: 1944-1991; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment; mean years since initial hire 31 years in men, 39 years in women..	Cox Proportional Hazards Model. Confounders adjusted for: age, year of birth, race, years since hire, plant, and pay status (ever vs never hourly worker).	Lowest exposure concentration for a significant adverse health outcome response: 0-0.429 ppm-yrs (women). Adjusted RR (95% CI) by decile of BD exposure (women) 0 vs. 0-<0.429 ppm-yrs: 3.29 (1.16-9.33)0 vs. 0.429-<1.3 ppm-yrs: 2.04 (0.73-5.69)0 vs. 1.3-<2.4 ppm-yrs: 2.73 (0.97-7.65)0 vs. 2.4-<5.1 ppm-yrs: 1.82 (0.65-5.05)0 vs. 5.1-<11.4 ppm-yrs: 1.59 (0.57-4.43)0 vs. 11.4-<16.5 ppm-yrs: 2.73 (0.97-7.69)0 vs. 16.5-<32.2 ppm-yrs: 1.45 (0.51-4.12)0 vs. 32.2-<58.9 ppm-yrs: 2.46 (0.94-6.48)0 vs. 58.9-<314.3 ppm-yrs: 1.23 (0.46-3.30)0 vs. 314.3+ ppm-yrs: 1.73 (0.60-4.96)No significant results for men.. The lowest exposure group (who had a mean exposure of 0.14 ppm yrs) had a significant positive association with lung cancer. No other exposure groups had a significant association, but all were non-significant positive. Non-significant, inconsistent associations were reported for deciles in men..	Sathiakumar et. al 2009 1600222 Medium
Lung cancer mortality	Health Effect: Lung/Respiratory-Lung cancer mortality-Cancer/Carcinogenesis-Lung cancer mortality-Mortality-Lung cancer mortality. Outcome measure: Linkage to vital records	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female, Male. Cohort (Retrosepctive). The study included 20,059 rubber industry workers (4101 women and 15,958 men) employed at 8 styrene-butadiene plants in the US and Canda.. Women hired: 1943-1991; Follow-up: 2002 , Men hired: 1944-1991; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment; mean years since initial hire 31 years in men, 39 years in women..	Cox Proportional Hazards Model. Confounders adjusted for: age, year of birth, race, years since hire, plant, and pay status (ever vs never hourly worker).	Lowest exposure concentration for a significant adverse health outcome response: continuous. Adjusted RR and 95% CI and Beta Coefficient and SE for the Relation Between butadiene (BD) Exposure and Lung Cancer, by Gender.*p < 0.05Women - Ever vs never exposed to BD: -RR (95% CI) 1.99 (1.28 - 3.10) *-Beta (SE) 0.68817 (0.22684) *Women -BD ppm-yrs, continuous: 1. All women, untransformed BD-RR (95% CI) 1.00 (1.00 - 1.00) -B (SE) 0.0002 (0.00089)2. All women, ln-transformed BD-RR (95% CI) 1.06 (1.01 - 1.12) *-B (SE) 0.05929 (0.02648) *3. BD ever-exposed women, untransformed BD-RR (95% CI) 1.00 (1.00 –1.00) -B (SE) 0.00124 (0.00112)4. BD-ever exposed women, ln-transformed BD-RR (95% CI) 0.85 (0.72– 0.99) * -B (SE) 0.16871 (0.07962) *No significant results for men.. Women workers ”ever” exposed to BD had a higher risk of lung cancer mortality. Exposure-response trends were inconsistent. Untransformed BD exposure associations were null. Natural logarithm-transformed BD exposure indicated a positive trend when the unexposed were included and an inverse trend when the unexposed were excluded. No exposure response trends were seen for BD among men..	Sathiakumar et. al 2009 1600222 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality-Immune/Hematological-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality-Mortality-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality. Outcome measure: Vital Records & Death Certificates	Occupational workers. Adults (18+), Older Adults (65+). United States & Canada; Louisiana, Texas, Kentucky, Ontario. Male. Cohort (Retrosepctive). 16,579 men who had worked at any of 6 synthetic rubber manufacturing plants in the US and Canada between 1943 and 1992 for at least one year.. Enrollment: 1943-1991; Follow-up for mortality ascertainment: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured a mean of 34 to 38 years prior to mortality.	Cox Proportional Hazards Model. Confounders adjusted for: age, year of birth, plant, race.	Lowest exposure concentration for a significant adverse health outcome response: 213.43-<289.91 cumulative ppm-years; continuous. Significant adjusted RR (95% CI) for increasing leukemia-specific exposure deciles: gp6 (107.78-<124.94 ppm-years) = 1.57 (0.70, 3.51); gp7 (213.43-<289.91 ppm-years) = 3.20 (1.42, 7.18); gp8 (289.91-<448.17 ppm-years) = 2.64 (1.18, 5.91); gp9 (448.17-<908.35 ppm-years) = 2.78 (1.24, 6.24); gp10 (908.35+ ppm-years) = 3.76 (1.59, 8.89). Significant adjusted beta (SE) for continuous cumulative BD ppm-years: untransformed BD = 2.9 x 10^-4 (1.0 x 10^-4); ln-transformed BD = 9.4 x 10^-2 (2.7 x 10^-2); log-10 transformed BD = 2.2 x 10^-1 (0.6 x 10^-1); square root of BD = 3.0 x 10^-2 (0.7 x 10^-2). Model comparisons: AIC values indicate similar fit for all transformations.. Using leukemia case specific deciles, RRs (95% CI) for increasing cumulative BD exposure vs. unexposed participants were positive above decile 2, and significant above decile 6. Beta coefficients for associations between leukemia and continuous BD variables were significant for untransformed BD and for all transformations examined (ln, log-10, square root)..	Sathiakumar et. al 2015 4659248 Medium
Non-Hodgkin's lymphoma (NHL) mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality-Immune/Hematological-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality-Mortality-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality. Outcome measure: Vital Records & Death Certificates	Occupational workers. Adults (18+), Older Adults (65+). United States & Canada; Louisiana, Texas, Kentucky, Ontario. Male. Cohort (Retrosepctive). 16,579 men who had worked at any of 6 synthetic rubber manufacturing plants in the US and Canada between 1943 and 1992 for at least one year.. Enrollment: 1943-1991; Follow-up for mortality ascertainment: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured a mean of 34 to 38 years prior to mortality.	Cox Proportional Hazards Model. Confounders adjusted for: age, year of birth, plant, race.	Lowest exposure concentration for a significant adverse health outcome response: 301.48-<355.58 cumulative ppm-years; continuous. Significant adjusted RR (95% CI) for increasing NHL-specific exposure deciles were observed for gp8 (301.48-<355.58 ppm-years) = 3.55 (1.46, 8.60) and gp9 (355.58-<490.66 ppm-years) = 2.96 (1.27, 6.91), but not for gp10 (490.66+ ppm-years) = 1.30 (0.55, 3.06). Significant adjusted beta (SE) for continuous cumulative BD ppm-years were not significant for non-Hodgkin's lymphoma.. Using NHL case specific deciles, RRs (95% CI) for increasing cumulative BD exposure vs. unexposed participants were positive for 7 of 10 declines, reaching significance for deciles 8 and 9. The magnitude of association declined in decile 10. Beta coefficients for associations between NHL and continuous BD variables were not statistically significant overall (p<0.10 for square root transformation among men hired before 1960)..	Sathiakumar et. al 2015 4659248 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Multiple myeloma mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality-Immune/Hematological-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality-Mortality-Leukemia mortality, Non-Hodgkin's Lymphoma mortality, Multiple Myeloma mortality. Outcome measure: Vital Records & Death Certificates	Occupational workers. Adults (18+), Older Adults (65+). United States & Canada; Louisiana, Texas, Kentucky, Ontario. Male. Cohort (Retrosepctive). 16,579 men who had worked at any of 6 synthetic rubber manufacturing plants in the US and Canada between 1943 and 1992 for at least one year.. Enrollment: 1943-1991; Follow-up for mortality ascertainment: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured a mean of 34 to 38 years prior to mortality.	Cox Proportional Hazards Model. Confounders adjusted for: age, year of birth, plant, race.	