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U.S. Environmental Protection Agency
EPA Docket Center (ORD Docket)
Mail Code: 28221T
1200 Pennsylvania Avenue, NE
Washington DC 20460

Re: Protocol for the Ethylbenzene IRIS Assessment (Preliminary Assessment Materials) (CASRN 100-41-4); EPA Docket No. EPA-HQ-ORD-2014-0526

Ladies and Gentlemen:

The Styrene Information and Research Center (SIRC) appreciates the opportunity to submit these comments on the Protocol for the Integrated Risk Information System (IRIS) Assessment of Ethylbenzene. 88 Fed. Reg. 10,320 (Feb.17, 2023). SIRC, formed in 1987, is a non-profit organization consisting of companies involved in the manufacture or processing of styrene, and companies that fabricate styrene-based products. Collectively, SIRC's membership represents the majority of the North American styrene industry. SIRC's charter also addresses the interests of ethylbenzene producers, and its use in the production of styrene monomer. SIRC serves as a leading resource for styrene and ethylbenzene exposure and health effects information developed over three decades of toxicological research and makes these findings readily available to industry, federal and state governments, and international agencies through publication in peer-review journals.

These comments supplement SIRC's prior October 18, 2017, written comments on the draft IRIS Assessment Plan (IAP) for ethylbenzene, its verbal comments at the EPA Science Advisory Board's Chemical Assessment Advisory Committee meeting on September 28, 2017, and the written information SIRC submitted in 2014 in response to EPA's problem formulation materials related to ethylbenzene.[1]

The draft ethylbenzene IRIS protocol is an activity in the IRIS systematic review process. The protocol follows the earlier IRIS IAP for ethylbenzene, which described what the ethylbenzene assessment will cover, with content on how the assessment will be conducted. The present report provides the methods that EPA is using to identify the relevant ethylbenzene health effects information and to evaluate this information for use in the IRIS assessment.

[1] *See* Document Nos. EPA-HQ-ORD-2017-0497-0007 (Oct. 18, 2017); EPA-HQ-ORD-2014-0526-0010 (Oct. 8, 2014); EPA–HQ–ORD–2014–0526-0009 (Sep. 11, 2014); EPA-HQ-ORD-2014-0526-0007 (Aug. 27, 2014); EPA–HQ–ORD–2014–0526–0006 (Aug. 20, 2014); EPA–HQ–ORD–2014–0526–0005 (Aug. 20, 2014); EPA–HQ–ORD–2014–0526-0004 (Aug. 19, 2014); EPA–HQ–ORD–2014–0526-0003 (Aug. 19, 2014); and EPA–HQ–ORD–2014–0526-0002 (Aug. 18, 2014).

Overall, the ethylbenzene draft protocol is well-organized and provides a thorough summary of EPA's plans for conducting the ethylbenzene IRIS assessment. The protocol does a good job describing the general details of EPA's generic methods for searching, screening, and inventorying the literature, problem formulation refinement, study evaluation for bias and sensitivity, extraction of data from studies, synthesis and integration of evidence, and dose-response assessment. But, as a methods report, the specifics of these processes as they will be applied to the ethylbenzene literature are limited. As a result, there are limited opportunities to provide meaningful review and comment on the Protocol.

The primary ethylbenzene-specific information in the Protocol is the Ethylbenzene Evidence Map Visualizations (Ethylbenzene Evidence Map Visualizations | Tableau Public) and the search results for ethylbenzene in the HERO database (HERO Search Results | Health & Environmental Research Online (HERO) | US EPA). These databases were, therefore, the focus on SIRC's review and the basis for our comments.

1. **The Protocol should include the basis for EPA's individual ethylbenzene study evaluation decisions.**

   The draft protocol provides detailed descriptions of the evaluation process that has been applied to the ethylbenzene literature but does not provide access to the specific evaluation findings for the articles/studies that were reviewed. As a result, it is unclear from the document what EPA's particular basis was for determining which of the individual studies screened from the HERO database were selected for inclusion in the Evidence Map Visualizations and which were excluded. The basis for the study-specific screening decisions should be made available for public comment early in the process. Because the Evidence Map Visualizations appear to represent the most important studies that will be considered in the ethylbenzene IRIS assessment, EPA should have the benefit of public comment on those study-specific screening choices before EPA prepares the assessment.

