MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

October 13, 2003

TO: 3,4-Difluorobenzonitrile file (CAS # 64248-62-0)

FROM: Gary Butterfield

SUBJECT: Screening level for 3,4-difluorobenzonitrile

3,4-Difluorobenzonitrile is also known as 3,4-DFBN. This is a white solid material, with a melting point of 50C. The molecular weight is 139.1 g/mol.

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 data was located for 3,4-difluorobenzonitrile during the literature searches. Dow Chemical provided summaries of several unpublished toxicity studies from their records.

In an acute oral study, Dow/Wall and Johnson (1988), groups of 3 female Fischer 344 rats were administered 3,4-difluorobenzonitrile via gavage at doses of 500 or 2000 mg/kg. All of the rats given 2000 mg/kg died, while all of the rats given 500 mg/kg survived the 14 day observation period.

In an acute inhalation study, Dow/Landry, Clements and Johnson (1996), a group of 5 male and 5 female F344 rats were exposed via nose-only exposure for 4 hours to a concentration of 430 ppm (or 2460 mg/m3). It is reported that this is the highest vapor concentration possible. A visual check of light scattering confirmed that aerosol was not present. All rats survived the exposure and 14-day observation period.

In a 28-day oral study (Dow/Takahashi and Macigaki (1993/4)) groups of Sprague-Dawley rats were administered 3,4-difluorobenzonitrile dissolved in olive oil via gavage at dose levels of 2, 15 or 100 mg/kg. The female rat NOEL was reported to be 2 mg/kg, while the male NOEL was 15 mg/kg. The effects observed in the females included: increased liver weight due to hypertrophy of hepatocytes, increased renal weight, acinar cell atrophy of Harder's gland, and high levels of total serum protein and albumin. The males had many of these same observations along with increased testicular weight.

For the purposes of determining a screening level, results from a longer term study is generally preferred over an acute study. Thus, the 28-day oral study female rat NOEL of 2 mg/kg provides the best basis for setting the ITSL. The equation from R232(1)(e) for 7-day oral study can be applied to the NOEL as follows.

$$\text{ITSL} = \frac{2\ \text{mg/kg}}{35 \times 100} \times \frac{1\ \text{kg}}{0.9\ \text{m3}} = 0.6\ \text{ug/m3 annual average}$$

The default rat inhalation rate of 0.9 m3/kg was used in the above calculation.

As a solid at ambient temperatures, 3,4-DFBN would therefore be expected to be emitted to ambient air as a particulate. The contribution of airborne 3,4-DFBN concentrations to ambient particulate levels should be considered when evaluating compliance with any of the NAAQS for particulate matter.

References:

Dow/Landry, Clements and Johnson. 1996. 3,4-difluorobenzonitrile: acute inhalation toxicity study in Fischer 344 rats. Lab report code DR-0284-6324-002. Submitted by Dow to DEQ Air Quality Div.

Dow/Takahashi and Macigaki. 1993/4. Twenty-eight day oral gavage in Sprague-Dawley rats and reverse mutation (Ames) test on 3,4-difluorobenzonitrile. Lab report code DR-0284-6324-004. Submitted by Dow to DEQ Air Quality Div.

Dow/Wall and Johnson. 1988. 3,4-difluorobenzonitrile: acute toxicologic properties. Lab report code DR-0284-6324-001. Submitted by Dow to DEQ Air Quality Div.