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Office of Research and Development
Office of Health and Environmental Assessment
Environmental Criteria and Assessment Office
Cincinnati OH 45268

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HEALTH EFFECTS ASSESSMENT FOR PYRENE

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Office of Emergency and Remedial Response
Office of Solid Waste and Emergency Response
Washington, DC 20460

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PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with pyrene. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the Chemical Abstracts, TOXLINE, CANCERLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to September, 1984. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1980a. Ambient Water Quality Criteria for Polynuclear Aromatic Hydrocarbons. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-069. NTIS PB 81-117806.

U.S. EPA. 1981. Hazard Profile on PAH. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, the AIS or acceptable intake subchronic, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for AIS estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure.

The AIC, acceptable intake chronic, is similar in concept to the ADI (acceptable daily intake). It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980b) for a discussion of this concept]. The AIC is route specific and estimates acceptable exposure for a given route with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for ranking reportable quantities; the methodology for their development is explained in U.S. EPA (1983a).

For compounds for which there is sufficient evidence of carcinogenicity, AIS and AIC values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980b). Since cancer is a process that is not characterized by a threshold, <u>any</u> exposure contributes an increment of risk. Consequently, derivation of AIS and AIC values would be inappropriate. For carcinogens, q_1*s have been computed based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, refer to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates presented.

There are essentially no toxicological data available concerning the effects of pyrene in animals or man. Existing criteria addressing PAHs as a class have been established to address the carcinogenic members of this group. Data are inadequate to assess the potential carcinogenicity of pyrene. Limited short-term *in vitro* and *in vivo* testing data have been primarily negative. AIS, AIC or carcinogenic potencies could not be estimated for this compound.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
BCF	Bioconcentration factor
CAS	Chemical Abstract Service
CS	Composite score
DNA	Deoxyribonucleic acid
PAH	Polycyclic aromatic hydrocarbons
TLV	Threshold limit value
TWA	Time-weighted average

1. ENVIRONMENTAL CHEMISTRY AND FATE

The relevant physical and chemical properties and environmental fate of pyrene (CAS No. 129-00-0) are as follows:

Chemical class:	PAH
Molecular weight:	202.24
Vapor pressure:	2.5×10^{-6} at 25°C (Mabey et al., 1981)
Water solubility:	0.132 mg/kg at 25°C (Wise et al., 1981)
Log octanol/water partition coefficient:	4.88 (U.S. EPA, 1980a)
BCF:	2800 (U.S. EPA, 1980a)
Half-life in air:	2 hrs->2 days (estimated)

The half-life value for pyrene in the atmosphere has been estimated from the observed decomposition of soot-adsorbed pyrene (58%) in artificial smog (Falk et al., 1956) and the photodecomposition study of Korfmacher et al. (1980). No estimated value for the half-life of pyrene in the aquatic media could be located in the available literature; however, photolysis of dissolved pyrene in the aquatic phase and adsorption onto particulate matter with subsequent sedimentation may be the important processes. Biodegradation of particulate-sorbed pyrene is likely to be an important removal process from sediment in the aquatic environment. (Callahan et al., 1979).

The fate of pyrene in soil is not known with certainty, but biodegradation is believed to be the most significant removal process (Santodonato et al., 1981). Based on its high soil adsorption coefficient (K_{OC}= 84,000) (Kenaga and Goring, 1980) and low water solubility, this compound is not likely to leach significantly from soils, particularly from soils containing high organic carbon content.

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

Mitchell and Tu (1979) reported that an aqueous suspension of pyrene was poorly absorbed from the gut of male Fischer 344 rats.

2.2. INHALATION

Mitchell and Tu (1979) reported rapid pulmonary absorption of a pyrene aerosol (300-500 µg/ℓ of air) by male Fischer 344 rats. Widespread tissue distribution was seen after 60 minutes of exposure.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

3.1.1. Oral. Pertinent data regarding the subchronic oral toxicity of pyrene in humans and experimental animals could not be located in the available literature.

3.1.2. Inhalation. Pertinent data regarding the subchronic inhalation toxicity of pyrene in humans and experimental animals could not be located in the available literature.

3.2. CHRONIC

3.2.1. Oral. Pertinent data regarding the chronic oral toxicity of pyrene in humans and experimental animals could not be located in the available literature.

3.2.2. Inhalation. Holland et al. (1980) administered uncharacterized oil shale containing PAH, including pyrene, to Syrian golden hamsters by inhalation of 50 mg respirable shale dust/m^3 for 4 hours/day, 4 days/week. The authors reported interim results indicating that shale dust caused little pulmonary epithelial or fibrotic reaction, but that retorted shales caused inflammation accompanied by fibrosis. Because of the uncharacterized nature of the test material, it is not possible to quantify these or future data from this study for use in risk assessment.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

3.3.1. Oral. Pertinent data regarding the teratogenicity of pyrene following oral administration could not be located in the available literature.

3.3.2. Inhalation. Weaver and Gibson (1979) exposed pregnant rats to graded airborne concentrations of uncharacterized oil shale containing PAH, including pyrene, on days 6-15 of gestation. No treatment-related teratogenic effects were observed during examination of fetuses obtained by

Caesarean section on day 20 of gestation. Because of the uncharacterized nature of the test material, it is not possible to quantify the data from this study for use in risk assessment.

3.4. TOXICANT INTERACTIONS

Pertinent data regarding the toxicant interactions of pyrene could not be located in the available literature.

