MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

November 10, 1998

TO: File for beta phenylethylamine (CAS #64-04-0)

FROM: Cathy Simon, Supervisor, Toxics Unit, Air Quality Division

SUBJECT: Change in the Initial Threshold Screening Level (ITSL)

The ITSL for beta phenylethylamine has been changed from 0.04 ug/m^3 to 0.1 ug/m^3 based on an annual averaging time.

The change in the ITSL was made due to a revision in the State's air toxic rules which became effective on November 10, 1998. Previously, the ITSL had been set pursuant to Rule 232(i). This rule sets the ITSL at a default value of 0.04 ug/m^3 (annual average) when no specific data are available to determine an ITSL. The November 10, 1998 revisions to the rules changed this default ITSL to a value of 0.1 ug/m^3.

No updated review of the literature has been done since the ITSL was originally set at a value of 0.04 ug/m^3, to determine if new data are available for this compound.

CAS:SLB

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

March 14, 1995

TO: File for β-Phenylethylamine (βPEA) (CAS # 64-04-0)

FROM: Dan O'Brien, Toxics Unit, Air Quality Division

SUBJECT: Screening Level Development Literature Search, Permit # 447-85 (Zeeland Chemical)

The initial threshold screening level (ITSL) for β-Phenylethylamine is 0.04 µg/m^3 based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: AQD chemical files, IRIS, HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP Management Status Report, EPB Library, IARC Monographs, CAS On-line and NLM/Toxline (1967 - October 24, 1994), CESARS, Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and Condensed Chemical Dictionary.

β-phenylethylamine is an endogenous amine found in the bodies of humans and other mammals. Structurally, it is epinephrine-like and acts as a sympathomimetic neurotransmitter. A number or articles exist in the scientific literature that deal with βPEA, dividing predominantly into three subgroups. First, articles were found in human medical and psychiatric journals which document concentrations of βPEA in the body fluids of humans afflicted with various mental and emotional disorders, and with phenylketonuria. Authors of these articles disagree on what the βPEA concentrations mean from a medical standpoint, as different reports show concentrations both elevated and lowered in cases with the same clinical diagnosis. One case report notes a woman's exposure to βPEA through ingestion of mistletoe, but since other chemicals were also present in the plant, the health effects manifest could not be causally linked to βPEA. A second group of publications concerns neurobehavioral effects displayed by rodents following exposure to βPEA in an experimental setting. While these report anxiety and seizures in dosed rodents, all of the studies utilized injections (subcutaneous, intraperitoneal, intracerebralventricular, *etc.*) as the route of exposure, and consequently are unusable for derivation of a screening level. The final group include *in vitro* teratogenicity studies of βPEA. These show the compound to be a proximate teratogen, causing neural tube and head fold defects in embryo cultures. While raising concern that similar effects could potentially occur in exposed humans, none of these articles is useful for establishing an initial threshold screening level (ITSL).

Of all the search results reviewed, only two citations were potentially of use in generating an ITSL. Both were in German. The first (Luthy and Schlatter, 1983), which included an English summary, is by design essentially a small double-blind clinical trial in which 27 healthy human volunteers were given 5 mg PEA orally in apple juice, or a placebo. According to the summary, "...phenylethylamine produced symptoms like headache, dizziness and discomfort in some

volunteers". Rule 232 of Act 348 provides no explicit method to utilize this type of data, and consequently, it was deemed unlikely to be useful in the derivation of a screening level, and the text of the article was not translated. The other (Hauschild, 1940) had no English summary, but brief examination of it by a native German speaker (Hartung, 1994) indicated it was an account of the pharmacology of the phenylalkylamines as a group. RTECS (1994) lists an oral LD_{Lo} in the rat = 800 mg/kg for βPEA and cites this article as a reference. While it was possible to locate this dose tabulated in the article, it was not possible to determine without translation whether the study conditions under which this dose was arrived at satisfied the minimum requirements for the study to be acceptable for screening level derivation (with respect to animal strain, dose levels and number of animals per dose level, observation period post-dose, purity of the test material, vehicle used, and method of statistical analysis). Since this reference provided the only potentially usable source of data with which to derive a screening level, the Division pursued translation of the study. The translation indicated that the study design and methods were not sufficiently documented to allow the article's use in deriving an ITSL. Among the deficiencies, there was no information on animal strain, number and concentrations of dose levels, the use/length of an observation period, agent purity, test vehicle, or the method used to derive the lethal dose value. Consequently, lack of usable data has necessitated setting the ITSL for βPEA at the default trace level.

Per section R 336.1232, rule 232, subrule (1)(i) of Act 348, the **ITSL** forβ-phenylethylamine = **0.04 µg/m^3**, and per rule 232, subrule (2)(c), an **annual averaging** time applies.

REFERENCES

Hartung, R. (1994). Personal communication, December 8, 1994.

Hauschild, F. (1940). Zur pharmakologie der phenylalkylamine [The pharmacology of phenylalkylamine]. *Naunyn-Schmiedeberg's archiv Fuer experimentelle pathologie und pharmakologie* **195**:647-680.

Luthy, J. and Schlatter, C. (1983). Biogene amine in lebensmitteln: Zur wirkung von histamin, tyramin und phenylethylamin auf den menschen [Biogenic amines in foods: Effects of histamine, tyramine and phenylethylamine on man]. *Z Lebensm Unters Forsch* **177**(6):439-443.

RTECS (1994). Phenylethylamine (64-04-0). *In*: Registry of Toxic Effects and Chemical Substances Database. National Institute for Occupational Safety and Health, Public Health Service, Centers for Disease Control, U.S. Department of Health and Human Services, and Canadian Centre for Occupational Safety and Health.

DO:ma
cc: A. Khan