MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for naptha (petroleum) light catalytic cracked (CAS # 64741-55-5)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: naptha (petroleum) light catalytic cracked ITSL change in the averaging time from 24 hrs to annual

DATE: February 7, 2017

The current ITSL for naptha (petroleum) light catalytic cracked is 5600 ug/m^3, with annual averaging time (AT).

Previously, the ITSL was established on December 5, 2003 at 5600 ug/m^3 with 24 hr averaging time (see attached justification memo). The averaging time (AT) assigned to the ITSL previously was 24 hours, as per the default methodology at that time (Rule 232(2)(b)). The ITSL derivation applied a total uncertainty factor (UF) = 300, which consisted of a UF = 10 for intraspecies variability, UF = 3 for interspecies extrapolation (with dosimetric adjustment) and UF = 10 for subchronic-to-chronic conversion. The current file review concludes that the AT for the ITSL may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b).

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

December 5, 2003

TO: File for naphtha (petroleum), light catalytic cracked (64741-55-5)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for *naphtha (petroleum), light catalytic cracked* is 5600 $\mu g/m^3$ based on a 24 hr 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):

> "*Naphtha (petroleum), light catalytic cracked*, also known as *light catalytic cracked naphtha (LCCN)*, is a complex combination of hydrocarbons produced by the distillation of products from a catalytic cracking process. It consists of hydrocarbons having carbon numbers predominately in the range of C4-C11 and boiling in the range of approximately minus 20C to 190C (-4F to 374F). It contains a relatively large proportion of unsaturated hydrocarbons."

Due to LCCN being on EPA's list of high production volume chemicals, a number of toxicity studies were available for review. These studies included an acute inhalation study provided by Marathon Oil Co.; a 13-week rat inhalation study sponsored by the American Petroleum Institute (API); and a 15-week rat inhalation study sponsored by the Petroleum Product Stewardship Council (PPSC). The 15-week study was for LCCN-distillates referred to as LCCN-D.

In the acute inhalation study, five young adult rats (strain not specified) of each sex were exposed to a target vapor concentration of 5.25 mg/L for 4 hours of LCCN. No animals died or exhibited clinical signs during the course of the exposures or during the 14-day observation period. No toxic signs of any significance were seen in animals of either sex that could be attributed to exposure. Histopathological examination of the lung tissues yielded minimal pulmonary findings, none that could be attributed to exposure of these animals to the compound. An LC_{50} was not determined since there were no deaths observed at the 5.25 mg/L concentration.

In a 13-week subchronic inhalation toxicity study sponsored by the American Petroleum Institute (API), four groups of 20 male and 20 female Sprague-Dawley rats were exposed to concentrations of 0, 1500, 2600, or 4500 ppm LCCN. Exposures were conducted six hours per day, five days per week, for thirteen consecutive weeks. During the exposure period,

observations for pharmacotoxic signs prior to and after exposure were conducted daily. Detailed observations for pharmacotoxic signs and body weights were conducted weekly over the course of the study. Various hematologic, serum biochemical and histopathologic evaluations were conducted after 13-weeks of exposure.

Results showed very few toxic responses were observed in male or female rats exposed to LCCN at levels up to 4520 ppm. At that exposure level, a 50 to 65% incidence of red tinged nasal discharge was observed in females and males, respectively. This sign was not observed in appreciable numbers of animals at lower exposure levels of 1510 and 2610 ppm. Males exposed to 4520 ppm exhibited depressed body weights, about 90% of controls, over most of the 13-week exposure. Males exposed to lower levels, and females at all exposure levels exhibited body weights similar to controls. There were no exposure-related differences for either males or females in any of the hematologic, serum biochemical or urinalysis parameters evaluated. After the 13-week exposure period there was a dose-related increase in liver weights for both males and females, approximately 15% for the high level group. These liver weight changes were associated with a trace severity of cellular hypertrophy, in 50 and 25% of the males and females, respectively. According to the study investigators, these weight changes probably reflect a nonspecific biochemical/physiologic response to the test material. This interpretation was supported by the normal levels of hepatic related serum enzymes. Kidney weights were elevated in male rats, approximately equally at all three exposure levels. Kidney weights for females were similar between exposed and control groups. The elevated male kidney weights were due to the alpha-2_u-globulin protein that effects male rats, but has no relevance in humans.

In summary, exposure to LCCN at 4520 ppm for 13-weeks produced mild but significant toxic responses in males, depressed body weights, typical hydrocarbon induced nephropathy, and increase in liver weights. Females were essentially unaffected by this exposure regimen, except for the increase in liver weights. According to the study investigators, based on the results of this study, the NOAEL for LCCN is 2610 ppm.