Lowest exposure concentration for a significant adverse health outcome response: None significant. nan. nan.	Sathiakumar et. al 2015 4659248 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lung and breast cancer mortality	Health Effect: Cancer/Carcinogenesis-All cancers mortality, all benign neoplasm mortality, buccal cavity and pharynx cancer mortality, , esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphopoietic cancer mortality, non-Hodgkin's lymphoma mortality, Hodgkin's lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality.-Mortality-Blood disorders mortality; mental disorders mortality; allergic, endocrine, metabolic, and nutritional disease combined mortality; nervous system disease mortality; circulatory disease mortality; non-malignant respiratory disease mortality; digestive disease mortality; genitourinary disease mortality; external causes mortality; other known and unknown causes mortality.-Mortality-All cancers mortality, all benign neoplasm mortality, buccal cavity and pharynx cancer mortality, , esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality,	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female. Cohort (Retrosepctive). 4,863 women workers at any of 8 North American Styrene-Butadiene Rubber manufacturing facilities. SBR Workers. 1943-2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment, 11 to 60 years prior to death.	Poisson Regression. Confounders adjusted for: age, years since hire, ever-hourly worker status.	Lowest exposure concentration for a significant adverse health outcome response: >0 to <1.9 ppm-years. Lung cancer: OR (95% CI) forQ1 vs ref = 2.7 (1.4 –5.1); Q2 vs ref = 1.8 (0.9 –3.5); Q3 vs ref = 2.0 (1.0–4.0); Q4 vs ref = 1.7 (0.8 –3.4). SMR (95% CI) for lung cancer mortality: All workers = 114 (93-138), ever-hourly workers = 159 (117-211); never-hourly workers = 93 (71-120); all workers using state population referent = 127 (104/154).. RRs for lung cancer mortality were significant for women in the lowest and third quartile of BD exposure relative to those who were unexposed; the association was non-monotonic. SMRs for lung cancer mortality were significant for SBR-exposed hourly workers, but not for hourly workers not exposed to SBR processes. Indirect estimated adjustment for smoking slightly attenuated lung cancer SMRs..	Sathiakumar et. al 2009 1330953 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Bladder cancer mortality	Health Effect: Cancer/Carcinogenesis-All cancers mortality, all benign neoplasm mortality, buccal cavity and pharynx cancer mortality, , esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphopoietic cancer mortality, non-Hodgkin's lymphoma mortality, Hodgkin's lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality.-Mortality-Blood disorders mortality; mental disorders mortality; allergic, endocrine, metabolic, and nutritional disease combined mortality; nervous system disease mortality; circulatory disease mortality; non-malignant respiratory disease mortality; digestive disease mortality; genitourinary disease mortality; external causes mortality; other known and unknown causes mortality.-Mortality-All cancers mortality, all benign neoplasm mortality, buccal cavity and pharynx cancer mortality, , esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality,	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female. Cohort (Retrosepctive). 4,863 women workers at any of 8 North American Styrene-Butadiene Rubber manufacturing facilities. SBR Workers. 1943-2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment, 11 to 60 years prior to death.	Standardized Mortality Ratio (SMR). Confounders adjusted for: age, years since hire, ever-hourly worker status.	Lowest exposure concentration for a significant adverse health outcome response: SBR-related operations hourly work; residual operations ever-hourly work. SMR (95% CI) for bladder cancer mortality:All workers = 174 (75-343), ever-hourly workers = 332 (122-723); never-hourly workers = 72 (9-259); all workers using state population referent = 186 (80-3664).. SMRs for bladder cancer mortality were positive for ever-hourly female workers. When examined by work process area, SMRs were significant for those in "residual" operations, not for SBR-related operations workers. Residual operations defined as working "in general services, in safety, in design and engineering, and, at the Canadian plant, in maintenance, technical, and other operations that could not be identified as related to SBR production.".	Sathiakumar et. al 2009 1330953 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality, non-Hodgkin's lymphoma mortality	Health Effect: Cancer/Carcinogenesis-All cancers mortality, all benign neoplasm mortality, buccal cavity and pharynx cancer mortality, , esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphopoietic cancer mortality, non-Hodgkin's lymphoma mortality, Hodgkin's lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality.-Mortality-All cancers mortality, all benign neoplasm mortality, buccal cavity and pharynx cancer mortality, , esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphopoietic cancer mortality, non-Hodgkin's lymphoma mortality, Hodgkin's lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality.-Immune/Hematological-Blood disorders mortality.. Outcome measure: ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female. Cohort (Retrosepctive). 4,863 women workers at any of 8 North American Styrene-Butadiene Rubber manufacturing facilities. SBR Workers. 1943-2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment, 11 to 60 years prior to death.	Standardized Mortality Ratio (SMR). Confounders adjusted for: age, years since hire, ever-hourly worker status.	Lowest exposure concentration for a significant adverse health outcome response: No significant findings for leukemia or lymphoma mortality in women. SMRs (95% CI) for leukemia mortality in women: All workers = 78 (38-144), ever-hourly workers = 46 (6-164); never-hourly workers = 95 (41-188). SMRs (95% CI) for non-Hodgkin's lymphoma mortality in women: All workers = 105 (59–173), ever-hourly workers = 154 (62–317); never-hourly workers = 82 (36–162).. SMRs for leukemia and non-Hodgkin's lymphoma mortality were not significant in female workers..	Sathiakumar et. al 2009 1330953 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lung cancer mortality	Health Effect: Cancer/Carcinogenesis-All cancers mortality, benign neoplasms mortality, leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, prostate cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, other cancers mortality-Mortality-All cancers mortality, benign neoplasms mortality. Leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, prostate cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, other cancer mortality-Lung/Respiratory-Lung cancer mortality.	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female, Male. Cohort (Retrosepctive). Workers at 8 North American Styrene-Butadiene Rubber facilities between 1943-1991. Men were included if they had been employed for at least one year. Women were included if they had been employed for at least one day.. Employment: 1943-1991. Follow-up for mortality: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment 18 to 66 years prior to death.	Cox Proportional Hazards Model. Confounders adjusted for: Within cohort analyses were adjusted for age, year and age at hire, sex, plant, ever-hourly status. SMRs were not adjusted, though some were stratified..	