MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for n-Butyl Glycidyl Ether (CAS No. 2426-08-6)

FROM: Cathy Simon, Air Quality Division

DATE: January 15, 2013

SUBJECT: Screening Level Update

A second initial threshold screening level (ITSL) of 160 µg/m^3 (8-hour averaging time) has been established for n-butyl glycidyl ether in addition to the existing ITSL of 300 µg/m^3 (one hour averaging time). This change is being made as part of a project to update ITSLs that are derived from outdated occupational exposure limits. The evaluation of data being done as part of this project is limited to identifying the most recent occupational exposure limit, and does not include a review of all the available scientific literature.

The original ITSL for n-butyl glycidyl ether was set in 1996 and was derived from the National Institute of Occupational Safety and Health (NIOSH) recommended exposure level - ceiling (REL-C) of 30 mg/m^3 (MDEQ, 1996). At that time, the American Conference of Governmental Hygienists (ACGIH) Threshold Limit Value (TLV) for n-butyl glycidyl ether was 25 ppm (133 mg/m^3) and was considered to be inappropriate for use in deriving the ITSL due to the lack of an adequate safety margin for the protection of human health (MDEQ, 1996). In 2005, the ACGIH adopted a new TLV – time weighted average (TWA) of 3 ppm (16 mg/m^3) (ACGIH, 2005). This new TLV (TWA) represents the most up to date and scientifically based TLV available from the ACGIH, and is considered appropriate to use for derivation of an ITSL. The new ITSL for n-butyl glycidyl ether was derived as follows:

$$ITSL = \frac{TLV}{100} = \frac{16\ \ mg/m^3}{100} = 0.16\ mg/m^3 = 160\ \mu g/m^3$$

The above ITSL of 160 µg/m^3 (8-hour averaging time) was derived pursuant to Rule 229(2)(b) of the Michigan Air Pollution Control Rules, and is consistent with the methodology of Rules 232(1)(c) and 232(2)(a). The previous ITSL of 300 µg/m^3 (one-hour averaging time) is still considered valid and is being retained.

References

ACGIH. 2005. n-Butyl Glycidyl Ether. Documentation of the Threshold Limit Values and Biological Exposure Indices. 7th Edition. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

MDEQ. 1996. *Memo from Michael Depa to File for n-Butyl Glycidyl Ether (CAS # 2426-08-6). Subject: Screening Level Determination.* February 9, 1996. Michigan Department of Environmental Quality, Air Quality Division.

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MICHIGAN DEPARTMENT OF ENVIRONNENTAL QUALITY

INTEROFFICE COMMUNICATION

February 9, 1996

TO: File for n-Butyl Glycidyl Ether (CAS# 2426-08-6)

FROM: Michael Depa, Toxics unit

SUBJECT: Screening Level Determination

The initial threshold screening level (ITSL) for n-butyl glycidyl ether is 300 µg/m³ based on a 1 hour averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, RTECS, ACGIH Threshold Limit Values, NIOSH Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, IARC Monographs, CAS Online (1967 - November 30, 1995), National Library of Medicine, Health Effects Assessment Summary Tables, and NW Status Report. Review of these sources found that EPA has not established an Rf C or RfD for n-butyl glycidyl ether. The ACGIH TLV for n-butyl glycidyl ether is 133 mg/m³. The NIOSH Ceiling REL is 30 mg/m³. Animal toxicity studies were available and are summarized below.

Groups of 10 male rats (strain not specified) were dose by inhalation to either 0, 38, 75, 150, or 300 ppm n-butyl glycidyl ether vapor for 7 hours per day, 5 days per week for a total of 50 exposures (~10 weeks) (Anderson et al., 1957) . At the level of 300 ppm there were five deaths, all occurring between the twentieth and thirty-fifth exposures. The animals in this group developed an emaciated appearance. One animal died in the 150 ppm dose group. There was a statistically significant decrease in weight gain in the 150 ppm ($p = 0.01$) and 300 ppm ($p = 0.05$) dose groups. There was a statistically significant ($p = 0.05$) increase in the relative kidney and lung weights in the 300 ppm dose group. There was no difference in the relative organ weight below the 300 ppm dose group. Three of 5 rats in the 300 ppm d'ose group had focal necrosis of the liver (the 5 rats that died during the experiment apparently were not examined). Atalectasis[1] appeared in the lungs of 4 controls and 18 of 35 dosed rats. These lesions did not appear to be related to the treatment. One animal exposed to 75 ppm had severe pneumonia and slight patchy atrophy of the testis. Five rats exposed to 150 ppm had bronchopneumonia. Three of the five survivors of the 300 ppm group had pneumonia; four had atrophic testes. There were no other findings among controls or animals exposed to 38 ppm. A LOAEL of 150 ppm (800 mg/m³) was identified based on decreased body weight and bronchopneumonia. A NOAEL of 75 ppm was also identified.

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1 Absence of gas from a part or the whole of the lungs, due to failure of expansion or resorption of gas from the alveoli.

