MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

February 3, 2004

TO: File for clarified oils (petroleum), catalytic cracked (64741-62-4)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for *clarified oils (petroleum), catalytic cracked*, also known as clarified slurry oil (CSO) is 12 $\mu g/m^3$ 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 on-line, RTECS, EPBCCD, EPB library, CAS-online, NLM-online, IARC on-line, NIOSH Pocket Guide, and ACGIH Guide.

A definition of this petroleum hydrocarbon distillate is provided by the Toxic Substance Control Act Chemical Substance Inventory (Initial Inventory; Volume 1; 1979):

"*clarified oils (petroleum), catalytic cracked* is a complex combination of hydrocarbons produced as the residual fraction from distillation of the products from a catalytic cracking process. It consists of hydrocarbons having carbon numbers predominately greater than C_{20} and boiling above approximately 350^0C (662^0F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons."

A complete reference check was conducted for CSO, but only two toxicity studies were available to derive an ITSL. The first study was an LD_{50} value supported with the minimum data reporting requirements for acute toxicity testing. The LD_{50} data was obtained from an abstract presented in the Journal of the American College of Toxicology. According to the abstract, 5 male and 5 female Sprague-Dawley rats were orally dosed by gavage at 25 g/kg body weight and observed for 14 days post dosing. Adverse effects included hypoactivity and diarrhea. An LD_{50} of 5.3 g/kg (4.0-7.0 g/kg C.I.) was determined for male rats, and an LD_{50} of 4.3 g/kg (2.7-5.5 g/kg C.I.) was determined for females. Therefore, an LD_{50} of 4.3 g/kg could be used to develop an ITSL for CSO.

The second study was a teratogenicity study. In this study, pregnant CD-rats were given a single oral dose on gestation days 11-14 of CSO to determine the teratogenic potency of

this compound. Previous dermal studies showed similar refinery streams to be developmentally toxic (manifested primarily as increased embryolethality and growth retardation) by the dermal route of exposure. However, there is no evidence for their being teratogenic. The present study was designed to further explore the suspected teratogenic potency of CSO while at the same time limiting embryolethality. To profile teratogenic effects as a function of gestation day, pregnant rats received a single oral dose at 2000 mg/kg CSO on one of gestation days (GD) 11-14. According to the study investigators, to profile effects as a dose response function, rats received a single oral dose of CSO on GD 12 at 125, 500, and 2000 mg/kg. Control animals were similarly treated but were administered tap water.

On GD 20, dams were necropsied and the fetuses evaluated for normal development. In general, evidence of maternal toxicity (i.e., decreased body weight gain, decreased thymus weight) was observed at doses greater than or equal to 500 mg/kg. CSO produced a significant increase in the incidence of resorptions on GD 11 and 12 at the mid- and high-dose levels. The no-observed-effect-level (NOEL) for resorptions was 500 mg/kg. A common pattern of external, visceral, and skeletal fetal malformations was observed for CSO and included cleft palate, diaphragmatic hernia, and paw and tail defects. The incidence of external and skeletal malformations was greatest on GD11 and 12 for fetuses exposed to CSO; the incidence of visceral anomalies was greatest on GD 11-13. The NOEL for external and visceral anomalies is 500 mg/kg and for skeletal anomalies is 125 mg/kg. The study investigators concluded, the present study clearly establishes CSO as a teratogen in the rat when administered via gavage on a single day of gestation.

Both the LD_{50} and the teratogenicity study were considered key studies to develop an ITSL for CSO. Minimum data requirements for acute toxicity testing did support the LD_{50} (4300 mg/kg) for this compound, but the LD_{50} only considers death as a toxicological endpoint. CSO also caused developmental effects at much lower dose levels of 500 or 2000 mg/kg in the teratogenicity study. The NOEL for this study was 125 mg/kg, and would result in an ITSL of 38 ug/m^3 (annual avg.) if based upon the 7-day NOAEL formula (Rule 232(1)(e)). However, there were data uncertainties associated with the teratogenicity study. The study investigators were interested in teratogenic effects of CSO as a function of gestation day so maternal rats were dosed on GD 11-14 rather than the typical GD 6-15. This limited the testing period by over half, which alters the OECD guidelines for teratogenicity testing. Although this uncertainty raised questions about using the teratogenicity data to develop an ITSL, there are arguments for its use. Animals did develop teratogenic effects at specific dose levels on a critical day of gestation, confirming that CSO affected the fetus at a sensitive time of development. A distinct range of doses also appeared to demarcate adverse fetal effects and no effects regardless of what gestation day the animals were dosed. Additionally, the 125 mg/kg dose level was a NOEL not a NOAEL. This would tend to support the argument that additional dosing would not have made a large difference in the results. To account for data uncertainties, the 7-day NOAEL formula allows for the addition of an uncertainty factor (UF) depending upon the quality of the data. The study did follow modified OECD guidelines. To account for these data uncertainties, a UF-3 seems

appropriate to use to derive an ITSL. The data quality was good, but the standard testing protocol was slightly adjusted to tease-out certain toxicological effects. An ITSL that is derived using the 7-day NOAEL formula with an added UF-3 would equal 12 ug/m^3 (annual avg). This value is similar to an ITSL derived from an LD_{50} (14 ug/m^3 annual avg) but accounts for developmental effects.

The ITSL was determined as follows:

NOEL = 125 mg/kg.
UF-10 for data uncertainties of single dosed animals over a shortened dosing period

$I = 0.80(0.319)^{0.8206} = 0.3133 m^3$

$$ITSL = \frac{NOEL}{3 \times 35 \times 100} \times \frac{W_A}{I_A} \times \frac{b}{a}$$

$$ITSL = \frac{125\ mg/kg/day}{3 \times 35 \times 100} \times \frac{0.319\ kg}{0.3133 m^3} \times \frac{1}{1} = 0.01212\ mg/m3$$

Conversion of mg/m3 to ug/m3

0.01212 mg/m3 x 1000 = 12.1 ug/m3

The ITSL for *clarified oils (petroleum), catalytic cracked* = 12 ug/m^3 based on annual averaging.

References:

1. Abstract: 1990. Acute toxicological evaluation of vacuum residuum. Journal of the American College of Toxicology, Part B. Vol. 1, No. 2; pg 136. Mary Ann Liebert, Publisher.

2. TSCA. 1979. Toxic Substance Control Act Chemical Substance Inventory (Initial Inventory; Volume 1. U.S. EPA, Office of Toxic Substances, Washington, DC 20460, May 1979.

3. Feuston, MH. 1996. Developmental toxicity of clarified slurry oil, syntower bottoms, and distillate aromatic extract administered as a single oral dose to pregnant rats. Journal of Toxicology and Environmental Health, 49:45-66.