2. **SIRC has identified a number of potentially relevant ethylbenzene articles/studies for the IRIS assessment that are not identified in the Ethylbenzene Evidence Map Visualizations or HERO database search for ethylbenzene.**

   EPA has developed the extensive HERO database of ethylbenzene information which appears to have identified the majority of the important studies that will be needed for the IRIS review. However, SIRC has identified a number of additional animal and human studies that may also contain useful key or supporting information for the IRIS review, but which were not located in a search of the ethylbenzene HERO database. These additional studies are listed in Table 1 (Animal studies) and Table 2 (Human studies) in the attachment. EPA is encouraged to review these additional studies to determine their value for the IRIS assessment of ethylbenzene.

3. **SIRC is aware of newly published and soon to be published ethylbenzene information that may be potentially relevant to the IRIS assessment.**

   SIRC historically has developed and continues to develop health and environmental effects and exposure information to improve the knowledge base for ethylbenzene. Recently, SIRC sponsored

two such projects that may provide useful information for the background and health effects IRIS assessment of ethylbenzene.

The first project was a 2022 update to the 2007 exposure assessment of ethylbenzene in North America conducted for the Voluntary Children's Chemical Evaluation Program. This update summarizes the current ethylbenzene concentrations in air and foods, exposures during the use of household and consumer products, nationally representative biomonitoring data, including expanded demographic groups, and a new survey of worker exposures in styrene production facilities. The key findings of the update are that: (1) the general population ethylbenzene exposures appear to have declined for all age groups; (2) the ethylbenzene/styrene chain of commerce contributes an estimated 0.1% to total air emissions and 7%-12% to dietary concentrations; (3) total estimated ethylbenzene intakes are consistent with biomonitoring data; (4) lactational transfer is not a significant exposure pathway for breastfed infants; and (5) production workers' exposure to ethylbenzene is well below occupational guidelines. The update was published in January 2023 as: Kester J.E. and Morgott DA. (2023). Ethylbenzene exposure in North America – an update. J Environ Exp Assess. 2:1. DOI: 10.20517/jeea.2022.22.

The second project provides a further perspective on the exposure concentrations that were found in the National Toxicology Program (NTP) studies to produce tumors in rodents (National Toxicology Program (1999) NTP Technical Report on the Toxicology and Carcinogenesis Studies of Ethylbenzene (CAS NO. 100-41-4) in F344/N Rats and B6C3F1 Mice (Inhalation Studies) National Toxicology Program, Research Triangle Park, NC). This study explored the kinetically-derived maximal dose (KMD) concept for ethylbenzene inhalation exposure. A manuscript for this study is in preparation and will be submitted for publication in a peer-reviewed journal. SIRC will provide EPA with the citation when available.

We hope you find SIRC's comments and information useful and encourage EPA to consider this information in its assessment of ethylbenzene. SIRC would be pleased to answer questions or provide additional details to support these comments.

Sincerely,

Ray Ehrlich

Ray Ehrlich
Executive Director

Attachment: Table 1 - Additional Ethylbenzene Animal Studies Not Identified in the HERO database for Ethylbenzene

Table 2 - Additional Ethylbenzene Human Studies Not Identified in the HERO database for Ethylbenzene

ATTACHMENT

Table 1. Additional Ethylbenzene Animal Studies Not Identified in the HERO database for Ethylbenzene.

