

“significant” risk reduction of a “material” adverse health effect to workers. Because OSHA operates under a different statute, employs different methodology, and will presumably have additional data at some point in the future, OSHA’s derivation of a permissible exposure limit (PEL) may result in a different number than the AEL we set using EPA’s own methodology and the data available today.

Today’s proposed decision to find nPB acceptable under the SNAP program is based in part on its relatively low ozone depletion potential when emitted within the continental United States. However, the ODP of nPB varies with latitude; therefore, this decision should not guide decisions of other countries. For example, nPB emitted closer to the equator has a significantly higher ozone depleting potential than nPB emitted from the middle and northern latitudes, which include the continental United States (for a further discussion, see section IV.B. below on Ozone Depletion Potential). EPA recommends that any decisions on the use of nPB outside the U.S. should be based on latitude-specific ODPs and volumes of the chemical projected to be used in those regions.

A. Toxicity

A primary concern regarding nPB use in the United States is its potential adverse health effects to exposed workers. Since EPA recommended a preliminary exposure guideline in 1999, additional studies have been conducted on the toxicity of nPB and its isomer, iPB. EPA has reviewed available toxicity data in order to develop a contamination limit for iPB and an Acceptable Exposure Limit (AEL)⁴ for occupational exposure to nPB that are protective of human health. EPA has also reviewed workplace exposure measurements from several facilities where nPB has been used.

1. What Acceptable Exposure Limit Is EPA Recommending for n-Propyl Bromide, and Why?

Today, EPA is recommending an AEL for nPB of 25 ppm as an eight-hour time-weighted average. Based upon currently available data, EPA believes that workers can be exposed to an average nPB concentration of 25 ppm without appreciable risk of adverse health effects. In addition, like many halogenated solvents, nPB has the potential to be absorbed through the

skin, so we recommend avoiding skin exposure to nPB by wearing protective clothing and flexible laminated gloves. The discussion below describes the derivation of the recommended AEL of 25 ppm for workplace exposure.

a. Summary of toxicity studies. EPA reviewed all the studies listed in docket numbers A-2001-07 and A-91-42 and the studies cited as references in Section XI at the end of this preamble. The epidemiological data on nPB are limited. An anecdotal report by Sclar described neurotoxic effects seen in one patient who used an nPB-based solvent (Sclar, 1999). Another recently published paper describes three women exhibiting signs of peripheral and central nervous system toxicity, such as stumbling, numbness, urinary incontinence, diarrhea, nausea, difficulty in concentrating, dizziness, and headaches which was attributed to nPB exposure (Ichihara, 2002a). Because detailed exposure data are not available in either of these papers, it is difficult to use this information in a risk assessment. Vibration sense deficits, decreased nerve conduction, and reduced scores on neurological functional tests were reported in female workers in China exposed to nPB between <1 ppm and 49 ppm (Ichihara *et al.*, 2002b). The study authors concluded that their findings suggest that exposure to nPB at levels below or around 50 ppm may affect peripheral and central nervous system function. However, because only an abstract of the study was available to EPA, it was not possible to determine if the exposures and effects were well-characterized or if the sample was large enough to draw reliable conclusions. As discussed below in section IV.A.1.e, “Feasibility of meeting the AEL for nPB in each industrial sector,” NIOSH has performed a number of health hazard evaluations with measured workplace exposures to nPB. However, only one of these studies attempted to assess health effects (NIOSH, 2002). In this study, NIOSH conducted a voluntary medical survey and performed a complete blood count on those workers who chose to participate (43 out of 70 workers participated). The medical survey included questions on whether workers had headaches at least once per week, and whether workers had difficulty having children. No exposure-response relationship could be identified from these data. The survey was not designed to fully characterize effects on the reproductive system, nor did the study employ a control group (a group of workers who were not exposed to nPB),

further limiting the utility of this data for risk assessment.

The acute toxicity of nPB has been studied in Sprague-Dawley rats for inhalation (Elf Atochem, 1997), oral (Elf Atochem, 1993), and dermal (Elf Atochem, 1995b) routes of exposure. The 4-hour LC50 (lethal concentration for 50% of the test animals) for inhalation of nPB was 35,000 mg/m³ (Elf Atochem, 1997), with death resulting from pulmonary edema. The LD50 (lethal dose for 50% of the test animals) for gavage dosing of nPB was greater than 2,000 mg/kg (Elf Atochem, 1993).

Animals receiving 2,000 mg/kg nPB dermally (with occlusion of the exposure area) showed no cutaneous reactions and no evidence of toxicity (Elf Atochem, 1995b). A skin sensitization test in Guinea pigs was also negative (Elf Atochem, 1995c).

Key chronic and subchronic toxicological studies on nPB include a 28-day inhalation study (ClinTrials, 1997a), a 90-day inhalation study (ClinTrials, 1997b), a two-generation reproductive toxicity study (WIL, 2001), and various papers and abstracts published in peer-reviewed scientific journals (Ichihara, 1998, 1999, 2000a, 2000b; Kim, 1999; Wang, 1999; Yu, 2001; Ichihara 2002a, 2002b). The results of these studies consistently show that sensitive health endpoints⁵ (*i.e.*, the biological effects occurring at the lowest levels of nPB exposure) include effects on the liver (centrilobular vacuolation—cellular changes in the central area of the liver) and on the male reproductive system (decreases in absolute and relative seminal vesicle weights, and reduced sperm count, motility and maturation, and effects on sperm shape).

The ClinTrials 90-day inhalation study showed liver effects at exposures of 400 ppm and above, which is consistent with the effects seen by Kim *et al.* (1999). Effects of nPB on the central and peripheral nervous system have also been reported, including peripheral nerve degeneration and axonal swelling in the spinal cord at 1000 ppm (Yu, 2001), degeneration of the myelin of peripheral nerves at 800 ppm (Ichihara, 1999), and significantly decreased hind limb grip strength (a measure of motor nerve function) at 400 ppm (Ichihara, 2000b).

Concerns over potential reproductive toxicity associated with nPB were initially raised because exposure to iPB,

⁴ An AEL is the SNAP program’s generic term for an eight-hour time-weighted average occupational exposure limit.

⁵ An endpoint is an observable or measurable biological event or chemical concentration (*e.g.*, metabolite concentration in a target tissue) used as an index of an effect of a chemical exposure.