Lowest exposure concentration for a significant adverse health outcome response: Ever exposed hourly worker employed <10 years at >=20 years since hire. Within-cohort RR (95% CI) for lung cancer mortality associated with having been ever vs never exposed to butadiene in women = 1.97 (1.33–2.90), in men = 0.93 (0.78–1.11), and overall = 1.07 (0.91–1.26). p-values for trend from unspecified exposure-respond analysis =0.96 in men, =0.97 in women, and = 0.87 in all subjects.SMRs (95% CI) for lung cancer mortality were: (i) among workers exposed to butadiene = 202 (152-264) in women and 88 (81-95) in men; (ii) among workers not exposed to butadiene = 86 (67-108) in women and 86 (73-100) in men. For men and women combined, the SMR (95% CI) for lung cancer mortality was significant for workers employed <10 years with >=20 years since hire = 119 (106-133). For men and women combined, the SMR (95% CI) for lung cancer mortality was inversely significant for workers employed <10 years with <20 years since hire = 64 (42-94). For all other subgroups characterized based on employment duration and lag since first hire SMRs were NS.. RRs for ever-exposure to butadiene were significant for lung cancer mortality in women, but not in men. The median (IQR) cumulative ppm-years of butadiene exposure among cases was 12 (2-58) in women and 81 (25-236) in men..	Sathiakumar et. al 2019 6592911 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Bladder cancer mortality	Health Effect: Cancer/Carcinogenesis- All cancers mortality, benign neoplasms mortality, leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, prostate cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, other cancers mortality-Mortality- All cancers mortality, benign neoplasms mortality. Leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, prostate cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, other cancer mortality-Renal/Kidney- Bladder cancer mortality, kidney cancer mortality.	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female, Male. Cohort (Retrosepctive). Workers at 8 North American Styrene-Butadiene Rubber facilities between 1943-1991. Men were included if they had been employed for at least one year. Women were included if they had been employed for at least one day.. Employment: 1943-1991. Follow-up for mortality: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment 18 to 66 years prior to death.	Standardized Mortality Ratio (SMR). Confounders adjusted for: SMRs were unadjusted, though some were stratified. Within cohort Cox models adjusted for age, year and age at hire, race, sex, plant and ever-hourly status..	Lowest exposure concentration for a significant adverse health outcome response: Ever exposed hourly worker employed >=10 years.. SMRs (95% CI) for bladder cancer mortality were 142 (106-186) for ever hourly workers employed for10+ years, vs 88 (52-139) for workers employed <10 years. SMRs (95% CI) for bladder cancer mortality were 131 (102-166) for ever hourly workers with 20+ years since hire, vs 38 (5-139) for workers with <20 years since hire. SMRs for bladder cancer were significant for workers employed 10+ years who also had 20+ years since hire = 148 (110-195), but not for other combinations of employment duration and time since hire. For bladder cancer mortality, the within-cohort Cox proportional hazard rate ratio (95% CI) for ever-vs never exposure to butadiene was 1.36 (0.78-2.38).. SMRs for bladder cancer mortality were significant among workers employed for 10+ years, or with 20+ years since hire. For bladder cancer mortality, the within-cohort Cox proportional hazard rate ratio (95% CI) for ever-vs never exposure to butadiene was not significant. The exposure response trend p-value was significant; however effect estimates were not provided, and the exposure used in the model was not characterized..	Sathiakumar et. al 2019 6592911 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Immune/Hematological-Leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality-Cancer/Carcinogenesis-All cancers mortality, benign neoplasms mortality, leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, prostate cancer mortality, breast cancer mortality, uterine cancer mortality, ovarian cancer mortality, other cancers mortality-Mortality-All cancers mortality, benign neoplasms mortality. Leukemia (lymphoid, myeloid subtypes) mortality, multiple myeloma mortality, Hodgkin's lymphoma mortality, non-Hodgkin's lymphoma mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, lung cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality,	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Female, Male. Cohort (Retrosepctive). Workers at 8 North American Styrene-Butadiene Rubber facilities between 1943-1991. Men were included if they had been employed for at least one year. Women were included if they had been employed for at least one day.. Employment: 1943-1991. Follow-up for mortality: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated during employment 18 to 66 years prior to death.	Standardized Mortality Ratio (SMR). Confounders adjusted for: SMRs were not adjusted, though some were stratified. Within cohort-analyses of mortality adjusted for age, year and age at hire, race, sex, plant and ever-hourly status..	Lowest exposure concentration for a significant adverse health outcome response: Ever exposed hourly worker employed >=10 years.. SMRs (95% CI) for leukemia mortality were 139 (107-176) for ever hourly workers employed for 10+ years, vs 89 (60-127) for ever-hourly workers employed <10 years. SMRs (95% CI) for leukemia mortality were significant for workers employed 10+ years who also had 20+ years since hire = 139 (106-179), but not for other combinations of employment duration and time since hire. The SMR (95% CI) for Non-Hodgkin's lymphoma was also significant for workers employed 10+ years who also had 20+ years since hire = 136 (102-177), but not for other combinations of employment duration and time since hire.For leukemia mortality, the within-cohort Cox proportional hazard rate ratio (95% CI) for ever-vs never exposure to butadiene was 1.39 (0.87-2.21) for all leukemia, 1.09 (0.54, 2.24) for lymphoid leukemia, and 1.47 (0.77, 2.84) for myeloid leukemia.. SMRs for leukemia and Non-Hodgkin's lymphoma mortality were significant for workers employed for 10+ years who also had 20+ years since hire. The SMR for leukemia was also positive but NS for workers employed for 10+ years who had a <20 year lag since hire. SMRs for other employment and hire date durations were less than 100. In within-cohort analyses, the exposure-response p-value for total and lymphoid, but not myeloid leukemia, were significant, but the exposure variable used in these analyses were not characterized. Analyzing ever vs never butadiene exposure, the within-cohort RR for lymphoid leukemia mortality was null, while the RR for myeloid leukemia was positive but not significant..	Sathiakumar et. al 2019 6592911 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality, chronic myelogenous leukemia [CML] mortality, chronic lymphocytic leukemia [CLL] mortality, acute myelogenous or monocytic leukemia [ALM] mortality, all lymphoid neoplasms mortality, and all myeloid neoplasms mortality	Health Effect: Cancer/Carcinogenesis-Leukemia mortality-Mortality-Leukemia mortality-Immune/Hematological-Leukemia mortality. Outcome measure: Data linkage to vital status databases; ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). Male workers employed for at least one year at styrene-butadiene rubber plants in the US and Canada between 1943 and 1991.. Hire dated: 1943-1991; Follow-up 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure during employment.	Poisson Regression. Confounders adjusted for: Age.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Beta (SE) per ppm-year of cumulative BD exposure for:- Chronic Lymphocytic Leukemia (CLL) mortality: 2.85 x 10^-3 (2.08 x 10^-3) [no lag]- Chronic Myelogenous Leukemia (CML) mortality: -2.26 x 10^-4 (5.51 x 10^-4) [15 year lag]- Acute Myelogenous Leukemia (AML) mortality: -4.75 x 10^-4 (4.35 x 10^-4) [no lag]. After adjustment for covariates selected based on statistical significance (vs a directed acyclic graph or other appropriate method), higher cumulative BD exposure was associated with increases in CLL mortality, but not with CML or AML mortality. Covariates in some models – but not the model for CLL – included duplicative measures of BD exposure which could attenuate effect estimates for the cumulative BD exposure variable..	