	Additional Ethylbenzene Animal Study Reference	Health System
1	Abduljalel, M.E., Al-Saadi, R.N. (2022). Toxicopathological effect of benzene, toluene, ethylbenzene, and xylenes (BTEX) as a mixture and the protective effect of citicoline in male rats followings 90-day 0ral exposure. Revista Electronica de Veterinaria. 23 (3): 399-414.	Hepatic Renal Nervous
2	Åstrand, I., Engström, J., Övrum, P. (1978). Exposure to xylene and ethylbenzene. I. Uptake, distribution and elimination in man. Scand. J. Work Environ. Health. 4:185-194.	Other (ADME)
3	Bardodej, Z., Bardodejova, E. (1970). Biotransformation of ethylbenzene, styrene and alpha-methylstyrene in man. Am. Ind. Hyg. Assoc. J. 32:1-5.	Other (ADME)
4	Unnamed study report. (2004). 4-ethylphenol, 1-phenylethanol S-phase response study in the kidneys of F344/Crl rats. Administration by gavage for 1 and 4 weeks. (reported in: https://echa.europa.eu/registration-dossier/-/registered-dossier/15377/7/8/?documentUUID=bfaf9621-eda4-4818-94d2-e4d2de3af5a1.)	Cancer (metabolite)
5	Unnamed study report. (2004). 4-ethylphenol, 1-phenylethanol cell proliferation study in the liver of B6C3F1 mice. Administration by gavage for 1 and 4 weeks. (reported in: https://echa.europa.eu/registration-dossier/-/registered-dossier/15377/7/8/?documentUUID=eb3a508c-ffcf-4ecb-ba1b-20a0ff4aef12)	Cancer (metabolite)
6	Cappaert, N.L.M. (2000). The damaging effects of noise and ethyl benzene on hearing. Thesis from University of Utrecht, The Netherlands	Nervous
7	Davidson, C.J., Svenson, D.W., Hannigan, J.H., Perrine, S.A., Bowen, S.E. (2022). A novel preclinical model of environment-like combined benzene, toluene, ethylbenzene, and xylenes (BTEX) exposure: Behavioral and neurochemical findings. Neurotoxicol. Teratol. 91:107076.	Nervous
8	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985). Genetic toxicology testing of 41 industrial chemicals. Mutat. Res. 153:157-177.	Other (Genotoxicity)
9	Duerksen-Hughes, P. J., Yang, J., Ozcan, O. (1999). Induction as a genotoxic test for twenty five chemicals undergoing in vivo carcinogenicity testing. Env. Hlth. Persp. 107(10):805-812.	Other (Genotoxicity)

	Additional Ethylbenzene Animal Study Reference	Health System
10	El Mastri, A. M., Smith, J. N., Williams, R. T. (1956). The metabolism of alkylbenzenes: n-Propylbenzene and n-butylbenzene with further observations on ethylbenzene. Biochem. J. 64:50-56.	Other (ADME)
11	Engelhardt, G. (2006). In vivo micronucleus test in mice with 1-phenylethanol. Arch. Toxicol. 80:868-872.	Other (Genotoxicity) (metabolite)
12	Freundt, K.J., Römer, K.G., Federsel, R.J. (1989). Decrease of inhaled toluene, ethyl benzene, m-xylene, or mesitylene in rat blood after combined exposure to ethyl acetate. Bull. Environ. Contam. Toxicol. 42:495-498.	Other (ADME)
13	Fuciarelli, A. F. (2000). Ethylbenzene two-week repeated-dose inhalation toxicokinetic study report. Battelle, Richland, Washington. Battelle Project #G002840-LQ. Conducted for the National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina. (cited in American Chemistry Council (ACC). (2007). Voluntary Children's Chemical Evaluation Program (VCCEP) Tier 1 Pilot Submission for Ethylbenzene (CAS No. 100–41-4). [Online] Available at: http://www.tera.org)	Other (ADME)
14	Gibson, D.P., Brauninger, R., Shaffi, H.S., Kerckaert, G.A, LeBoeuf, R.A., Isfort, R.J., Aardema, M.J. (1997). Induction of micronuclei in Syrian hamster embryo cells: Comparison to results in the SHE cell transformation assay for National Toxicology Program test chemicals. Mutat. Res. 392:61-90.	Other (Genotoxicity)
15	Kawai, T., Yasugi, T., Mizunuma, K., Horiguchi, S., Iguchi, H., Uchida, Y., Iwami, O., Ikeda, M. (1992). Comparative evaluation of urinalysis and blood analysis as means of detecting exposure to organic solvents at low concentrations. Int. Arch. Occup. Environ. Health. 64:223-234.	Other (ADME)
16	Kerckaert, G. A., Brauninger, R., Leboef, R.A., Isfort, R.A. (1996). Use of the Syrian hamster embryo cell transformation assay for carcinogenicity prediction of chemicals currently being tested by the National Toxicology Program in rodent bioassays. Env. Health Persp. 104 (Suppl. 5):1075-1084.	Other (Genotoxicity)
17	Lewis, D. V. F., Sams, C., Loizou, G. D. (2002). A Quantitative Structure Activity Relationship analysis on a Series of Alkyl Benzenes Metabolized by Human Cytochrome P450 CYP2E1. J. Biochem. Mol. Toxicol. 17:47-52.	Other (ADME)
18	McDougal, J.M., Pollard, D.L., Weisman, W., Garrett, C.M., Miller, T.E. (2000). Assessment of skin absorption and penetration of JP8 jet fuel and its components. Toxicol. Sci. 55:247-255.	Other (ADME)

