U.S. Army Center for Health Promotion and Preventive Medicine

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Wildlife Toxicity Assessment for Phenanthrene

JANUARY 2006

Prepared by
Health Effects Research Program
Environmental Health Risk Assessment Program

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FINAL REPORT
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Department of the Army
U.S. Army Center for Health Promotion and Preventive Medicine

Wildlife Toxicity Assessment for Phenanthrene

CAS No. 85-01-8 **January 2006**

1. Introduction

Phenanthrene is one of more than 200 structurally related polycyclic aromatic hydrocarbons (PAHs) that are produced during the incomplete combustion of organic matter (HSDB 2001). The compounds have been detected in tobacco smoke, automobile exhausts, barbecued meat, garbage incineration, and wood burning. Along with other PAHs, phenanthrene has also been detected in used motor oils, crude oils and lubricating fluids. According to IARC (1983), and the ATSDR (1995), phenanthrene has been identified in ambient air, surface and drinking water, and in foods, all of which could serve as sources of phenanthrene for wildlife. Although the compound is not produced commercially in the United States, the Agency for Toxic Substances and Disease Registry (ATSDR) reports that a small amount of purified phenanthrene is imported, for use in the manufacture of explosives, pesticides, drugs, the chemical phenanthrene-quinone, and some dyes, and in research (ATSDR 1995).

This Wildlife Toxicity Assessment summarizes the current knowledge of the toxicological impacts of phenanthrene on wildlife. Evaluating the toxicity of phenanthrene is intended to contribute to the derivation of toxicity reference values (TRVs) that could serve as screening-level benchmarks for wildlife in the vicinity of contaminated sites. The protocol for the development of this assessment is documented in the U.S. Army Center for Health Promotion and Preventive Medicine Technical Guide 254, *Standard Practice for Wildlife Toxicity Reference Values* (USACHPPM 2000). TRVs are not here derived for phenanthrene at this time, due mainly to a paucity of relevant data. This summary should nevertheless contribute to the overall risk management process by helping to identify the most critical research needs.

2. Toxicity Profile

2.1 Literature Review

Relevant biomedical, toxicological, and ecological databases were electronically searched April 20, 2001, using Dialog to identify primary reports of studies and reviews on the toxicology of phenanthrene. Separate searches were carried out linking the compound to laboratory mammals, birds, reptiles and amphibians (combined), or wild mammals and birds. In general, a two-tiered approach was used in which all citations were first evaluated as titles and "key words in context." All available abstracts of those

articles that were identified as possibly relevant to TRV development in the first tier were then evaluated for retrieval in the second tier. For phenanthrene, 22 articles were marked for retrieval from 157 initial hits. Details of the search strategy and the results of the search are documented in Appendix A.

In addition to searches using Dialog, the Defense Technical Information Center (DTIC) was searched for reports on the toxicology of phenanthrene. Secondary references and sources of information on phenanthrene included an ATSDR *Toxicological Profile for Polycyclic Aromatic Hydrocarbons* (ATSDR 1995), the National Library of Medicine's Hazardous Substances Databank (HSDB 2001), the U.S. Environmental Protection Agency's (U.S. EPA) Integrated Risk Information System (IRIS) (U.S. EPA 2001), and Health Effects Assessment Summary Tables (U.S. EPA 1997).

2.2 Environmental Fate and Transport

Formation of PAHs during the combustion of organic matter could result in direct exposure of wildlife to phenanthrene via inhalation and dermal contact, or by indirect exposure as the compound enters the food chain following deposition to soil and surface water. Natural sources of such emissions include forest fires and volcanoes. Anthropogenic sources include emissions from power stations and steel mills, the burning of garbage and wood, and the production of coal tar, coke, and asphalt. (ATSDR 1995). Particulates and vapors from diesel emissions contain an abundance of three-ringed compounds such as phenanthrene. Overall, this and other PAHs have a widespread distribution in environmental media, largely in the parts per billion concentration range.

Transport and partitioning of PAHs in the environment depend on the physical-chemical characteristics of each compound (see Table 1). For example, low molecular weight PAHs such as phenanthrene have organic carbon partition coefficients (K_{oc}) in the 10^3–10^4 range, indicative of a moderate absorption capacity in soil and sediments. Because of their low aqueous solubility, water-borne PAHs tend to sorb to particles that settle to the bottom or possibly remain suspended in the water column. Nonetheless, ATSDR (1995) has indicated that, to some extent, lower molecular weight PAHs (such as phenanthrene) can volatilize to the atmosphere at the surface of a contaminated water body.

Phenanthrene may be assumed to share the capacity of other PAHs to bioconcentrate in terrestrial and aquatic food chains. This may result in greater exposure for organisms high in the food chain. However, those organisms possessing the aryl hydrocarbon hydroxylase (AHH) enzyme systems should be able to metabolize the compound, thereby preventing bioaccumulation, thus species lacking this system might receive greater exposure and contribute to bioaccumulation. The compound may also undergo photolytic and oxidation reactions in the environment, with the reported formation of an arene oxide in the latter case (ATSDR 1995). By contrast, the major photoproduct of phenanthrene is 9,10-phenanthrenequinone.