Sielken, 2007 6544022 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality, chronic myelogenous leukemia [CML] mortality, chronic lymphocytic leukemia [CLL] mortality, acute myelogenous or monocytic leukemia [ALM] mortality, all lymphoid neoplasms mortality, and all myeloid neoplasms mortality	Health Effect: Cancer/Carcinogenesis- Leukemia mortality- Mortality- Leukemia mortality- Immune/Hematological- Leukemia mortality. Outcome measure: Data linkage to vital status databases; ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). Male workers employed for at least one year at styrene-butadiene rubber plants in the US and Canada between 1943 and 1991.. Hire dated: 1943-1991; Follow-up 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure during employment.	Cox Proportional Hazards Model. Confounders adjusted for: Age.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Beta (SE) per ppm-year of cumulative BD exposure for:- Chronic Lymphocytic Leukemia (CLL) mortality: 4.15 x 10^-4 (1.32 x 10^-4) [no lag]- Chronic Myelogenous Leukemia (CML) mortality: 4.11 x 10^-4 (7.22 x 10^-4) [15 year lag]- Acute Myelogenous Leukemia (AML) mortality: -2.20 x 10^-4 (5.67 x 10^-4) [no lag]. After adjustment for covariates selected based on statistical significance (vs a directed acyclic graph or other appropriate method), higher cumulative BD exposure was associated with increases in CLL mortality, but not with CML or AML mortality. Covariates in some models – but not the model for CLL – included duplicative measures of BD exposure which could attenuate effect estimates for the cumulative BD exposure variable..	Sielken, 2007 6544022 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality, chronic myelogenous leukemia [CML] mortality, chronic lymphocytic leukemia [CLL] mortality, acute myelogenous or monocytic leukemia [ALM] mortality, all lymphoid neoplasms mortality, and all myeloid neoplasms mortality	Health Effect: Mortality-Leukemia mortality, chronic myelogenous leukemia [CML] mortality, chronic lymphocytic leukemia [CLL] mortality, acute myelogenous or monocytic leukemia [ALM] mortality, all lymphoid neoplasms mortality, and all myeloid neoplasms mortality-Immune/Hematological-Leukemia mortality, chronic myelogenous leukemia [CML] mortality, chronic lymphocytic leukemia [CLL] mortality, acute myelogenous or monocytic leukemia [ALM] mortality, all lymphoid neoplasms mortality, and all myeloid neoplasms mortality-Cancer/Carcinogenesis-Leukemia mortality, chronic myelogenous leukemia [CML] mortality, chronic lymphocytic leukemia [CLL] mortality, acute myelogenous or monocytic leukemia [ALM] mortality, all lymphoid neoplasms mortality, and all myeloid neoplasms mortality. Outcome measure: Data linkage to vital status databases; ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). Workers at 6 styrene butadiene rubber plants in the United States and Canada. Other papers describe the cohort as comprising over 16,000 male workers employed for at least one year between 1943 and 1991.. Employed: 1943 to 1991. Follow-up: reported elsewhere through 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure during employment.	Cox Proportional Hazards Model. Confounders adjusted for: Age. Models examined other potential confounders which varied..	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Beta (95% CI) for cumulative BD ppm-years.-All leukemia: full sample = 0.00029 (0.00009-0.00049); association remained significant in subsample with cumulative BD exposure <=400 ppm-years 0.00283 (0.00065-0.00501). -Chronic lymphocytic leukemia: full sample = 0.00042 (0.00017-0.00067); association remained significant in subsample with cumulative BD exposure <=500 ppm-years 0.00411 (0.00123-0.00699). All lymphoid neoplasms: full sample = 0.00023 (0.00004-0.00042); association remained significant in subsample with cumulative BD exposure <=1000 ppm-years 0.00157 (0.00005-0.00309).. Cumulative BD exposure was associated with significantly increased mortality from leukemia overall, the CLL subtype, and with all lymphoid neoplasm mortality. Associations were not significant for myeloid neoplasms or other leukemia subtypes. Models that included both all exposure and exposure limited to a time lag of 40+ years had statistically significant slopes for cumulative BD exposure..	Sielken et. al 2013 1798799 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Total leukemia	Health Effect: Cancer/Carcinogenesis-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Mortality-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Immune/Hematological-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia. Outcome measure: Data linkage and medical records, ICD-9 codes 204.0, 205.0, 206.0, 207.0, 204.1, 205.1, 207.1, 204.9, 205.9, 207.8	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry (enrolled=16585, decedents = 5593). Employed: 1943->1992; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured while working at a relevant industry plant.	Cox Proportional Hazards Model.	Lowest exposure concentration for a significant adverse health outcome response: </=400 ppm-years. Per unit increase in cumulative BD ppm-years, beta coefficient (SE), 95% CI, p-valueAll: 0.00029 (SE= 0.00010), 95% CI: 0.00009, 0.00049, p-value = 0.0263</= 1338 ppm-years: 0.00121 (SE= 0.00036), 95% CI: 0.00051, 0.00191, p-value = 0.0024</= 1000 ppm-years: 0.00145 (SE= 0.00047), 95% CI: 0.00054, 0.00236, p-value = 0.0045</= 500 ppm-years: 0.00296 (SE= 0.00086, 95% CI: 0.00127, 0.00465, p-value = 0.0014</= 400 ppm-years: 0.00283 (SE= 0.00111), 95% CI: 0.00065, 0.00501, p-value = 0.0156. Significant associations between cumulative BD ppm-years and leukemia were found for models including exposure in ranges limited to thresholds above <=300 ppm-years. Data shown in Table 6 provides additional insight into these results, as there was an observed decrease in power as ppm-years decreased (fewer person-years and case counts were included)..	Sielken et. al 2011 1940484 Low
Chronic lymphocytic leukemia	Health Effect: Cancer/Carcinogenesis-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Mortality-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Immune/Hematological-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia. Outcome measure: Data linkage with ICD codes, medical records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry (enrolled=16585, decedents = 5593). Employed: 1943->1992; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured while working at a relevant industry plant.	Cox Proportional Hazards Model.	Lowest exposure concentration for a significant adverse health outcome response: </=500 ppm-years. Per unit increase in cumulative BD ppm-years, beta coefficient (SE), 95% CI : All: 0.00042 (SE= 0.00013), 95% CI: 0.00017, 0.00067, p-value = 0.0195</= 1338 ppm-years: 0.00160 (SE= 0.00057), 95% CI: 0.00048, 0.00272, p-value = 0.0145</= 1000 ppm-years: 0.00210 (SE= 0.00073), 95% CI: 0.00067, 0.00353, p-value = 0.0110</= 500 ppm-years: 0.00411 (SE= 000147), 95% CI: 0.00123, 0.00699, p-value = 0.0101. Significant associations were found for all intervals above 400 ppm-years. Table 6 provides additional insight into this table, as there was an observed decrease in power as ppm-years decreased..	Sielken et. al 2011 1940484 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Chronic lymphocytic leukemia	Health Effect: Cancer/Carcinogenesis-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Mortality-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Immune/Hematological-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia. Outcome measure: Data linkage with ICD codes, medical records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry (enrolled=16585, decedents = 5593). Employed: 1943->1992; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured while working at a relevant industry plant.	Cox Proportional Hazards Model.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Chronic lymphocytic leukemiaCumulative butadiene ppm-years: Max log likelihood: -205.66, beta = 0.000417 (statistically significantly different than zero at the 5% significance level). Significant association between cumulative butadiene ppm-years and chronic lymphocytic leukemia. There were no other significant associations for chronic myelogenous leukemia or acute myelogenous leukemia..	Sielken et. al 2011 1940484 Low