	Additional Ethylbenzene Animal Study Reference	Health System
19	McGregor, D.B., Brown, A., Cattanach, P., Edwards, I., McBridle, D., Riach, C., Caspary, W.J. (1988). Responses of the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay: III. 72 coded chemicals. Environ. Mol. Mutagen. 12:85-154.	Other (Genotoxicity)
20	McMahon, R.E., Sullivan, H.R. (1968). The nature of the in vivo conversion of L(-) methylphenylcarbinol to D(-) mandelic acid in the rat. Pharmacologist. 10:203-208.	Other (ADME)
21	McMahon, R. E.; Sullivan, H. R. (1969). The microsomal oxygenation of ethylbenzene, iso-topic, stereochemical and induction studies. Arch. Biochem. Biophys. 132:575-577.	Other (ADME)
22	Moore, R. J., Anderson, D. J., Mottaz, H. M., Dill, J. A., Westerberg, R. B., Graves, S. W., Smith, C. S., Fuciarelli, A. F. (1998). Sub-chronic toxicokinetic studies following whole-body inhalation exposures of Fischer 344/N rats and B6C3F1 mice to 75 and 750 ppm ethylbenzene. The Toxicologist. 42:253 (Abstract #1249).	Other (Toxicokinetics)
23	Muhammad, F., Monteiro-Riviere, N.A., Baynes, R.E., Riviere, J.E. (2005). Effect of in vivo jet fuel exposure on subsequent in vitro dermal absorption of individual aromatic and aliphatic hydrocarbon fuel constituents. J. Toxicol. Environ. Health. Part A, 68:719–737.	Other (ADME)
24	Nakajima, T., Sato, A. (1979). Enhanced activity of liver drug-metabolizing enzymes for aromatic and chlorinated hydrocarbons following food deprivation. Toxicol. Appl. Pharmacol. 50:549-556.	Other (ADME)
25	*Nishihara, T., Nishikawa, J., Kanayama T., Dakeyama F., Saito, K., Imagawa M., Takatori, S., Kitagawa Y., Hori, S., Utsumi H. (2000). Estrogenic activities of 517 chemicals by yeast two hybrid assay. J. Health Science. 46:282-298.	Endocrine
26	NTP. (1990). Technical Report on the toxicology and carcinogenesis studies of alpha-methylbenzyl alcohol (Cas 98-85-1) in F344/N rats and B6C3F1 mice (gavage studies). NTP. Testing laboratory: NIEHS campus in Research Triangle Park, NC	Cancer (metabolite)
27	Pedersen, D.C., Schatz, R.A. (1999). Pulmonary metabolism of ethylbenzene following exposure to rats. The Toxicologist. 48:408 (Abstract #1926).	Other (ADME)
28	Pyykko, K. Paavilainen, S., Metsa-Ketela, T., Laustiola, K. (1987). The increasing and decreasing effects of aromatic hydrocarbon solvents on pulmonary and hepatic cytochrome P-450 in the rat. Pharmacol. Toxicol. 60:288-293.	Other (ADME)

