Opinion/Recommendation

Occupational Exposure Limits for ethyldiene norbornene, ethyleneimine, benomyl, and 2,3-epoxypropyl methacrylate, and classifications on carcinogenicity

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

Atsuko Araki, Kenichi Azuma, Ginji Endo, Yoko Endo, Tetsuhiito Fukushima, Kunio Harada, Hajime Hori, Seichi Horie, Hyogo Horiguchi, Masayoshi Ichiba, Gaku Ichihara, Masayuki Ikeda, Tatsuya Ishitake, Akiyoshi Ito, Yuki Ito, Satoko Iwasawa, Takeyasu Kakumi, Michihiro Kamijima, Kanae Karita, Takahiko Katoh, Toshio Kawai, Toshihiro Kawamoto, Shinji Kumagai, Yukinori Kusakai, Akiko Matsumoto, Muneyuki Miyagawa, Hiroyuki Miyauchi, Yasuo Morimoto, Kasuke Nagano, Hisao Naito, Tamie Nakajima, Makiko Nakano, Tetsuo Nomiyama, Hirokazu Okuda, Masayuki Okuda, Kazuyuki Omae, Haruhiko Sakurai, Kazuhiro Sato, Tomotaka Sobue, Yasushi Suwazono, Toru Takebayashi, Tatsuya Takeshita, Akito Takeuchi, Ayano Takeuchi, Masatoshi Tanaka, Shigeru Tanaka, Teruoji Tsukahara, Masashi Tsunoda, Susumu Ueno, Jun Ueyama, Yumi Umeda, Kenya Yamamoto, Yuko Yamano, Takenori Yamauchi and Eiji Yano

1 Hokkaido University, 2 Kindai University, 3 Japan Industrial Safety and Health Association, 4 Fukushima Medical University, 5 University of Occupational and Environmental Health, Japan, 6 Kitasato University, 7 Saga University, 8 Tokyo University of Science, 9 Kyoto University, 10 Kurume University, 11 Nagoya City University, 12 National Defense Medical College, 13 Kyorin University, 14 Kumamoto University, 15 University of Fukui, 16 Teikyo University, 17 Fujita Health University, 18 Chubu University, 19 Keio University, 20 Shinshu University, 21 Japan Bioassay Research Center, 22 Yamaguchi University, 23 Osaka University, 24 Chiba University, 25 Wakayama Medical University, 26 Jumonji University, 27 Nagoya University, 28 The University of Tokyo, 29 Showa University, 30 corresponding author and independent consultant

Occupational Exposure Limits (OELs) for Chemical Substances

Ethyldiene norbornene [CAS No. 16219-75-3] is a white to colorless liquid (boiling point 148°C, vapor pressure 560 Pa (20°C)) with a characteristic odor used for the production of automobile synthetic rubber products, ethylene propylene diene methylene linkage. The OEL-Mean of 2 ppm (10 mg/m³) is proposed based on the results of animal experiments. In the 14-week inhalation exposure...
experiment (5 to 150 ppm) with Fischer 344 rats, swelling and crust formation around the eyes were observed in the female group of 5 ppm or more, and the effects on the thyroid gland (e.g., follicular colloid reduction, hyper trophy, and hyperplasia of follicular epithelial cells, etc.) was observed in the group of 25 ppm or more in males and females. Although the implantation rate and the fertility rate decreased in animals and the incidence of skeletal mutation of the three species of pediatric animals was increased, these effects were observed at concentrations where an increase in the relative weight of the liver to the mother was observed. Thus, we propose the Group 3 for reproductive toxicity.

Ethyleneimine [CAS No. 151-56-4] is a colorless corrosive liquid with ammonia odor (boiling point 56°C) and vapor pressure of 160 torr (21.33 kPa) (20°C). It is used as production raw materials of pharmaceutical intermedi ate, polyethyleneimine, amino ethylation acrylic polymers, and the aziridine-based crosslinking agent. This chemical was recommended at 0.5 ppm (0.88 mg/m³) for OEL-M in 1966, added a skin absorption mark in 1990, categorized Group 2B for class of carcinogenicity in 2001, and was classified Group 3 as a reproductive toxicant in 2014. The Japan Society for Occupational Health (JSOH) reevaluated the OEL and other classifications by examining subsequent reports this time. The JSOH proposes 0.05 ppm (0.09 mg/m³) as OEL-M for ethylene imine based on the results that observed effects such as bronchitis and liver and renal denaturation in a rat inhalation experiment of 10 mg/m³ (5.7 ppm) for 4 hr/day and 1.5 months, and the reproductive toxicity such as decreases in the pregnancy rate exposed to 10 mg/m³ of ethyleneimine among pregnancy rats. The skin absorbency, a carcinogenic classification (Group 2B), and a genotoxicity classification (Group 3) remains the same.

Benomyl [CAS No.17804-35-2] is a carbamate fungicide broadly used for rice, wheat, fruits, vegetables, and flowers, among others, and benomyl wettable powder and benomyl-tiuram wettable powder are registered pesticides 50 and 200 mg/m². Since benomyl to call for attention. 2,3-Epoxypropyl methacrylate (Glycidyl methacrylate, GMA) [CAS No. 106-91-2] is a colorless liquid with a characteristic odor (boiling point 189°C, vapor pressure of 0.42 kPa at 25°C) that reacts violently with strong acids, strong bases, and strong oxidants with the generation of fire hazard. It is used mainly as a raw material in the manufacture of acrylic resin, diluent of epoxide-based adhesive, stabilizing agent of polystyrene chloride, ion-exchange resin, and binder of printing ink. The results of carcinogenicity and genotoxicity studies suggested a possible non-threshold carcinogen for rodents. However, because there is no available scientific knowledge of car cinogenicity in humans, assessing a dose-response relationship in human as a non-threshold carcinogen admits to large uncertainty. Therefore, the JSOH proposes 0.01 ppm (0.06 mg/m³) as the OEL-M for GMA, according to the dose-dependent pathological changes in olfactory and respiratory epithelia in the nasal cavity at concentrations of ≥0.6 ppm in the results of 2-year inhalation studies of B6D2F1/Crlj mice (0.6-10 ppm). In the assessment, an uncertainty factor for the severity of carcinogenic effect was taken into account. There was sufficient evidence in rats and mice of the carcinogenicity of GMA. The carcinogenicity classification is proposed as Group 2A. In the evaluation, it was taken into account that GMA is mutagenic in a wide range of in-vivo and in-vitro test systems. The OEL-M was set based on the non-carcinogenic effects. Thus, ψ notation is indicated for attention message. Skin absorption notation is indicated and skin occupational sensitizer classification is proposed as Group 2. The reproductive toxicant classification is proposed as Group 3.  

Classifications on Carcinogenicity

Regarding the carcinogenicity classification, 2-nitrotoluene is proposed to be a Group 2A carcinogen. The proposed Group 2B carcinogens are vinylidene chloride, quinoline, diazinon, 2,4,6-Trichlorophenol, pyridine, 1-tert-Butoxypropan-2-ol, malathion and β-Myrcone.

The latest OEL recommendations (2018-2019) will appear in the September issue of the Journal of Occupational Health (Volume 60, Number 5). A brief summary of the proposal will be posted on the society’s website (https://www.sanei.or.jp/oel-eng) in September.

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

Conflicts of interest: The committee declares that have no conflicts of interest.
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