

controls (see Section IV.A.1.e., "Feasibility of meeting the AEL for nPB in each industrial sector"). The AEL of 18 ppm was derived using assumptions that some may consider conservative. Following the SNAP principle referenced above, some slight adjustment of the AEL may be warranted after applying judgment based on the available data, and after considering alternative derivations.

To assess how much of an adjustment may be appropriate that would still be protective of human health, EPA considered potential sources of conservatism in the AEL derivation—specifically, the use of the BMDL in the F1 generation as a point of departure. To assess the magnitude of this conservatism, we derived an AEL based on the BMDL for reduced sperm motility in the F0 generation (282 ppm), the second most sensitive endpoint found in the 2-generation study. Deriving an HEC (296 ppm), and applying the same uncertainty factors as applied to the F1 generation (3 for intraspecies variability and 3 for differences in pharmacodynamics), would result in an occupational exposure limit of approximately 30 ppm. A derivation based on F0 data could be considered as a reasonable and protective upper bound for the occupational exposure limit. EPA requests comment on whether it is appropriate to interpret 30 ppm as an upper bound for an occupational exposure limit.

EPA has determined that 18 ppm is a reasonable but possibly conservative starting point, and that exposure to 25 ppm would not pose substantially greater risks, while still falling below an upper bound on the occupational exposure limit. An AEL of 25 ppm would reduce overall risk to worker health while adhering to EPA's SNAP guiding principle of not finding a substitute unacceptable unless the proposed substitute is clearly more harmful than other alternatives. EPA specifically requests comment on this approach.

Dermal Exposure. EPA believes that workers should use good workplace practices and proper handling procedures to avoid unnecessary dermal exposure to all industrial solvents, including nPB. Similar to other halogenated solvents, nPB may defat the skin and may cause local irritation due to this characteristic. A skin notation is applied to those chemicals where "dermal absorption contributes substantially to the overall systemic toxicity" (skin notation documentation for methyl chloride; ACGIH, 1991). As described previously, the available

acute dermal toxicity study in rats (Elf Atochem, 1995) indicates that acute dermal exposure to nPB does not result in systemic toxicity. Because significant dermal absorption of nPB was not demonstrated in this study, EPA is not including a skin notation for nPB along with our recommended AEL in the comments section of the regulatory text. The database regarding dermal toxicity for nPB is not as conclusive as the data for chemicals that have a skin notation, (e.g., methyl chloride, dichlorvos). To apply a skin notation to nPB would imply that the dermal toxicity of this compound is similar to that of these other compounds. It is also noteworthy that there is no skin notation for other halogenated solvents such as methylene chloride or perchloroethylene, and there is no evidence that absorption through the skin is greater for nPB than for the other halogenated compounds. Thus, in EPA's judgement the database currently does not support the need for a skin notation for nPB.

However, we note that the acute dermal study did not provide information regarding chronic dermal absorption. Further, NIOSH evaluated the potential of nPB to permeate skin and promote chronic, systemic toxicity using a mathematical model and the log octanol:water coefficient for nPB, which is approximately 2. This evaluation found that nPB dermal exposure may be an additional source of exposure to workers if the unprotected skin of both hands is exposed (NIOSH, 2003). Given the above information, EPA specifically requests comment on whether to add a skin notation to our recommended AEL in the final rule if there are data that support this change.

c. Overview of the Evaluation of Risks to Human Reproduction (CERHR)

Expert Panel Report on nPB. In December 1999, NIOSH submitted an assessment nomination to the National Toxicology Program's (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) for both nPB and iPB. The NTP and the National Institute of Environmental Health Sciences (NIEHS) established CERHR in June 1998. CERHR's purpose is to provide timely, unbiased, scientifically sound evaluations of human and experimental evidence for adverse effects on reproduction, including development, caused by agents to which humans may be exposed.

nPB (1-Bromopropane) was nominated by NIOSH and selected for evaluation by the CERHR based primarily on documented evidence of worker exposures and published evidence of reproductive and developmental toxicity in rodents (this

evidence is reviewed above in section IV.A.1.a). The evaluation of nPB was a four-month effort by a ten-member Expert Panel of academic, private and government scientists that culminated in a public meeting in December 2001. At that meeting, the Expert Panel reviewed the scientific evidence on nPB and reached conclusions regarding its potential effects on human reproduction and development. The Expert Panel Report on nPB was issued in March 2002 (CERHR, 2002a). An Expert Panel Report on iPB was issued at the same time and is discussed in section IV.A.4. of this preamble (CERHR, 2002b).

The Expert Panel Report on nPB is intended to: (1) Interpret the strength of scientific evidence that a given exposure or exposure circumstance may pose a hazard to reproduction and the health and welfare of children; (2) provide objective and scientifically thorough assessments of the scientific evidence that adverse reproductive/developmental health effects are associated with exposure to specific chemicals or classes of chemicals, including descriptions of any uncertainties that would diminish confidence in assessment of risks; and (3) identify knowledge gaps to help establish research and testing priorities.

NTP-CERHR sought public comment on the Expert Panel Report through a Federal Register notice on March 8, 2002 (67 FR 10734). The NTP has issued a final report, and has published all the public comments that were received on that report. These documents may be accessed through the CERHR Web site at <http://cerhr.niehs.nih.gov/news/bromo/index.html>.

The conclusions of the March 2002 Expert Panel Report on nPB were as follows:

- Available human data are insufficient to draw conclusions on the potential for reproductive or developmental toxicity.
- Available toxicological data were sufficient to conclude that nPB exposure can induce developmental and reproductive toxicity in rats. In evaluating the potential effects on human reproduction, the rat data are assumed to be relevant for humans.
- The mechanisms that lead to reproductive or developmental toxicity are unknown.
- There are no relevant kinetic or metabolism data for nPB to compare human and animal exposure levels.

The Expert Panel identified LOAELs from the body of animal data as follows:

- A LOAEL for male reproductive effects of 200 ppm based on decreases in absolute and relative seminal vesicle weight reported in Ichihara (2000b). A