	Additional Ethylbenzene Animal Study Reference	Health System
29	Römer, K.G., Federsel, R.J., Freundt, K.J. (1986). Rise of inhaled toluene, ethyl benzene, m-xylene, or mesitylene in rat blood after treatment with ethanol. Bull. Environ. Contam. Toxicol. 37:874-876.	Other (ADME)
30	Sakazaki, H., Ueno, H., Umetani, K., Utsumi, H., Nakamuro, K. (2001). Immunological evaluation of environmental chemicals utilizing mouse lymphocyte mitogenesis test. J. Health Sci. 47(3):258-271.	Immune
31	Sato, A., Nakajima, T. (1987). Pharmacokinetics of organic solvent vapors in relation to their toxicity. Scand. J. Work Environ. Health. 13:81-93.	
32	Smyth, H.F., Jr., Carpenter, C.P., Weil, C.S., Pozzani, U.C., Striegel, J.A. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.	Acute
33	Tsurata, H. (1982). Percutaneous absorption of organic solvents. III. On the penetration rates of hydrophobic solvents through the excised rat skin. Ind. Health. 20:335-345.	Other (ADME)
34	Vaalavirta, L.; Tähti, H. (1995). Astrocyte membrane Na+, K+ ATPase and Mg2+ ATPase as targets of organic solvent impact. Life Sciences 57:2223-2230.	Nervous
35	Wollny, H.E. (2000). Cell mutation assay at the thymidine kinase locus (TK+/-) in mouse lymphoma L5178Y cells (soft agar method) with ethylbenzene. RCC-CCR Project No. 635300. RCC-Cytotest Cell Research GmbH, Germany. (cited in American Chemistry Council (ACC). (2007). Voluntary Children's Chemical Evaluation Program (VCCEP) Tier 1 Pilot Submission for Ethylbenzene (CAS No. 100–41-4). [Online] Available at: http://www.tera.org)	Other (Genotoxicity)
36	Yuan, W., White, T.B., White, J.W., Strobel, H.W., Backes, W.L. (1995). Relationship between hydrocarbon structure and induction of P450: Effect on RNA levels. Xenobiotica. 25:9-16.	Other (ADME)
37	Yuan, W., Sequeira, D.J., Cawley, G.F., Eyer, C.S., Backes, W.L. (1997). Time course for the modulation of hepatic cytochrome P450 after administration of ethylbenzene and its correlation with toluene metabolism. Arch. Biochem. Biophys. 339: 55-63.	Other (ADME)
38	Yuan, W., Serron, S.C., Cawley, G.F., Eyer, C.S., Backes, W.L. (1997) Ethylbenzene modulates the expression of different cytochrome P-450 isozymes by discrete multistep processes. Biochem. Biophys. Acta. 1334:361-372.	Other (ADME)

*Article found in HERO but not in ethylbenzene search of HERO

Table 2. Additional Ethylbenzene Human Studies Not Identified in the HERO database for Ethylbenzene.

