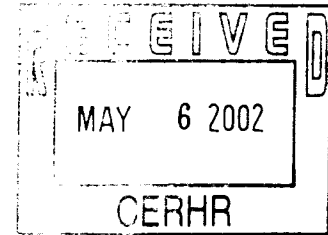


Shelby.Michael

From: Rich Morford
Sent: Monday, May 6, 2002 4:58 PM
To: Shelby.Michael
Subject: Expert Panel Review of 1-bromopropane



Dr. Shelby:

Please include the following remarks in the public file regarding the Expert Panel report on 1-bromopropane.

I have reviewed the report NTP-CERHR Expert Panel Report on the Reproductive and Developmental Toxicity of 1-bromopropane. We are in basic agreement with the Panel's conclusions. However, we feel the following criticisms of the report are warranted.

1. Our main criticism of the report is that the review itself was premature. We do not believe there exists any emergency situation which warranted a review at this particular time. Prior to the Panel meeting, the industry identified more information that was known to be potentially available within months to a year. Had their been adequate time, the industry may have provided additional raw data for some of the studies discussed as abstracts or identified but not considered due to lack of peer review. Since that time, more information has been identified as becoming available within the next year.

A review of 1-bromopropane late in 2002 or early 2003 could have been more complete as many of the critical data needs asserted in the report may well have been filled by that time.

Below is an update of information which is or will become available this year:

A) The Okuda reproductivity study from Japan has been published in Japanese and is now being translated.

B) A Japanese study Effects of 1-bromopropane, 2-bromopropane and 1,2 dichloropropane on the estrous cycle and ovulation of F344 Rats was published in Toxicology Letters.

C) NIOSH is completing two additional human medical studies regarding human exposure

to nPB within the adhesive industry. We are told these are likely to become available within sixty days.

D) Available to the Panel as an abstract only, the study Metabolism of Inhaled 1-bromopropane Vapor in Rats is due shortly.

E) A fairly reliable translation of four articles published in Russian journals in the 1970s has become available to us. These appear to be the original studies from which the intraperitoneal exposure effects reported by secondary sources are based. These studies include information on the clearance rate for nPB in rats. Interestingly, the National Cancer Institute cites these studies in their nomination of n butyl bromide to the NTP.

F) As earlier reported, the Doull/Rozman assessment has been peer reviewed excepted for publication in the ACGIH journal Applied Occupational and Environmental Hygiene.

G) Dr. Stelljes is completing the final draft of a report based on his bench mark dose method study for a peer review journal. We expect the paper to be accepted and published sometime in late 2002.

H) Dr Adali of Enviro Med Laboratories will begin human cell bioassays of eight additional solvents in June. These results, along with the previous results submitted to the NTP will be submitted for peer review in the third quarter of 2002.

I) The report Detection of N-Acetyl-S-Propylcysteine in the Urine of Workers Exposed to 1-bromopropane, available as an abstract to the Panel, is expected to be available in the near future.

J) A preliminary USEPA report on the adhesive sector, from their Design for Environment program, is due shortly. This report discusses general population and occupational exposure to nPB. We can provide a preliminary copy if that serves your purposes.

K) The study Biological Monitoring of Occupational Exposure to 1-bromopropane by means of urinalysis for 1-bromopropane and bromide ion was recently published in Biomarkers journal. The lack of detection of n-propanol in worker's urine tends to support the metabolic pathway proposed by Jones

and Walsh.

2) As discussed below, the Sclar case report has no usefulness for any scientific assessment. Please review the Great Lakes letter to the USEPA regarding this "study" which I will forward to you shortly.

3) An open mind is essential to a scientific review of any subject. However, the Panel refused to review much occupational exposure data available from industry sources. A clear animosity toward industry sponsored research regarding occupational exposure was exhibited by certain members of the expert panel. This bias has no place in these proceedings, especially as the Panel members were acting as governmental representatives. Such intransigent, biased attitudes toward industry by panel members can call into question the integrity of the entire report.

