

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

October 21, 1994

TO: File for Tolazamide (1156-19-0)
FROM: Marco Bianchi *Marco Bianchi*
SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for tolazamide is $17 \mu\text{g}/\text{m}^3$ based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

A complete reference check was conducted for tolazamide, but only limited information was available. Upjohn provided an in-house oral and IP LD_{50} study for tolazamide on mice and rats, respectively. The mouse IP study revealed a calculated IP LD_{50} of 2239 mg/kg, with total mortality at 3200 mg/kg (10/10).

In contrast, five groups of five rats per group were given a single oral dose of 2000, 2500, 3200, 4000, and 5000 mg/kg body weight of tolazamide suspended in 1% CMC vehicle. No deaths were observed for any of the test animals, and only salivation was noted in dose groups 2500 mg/kg and higher. To verify using 5000 mg/kg as a surrogate LD_{50} , the lowest human therapeutic dose (Physicians Desk Reference, 1994) was calculated for comparison. This calculation showed that 5000 mg/kg can be appropriately used for ITSL derivation.

The ITSL was derived as follows:

The LD_{50} for this study was determined to be 5000 mg/kg.

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$\text{LD}_{50} = 5000 \text{ mg/kg}$

$$\text{ITSL} = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{5000}{0.167 \times 0.900} = 0.0166 \text{ mg/kg}$$

$0.0166 \text{ mg/kg} \times 1000 = 16.6$ or $17 \mu\text{g}/\text{m}^3$ based on annual averaging.

The ITSL for tolazamide = $17 \mu\text{g}/\text{m}^3$ based on annual averaging.

MB:ma