

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

June 8, 2005

TO: Memo to File for Triisopropanolamine (TIPA) CAS #122-20-3
FROM: Margaret M Sadoff
RE: Derivation of Initial Threshold Screening Level (ITSL)

The Initial Threshold Screening Level for TIPA is 19 ug/m³ with an annual averaging time.

A search of the literature and the following databases was performed for information regarding TIPA: American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values, National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Integrated Risk Information System (IRIS), NIOSH's Registry of Toxic Effects of Chemical Substances (RTECS), Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, CAS Online (1967 to December 2003), Hazardous Substance Data Bank (HSDB), National Library of Medicine/Toxline, Health Effects Assessment Summary Tables (HEAST), and National Toxicology Program (NTP) Study Database.

There is limited detailed toxicity information on TIPA in the database. RTECs lists an LD50 in rats as 4730 mg/kg and in mice as 2520 mg/kg. Study details are not available. DOW has published results of developmental studies showing that TIPA salts are less toxic to the fetus than to the mother in rats and rabbits. However, TIPA salts have a different CAS number than TIPA and were tested in combination with other salts of 2,4-D. Safety assessments on the use of TIPA and related compounds as cosmetic ingredients showed that these ingredients are "practically nontoxic" and are safe up to concentrations of 1%. A note was added that these ingredients should not be used in products containing N-nitrosating agents due to the potential for mutagenic activation. Genetics toxicology tests (Salmonella) conducted by NTP on the single chemical TIPA were negative. The FAO and WHO Working groups published their toxicological evaluations of pesticide residues in food including 2,4-D acid, salts, and esters. They reported oral LD50 values in rats and rabbits were between 699 and 2,322 mg/kg/bw/day. The LC50 for rabbits was between 1.8 and 10.7 mg/L (1,800 to 10,700 mg/m³). A European study reported results from two week and 30-day administrations of TIPA in rats via ingestion of drinking water. Results from the 30 day study were a NOAEL of 0.14 g/kg/bw/day and a LOAEL of 0.26 g/kg/bw/day. Effects at the LOAEL were changes in liver, kidney, spleen and testicles. Study details were not available.

DOW conducted an acute oral toxicity study in Fischer 344-derived CDF male rats which is of sufficient quality from which to derive an ITSL pursuant to Rule 232(h). Toxicity tests were conducted as an 85% solution of TIPA 99.6% triisopropanolamine, 0.42% diisopropanolamine, < 0.02% monoisopropanolamine and 0.03% water) in distilled water. Six rats per dose group were given a single dose of the test material via oral gavage. The dose groups and incidence of mortality are given below:

TIPA as 85% solution mg/kg	Mortality
603	0/6
1300	0/6
2500	0/6
5000	1/6
10,000	6/6

Following the administered dose, all rats exhibited lethargy. Rats in the two highest dose groups exhibited rough coats. In addition, dark exudates around the eyes were observed in the 5000 mg/kg dose group. Pale watery eyes and diarrhea were additional symptoms exhibited by the 10,000 mg/kg group. All surviving rats exhibited weight gain during the 2 week post treatment observation period. No treatment related effects were observed upon pathological examination of survivors 2-weeks post-treatment.

The single dose oral LD50 for male rats was determined to be 5994 mg/kg (95CI = 4,533 to 8,735 mg/kg) as calculated by the moving average method of analysis. The ITSL calculation as per Rule 232(h) is as follows:

$$\begin{aligned}
 \text{ITSL} &= \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{\text{LD50 (mg/kg)} \times \text{Weight}}{0.167 \times \text{Inhalation Rate}} \\
 &= \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{5994 \times 0.10^*}{0.167 \times 0.095^{**}} = 0.0189 \text{ mg/m}^3
 \end{aligned}$$

≈ 19 ug/m³, annual averaging time

The Initial Threshold Screening Level for TIPA is 19 ug/m³ with an annual averaging time.

*Average weight as given in DOW study (range = 0.074 to 0.133 kg)

** Inhalation rate using 1988 EPA IR value (0.952 m³/kg/d) and study body weight average (0.1 kg).