Hine et al. (1956) tested n-butyl glycidyl ether in two acute lethal concentration studies. The 4 hour LC50 for the mouse (Webster strain; n = 5 or 6/group; 20 to 28 grams body weight) was found to be greater than 3500 ppm n-butyl glycidyl ether vapor (> 18,600 mg/m^3). The 8 hour LC50 for the rat (Long-Evans strain; n = 6/group; 110-140 gram body weight) was found to be 1030 ppm (890-1240 ppm) (5485 mg/m^3)

In another study, groups of 10 rats (CA TIF:RAIF, male and female) were dosed with mean concentrations of 0, 84, 470, or 1013 mg/m^3 n-butyl glycidyl ether for 6 hours per day, 5 days per week for 28 days (Gatz, 1985) . All organs were weighed. Statistical analysis was performed on absolute organ weights, organ weight to body weight ratios, and organ weight to brain weight ratios. A thorough hematological and serum chemistry analysis was performed. Histopathology was performed on all the organs. Nasal passages were sectioned in three different levels. The body weights of the male animals in the high dose level group were significantly decreased compared with controls after the second week of exposure. There was a slight decrease in body weights in the high dose (1013 mg/m^3) female group but it was not significantly different. There were changes in the fasting glucose in the high dose groups and elevated aspartate transferase levels in serum of high dose males and slightly increased hemoglobin in the high dose male rats. Mean cell volume (MCV) was statistically increased in the 470 mg/m^3 and 1013 mg/m^3 dose females. In the male dose groups the lymphocytes were significantly increased in the low and medium dose, but not in the high dose group. Histopathological examination revealed a degeneration of the olfactory mucosa and hyperplastic/metaplastic changes of the ciliated respiratory epitheliurn, both changes were more apparent in males than in females. These changes were present in the high and medium dose groups but not in the low dose group. Relative and absolute testes weights were normal. There was a statistically significant increase in the brain to body weight ratio in the high dose male group. There were no other differences in the male organ or organ to body weight ratios. In the high dose females there was a statistically significant decreased liver/brain ratio, however, there were no microscopic changes observed in the liver. The only histopathological changes found during the microscopic evaluation which can be related to the treatment by inhalation were observed in the nasal cavity. Two types of changes, both dose related, were observed: a degeneration of the olfactory mucosa and hyperplasia/metaplastic changes of the ciliated respiratory epithelium. Other parts of the respiratory tract were analyzed and found to be normal. A LOAEL of 470 mg/m^3 was identified based on increased lymphocytes, mean cell volume and olfactory hyperp1aia in male and female rats. A NOAEL of 84 mg/m^3 was also identified. It should be noted that the dose of 84 mg/m^3 could be considered a LOAEL based on the significantly increased lymphocyte count in the male rats. However, this response to n-butyl glycidyl ether was not seen at the high dose and was deemed not related to the exposure.

The ACGIH Documentation of Threshold Limit Values for n-butyl glycidyl ether was analyzed in order to determine the adequacy of the TLV. The

TLV of 25 ppm (133 mg/m³) was based on a 8 hour 1030 ppm LC50 in rats (see Hines et al., 1956 above) and, “incorporating a safety factor”.

This safety factor is roughly 40. It was deemed that this is an inadequate safety margin for the protection of human health, especially with regard to the bronchopneumonia and decreased weight gain seen at 150 ppm (800 mg/m³) as noted by Anderson et. al. (1957, see above summary). In contrast, the NIOSH recommended exposure level (REL) of 5.6 ppm - Ceiling (30 mg/m³) was deemed adequate to protect against respiratory and possible testicular effects (NIOSH, 1978). The ITSL was determined using the NIOSH REL according to Rule 232(1)(c). The calculation is shown below.

ITSL OEL/100

where, OEL is either the NIOSH REL or the ACGIH TLV.

ITSL = 30 mg/m³/100
ITSL = 0.3 mg/m³
ITSL = 300 µg/m³

The averaging time was determined according to Rule 232(2)(a) to be 1 hour. The ITSL for n-butyl glycidyl ether is 300 µg/m³ based on a 1-hour averaging time.

References

ACGIH. 1991. American Conference of Governmental Industrial Hygienists Documentation of Threshold Limit Values and Biological Exposure Indices. 6th edition. Cincinnati OH, pages 180-181.

Anderson, H., Hine, C., Guzman, P., Wellington, J. 1957. Chronic vapor toxicity of n-butyl glycidyl ether. Confidential Report To: Shell Development Company, Emeryville California. From: Department of Pharmacology and Experimental Therapeutics, University of California School of Medicine, San Francisco. Obtained from EPA/OTS Doc# 88- 7800213. Chronic vapor toxicity of n-butyl glycidyl ether with attachments and cover letter dated 7/12/78.

Gatz, R. 1985. Final report on the toxic effects of a 28-day inhalation exposure to butyl glycidyl ether (TK-10408) in the rat. Confidential report to CIBY-GEIGY AG 4002 Basel Switzerland. Battelle, Center for Toxicology and Biosciences. 7 Route de Drize, 1227 CarougeGeneva, Switzerland. Obtained from EPA/OTS Doc4t 86-870001327. line. C., Kodama, J., wellington, J., Dunlap, M., Anderson, H. 1956. The toxicolcqy of glycidol and some glyciyl ethers. A. M. A. Achieves of Industrial Health. Vol 14. 250-264.

NIOSH. 1978. Glycidyl Ethers. Current Intelligence Bulletin 29. Us Department of Health, Education and welfare. Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health. DI-IEW (NIOSH) Publication No. 79-104.

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