

Miller, Diane M. (CDC/NIOSH/EID)

From: Paul Dugard [pdugard@mindspring.com]
Sent: Tuesday, December 15, 2009 5:03 PM
To: NIOSH Docket Office (CDC)
Subject: Re: 1-Bromopropane: Request for Information
Attachments: nPB Rusch OEL Calc 2007.pdf

Dear Sir:

Please find attached derivation of an occupational exposure limit (OEL) for nPB that employs the standard methodology used by responsible companies. This example was prepared by Dr George Rusch of Honeywell for use in discussions with US EPA. This treatment predates the finding of "clear evidence of carcinogenicity" in rats and mice in the NTP bioassays,

Sincerely,

Paul H. Dugard, PhD

-----Original Message-----

From: Paul Dugard
Sent: Dec 14, 2009 7:03 PM
To: nioshdocket@cdc.gov
Subject: 1-Bromopropane: Request for Information

Dear Sir:

Please find attached the response to the request for information on 1-bromopropane (nPB) published in the Federal Register of September 16, 2009. The items attached are the review of the toxicity and occupational exposure limits for nPB prepared by the Halogenated Solvents Industry Alliance (HSIA), an abstract of the draft report of the carcinogenicity and other studies conducted on behalf of the NTP and the report of the findings of the Technical Reports Review Subcommittee of the NTP. The full draft report of the NTP studies is available via the NTP website. An assessment of the occupational exposure limit by Dr. G. Rusch could not be submitted in electronic format and will be submitted in hard copy, or in a scanned version.

Thank you for the opportunity to contribute information.

Sincerely,

Paul H. Dugard, PhD
Director of Scientific Programs

Halogenated Solvents Industry Alliance, Inc.
1300 Wilson Boulevard
Arlington, VA 22209

Telephone (direct line): 703-741-5781

Development of OELs

Approach for n-Bromopropane

Considerations:

- Is our Point of Departure (POD) a NOEL or LOEL
- The POD should represent the most sensitive endpoint
- Is the data from Man or Animals

Approaches:

- If we use LOEL first estimate NOEL (data dependant)
- If data is from animal study apply extrapolation factor to estimate exposure level in man that can result in similar effect. (typically 3x to 30x)
- Then apply safety factor to include variability among members of the worker population (typically 3X or 10X)
- If POD is from human data apply safety factor to include all members of general population (typically 3X or 10X)

Development of OELs

Approach for n-Bromopropane from animal data

Study	POD	Extrapol. Factor	Safety Factor	Est. OEL
Decrease in seminal vessel weight Ichihara et al.(2000)	200 ppm	10 since this is an effect level	3 since it is a sens. Effect	6.7 ppm
Decrease in grip strength at 200 ppm Ichihara et al.(2000)	200 ppm	10 since this is an effect level	3 since it is a sens. Effect	6.7 ppm
Cerebrum decrease in enolase activity Wang et al, (2003)	200 ppm	10 since this is an effect level	3 since it is a sens. Effect	6.7 ppm
Decrease in muscle strength Honma et al.(2003)	50 ppm LOEL 10 ppm NOEL	3 from NOEL	3 since it is a sens. Effect	1.0 ppm

Development of OELs

Approach for n-Bromopropane from human data

Study	POD	Safety Factor	Est. OEL
<p>Diminished foot sensitivity to tuning fork vibration Ichihara et al. (2004)</p>	<p>2.92 ppm <i>- geometric mean</i> (0.34-49.19 ppm)</p>	<p>3 (sens. endpoint but wide variation on exposure level)</p>	<p>1.0 ppm</p>
<p>Severe peripheral neuropathy Majersik et al. (2007)</p>	<p>130 ppm (91-176 ppm)</p>	<p>30 (severe effect level est. 10 x to NOEL & 3X general population)</p>	<p>4.3 ppm</p>