Shelby.Michael

From: Sandi Murphy
Sent: Thursday, September 27, 2001 4:17 PM
To: Shelby@niehs.nih.gov
Cc: Valerie_FROMENT/MICHELET/ATO_SA/ATO%ATOCHEM; Kirsten Makel
Subject: Bromopropane Expert Panel

english translation ATOBNP .doc

Dear Dr. Shelby:

ATOFINA is a producer of n-propylbromide (nPB). We are aware of the toxicology data for this material and for isopropyl bromide. Several years ago, as part of our Product Stewardship Program the decision was made not to market nPB for solvent uses. The toxicology database was reviewed recently and this business decision was reaffirmed. We would like to share our views with the scientists who will serve on the Bromopropane Expert Panel. A copy of our position statement is attached.

If you have any questions, please feel free to contact me at 215 419-5881 or by email: sandi.murphy@atofina.com.

Thank you for this consideration.

Sandra Murphy

(See attached file: english translation ATOBNP .doc)

ATOFINA

n-propyl bromide and solvent use
Confirmation of ATOFINA's position relating to potential health risks

In December 1997, according to its policy on Responsible Care and in response to the questions of its customers, ATOFINA (formerly ELF ATOCHEM) expressed concerns about the use of n-propyl bromide (nPB or 1-bromopropane, CAS 106-94-5) as a solvent.

In solvent applications where exposures cannot easily be kept under control, the potential to cause adverse health effects was the key reason for this position. In such critical fields as reproduction and carcinogenicity, no toxicological data were available yet potential effects on health were suggested by the chemical reactivity of nPB and its structural relationship with a family of brominated chemicals already under suspicion.
Indeed:

- nPB is a chemical reaction agent used for alkylation. This reaction, if expressed at the biological level, could be expected to cause serious effects on health such as reprotoxic, genotoxic and / or carcinogenic effects. In 1997, the data in our possession already showed a possible genotoxic potential.

- nPB is a part of a toxicologically suspect family in which several compounds have toxic properties identified in animals and confirmed in humans. In 1995 and then in 1996, we learned that isopropyl bromide (iPB), the structural isomer of nPB, had caused serious reproductive function problems (oligospermia, amenorrhoea) in Korean and then in Chinese workers as well as blood effects (anemia, pancytopenia) following its use as a degreasing solvent. These toxic effects of iPB have since been confirmed in animal studies.

Today, the new toxicological data available indicate that some effects of nPB and iPB are similar in animals. As the effects observed in animals for iPB have also been demonstrated in humans when used as solvent, the concerns expressed in 1997 about the potential effects of nPB in solvent applications are reinforced.

Considering the available studies on nPB, the following effects have been observed:

REPROTOXIC EFFECTS
The first screening studies of reprotoxic potential showed that, in male rats, nPB decreases the number and the motility of sperm cells together with abnormalities of their morphology. This impairment might reflect an effect in the spermiation process (3). This type of effect can be compared with that of iPB which is responsible for testicular atrophy as well as an impairment in number and motility of sperm cells (3, 4).
In female rats, a first communication (10) pointed out that nPB causes an increase in the number of irregular oestrous cycles; disturbance of the ovarian cycle has also been observed with iPB (6).
Recently, a two-generation reproductive toxicity study in rats has confirmed the effects of nPB on reproductive capacities. Impairments of ovarian cyclicity and effects on sperm cell viability have been confirmed together with an impact on the animals' fertility (1).

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NEUROTOXIC EFFECTS

A decrease of the nerve conduction velocity as well as histological effects in the peripheral and central nervous system were reported in rats after repeated administration of nPB (2, 8, 12, 13). For iPB, on the other hand, solely a peripheral neurotoxicity with effects on the nervous conduction has been shown (11, 13).

HEMATOTOXIC EFFECTS

According to the available data, nPB has little or no hematotoxic effects in rats (5, 9) while iPB is responsible for anemia and even for pancytopenia with impairment of the bone marrow (7).

Based on the current knowledge available on nPB and the toxic effects highlighted in animals, the assessment of ATOFINA leads to the conclusion that an 8-hour occupational exposure limit value (OEL) in humans should not exceed 5 ppm.

Because: - potential excessive exposures to any volatile solvent in open applications cannot be easily prevented,
- it is difficult to keep exposure levels of nPB below this OEL,
- and, it is difficult to control the distribution of marketed solvents to prevent uncontrolled industrial uses or other misuses of the product,

ATOFINA CONFIRMS ITS POSITION AND HAS DECIDED NOT TO MARKET NPB IN SOLVENT APPLICATIONS.

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