4. CARCINOGENICITY

4.1. HUMAN DATA

4.1.1. Oral. Pertinent data regarding the carcinogenic effects of oral exposure to pyrene in humans could not be located in the available literature.

4.1.2. Inhalation. Pertinent data regarding the carcinogenic effects of inhalation exposure to pyrene in humans could not be located in the available literature.

4.2. BIOASSAYS

4.2.1. Oral. Pertinent data regarding the carcinogenic effects of orally administered pyrene to experimental animals could not be located in the available literature.

4.2.2. Inhalation. Pertinent data regarding the carcinogenic effects of inhalation exposure to pyrene in experimental animals could not be located in the available literature.

4.3. OTHER RELEVANT DATA

Pyrene was negative in the reverse mutation assay with Salmonella typhimurium (LaVoie et al., 1979; Nagao and Sugimura, 1978); in mammalian cell mutagenesis assays in the presence of a metabolizing enzyme system (Maher and McCormick, 1978); in the Escherichia coli WP2/WP100 rec assay in the presence or absence of exogenous mammalian activation (Mamber et al., 1983); and in the L51F8Y/TK assay with or without a mammalian metabolic activation system (Amacher and Turner, 1982).

Pyrene significantly induced unscheduled DNA synthesis in cultured rat hepatocytes (Althous et al., 1982). Chen (1983) reported that pyrene binds to DNA; at least two binding sites were identifiable.

4.4. WEIGHT OF EVIDENCE

The carcinogenicity of oral or inhalation exposures of humans or animals to pyrene have not been evaluated. When applied dermally, pyrene is regarded as a noncarcinogen (Santodonato et al., 1981; U.S. EPA, 1981). Pyrene was ineffective as a complete carcinogen when applied to the skin of mice (LaVoie et al., 1979). Mouse skin is known to be highly sensitive to the effects of carcinogenic PAH. Pyrene is not an effective tumor initiator for mouse skin (Wood et al., 1980).

IARC (1983) reported that there was insufficient evidence regarding the carcinogenic risk to humans and experimental animals associated with oral or inhalation exposure to pyrene. Applying the criteria for evaluation of the overall weight of evidence for the carcinogenic potential for humans proposed by the Carcinogen Assessment Group of the U.S. EPA (Federal Register, 1984), pyrene is most appropriately designated a Group D - Not Classified chemical.

5. REGULATORY STANDARDS AND CRITERIA

Exposure criteria and TLVs have been developed for PAH as a class, as well as for several individual PAHs. The OSHA has set an 8-hour TWA concentration limit of 0.2 mg/m³ for the benzene-soluble fraction of coal tar pitch volatiles (anthracene, benzo[a]pyrene, phenanthrene, acridine, chrysene, pyrene) (Code of Federal Regulations, 1981). NIOSH (1977) recommends a concentration limit for coal tar, coal tar pitch, creosote and mixtures of these substances of 0.1 mg/m³ of the cyclohexane-extractable fraction of the sample, determined as a 10-hour TWA. NIOSH (1977) concluded that these specific coal tar products, as well as coke oven emissions, are carcinogenic and can increase the risk of lung and skin cancer in workers. NIOSH (1977) also recommends a ceiling limit for exposure to asphalt fumes of 5 mg airborne particulates/m³ of air.

Environmental quality criteria, which specify concentration limits intended to protect humans against adverse health effects, have been recommended for PAH in ambient water. The U.S. EPA (1980a) has recommended a concentration limit of 28 ng/ℓ for the sum of all carcinogenic PAHs in ambient water. This value is based on a mathematical extrapolation of the results from studies with mice treated orally with benzo[a]pyrene, and acknowledges the conservative assumption that all carcinogenic PAHs are equal in potency to benzo[a]pyrene. On the basis of the animal bioassay data, daily consumption of water containing 28 ng/ℓ of carginogenic PAHs over an entire lifetime is estimated to keep the lifetime risk of cancer development below one chance in 100,000.

The EPA has not recommended an ambient water quality criterion for noncarcinogenic PAHs as a class. The U.S. EPA (1980a) acknowledged that data suitable for quantitative risk assessment of noncarcinogenic PAHs are essentially nonexistent.

6. RISK ASSESSMENT

6.1. ACCEPTABLE INTAKE SUBCHRONIC (AIS)

6.1.1. Oral. The lack of subchronic oral data precludes the derivation of an oral AIS for pyrene.

6.2.1. Inhalation. The lack of subchronic inhalation data precludes the derivation of an inhalation AIS for pyrene.

6.2. ACCEPTABLE INTAKE CHRONIC (AIC)

6.2.1. Oral. The lack of chronic and subchronic oral data precludes the derivation of an oral AIC for pyrene.

6.2.2. Inhalation. The lack of chronic and subchronic inhalation data precludes the derivation of an inhalation AIC for pyrene. U.S. EPA (1983b) reviewed the inhalation studies of Holland et al. (1980) in hamsters and Weaver and Gibson (1979) in pregnant rats and concluded that data were insufficient for computation of a CS for pyrene.

6.3. UNIT CARCINOGENIC RISK (q_1^*)

6.3.1. Oral. The lack of oral carcinogenicity data precludes the derivation of a unit carcinogenic risk for pyrene.

6.3.2. Inhalation. The lack of inhalation carcinogenicity data precludes the derivation of a unit carcinogenic risk for pyrene.

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