In a companion study to the API study listed above, the PPSC sponsored a 15-week inhalation study exposing Sprague-Dawley rats to a distillate of LCCN. Target concentrations of LCCN-D were 0, 750, 2500, and 7500 ppm for 6 hrs/day 5 days/week. Neurotoxicity was evaluated by motor activity assessment and a functional observational battery. Neuropathologic examination of selected neuronal tissues from animals in the control and high-exposure groups was also conducted. No compound-related effects were seen on survival, clinical chemistry, food consumption, or physical signs. No evidence of neurotoxicity was seen at any exposure level. Slight decreases in hematocrit and hemoglobin concentrations were seen in male rats at the end of exposure to 7500 ppm. However, values were within normal physiological ranges and recovery occurred. Slight decreases in mean body weights and body weight gain were observed in high-exposure females during the first 7 weeks of exposure, but this decrease was not seen during the second half of the study. Male nephropathy involving hyaline droplet formation and alpha-2u-globulin accumulation was seen in mid- and high-exposure males, an effect not relevant to humans. The incidence and severity of goblet cell hypertrophy/hyperplasia and respiratory epithelium hyperplasia in the nasoturbinal tissues were greater in high-exposure animals, but recovery occurred. According to the study investigators, none of the effects observed were considered toxicologically significant. They established a NOEL for subchronic and neural toxicity of LCCN-D at 2500 ppm.

The 13-week API study presented above included the necessary data requirements to derive an Inhalation Reference Concentration (RfC). The study is of sufficient duration; it examined a

number of physical, histological and pathological parameters; and its NOAEL was supported by 15-week companion study at a similar no-observable-effect-level. The companion study was strong enough to establish an RfC in its own right, but because it is comprised of a slightly different blend of petroleum hydrocarbons, it is not classified with the same CAS number as LCCN. LCCN-D was shown to have lighter components in the C5 to C7 carbon range comprising ~93%, as compared to ~75% for LCCN. The companion study seems an appropriate support study because it was conducted specifically to address the neurotoxicity of LCCN under exposures similar in level and composition to those encountered by humans both in the workplace and during vehicle refueling. The outcome of this study provides a distinct exposure threshold of adverse effects similar to the API study, resulting in greater confidence in that NOAEL. Therefore, the ITSL will be based a NOAEL of 2610 ppm (API, 1987).

The ITSL was determined as follows:

NOAEL = 2610 ppm or 9380 mg/m^3 (as determined from Lapin, 2001)

Adjust for Exposure Regimen

$NOAEL_{[ADJ]}$ = E (mg/m^3) x D (h/24h) x W (days/7 days)

E = experimental dose level
D = number of hours exposed/24 h; and
W = number of days of exposure/7 days

$NOAEL_{[ADJ]}$ = 9380 mg/m^3 x 6h/24h x 5days/7days

$NOAEL_{[ADJ]}$ = 1675 mg/m^3

Dosimetric Adjustments and Calculation of $NOAEL_{[HEC]}$

$$NOAEL_{[HEC]} = NOAEL_{[ADJ]} \times \frac{(H_{b/g})_A}{(H_{b/g})_H}$$

$NOAEL_{[HEC]}$ = the NOAEL or analogous effect level obtained with an alternative approach, dosimetrically adjusted to an HEC;

$NOAEL_{[ADJ]}$ = described above; and

$(H_{b/g})_A/(H_{b/g})_H$ = the ratio of the blood:gas (air) partition coefficient of the chemical for the laboratory animal species to the human value. The value of 1.0 is used for the ratio if $(H_{b/g})_A > (H_{b/g})_H$.

$$NOAEL_{[HEC]} = 1675\ mg/m^3 \times \frac{1}{1}$$

$NOAEL_{[HEC]}$ = 1675 mg/m^3

Uncertainty Factors

3 = factor of 3 ($10^{1/2}$) was applied for interspecies extrapolation rather than 10 because of the dosimetric adjustment from rat to human
10 = sensitive populations
10 = subchronic to chronic study

$$\frac{1675 \text{ mg/m3}}{3 \times 10 \times 10} = 5.583 \text{ mg/m3}$$

Conversion of mg/m^3 to ug/m^3

$$5.583 \text{ mg/m3} \times \frac{1{,}000 \text{ ug}}{1 \text{ mg}} = 5583 \text{ ug/m}^3$$

The ITSL for *naphtha (petroleum), light catalytic cracked* = 5600 ug/m^3 based on a 24 hr. averaging.

References:

1. API. 1984. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats, *light catalytic cracked* naphtha. API sample 81-04. Study conducted under contract PS-45 by Litton Bionetics, Inc. Kensington, MD, February, 1984. Marathon Oil/API Med Res Publ 31-30680. EPA/OTS Doc #FYI-AX-0587-0411.

2. API. 1987. Thirteen week subchronic inhalation toxicity study on a petroleum-derived hydrocarbon in rats. API-81-03. Study conducted by International Research and Development Corporation.

3. Lapin, C. et al. 2001. Toxicity evaluation of petroleum blending streams:inhalation subchronic toxicity/neurotoxicity study of a light catalytic cracked naphtha distillate in rats. International Journal of Toxicology, 20:307-319.

4. 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.