MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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June 2, 2006

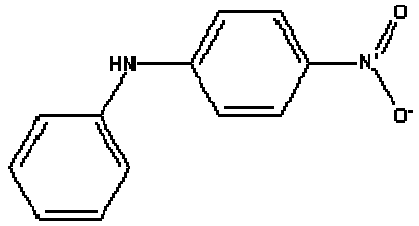
TO: **File for N-nitrodiphenylamine, CAS# 836-30-6**

FROM: **Margaret M. Sadoff, AQD, Toxics Unit**

RE: **Development of Screening Level**

The ITSL for N-nitrodiphenylamine is 1 ug/m3 with an annual average.

A search of the literature and the following databases was performed for information regarding N-nitrodiphenylamine: 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), Registry of Toxic Effects of Chemical Substances (RTECS), Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, CAS Registry Online, Hazardous Substance Data Bank (HSDB), National Library of Medicine/Toxline, Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Study Database, Entrez PubMed, and CalEPA's Toxicity Values Database.



N-nitrodiphenylamine MW = 214

Description

N-nitrodiphenylamine exists as a yellow needle-like solid with a negligible vapor pressure at room temperature. However, harmful concentrations of airborne particles can be reached quickly when dispersed (WHO International Chemical Safety Cards, ICSC 0804). Due to its nitroaromatic structure, this chemical is considered to have the potential to cause methemoglobin formation in humans. A manufacturer's internal atmospheric occupational exposure guideline is listed as 3 mg/m3, set on a structure-activity relationship basis for substances known to produce methemoglobinemia in humans. (Source: IPCS Inchem, Screening Information Data Set for High Production Volume Chemicals, online at http://www.inchem.org).

There is very little data available from which an ITSL can be derived.

RTECs reports a rat LD50 of 7,940 mg/kg.

In two subchronic studies, rats were fed up to 5,000 ppm in the diet for 90 days. The most notable clinical pathology finding was in hematological parameters and included increased reticulotcyte counts, dose related increase in methemoglobin, and decreases in hematocrit, hemoglobin and RBC counts. Other findings included decreased body weight gain, histopathological effects on kidneys in males, elevated liver weights in females, splenic congestion and slight anemia. The reported NOEL is 800 ppm (57 mg/kg/day). Although a 90-day oral study would be sufficient to calculate an RfD based ITSL, this is a German study and study detail is not available in English.

One oral study was found for reproductive toxicity in rats as performed by Monsanto Co. (TsCATS submission). A NOEL of 250 mg/kg/day was reported for lack of reproductive toxicity and no reported maternal or fetal toxicity. Using R232(1)e, this value would give an ITSL of 75 ug/m3 on an annually averaged basis but since the study was limited to reproductive effects only, it is not appropriate on which to base an ITSL for a chemical with known effects on the blood at lower doses in experimental animals.
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Lastly, one 21-day inhalation study in rats was found, also in German with the abstract published in English. (Source: Anonymous. In German. Abstract in English. Toxikologische Bewertung. Heidelberg, Berufsgenossenschaft der chemischen Industrie Vol. 274 (1994) 13p. Also reported by IPCS Inchem). There was sufficient detail in the abstract from which to derive an ITSL utilizing R232(1)d with the modification noted below*. Inhalation of 29 or 52 mg/m3 nitrodiphenylamine for 21 days, 6 hours/day, 5 days/wk caused raised methemoglobin levels and other hematological effects (not defined) as well as increased liver weights and respiratory irritation in rats. The NOEL from this study was reported as 8.5 mg/m3. The calculation for the ITSL of 1 ug/m3 on an annually averaged basis is given below:

$$\text{ITSL} = \frac{\text{NOAEL}}{\mathbf{35} \times 100} \times \frac{\text{hrs exposed/day}}{\text{24 hrs per day}}$$

$$= \frac{\text{8.5 mg/m3}}{\mathbf{20} \times 100} \times \frac{\text{6 hrs}}{\text{24 hrs}}$$

$$= 0.00106 \text{ or } \sim \mathbf{1\ ug/m3, annual\ average}$$

***The factor of 35 based on a 7-day study was reducted to a factor of 20 for a 21-day study.**