	Additional Ethylbenzene Human Study Reference	Health System
39	Beskid, O., Dusek, Z., Solopsky, I., Sram, R.J. (2006). The effects of exposure to different clastogens on the pattern of chromosomal aberrations detected by FISH whole chromosome painting in occupationally exposed individuals. Mut. Res. 594:20-29.	Other (Genotoxicity)
40	Casey, J. A., Goin, D. E., Rudolph, K. E., Schwartz, B. S., Mercer, D., Elser, H., Eisen, E. A., Morello-Frosch, R. (2019). Unconventional natural gas development and adverse birth outcomes in Pennsylvania: The potential mediating role of antenatal anxiety and depression. Environ Res. 177:108598.	Reproduction Developmental
41	Cao, Y.M., Jiang, X.Y., Min, C.Y., Liu, J. (2022). Acute toluene, xylene and ethylbenzene poisoning leads to neurological sequelae: a case report. Zhonghua lao dong wei sheng zhi ye bing za zhi = Zhonghua laodong weisheng zhiyebing zazhi = Chinese journal of industrial hygiene and occupational diseases, 40 (7), pp. 532-534. 2022.	Nervous
42	Cushing, L. J., Vavra-Musser, K., Chau, K., Franklin, M., & Johnston, J. E. (2020). Flaring from Unconventional Oil and Gas Development and Birth Outcomes in the Eagle Ford Shale in South Texas. Environ. Health Perspect. 128(7):77003.	Reproduction Developmental
43	Hesam, M., Shakerkhatibi, M,, Samadi, M.,; Poorolajal, J., Rahmani, A., Rafieemehr, H. (2020). Long-term exposure to outdoor VOCs and lung function in urban adults: a cross-sectional study in Tabriz an industrialized city in the northwest of Iran. Human and Ecological Risk Assessment. 26: 1512-1528	Respiratory
44	Janitz, A. E., Dao, H. D., Campbell, J. E., Stoner, J. A., Peck, J. D. (2019). The association between natural gas well activity and specific congenital anomalies in Oklahoma, 1997-2009. Environ Int. 122:381-388.	Developmental
45	Jiménez, T., Pollán, M., Domínguez-Castillo, A., Lucas, P., Sierra, M.A., de Larrea-Baz, N.F., González-Sánchez, M., Salas-Trejo, D., Llobet, R., Martínez, I., Nieves Pino, M.N., Martínez-Cortés, M., Pérez-Gómez, B., Lope, V., García-Pérez, J. (2022). Residential proximity to industrial pollution and mammographic density Sci. Total Environ. 829:154578.	Endocrine
46	Lawrence, K.G., Niehoff, N.M., Keil, A.P., Jackson, W.B., Christenbury, K., Stewart, P.A., Stenzel, M.R., Huynh, T.B., Growth, C.P., Ramachandran, G., Banerjee, S., Pratt, G.C., Curry, M.D., Engel, L.S., Sandler, D.P. (2022). Associations between airborne crude oil chemicals and symptom-based asthma. Environ. Int. 167:107433.	Respiratory

	Additional Ethylbenzene Human Study Reference	Health System
47	*Lei, T., Qian, H., Yang, J., Hu, Y. (2023). The association analysis between exposure to volatile organic chemicals and obesity in the general USA population: A cross-sectional study from NHANES program. Chemosphere, 315, art. no. 137738	Endocrine
48	Liao, Q., Du, R., Ma, R., Liu, X., Zhang, Y., Zhang, Z., Ji, P., Xiao. M., Cui, Y., Xing, X., Liu, L., Dang, S., Deng, Q., Xiao, Y. (2022). Association between exposure to a mixture of benzene, toluene, ethylbenzene, xylene, and styrene (BTEXS) and small airways function: A cross-sectional study. Environ. Res. 212(Pt D):113488.	Respiratory
49	Liao, Q., Zhang Y., Ma, R., Zhang, Z., Ji, P., Xiao, M., Du, R., Liu, L., Cui, Y., Xing, X., Liu, L., Dang, S., Deng, Q., Xiao, Y. (2022). Risk assessment and dose-effect of co-exposure to benzene, toluene, ethylbenzene, xylene, and styrene (BTEXS) on pulmonary function: A cross-sectional study. Environ. Pollut. 310:119894.	Respiratory
50	López-Vargas, R., Méndez-Serrano, A., Albores-Medina, A., Oropeza-Hernández, F., Hernández-Cadena, L., Mercado-Calderón, F., Alvarado-Toledo, E., Herrera-Morales, S., Arellano-Aguilar, O., García-Vargas, G., & Montero-Montoya, R. (2018). Oxidative stress index is increased in children exposed to industrial discharges and is inversely correlated with metabolite excretion of voc. Environ. Mol Mutagen. 59(7): 639-652.	Other
51	*Mendy, A., Burcham, S., Merianos, A.L., Mersha, T.B., Mahabee-Gittens, E.M., Chen, A., Yolton, K. (2022). Urinary volatile organic compound metabolites and reduced lung function in U.S. adults. Respiratory Medicine, 205, art. no. 107053.	Respiratory
52	Moradkhani, H., Leili, M., Puralajal, J., Mazaheri Tehrani, A., Hossein Panahi, A., Samadi, M.T., Beheshtifar, S. (2022) Association between BTEX (benzene, toluene, ethylbenzene and xylene) concentration in ambient air with hematological and spirometric indices: a population-based study. Human and Ecological Risk Assessment. 28 (5-6): 490-506.	Hematologic Respiratory
53	Neghab, M., Nourozi, M. A., Shahtaheri, S. J., Mansoori, Y., Bazzaz, J. T., Nedjat, S. (2018). Effects of Genetic Polymorphism on Susceptibility to Nephrotoxic Properties of BTEXs Compounds. J. Occup. Environ. Med. 60(8):e377-e382.	Other (Genotoxicity)
54	Nicole, W. (2020). On wells and wellness: Oil and gas flaring as a potential risk factor for preterm birth. Environ. Health Perspect. 128(11): 114004.	Reproduction Developmental