Total leukemia	Health Effect: Cancer/Carcinogenesis-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Mortality-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia-Immune/Hematological-Total leukemia mortality, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia. Outcome measure: Data linkage and medical records, ICD-9 codes 204.0, 205.0, 206.0, 207.0, 204.1, 205.1, 207.1, 204.9, 205.9, 207.8	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry (enrolled=16585, decedents = 5593). 1943-Employed: 1943->1992; Follow-up: 1998.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure measured while working at a relevant industry plant.	Cox Proportional Hazards Model.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Total leukemiaCumulative butadiene ppm-years: Max log likelihood: -692.08, beta = 0.000290 (statistically significantly different than zero at the 5% significance level). Significant association between cumulative butadiene ppm-years and total leukemia. There were no other significant associations between total leukemia and the other exposure variables analyzed..	Sielken et. al 2011 1940484 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Cancer/Carcinogenesis- Leukemia mortality- Mortality- Leukemia mortality- Immune/Hematological- Leukemia mortality. Outcome measure: Linkage to mortality databases	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada. Male. Cohort (Retrosepctive). Male styrene-butadiene rubber workers employed for at least one year between 1943 and 1991. SBR Workers. Hire dates: 1943-1991; Follow-up: 1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Occupational exposure for at least one year during adulthood.	Poisson Regression. Confounders adjusted for: age, calendar year, years since hire, and styrene co-exposure.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Beta = 0.00157 (95% CI not provided). 1,3 butadiene exposure was approximately linearly associated with an increased risk of leukemia mortality..	Sielken et. al 2001 1942871 Low
Acute Lymphocytic Leukemia	Health Effect: Cancer/Carcinogenesis- Acute Lymphocytic Leukemia- Immune/Hematological- Acute Lymphocytic Leukemia. Outcome measure: Cancer registry	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; Texas. Female, Male. Case-Control. 1,248 cases with ALL diagnosed before age 5 years identified from the Texas Cancer Registry, and 12,172 controls matched on birth month and year.. 1995 - 2011.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure during pregnancy estimated from EPA National Air Toxics data geocoded to maternal address at delivery.	Logistic Regression. Confounders adjusted for: birth year and month, census tract, maternal age, infant birth weight, infant gender, maternal race/ethnicity.	Lowest exposure concentration for a significant adverse health outcome response: Medium. OR (95% CI) for Q2vs Q1: 1.23 (1.03 - 1.46)OR (95% CI) for Q3 vs Q1: 1.23 (1.04 - 1.47)OR (95% CI) for Q4 vs Q1: 1.28 (1.08 - 1.52). Significant positive associations reported for all quartiles in multivariate single-pollutant models, p-value not provided..	Symanski et. al 2016 3358047 Medium
Acute Lymphocytic Leukemia	Health Effect: Cancer/Carcinogenesis- Acute Lymphocytic Leukemia- Immune/Hematological- Acute Lymphocytic Leukemia. Outcome measure: Cancer registry	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; Texas. Female, Male. Case-Control. 1,248 cases with ALL diagnosed before age 5 years identified from the Texas Cancer Registry, and 12,172 controls matched on birth month and year.. 1995 - 2011.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure during pregnancy estimated from EPA National Air Toxics data geocoded to maternal address at delivery.	Logistic Regression. Confounders adjusted for: birth year and month, census tract, maternal age, infant birth weight, infant gender, maternal race/ethnicity, benzene.	Lowest exposure concentration for a significant adverse health outcome response: Medium. OR (95% CI) for Q2vs Q1: 1.22 (1.00, 1.50)OR (95% CI) for Q3 vs Q1: 1.28 (1.01, 1.63)OR (95% CI) for Q4 vs Q1: 1.40 (1.06, 1.86). Significant positive associations reported for all quartiles in multivariate benzene co-pollutant adjusted models, p-value not provided..	Symanski et. al 2016 3358047 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Acute Lymphocytic Leukemia	Health Effect: Cancer/Carcinogenesis-Acute Lymphocytic Leukemia-Immune/Hematological-Acute Lymphocytic Leukemia. Outcome measure: Cancer registry	General public, Pregnant people. Infant (0-1), Toddler (2-3), Preschool (3-5), Adults (18+). United States; Texas. Female, Male. Case-Control. 1,248 cases with ALL diagnosed before age 5 years identified from the Texas Cancer Registry, and 12,172 controls matched on birth month and year.. 1995 - 2011.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure during pregnancy estimated from EPA National Air Toxics data geocoded to maternal address at delivery.	Logistic Regression. Confounders adjusted for: birth year and month, census tract, maternal age, infant birth weight, infant gender, maternal race/ethnicity, polycyclic organic matter.	Lowest exposure concentration for a significant adverse health outcome response: Medium. OR (95% CI) for Q2vs Q1: 1.26 (1.05, 1.52)OR (95% CI) for Q3 vs Q1: 1.23 (0.99, 1.53)OR (95% CI) for Q4 vs Q1: 1.24 (0.97, 1.60). Positive but non-significant associations reported for all quartiles in multivariate polycyclic organic matter adjusted model, p-value not provided..	Symanski et. al 2016 3358047 Medium
Leukemia mortality	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records, ICD code 204-208	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=12412). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Standardized Mortality Ratio (SMR). Confounders adjusted for: 0.	Lowest exposure concentration for a significant adverse health outcome response: 20-99 ppm-years. Cumulative exposure (ppm-years): SMR (95% CI)0: 86 (35-178)>0-19: 103 (56-172)20-99: 202 (120-320)100-199: 213 (85-438)200+: 331 (107-773). Significant SMRs were reported for individuals with cumulative exposure of 20-99 ppm-years and 200+ ppm-years..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia mortality	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records, ICD code 204-208	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=12412). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: 10-year age and calendar period groups.	Lowest exposure concentration for a significant adverse health outcome response: 20-99 ppm-years. Cumulative exposure (ppm-years): Poisson rate ratios0: 1.0>0-19: 1.120-99: 2.2100-199: 2.6200+: 4.6. Significance for rate ratios was not reported..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
All person-years, underlying cause of death, and contributing cause of death for leukemias	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records, ICD code 204-208	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=12412). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age (40-49, 50-59, 60-69, 70-79, 80+), calendar period (1950-59, 1960-69, 1970-79, 1980-89, 1990-91), years since hire (10-19, 20-29, 30+), race (black, other), and styrene.	Lowest exposure concentration for a significant adverse health outcome response: nan. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)>0-19 vs. 0 ppm-years: 1.1 (0.4-5.0)20-99 vs. 0 ppm-years: 1.8 (0.6-5.4)100-199 vs. 0 ppm-years: 2.1 (0.6-7.1)200+ vs. 0 ppm-years: 3.6 (1.0-13.2). No significant RRs reported..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
