

RECOMMENDATION

Occupational exposure limits for ethyl benzene, dimethyl terephthalate and hydrogen fluoride, and carcinogenicity and reproductive toxicant classifications

The Committee for Recommendation of Occupational Exposure Limits, Japan Society for Occupational Health

Correspondence: Tetsuo Nomiyama, Department of Preventive Medicine and Public Health, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano 390-8621, Japan.

Email: nomiyama@shinshu-u.ac.jp

1 | OCCUPATIONAL EXPOSURE LIMITS FOR CHEMICAL SUBSTANCES

Ethylbenzene [CAS No. 100-41-4] is a colorless liquid (boiling point 136.2°C, vapor pressure 1.27 kPa [25°C]) that is used as a raw material in the manufacture of styrene monomer, plastic, and rubber, and is a component of mixed xylene. This chemical was recommended at 100 ppm (430 mg/m³) for OEL-M in 1978, and revised at 50 ppm (217 mg/m³) and categorized Group 2B for class of carcinogenicity in 2001, and classified Group 2 as a reproductive toxicant in 2014. The JSOH reevaluated the occupational exposure limits (OEL) by examining subsequent reports this time, and proposed 20 ppm as OEL-M for ethylbenzene based on significant hearing loss in workers exposed to 30 ppm and noise in comparison with workers exposed to only noise,¹ significant loss of outer hair cell of cochlear nerve at concentrations ≥ 200 ppm in 13 weeks inhalation study (0, 200, 400, 600, 800 ppm) in SD rats,² and significant increase of auditory threshold ≥ 400 ppm in 5 days inhalation study (0, 300, 400, 550 ppm) in WAG/Rij rats.³ Skin absorption notation is indicated, and classifications of carcinogenic (Group 2B) and reproductive toxicant (Group 2) remain the same.

Dimethyl terephthalate [CAS No. 120-61-6] is white flakes (melting point 140°C, boiling point 288°C), and used as a material in the manufacture of polybutylene

terephthalate, film, polyester fiber. The JSOH proposed 8 mg/m³ as OEL-M for dimethyl terephthalate based on the results of animal experiment.⁴ Nose rubbing, preening, and blinking were found at the concentration of 86.4 mg/m³, but not at that of 16.5 mg/m³ in male Long-Evans rats for 5 days 4-hour inhalation exposures per week for 58 days.

Hydrogen fluoride [CAS No. 7664-39-3] is colorless corrosive gas and/or fume (melting point - 83°C, boiling point 20°C, vapor pressure 122 kPa [25°C]). It is used as a raw material of fluorine compounds, alkylating agent, and etching agent for glass and silica. The OEL-Ceiling, defined as the reference value to the maximal exposure concentration of the substance during a working day at or below which adverse health effects do not appear in most workers, of 3.0 ppm (2.5 mg/m³) is proposed based on the increased symptom scores from upper airways of human volunteer experiments.^{5,6} Symptoms in upper airways in human volunteers exposed to 2.5-5.2 mg/m³ were significantly increased compared to those exposed to 0.2-0.6 and 0.7-2.4 mg/m³. In another human volunteer experiment, five volunteers suffered face flush at 5 days 6-hour exposures per week during 10-50 days. Skin absorption notation is indicated.

2 | CLASSIFICATIONS ON CARCINOGENICITY

N,N-dimethylformamide is proposed to be a Group 2A carcinogen. Proposed Group 2B carcinogens are ethylbenzene, 4-chlorobenzotrifluoride, and 1-bromo-3-chloropropane.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Journal of Occupational Health* published by John Wiley & Sons Australia, Ltd on behalf of The Japan Society for Occupational Health

3 | OTHER CLASSIFICATIONS

Reproductive toxicants classification for ethylbenzene is proposed as Group 2.

The latest OEL recommendations (2020-2021) will appear in the Environmental and Occupational Health Practice (Volume 2) as an open access. A brief summary of the proposal will be posted at the society's website (<https://www.sanei.or.jp/oel-eng>) in September.

DISCLOSURE

Approval of the research protocol: N/A. *Informed consent:* N/A. *Registry and the registration no. of the study/trial:* N/A. *Animal studies:* N/A. *Conflict of interest:* None declared.

AUTHOR CONTRIBUTIONS

All the authors contributed draft preparation and deliberation of the proposals in the committee. The corresponding author (TN) developed and finalized the article based on the comments from all other authors' feedback.