	Additional Ethylbenzene Human Study Reference	Health System
55	Niehoff, N.M., Gammon, M.D., Keil A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environ. Int. 130:104897.	Cancer
56	Niu, Z., Wen, X., Wang, M., Tian, L., Mu, L. (2022). Personal exposure to benzene, toluene, ethylbenzene, and xylenes (BTEXs) mixture and telomere length: a cross-sectional study of the general US adult population. Environ. Res. 209:112810.	Other (Genotoxicity)
57	Partha, D.B., Cassidy-Bushrow, A.E., Huang, Y. (2022). Global preterm births attributable to BTEX (benzene, toluene, ethylbenzene, and xylene) exposure. Science of the Total Environment, 2022838, art. no. 156390.	Reproduction Developmental
58	Roshan, S.J., Mansoori, Y., Hosseini, S.R., Sabour, D., Daraei, A. (2022). Genetic variations in ATM and H2AX loci contribute to risk of hematological abnormalities in individuals exposed to BTEX chemicals J Clin Lab Anal. e24321.	Hematologic
59	Rubes, J., Sipek, J., Kopecka, V., Musilova, P., Vozdova, M. (2021). Semen quality and sperm DNA integrity in city policemen exposed to polluted air in an urban industrial agglomeration. International Journal of Hygiene and Environmental Health. 237: 13835-13835.	Reproduction
60	Sisto, R., Cavallo, D., Ursini, C. L., Fresegna, A. M., Ciervo, A., Maiello, R., Paci, E., Pigini, D., Gherardi, M., Gordiani, A., L'Episcopo, N., Tranfo, G., Capone, P., Carbonari, D., Balzani, B., & Chiarella, P. (2020). Direct and oxidative DNA damage in a group of painters exposed to VOCs: Dose - response relationship. Front Public Health. 8: 445.	Other
61	Tran, K. V., Casey, J. A., Cushing, L. J., Morello-Frosch, R. (2020). Residential proximity to oil and gas development and birth outcomes in California: A retrospective cohort study of 2006-2015 Births. Environ. Health Perspect. 128(6): 67001.	Reproduction Developmental
62	Vyskocil, A., Leroux, T., Truchon, G., Lemay, F., Gendron, M., Gagnon, F., Majidi, N. E., Viau, C. (2008). Ethylbenzene should be considered ototoxic at a occupationally relevant exposure concentrations. Toxicol. Ind. Health. 24:241-246.	Nervous
63	Yu, L., Wang, B., Liu, W., Xu, T., Yang, M., Wang, X., Tan, Q. (2022). Cross-sectional and longitudinal associations of styrene and ethylbenzene exposure with heart rate variability alternation among urban adult population in China. Sci Total Environ. 845:157231.	Cardiovascular

	Additional Ethylbenzene Human Study Reference	Health System
64	Zhang, Y., Liu, Y., Li, Z., Liu, X., Chen, Q., Qin, J., Liao, Q., Du, R., Deng, Q., Xiao, Y., Xing, X.(2022). Effects of coexposure to noise and mixture of toluene, ethylbenzene, xylene, and styrene (TEXS) on hearing loss in petrochemical workers of southern China. Environmental Science and Pollution Research. DOI: 10.1007/s11356-022-24414-6	Nervous

*Article found in HERO but not in ethylbenzene search of HERO