All person-years, and all underlying cause of death with leukemia	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records, ICD code 204-208	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=12412). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year).	Poisson Regression. Confounders adjusted for: age (40-49, 50-59, 60-69, 70-79, 80+), calendar period (1950-59, 1960-69, 1970-79, 1980-89, 1990-91), years since hire (10-19, 20-29, 30+), race (black, other), and styrene.	Lowest exposure concentration for a significant adverse health outcome response: 0. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)>0-19 vs. 0 ppm-years: 1.4 (0.4-4.8)20-99 vs. 0 ppm-years: 2.3 (0.7-7.9)100-199 vs. 0 ppm-years: 2.6 (0.7-10.0)200+ vs. 0 ppm-years: 4.2 (1.0-17.4). No significant RRs reported..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Chronic lymphocytic leukemia	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=17964). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year.	Poisson Regression. Confounders adjusted for: age, race, calendar period, years since hire, styrene.	Lowest exposure concentration for a significant adverse health outcome response: 0. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)20-99 vs. 0 ppm-years: 1.6 (0.5-5.4)100+ vs. 0ppm-years: 1.7 (0.4-8.2). No significant RRs reported. Analysis was restricted to aged 50+, years since hire 20+ and calendar years 1970-91.	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Chronic myelogenous leukemia	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=17964). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year.	Poisson Regression. Confounders adjusted for: age, race, calendar period, years since hire, styrene.	Lowest exposure concentration for a significant adverse health outcome response: 0. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)20-99 vs. 0 ppm-years: 0.8 (0.2-3.2)100+ vs. 0 ppm-years: 1.3 (0.3-6.3). No significant RRs reported. Analysis was restricted to individuals aged 40-79 and calendar years 1950-89..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Acute myelogenous leukemia	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=17964). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year.	Poisson Regression. Confounders adjusted for: age, race, calendar period, years since hire, styrene.	Lowest exposure concentration for a significant adverse health outcome response: 100+ ppm-years. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)20-99 vs. 0 ppm-years: 11.6 (0.9-175)100+ vs. 0 ppm-years: 12.2 (1.2-112). Significant positive association reported for 100+ ppm-years of 1,3-butadiene exposure compared to <20 ppm-years and acute myelogenous leukemia. Analysis was restricted to ages 40+, calendar year 1960+, and years since hire 20+.	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Acute unspecified leukemia	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=17964). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year.	Poisson Regression. Confounders adjusted for: age, calendar period, years since hire, styrene.	Lowest exposure concentration for a significant adverse health outcome response: 0. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)20-99 vs. 0 ppm-years: 2.3 (0.5-10.8)100+ vs. 0ppm-years: 3.9 (0.6-27.6). No significant RRs reported. Analysis was restricted to ages 40-69 and 80+, white race, and calendar years 1960+.	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
non-Hodgkin's lymphoma	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=12412). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year.	Poisson Regression. Confounders adjusted for: age, calendar period, years since hire, race, styrene.	Lowest exposure concentration for a significant adverse health outcome response: N?A. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)>0-19 vs. 0 ppm-years: 2.3 (0.4-11.8)20-99 vs. 0 ppm-years: 0.8 (0.1-4.8)100-199 vs. 0 ppm-years: 2.5 (0.4-14.7)200+ vs. 0 ppm-years: 1.6 (0.2-13.0). No significant RRs reported. Analyses were restricted to ages 40+ and calendar years 1960+..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Multiple myeloma	Health Effect: Immune/Hematological-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Cancer/Carcinogenesis-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia-Mortality-Leukemia mortality, chronic lymphocytic leukemia mortality, chronic myelogenous leukemia mortality, acute myelogenous leukemia mortality, acute unspecified leukemia. Outcome measure: Personnel and vital statistics records	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; North America. Male. Cohort (Retrosepctive). Male workers in the styrene-butadiene-rubber industry in North America (Enrolled n=12412). SBR Workers. 1950-1992.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure estimated during employment prior to outcome (at least 1 year.	Poisson Regression. Confounders adjusted for: age, calendar period, years since hire, race, and styrene.	Lowest exposure concentration for a significant adverse health outcome response: 0. Cumulative exposure (ppm-years): Poisson regression rate ratios (95% CI)20-99 vs. 0 ppm-years: 1.0 (0.3-3.0)100+ vs. 0 ppm-years: 0.5 (0.1-4.5). No significant RRs reported. Analysis was restricted to ages 40+, years since hire 10+, and calendar years 1950-89..	UAB, 1995 5665016 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lung cancer	Health Effect: Cancer/Carcinogenesis-Lung cancer mortality, breast cancer mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Mortality-Lung cancer mortality, breast cancer mortality, all cause mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Lung/Respiratory-Lung cancer mortality, nonmalignant respiratory disease mortality, larynx cancer mortality. Outcome measure: ICD codes (not specified)	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; Kentucky, Texas, Louisiana; Ontario. Female. Cohort (Retrosepctive). Women employed at 8 styrene-butadiene rubber plants in North American (n=4,863). Recruitment: 1943-1991; follow-up: through 2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Unclear Exposure during employment at one of eight styrene-butadiene rubber plants.	Poisson Regression. Confounders adjusted for: age, years since hire, ever-hourly status.	Lowest exposure concentration for a significant adverse health outcome response: >0 - <1.9 ppm-years. RR (95% CI) for Q1 vs. no exposure: 2.7 (1.4 - 5.1)RR (95% CI) for Q2 vs. no exposure: 1.8 (0.9 - 3.5)RR (95% CI) for Q3 vs. no exposure: 2.0 (1.0 - 4.0)RR (95% CI) for Q4 vs. no exposure: 1.7 (0.8 - 3.4). Significant positive association reported for Q1 versus zero exposure, with results for other quartiles positive but not significant (Table 16). Results were similar in a model using a different characterization of the exposure variable (high 1,3-butadiene exposure tasks) (Table 17)..	UAB, 2007 6544020 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lung cancer	Health Effect: Cancer/Carcinogenesis-Lung cancer mortality, breast cancer mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Mortality-Lung cancer mortality, breast cancer mortality, all cause mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Lung/Respiratory-Lung cancer mortality, nonmalignant respiratory disease mortality, larynx cancer mortality. Outcome measure: ICD codes (not specified)	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; Kentucky, Texas, Louisiana; Ontario. Female. Cohort (Retrosepctive). Women employed at 8 styrene-butadiene rubber plants in North American (n=4,863). Recruitment: 1943-1991; follow-up: through 2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Unclear Exposure during employment at one of eight styrene-butadiene rubber plants.	