On the other hand, it is very interesting then that industry representatives were asked for help from NIOSH to study clearance rates for NPB in exposed workers.

The industry understands that the Panel need not accept industry conclusions on what the data means. However, since the Panel members are all experts by definition, they certainly have the capability and expertise to make their own review of the data and decide the relevance and weight to be given the data in their review.

4) We are disappointed that the Panel did not note or discuss differences in reported effects between the various studies, i.e. liver effects in the Ichihara study and BSOC two generational study.

5) The general rules for the Panel should include some means to note for the record facts and circumstances surrounding toxicological studies which question the validity of reported effects. An example is the developmental report used as the basis for the Panel's conclusion. This report seems to have been held secret for nearly two years without explanation and was done at the same facility and at the same time as an two generation test which was aborted due to reproductive problems with the control group. The Panel itself was unanimous in its disapproval of the authors statements regarding the significance of observed effects which led to the Panel's own bench mark dose review. Further, the study reported effects on food intake and weight which were not consistent with other similar studies.

The rigorous scientific standard called for by the Panel's rules is not met if these questions are unanswered, let alone undiscussed. The procedure for the Panel should include some means to bring questions such as these into the discussion.

Below are comments specific to certain Sections of the report.

1.1.4

1-bromopropane contamination is now typically at or below .05% and the industry continues to improve manufacturing capability to further reduce 2-bromopropane content.

1.2

The International Brominated Solvents Association, whose members include Enviro Tech International, Inc., PolySystems USA, Dead Sea Bromine Group and Tulstar Industries, among others, has been formed to assist in educating the public and solvent users on the safe use of brominated solvents. The IBSA has taken the lead in industry efforts for the safe and environmentally friendly use and reasonable regulation of brominated solvents .

A preliminary report from the USEPA concludes that, based on two model situations, exposure of the general population to nPB, in each scenario studied, was below the yet to be announced RfC for n propyl bromide.

The USEPA's Design for Environment study of adhesive applications also contains general public exposure estimates and should be available in the near future.

1.2.2

Standing on its own, listing manufacturers who no longer manufacture solvents is misleading. As the report deals exclusively with toxicity, in inference is that these companies do not produce nPB due to toxicity. Atofina is the only company to "say" they will not produce nPB for solvent use due to toxicity questions. A note should be included in the report which states that business reasons and economic and marketplace pressures may also be involved in the decision whether to or not to produce nPB.

1.2.3

Statements such as "unspecified amounts of 1-BP were detected from unreported locations" and "unreported levels" were detected in waxes, liquid pastes and detergents obviously do not meet the standard set for inclusion of information into this report and offer no useful scientific information. All statements such as these secondary should be deleted since they can not stand up to the most minimal scientific scrutiny, let alone the rigorous scientific standard by which the Panel works.

Recent studies from the NOAA have determined the degradation products of nPB. This report should be available shortly

1.2.4

Again, much data is available as to occupational exposure from members of the industry. Much if not all of this information was and is available to the Panel. Biological monitoring studies have been completed and should be published shortly.

2.2.1

Without discussing this subject again at length, we believe the connection of any substance to the symptoms of the subject can not be scientifically defended. This "study" is of no usefulness toward scientific understanding and should be entirely deleted from the report. I will forward additional information from Great Lakes regarding information they received on the subject. This "study" illustrates the case against the presumption of validity given to peer reviewed studies.

I have been told that the raw data from the NIOSH tests should become available. We will forward this information to the NTP when it does become public.

5.3

Again, there is considerable, not limited, occupational exposure data available. The clear animosity toward industry sponsored data should be unacceptable in this type of review.

5.4

Again, there is considerable, not limited, occupational exposure data available. There exist only unverified and unsubstantiated claims of nPB in consumer products. Little will be gained by a study of

consumer products until such products can be identified as existing.

We will send copies of the studies and reports mentioned herein to the NTP-CERHR as we receive them.

Please let me know if you have any comments or questions.

Cordially

Richard Morford

General Counsel

Enviro Tech International, Inc.