REFERENCES

1. Zhang M, Wang Y, Wang Q, Yang D, Zhang J, Wang F, Gu Q. Ethylbenzene-induced hearing loss, neurobehavioral function, and neurotransmitter alterations in petrochemical workers. *J Occup Environ Med.* 2013;55(9):1001–1006.
2. Gagnaire F, Langlais C, Grossmann S, Wild P. Ototoxicity in rats exposed to ethylbenzene and to two technical xylene vapours for 13 weeks. *Arch Toxicol.* 2007;81(2):127–143.
3. Cappaert NL, Klis SF, Baretta AB, Muijser H, Smoorenburg GF. Ethyl benzene-induced ototoxicity in rats: a dose-dependent mid-frequency hearing loss. *J Assoc Res Otolaryngol.* 2000;1(4):292–299.
4. Krasavage WJ, Yanno FJ, Terhaar CJ. Dimethyl terephthalate (DMT): acute toxicity, subacute feeding and inhalation studies in male rats. *Am Ind Hyg Assoc J.* 1973;34(10):455–462.
5. Lund K, Ekstrand J, Boe J, Sørstrand P, Kongerud J. Exposure to hydrogen fluoride: an experimental study in humans of concentrations of fluoride in plasma, symptoms, and lung function. *Occup Environ Med.* 1997;54(1):32–37.
6. Largent EJ. *Fluorosis—The Health Aspects of Fluorine Compounds.* Columbus, OH: Ohio State Uni Press; 1961:34–48.

MEMBERS OF THE COMMITTEE FOR RECOMMENDATION OF OCCUPATIONAL EXPOSURE LIMITS, JAPAN SOCIETY FOR OCCUPATIONAL HEALTH

Atsuko Araki¹, Kenichi Azuma², Ginji Endo³, Yoko Endo⁴, Tetsuhito Fukushima⁵, Kunio Hara⁶, Hajime Hori⁶, Masayoshi Ichiba⁷, Tatsuya Ishitake⁸, Gaku Ichihara⁹, Akiyoshi Ito⁶, Yuki Ito¹⁰, Satoko Iwasawa¹¹, Takeyasu Kakamu⁵, Michihiro Kamijima¹⁰, Kanae Karita¹², Takahiko Katoh¹³, Toshio Kawai¹⁴, Toshihiro Kawamoto³, Reiko Kishi¹, Shinji Kumagai, Yukinori Kusaka¹⁵, Muneyuki Miyagawa¹⁶, Hiroyuki Miyauchi⁶, Yasuo Morimoto⁶, Kasuke Nagano¹⁷, Hisao Naito¹⁸, Tamie Nakajima¹⁹, Makiko Nakano²⁰, Tetsuo Nomiyama^{21,‡}, Hirokazu Okuda²², Masayuki Okuda²³, Kazuyuki Omae²⁰, Kazuhiro Sato¹⁵, Tomotaka Sobue²⁴, Yasushi Suwazono²⁵, Toru Takebayashi²⁰, Tatsuya Takeshita²⁶, Teruomi Tsukahara²¹, Masashi Tsunoda¹¹, Jun Ueyama²⁷, Yumi Umeda²², Kenya Yamamoto²⁸, Yuko Yamano²⁹, Takenori Yamauchi²⁹ and Eiji Yano¹⁶

Authors listed alphabetically.

¹Hokkaido University, ²Kindai University, ³Japan Industrial Safety and Health Association, ⁴Endo Occupational Health Consultant Office, ⁵Fukushima Medical University, ⁶University of Occupational and Environmental Health, Japan, ⁷Saga University, ⁸Tokyo University of Science, ⁹Kurume University, ¹⁰Nagoya City University, ¹¹National Defense Medical College, ¹²Kyorin University, ¹³Kumamoto University, ¹⁴Kansai Technical Center for Occupational Medicine, ¹⁵University of Fukui, ¹⁶Teikyo University, ¹⁷Nagano Toxicologic-Pathology Consulting, ¹⁸Kinjo Gakuin University, ¹⁹Chubu University, ²⁰Keio University, ²¹Shinshu University, ²²Japan Bioassay Research Center, ²³Yamaguchi University, ²⁴Osaka University, ²⁵Chiba University, ²⁶Wakayama Medical University, ²⁷Nagoya University, ²⁸Showa University, and [‡] corresponding author