Poisson Regression. Confounders adjusted for: age, years since hire, ever-hourly status, dimethyldithiocarbamate levels.	Lowest exposure concentration for a significant adverse health outcome response: >0 - <1.9 ppm-years. RR (95% CI) for Q1 vs. no exposure: 2.6 (1.3 - 5.2)RR (95% CI) for Q2 vs. no exposure: 1.7 (0.8 - 3.5)RR (95% CI) for Q3 vs. no exposure: 1.9 (0.9 - 4.0)RR (95% CI) for Q4 vs. no exposure: 1.7 (0.7 - 4.2). Significant positive association reported for Q1 versus zero exposure, with results for other quartiles positive but not significant in models adjusted for dimethyldithiocarbamate (Table 16). Results were similar but slightly attenuated in a model using a different characterization of the exposure variable (high 1,3-butadiene exposure tasks) (Table 17)..	UAB, 2007 6544020 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-Lung cancer mortality, breast cancer mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Mortality-Lung cancer mortality, breast cancer mortality, all cause mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Immune/Hematological-Lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mor-	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; Kentucky, Texas, Louisiana; Ontario. Female. Cohort (Retrosepctive). Women employed at 8 styrene-butadiene rubber plants in North American (n=4,863). Recruitment: 1943-1991; follow-up: through 2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Unclear Exposure during employment at one of eight styrene-butadiene rubber plants.	Standardized Mortality Ratio (SMR). Confounders adjusted for: race, age, calendar time.	Lowest exposure concentration for a significant adverse health outcome response: continuous. SMR (95% CI): 79 (38 - 145). No significant associations for leukemia expected and observed deaths among occupational population compared to general population..	UAB, 2007 6544020 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Bladder cancer	Health Effect: Cancer/Carcinogenesis-Lung cancer mortality, breast cancer mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Mortality-Lung cancer mortality, breast cancer mortality, all cause mortality, all cancer mortality, buccal cavity and pharynx cancer mortality, esophageal cancer mortality, stomach cancer mortality, colorectal cancer mortality, liver cancer mortality, pancreatic cancer mortality, larynx cancer mortality, uterine cancer mortality, ovarian cancer mortality, bladder cancer mortality, kidney cancer mortality, brain cancer mortality, lymphohematopoietic cancer mortality, Non-Hodgkin lymphoma mortality, Hodgkin lymphoma mortality, leukemia mortality, multiple myeloma mortality, other cancer mortality-Renal/Kidney-Bladder cancer mortality, kidney cancer mortality. Outcome measure: ICD codes (not specified)	Occupational workers. Adults (18+), Older Adults (65+). United States, Canada; Kentucky, Texas, Louisiana; Ontario. Female. Cohort (Retrosepctive). Women employed at 8 styrene-butadiene rubber plants in North American (n=4,863). Recruitment: 1943-1991; follow-up: through 2003.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Unclear Exposure during employment at one of eight styrene-butadiene rubber plants.	Standardized Mortality Ratio (SMR). Confounders adjusted for: race, age, calendar time.	Lowest exposure concentration for a significant adverse health outcome response: continuous. SMR (95% CI): 186 (80 - 366). No significant associations for bladder cancer expected and observed deaths among occupational population compared to general population..	UAB, 2007 6544020 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Leukemia	Health Effect: Cancer/Carcinogenesis-Mortality from all leukemias, lymphoid leukemia, myeloid leukemia, multiple myeloma, non-Hodgkin's lymphoma, and bladder/urinary cancer.-Immune/Hematological-Mortality from all leukemias, lymphoid leukemia, myeloid leukemia, multiple myeloma, and non-Hodgkin's lymphoma.-Mortality-Mortality from all leukemias, lymphoid leukemia, myeloid leukemia, multiple myeloma, non-Hodgkin's lymphoma, and bladder/urinary cancer.. Outcome measure: ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada; Texas, Kentucky, Louisiana, Ontario. Female, Male. Cohort (Retrosepctive). Male and female workers employed between 1943 and 1992 any of six styrene-butadiene rubber facilities in the United States and Canada, followed for mortality through 2009 (n=21,087). North American Styrene-Butadiene Rubber (SBR) cohort. Employed 1943-1991; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated based on work history prior to outcome.	Cox Proportional Hazards Model. Confounders adjusted for: age, BD high-intensity tasks (HITs) frequency.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Increase in risk of leukemia per unit increase in cumulative BD ppm-years exposure:-adjusted for BD HITs: Slope (SD) = 0.0001316 (0.0001079) per BD ppm-year, ns-not adjusted for BD HITs: Slope (SD) = 0.0002808 (0.0000838) per BD ppm-year, $p<0.01$. There was a significant increase in risk of leukemia associated with increasing cumulative BD exposure without adjusting for the frequency of high-intensity (>100 ppm) BD exposure tasks. The association with leukemia was not significant after this adjustment. Associations with lymphoid leukemia were significant before but not after HITs adjustment. However, associations were not significant for Myeloid leukemia, multiple myeloma, or non-Hodgkins' lymphoma..	Valdez-Flores et. al 2022 11531254 Low
Bladder cancer	Health Effect: Cancer/Carcinogenesis-Mortality from all leukemias, lymphoid leukemia, myeloid leukemia, multiple myeloma, non-Hodgkin's lymphoma, and bladder/urinary cancer.-Renal/Kidney-Mortality from bladder/urinary cancer.-Mortality-Mortality from all leukemias, lymphoid leukemia, myeloid leukemia, multiple myeloma, non-Hodgkin's lymphoma, and bladder/urinary cancer.. Outcome measure: ICD codes	Occupational workers. Adults (18+), Older Adults (65+). United States and Canada; Texas, Kentucky, Louisiana, Ontario. Female, Male. Cohort (Retrosepctive). Male and female workers employed between 1943 and 1992 any of six styrene-butadiene rubber facilities in the United States and Canada, followed for mortality through 2009 (n=21,087). North American Styrene-Butadiene Rubber (SBR) cohort. Employed 1943-1991; Follow-up: 2009.	Occupational assignment (by job title, job-exposure matrix, questionnaire, etc.) Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated based on work history.	Cox Proportional Hazards Model. Confounders adjusted for: age, BD high-intensity tasks (HITs) frequency.	Lowest exposure concentration for a significant adverse health outcome response: Continuous. Increase in risk of bladder/urinary cancer per unit increase in cumulative BD ppm-years exposure:-adjusted for BD HITs: Slope (SD) = 0.0002802 (0.0000852) per BD ppm-year, $p<0.05$-not adjusted for BD HITs: Slope (SD) = 0.0003159 (0.0000813) per BD ppm-year, $p<0.01$. There was a significant increase in risk of bladder/urinary associated with increasing cumulative BD exposure both with and without adjusting for the frequency of high-intensity (>100 ppm) BD exposure tasks. The association was attenuated after HITs adjustment..	Valdez-Flores et. al 2022 11531254 Low

