MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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August 12, 1996

To: File for Potassium Hydroxide (CAS # 1310-58-3)

From: Dan O'Brien Toxics Unit, Air Quality Division

Subject: Initial Threshold Screening Level (ITSL) for potassium hydroxide (KOH)

The initial threshold screening level for potassium hydroxide is 20 µg/m³ based on a 1 hour averaging time

The following references or databases were searched to identify data to determine the ITSL: AQD chemical files, IRIS, HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP Management Status Report, EPB Library, IARC Monographs, CAS On-line and NLM/Toxline (1967 January 23, 1996), CESARS, Patty's Industrial Hygiene and Toxicology, Merck Index and Condensed Chemical Dictionary.

KOH is a white to yellowish caustic, strongly alkaline solid that readily absorbs water to become a liquid. Its principal use is in the manufacture of soft and liquid soaps (Pierce, 1993; ACGIH, l992a; Merck, 1983). Other applications include use as a mordant for wood; in paint and varnish removers and in drain cleaners; in organic synthesis and the production of other potassium compounds; in photoengraving, lithography and printing inks; in electroplating; for mercerizing of cotton; in dyestuffs; as an electrolyte in alkaline storage batteries; for bleaching; in herbicides and liquid fertilizers; and as a food additive (Hawley, 1981). It has been applied medically for debudding of the horns of calves (Merck, 1983). The compound is extremely corrosive to tissues, due to its reaction with protein, saponifying effect on liquids and liquefactive necrotic effects on cells (Krenzelok, 1992; Fernando, 1987). Inhalation in any form (aerosol or dust) is strongly irritating to the upper respiratory tract, and severe injury is usually avoided by the self-limiting sneezing, coughing and discomfort. Contact with the eyes, if not treated immediately, can lead to severe and permanent ocular damage (Pierce, 1993). In accidents where elemental potassium has been allowed to react with moisture, the explosive exothermic reaction that resulted has produced KOU aerosols. The particles evolved are respirable (-.4 µm in diameter), can be deposited throughout the lower bronchial tree, and due to their irritant properties can produce potentially life threatening pulmonary edema (Krenzelok, 1992), which can have a latency of 5 to 72 hours (Pierce, 1993).

Much of what is known about the toxicity of KOH in humans derives from case reports and case series concerning either accidental ingestion the chemical, usually by children, in the form of cleaners (Spechler, 1992; Zargar et al., 1992; Edmondson, 1987; v.Mühlendahl et al., 1978) or in button batteries (Thompson et al., 1990: Fernando, 1987). Such incidents have been documented in veterinary medicine (Kore and Kiesche-Nesselrodt, 1990), and

the dog has received some attention as an animal model for button battery intoxications in humans (Yamashita et al., 1987; Litovitz et al., 1984). Similar cases have resulted from human suicide attempts utilizing KOH (Palmer, 1958). Patients present with clinical signs of hypersalivation, retching, emesis, dyspnea and immediate and severe pain. The clinical course of these intoxications generally involves ulceration of mucous membranes, perforation of the esophagus and stomach, and aspiration pneumonitis. Although airway injuries are rare, tissue edema and mucosal sloughing in the pharynx and upper airways can lead to airway obstruction and acute atelectasis (1-tallagan and Smith, 1994). Fatal outcome is usually due to shock, cardiovascular collapse, and/or asphyxia. If the patient survives the initial phase of the poisoning, infection in damaged tissues and esophageal strictures and stenosis (often requiring surgical intervention) may be expected subsequently (ACGIH, 1992a,b). ACGIH also reports a single case of esophageal carcinoma at the site of a hydroxide-induced stricture (Lansing et al., 1969). In contrast to the relatively large amount of data available on the toxic effects of KOH following oral exposure, little quantitative information has been published concerning the chemical's effects and dose/response relationships following inhalation exposure. Indeed, even the American College of Governmental Industrial Hygienists Threshold Limit Value (ACGIH-TLV) for KOH is based upon data for sodium hydroxide (NaOH) [1310- 73-2] by analogy (discussed below).

Little animal data concerning the toxicity of KOH was discovered in our searches. KOH was a minor constituent (1-2%) in one of seven machining fluids to which mice were exposed by aerosol inhalation (Schaper and Detwiler, 1991). However, it was present in such a small amount, with over half of the fluid mixture composed of heavy paraffinic distillate, that it is not possible to delineate what effects in the test animals, if any, might have been due to KOH. RTECS also lists a rat oral LD50 of 273 mg/kg, with the remainder of the acute toxicology citations having to do with dermal or ocular exposures.

