

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

December 1, 2003

TO: 2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine file
(CAS # 166524-75-0)

FROM: Gary Butterfield

SUBJECT: Screening level for 2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine

2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine is also known as DEDS. This material is a light beige solid.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH) Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), Michigan Department of Environmental Quality (DEQ) library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1968 - May 2003), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

The CAS and NLM on-line literature searches were conducted on May 5, 2003. No toxicity information was located during the literature searches. Dow Chemical was able to supply summaries of several unpublished toxicity studies - two acute oral studies, one acute inhalation study and one 4-week inhalation study.

In the acute oral studies, Dow/Gilbert (1994a, 1994b), groups of three female F344 rats were administered a single dose of 2000 mg/kg DEDS and observed for two weeks. There were no deaths observed in either of the oral studies.

In the acute inhalation study, Dow/Ciezlak (1994), a group of 5 male and 5 female F344 rats experienced a four-hour, nose-only exposure to 6.07 mg/L of DEDS dust with MMAD of 3 μ m and GSD of 2.48. There were no deaths observed during the 14-day observation period.

In the four-week inhalation study, Dow/Kirkpatrick (2001), groups of 10 male and 10 female F344 rats were exposed to aerosol via nose-only to concentrations of 0, 20, 60 or 200 mg/m³ for 6 hours per day, 5 days per week for a total of 20 exposures. Half of the rats were sacrificed at the end of the four-week exposure, while the other half were held for a 10-week recovery period. In the rats sacrificed at the end of the exposure period, the lungs had inflammation at all dose levels. The lung organ weights were also increased. There was an increased degree of inflammation with increasing doses. The nasal cavity of rats exposed to 200 mg/m³ had mucous cell hyperplasia. Rats sacrificed at the end of the recovery period had recovered from any treatment related effects. The lowest exposure level, 20 mg/m³, can be considered to be showing reversible adverse effects occurring at end of exposure, and will be considered to be a LOAEL.

It is generally preferable to use a longer term exposure study when setting a screening level. Thus, the use of the four-week study will provide the best basis for establishing the ITSL. The ITSL can be based on the 20 mg/m³ LOAEL and the equation from R232(1)(e), where the UF of 35 for the seven-day exposure was changed to 20 to account for a four-week exposure. The UF of 3 was used to adjust the LOAEL to a NOAEL rather than the standard 10 fold factor, because the EPA 1994 RfC document considers hyperplasia to be a relatively minor adverse effect, especially when recovery is also reported, as in this study.

The screening level can be calculated as follows.

$$\text{ITSL} = \frac{20 \text{ mg/m}^3}{20 \times 100 \times 3} \times \frac{6}{24} = 0.8 \text{ ug/m}^3 \text{ annual average}$$

It should also be noted that DEDS is a solid at ambient temperatures, and would therefore be expected to be emitted to ambient air as a particulate. The contribution of airborne DEDS concentrations to ambient particulate levels should be considered when evaluating compliance with any of the NAAQS for particulate matter.

References:

Dow/Ciezlak. 1994. 2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine (DEDS): acute aerosol inhalation toxicity study in Fischer 344 rats. Lab Report Code: HET DR-0336-0483-003. Summary provided by Dow Chemical for DEQ Air Quality Division.

Dow/Gilbert. 1994a. 2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine (DEDS): acute oral toxicity study in Fischer 344 rats. Lab Report Code: HET DR-0336-0483-001. Summary provided by Dow Chemical for DEQ Air Quality Division.

Dow/Gilbert. 1994b. 2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine (DEDS): acute aerosol inhalation toxicity study in Fischer 344 rats. Lab Report Code: HET DR-0336-0483-002. Summary provided by Dow Chemical for DEQ Air Quality Division.

Dow/Kirkpatrick. 2001. 2,2'-dithiobis(5-ethoxy-7-fluoro[1,2,4]triazolo(1,5c)pyrimidine (DEDS): 4 week repeated dose nose only aerosol inhalation toxicity and 10-week recovery study in Fischer 344 rats. CHEC file #: DECO HET DR-0336-0483-011. Summary provided by Dow Chemical for DEQ Air Quality Division.