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Acute lymphocytic leukemia	Health Effect: Cancer/Carcinogenesis-Lymphohematopoietic cancer incidence (leukemia, non-Hodgkin's lymphoma, Hodgkin's disease, acute lymphocytic leukemia, acute myeloid leukemia)-Immune/Hematological-Lymphohematopoietic cancer incidence (leukemia, non-Hodgkin's lymphoma, Hodgkin's disease, acute lymphocytic leukemia, acute myeloid leukemia). Outcome measure: NR	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17), Adults (18+). United States of America; Harris, Liberty, Montgomery, Chambers, Fort Bend, Waller, Brazoria, and Galveston Counties, Texas. Female, Male. Ecological. 997 cases of lymphohematopoietic cancer among children < 20 years of age from the Texas Cancer Registry (TCR), a North American Association of Central Cancer Registries. Ultimately, 670 cases of leukemia (510 cases of ALL and 92 cases of AML), 146 Hodgkin's disease cases, and 137 cases of NHL were included as eligible for analysis.. Diagnosis: 1995-2004.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated from 1999 US EPA ASPEN model data.	Poisson Regression. Confounders adjusted for: age at diagnosis, sex, race/ethnicity, and community-level socioeconomic status (cSES) (percent high school diploma, percent professional degree, median household income, median house value, median rent, and percent below poverty).	Lowest exposure concentration for a significant adverse health outcome response: NR. RR (95% CI) for "Medium-low" exposure vs "Low" exposure = 1.31 (1.02 - 1.68)RR (95% CI) for "Medium-high" exposure vs "Low" exposure = 1.31 (1.00 - 1.71)RR (95% CI) for "High" exposure vs "Low" exposure = 1.32 (0.98 - 1.77). Significant positive associations were reported "medium-low" and "medium-high" exposure relative to "Low exposure" and the trend test approached significance (p=0.056)..	Whitworth et. al 2008 622776 Medium

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Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
All leukemia	Health Effect: Cancer/Carcinogenesis-Lymphohematopoietic cancer incidence (leukemia, non-Hodgkin's lymphoma, Hodgkin's disease, acute lymphocytic leukemia, acute myeloid leukemia)-Immune/Hematological-Lymphohematopoietic cancer incidence (leukemia, non-Hodgkin's lymphoma, Hodgkin's disease, acute lymphocytic leukemia, acute myeloid leukemia). Outcome measure: ICD-10 codes C91-C95	General public. Infant (0-1), Toddler (2-3), Preschool (3-5), Middle childhood (6-11), Teens (12-17), Adults (18+). United States of America; Harris, Liberty, Montgomery, Chambers, Fort Bend, Waller, Brazoria, and Galveston Counties, Texas. Female, Male. Ecological. 997 cases of lymphohematopoietic cancer among children < 20 years of age from the Texas Cancer Registry (TCR), a North American Association of Central Cancer Registries. Ultimately, 670 cases of leukemia (510 cases of ALL and 92 cases of AML), 146 Hodgkin's disease cases, and 137 cases of NHL were included as eligible for analysis.. Diagnosis: 1995-2004.	Outdoor air Exposure Route: Inhalation Chronic (more than 28 days) Exposure estimated from 1999 US EPA ASPEN model data.	Poisson Regression. Confounders adjusted for: age at diagnosis, sex, race/ethnicity, and community-level socioeconomic status (cSES) (percent high school diploma, percent professional degree, median household income, median house value, median rent, and percent below poverty).	Lowest exposure concentration for a significant adverse health outcome response: NR. RR (95% CI) for "Medium-low" exposure vs "Low" exposure = 1.22 (0.98 - 1.52)RR (95% CI) for "Medium-high" exposure vs "Low" exposure = 1.25 (0.99 - 1.58)RR (95% CI) for "High" exposure vs "Low" exposure = 1.40 (1.07 - 1.81). Significant positive associations were reported for "high" vs. "low" exposure, and for the trend across all exposure levels..	Whitworth et. al 2008 622776 Medium

Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lung cancer	Health Effect: Cancer/Carcinogenesis-Lung cancer (incident)-Lung/Respiratory-Lung cancer (incident). Outcome measure: Interviews and Cancer Registry records	General public. Adults (18+), Older Adults (65+). China; Shanghai. Male. Nested Case-Control. Male smokers from the Shanghai Cohort Study (n=343 cases, n=392 controls). Shanghai Cohort Study. Recruitment: 1986-1989; Follow-up: through 2006..	Biomonitoring Biomonitoring matrix: Urine Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Chronic (more than 28 days) Exposure measured via biomonitoring at baseline. Mean smoking duration was 30.8 years in controls, 34.4 years in cases. Smoking was presumed to be the major route of 1,3-butadiene exposure..	Logistic Regression. Confounders adjusted for: age, neighborhood of residence, duration of biospecimen storage before assay, number of cigarettes smoked per day, number of years of smoking at baseline.	Lowest exposure concentration for a significant adverse health outcome response: >=18.9 pmol/mg creatinine. OR (95% CI) for:Q2 (4.31-8.56 pmol/mg creatinine) vs. Q1 (<4.31 pmol/mg creatinine): 1.25 (0.79-1.98)Q3 (8.57-18.8 pmol/mg creatinine) vs. Q1 (<4.31 pmol/mg creatinine): 1.20 (0.76-1.90)Q4 (>=18.9 pmol/mg creatinine) vs. Q1 (<4.31 pmol/mg creatinine): 1.75 (1.12 - 2.75)p-trend=0.018. Significant positive association reported for highest quartile of urinary MHBMA from smoking adjusted models. Q2 and Q3 were positive but not significant. Positive but not significant results also reported for Q2 and Q4 in models additionally adjusted for urinary NNAL and PheT (biomarkers of tobacco carcinogens PAH and NNK)..	Yuan et. al 2012 1508766 Medium

Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Lymphocyte number, lymphocyte percent of white blood cell count	Health Effect: Immune/Hematological- White blood cell count, granulocytes, lymphocytes, lymphocyte %, erythrocytes, platelets. Outcome measure: Blood sample collection	Occupational workers. Adults (18+). China; Yanshan. Female, Male. Cross-Sectional. 79 workers from polybutadiene rubber production facility (n = 41 exposed workers, n = 38 unexposed workers). NR.	Indoor air Exposure Route: Inhalation Acute (less than 24 hours) Exposure assessed in air samples collected at the breathing zone using personal samplers during a 6-hour shift.	Spearman correlation.	Lowest exposure concentration for a significant adverse health outcome response: continuous. Spearman correlation coefficient between 1,3-butadiene in air samples and lymphocyte number among exposed workers = 0.52 (p = 0.001)Spearman correlation coefficient between 1,3-butadience in air samples and lymphocyte % among exposed workers = 0.46 (p = 0.003). Significant positive correlation between 1,3-butadience in personal air samples and both lymphocyte number and lymphocyte percent of total white blood cell count among workers with jobs exposed to 1,3-butadiene..	Hayes et. al 2000 5586518 Low

Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
Sensorineural hearing loss	Health Effect: Ocular/Sensory-Sensorineural hearing loss. Outcome measure: Mean bilateral high-frequency thresholds at 4000, 6000, and 8000 HZ (PTA4,6,8) assessed using an AD226 audiometer	General public. Adults (18+), Older Adults (65+). United States. Female, Male. Cross-Sectional. Adults age 20-69 in the United States (n=849). National Health and Nutritional Examination Surveys (NHANES). 2011-2012.	Biomonitoring Biomonitoring matrix: Urine Exposure Route: Unclear/Uncertain (dust, biomarker without indication of exposure route, etc.) Unclear Exposure measured at time of outcome assessment.	ANCOVA. Confounders adjusted for: Age, history of noise exposure.	Lowest exposure concentration for a significant adverse health outcome response: Not applicable, analytic approach was ANCOVA. ANCOVA p-values:3,4-dihydroxybutyl (no history of noise exposure): 0.0033,4-dihydroxybutyl (history of noise exposure): 0.563-hydroxy-3-butenyl (no history of noise exposure): 0.043-hydroxy-3-butenyl (history of noise exposure): 0.292Note results for 3-hydroxy-3-butenyl (no history of noise exposure) were not considered statistically significant after correction for false discovery rate.. 3,4-dihydroxybutyl was associated with sensorineural hearing loss among participants without a history of noise exposure..	Pudrith et. al 2019 5660361 Low