Search of the literature pointed out a number of human epidemiological studies, a case series and a case report associated with KOH. Several of these studies (Wild et al., 1995; Graham et al., 1984; Attfield et al., 1982; Markham and Tan, 1981) appeared in on-line searches for KOH, but none of them documented exposure to KOH[1]. Two others used job descriptions (Johnson et al., 1987) and likely occupational exposures as characterized by an industrial toxicologist (Morris et al., 1986) to assess the association between occupational exposures and childhood nervous system tumors and between occupational exposures and multiple myeloma, respectively. In the former study the investigators executed a case-control design comparing the occupations of the fathers of children who died of cancers of the brain and spinal cord in Texas between 1964 and 1980 with the occupations of fathers of healthy control children chosen by a random sample of birth certificates. Multiple occupations were studied; assessment of exposures was limited to a qualitative listing of plausible chemical exposures which might be expected in a given broad

[1] All of these studies were conducted in groups of potash (potassium carbonate [584-08-7]) miners. Three of the studies (Graham et al., 1984; Attfield et al., 1982; Markham and Tan, 1981) were cross-sectional studies principally of respiratory outcomes as measured by self-reported symptoms and spirometry. All three reported largely negative findings. The fourth (Wild et al., 1995) was a retrospective cohort study of mortality rates in 8199 potash mine employees. Unlike the other studies, the authors' primary exposure of interest in this study was heat (rather than potash dust), and its effect on mortality rates from ischemic heart diseases.

occupational category. These authors found a high degree of association between paternal employment as a graphic arts worker Odds Ratio (OR) = 21.9; 95% Confidence Interval [CI] (1.2-397.2)) and having had a child who died of a childhood nervous system tumor. With respect to chemical exposures in this group of workers, the authors note that, "The printing and graphic arts industries involve occupational exposure to a large array of chemicals, including anilines, chromates, inks, oxalic acid, sodium and potassium hydroxides, paper dusts, and solvents among others". While valuable within the limits of its design, the inability to accurately characterize these workers' exposure to KOH makes it impossible to tell how much, if any, of the association observed might have been due to KOH. Moreover, because the OR was based on a small number of deaths (5 among the cases vs. none among the controls), the effect estimate is very imprecise; the CI suggests that children who died of nervous system tumors were anywhere between 0.2 and -400 times as likely to have had fathers who were graphics arts workers as were control children.

In the study by Morris et al. (1986), the authors conducted a case-control study of all incident cases of multiple myeloma diagnosed in Detroit, Seattle, Salt Lake City and Atlanta between 7/1/77 and 6/30/84, which amounted to 698 cases. These were compared with 1683 controls for various chemical exposures. Two methods were used. Via interview, both groups of subjects were asked whether they were "highly exposed" to products or fumes of a variety of categories of chemicals. For comparison with self-reported exposures, in the second method, a toxicologist was asked to evaluate what chemical exposures were likely for each subject based on occupational and other information obtained in the interviews. The chemical exposure category which would have included KOH was "alkalis", and for this category, the ORs of being diagnosed with multiple myeloma compared to controls were 1.0 [CI (0.5-1.9)] using self- reported alkali exposure as a metric, and 1.2 [CI (0.6-2.5)] using the toxicologist's assessment of likely exposure. Consequently, this study does not provide strong evidence of an association between KOH exposure and the incidence of multiple myeloma. Neither of these two studies provides sufficiently well-characterized KOH exposure data to aid in the quantitative derivation of a screening level.

Gordon (1987) published a paper regarding a case series of workers exposed to multiple chemicals[2] in radiology departments. This author reported non-specific symptoms, most of which were respiratory or cardiac (chest pain, catarrh, rhinitis, shortness of breath, arrhythmias, etc.), which eventually required that the workers be transferred out of contact with the radiographic chemical fumes. In general, symptoms subsided following removal from exposure. Some of the reported cases had abnormal chest radiographic findings. While not specifically implicating any particular component chemical of these mixtures, the author seems to emphasize the possible etiologic role of glutaraldehyde. A case report which was part of a Toxic Substance Control Agreement submission from Honeywell Corporation (EPA/CTS. 1992) describes a case of chronic obstructive lung disease in a woman in her late thirties exposed to a mixture of chemicals, one of which was KOH. Employed for nine years, this woman was forced by her condition to leave work in 1990. She experienced cough, lethargy, and dizziness beginning in 1987. The case worked in a

[2] Hydroguinone, diethylene glycol, acetic acid, glutaraldehyde, sodium sulphite, KOH, ammonium thiosulphate, sodium sulphate and aluminum sulphate, among others.

beryllium (Be) exposure area, and the only exposure information that was reported was for Be, which was present at concentrations < 10% of the Occupational Safety and Health Administration (OSHA) limit. Her diagnosis was not associated with exposure to any particular chemical by her occupational physicians. Clearly, due to the presence of KOH only in mixtures and the lack of quantitative exposure data for KOH, neither of these reports provides adequate data for derivation of a screening level.

No reproductive, teratogenicity or carcinogenicity studies of KOH were found in our searches. With respect to mutagenicity, Monta et al. (1989) recorded increased clastogenesis (chromatid breaks, chromosome exchanges and percentage of aberrant cells) in Chinese Hamster Ovary (CHO) cells at pHs of 9.8 and 10.4 where KOH was used to raise the pH of the medium. However, these rates were only increased in the presence of rat S9, and the authors urged caution in the interpretation of KOH as mutagenic, giving the impression that they believed the mutations were due to the absolute effects of pH rather than other mutagenic characteristics of KOH.

Both the National Institute for Occupational Safety and Health (NIOSH) and ACGIH have developed Occupational Exposure Limits (OELs) for KOH; both are ceiling limits of 2 mg/m^3 according to RTECS (1992), although NIOSH (1994) does not explicitly designate its OEL as ceiling. In its Threshold Limit Value (TLV) documentation, ACGIH (1992a) notes that "there are very few relevant data upon which to base a TLV for potassium hydroxide. Similar to sodium hydroxide, potassium hydroxide is extremely corrosive to tissue. Accordingly, by analogy with sodium hydroxide[3], a TLV-Ceiling of 2 mg/m^3 is recommended for potassium hydroxide". Referring to the TLV documentation for sodium hydroxide (NaOH) (ACGIH, 1992b), the TLV for both compounds appears to be based on an observation of Patty (1949) that 2 mg of NaOH/m^3 of air was "a concentration that is noticeably, but not excessively, irritant". ACGIH (1992b) also notes two accounts that "indicated noticeable irritation at concentrations of sodium hydroxide aerosol below 2 mg/m^3". One Citation reported nasal, ocular and throat irritation in cleaning workers where air concentrations of NaOH were between 0.005 and 0.7 mg/m^3, while the second notes eye and throat irritation in two individuals exposed to NaOH concentrations between 0.24 and 1.86 mg/m^3. The second report also notes that a third person exposed to 0.28 mg/m^3 experienced no irritation, so the possibility that substantial individual variation in sensitivity exists cannot be excluded. The TLV documentation points out, however, that both accounts suffered from inadequacies, the first because other solvents (e.g., Stoddard Solvent) were also present at concentrations as high as 780 mg/m^3, and the second because NIOSH "considered these data inadequate for correlation of exposure and effect".

Derivation of the ITSL: In choosing data for screening level development, preference is generally given to human epidemiologic data or chronic laboratory animal studies which can be used to derive a Reference Concentration (RfC). Such data were not found in our searches. When adequate data for RfC calculation are not available, next preference is given to oral data for calculation of a Reference Dose (RfD) if available data do not indicate that extrapolation from the oral to the inhalation route of exposure is inappropriate. In the

[3] It should be noted, however, that the same reference notes that "some evidence suggests that potassium hydroxide can pose a greater hazard than sodium hydroxide" and cites Ashcraft and Padula (1974).

case of KOH, ocular and upper airway irritation are the predominant toxic signs exhibited following inhalation exposure, suggesting portal-of-entry effects that may not be accurately accounted for by the use of oral data.

The next most appropriate alternative is an ITSL based upon an OEL. Given the unavailability of other inhalation data of sufficient quality for derivation of an RfC, and the inappropriateness of the use of oral data as noted above, the ACGIH-TLV is used here for the calculation of an ITSL for KOH. The TLV is used in preference to the NIOSH Recommended Exposure Limit (REL) since a ceiling limit is likely to be more protective than a time-weighted average (TWA) limit which may not reflect fluctuating KOH concentrations in excess of 2 mg/m^3 that simply average out over an 8 hour period (as noted previously, data on whether or not the REL is a ceiling limit are conflicting).

Per Rule 232(1) (C) of Act 348:

ITSL = OEL x 1/100 = 2 mg/m^3 x 1/100 = 0.02 mg/m^3 x 1000 µg/mg = 20 µg/m^3

where the factor of 1/100 is a safety factor to account for: 1) differences in susceptibility between the healthy, adult worker population as compared to the general population which may include individuals or subpopulations more sensitive to the effects of exposure to KOH and 2) the difference in exposure duration for the worker population as opposed to the general population. The factor is derived as follows:

Safety factor = 40hours/168 hours x 30years/70years x 1/10 = 1/100

The first term adjusts for the difference between a 40 hour work week and the total hours in a week; the second factor adjusts for the difference between assumed working life of 30 years and an assumed total lifespan of 70 years; and the third factor is a standard ten-fold uncertainty factor to extrapolate from the healthy worker to sensitive individuals in the general population.

Consistent with 232(2) (a), since the OEL used here is based on ceiling threshold limit, a 1 hour averaging time applies.

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