Aerobic biodegradation of PAHs is likely to be a significant breakdown mechanism for compounds such as phenanthrene, since different species of bacteria, algae, and fungi possess the necessary molecular architecture (the AHH enzyme system) to catabolize the compound.

Table 1. Summary of Physical-Chemical Properties of Phenanthrene

CAS No.	85-01-8
Molecular weight	178.2
Color	Colorless
Physical state	Plates, crystals, leaflets
Melting point	100 °C
Boiling point	340 °C
Odor	faint aromatic
Solubility in water	1.2 – 1.3 mg/L at 25 °C: soluble in benzene, ethanol, ether, toluene, carbon tetrachloride and carbon disulfide
Partition coefficients:	
Log K_{ow}	4.45 – 4.57
Log K_{oc}	4.15 – 4.36
Vapor pressure at 25 ^{o}C	6.8×10^{-4} mm Hg
Henry's Law constant at 25 ^{o}C	2.56×10^{-5} atm.m^3/mole
Conversion factors	1 ppm = 7.3 mg/m^3
	1 mg/m^3 = 0.137 ppm

Sources: ATSDR (1995), HSDB (2001)

2.3 Summary of Mammalian Toxicity

2.3.1 Mammalian Toxicity - Oral

Secondary sources have pointed to the overall absence of toxicological information on phenanthrene (Faust 1993; U.S. EPA 2001). For example, the U.S. EPA's IRIS record for phenanthrene reports no data on which to derive a chronic oral reference dose (RfD) or inhalation reference concentration, and inadequate data on which to derive a carcinogenic slope factor for the compound (U.S. EPA 2001). Similarly, the International Agency for Research on Cancer (IARC) concluded that the data were inadequate to permit an evaluation of the carcinogenicity of phenanthrene to experimental animals (IARC 1983). In general, the literature searches supporting this evaluation of the toxic potential of phenanthrene in wildlife have confirmed the earlier conclusions about the lack of experimental evidence.

2.3.1.1 Mammalian Oral Toxicity – Acute

No data are available.

2.3.1.2 Mammalian Oral Toxicity – Subacute

No data are available.

2.3.1.3 Mammalian Oral Toxicity – Subchronic

No data are available.

2.3.1.4 Mammalian Oral Toxicity – Chronic

No data are available.

2.3.1.5 Mammalian Oral Toxicity – Other

No relevant studies are available.

2.3.1.6 Studies Relevant for Mammalian TRV Development for Ingestion Exposures

There are no studies available in the scientific literature that provides data directly applicable to TRV development for wildlife exposed to phenanthrene via ingestion. In fact, available information on the oral toxicity of phenanthrene was insufficient to enable the U.S. EPA to develop a human health RfD for the compound (U.S. EPA 2001). Therefore, a TRV for phenanthrene cannot be derived at this time.

2.3.2 Mammalian Inhalation Toxicity

No data are available.

2.3.3 Mammalian Dermal Toxicity

The capacity of phenanthrene to induce tumors in the mouse skin-painting assay has been summarized by Faust (1993), ATSDR (1995) and on IRIS (U.S. EPA 2001). In general, the compound appears to be inactive in these systems. For example, dermal application of 5 percent phenanthrene in solvent, three times weekly for one year, did not induce skin tumors in mice (Roe and Grant 1964). Similarly, in two-stage skin initiation-promotion assays, the overwhelming weight of evidence indicates an inability of phenanthrene to initiate papilloma formation, irrespective of the experimental protocol employed (Faust 1993).

2.3.4 Mammalian Toxicity – Other

2.3.4.1 Mammalian Toxicity- Other- Acute

Simmon et al. (1979) reported a median lethal dose (LD_{50}) for phenanthrene of 700 mg/kg in mice (strain unstated) when the compound was administered intraperitoneally. Yoshikawa et al. (1985) found that single intraperitoneal injections of 150 mg/kg phenanthrene produced some slight hepatotoxicity and

effects on blood chemistry in rats. Though not applicable to derivation of a TRV, these studies still provide toxicity information bearing on the potential effects to wildlife.

2.3.4.2 Mammalian Toxicity-Other- Subacute

In one of the few published experiments to explore the toxicological effects of phenanthrene, the compound was administered to male Holtzman and Charles River rats (12 animals/group) for 7 days via intraperitoneal injection (0.35 mg/rat/day) (Gershbein 1975). Rats were terminated three days later at which point the body weights and excised liver weights were recorded and compared to those of untreated controls. The near identity in group-specific body weights and the close similarity between the liver weights of test versus control animals indicated that phenanthrene had little toxic impact on the subjects at the administered dose. The use of this dose (approximately 1.38 mg/kg-day) as a No-Observed-Adverse-Effects-Level (NOAEL) is complicated, and of extremely low confidence, since no toxic effects of phenanthrene have been defined in this or any other study. Furthermore the use of a single dose level precludes the delineation of the compound's toxicological threshold.

2.3.5. Studies Relevant for Mammalian TRV Development

In the single study that was identified as potentially relevant to TRV development, the absence of any toxicological consequences of phenanthrene administration in rats at the only dose tested did not allow a dependable Low-Observed-Adverse-Effect-Level (LOAEL) or No-Observed-Adverse-Effect-Level (NOAEL) to be identified (Gershbein 1975). Physiological experiments by Rahman et al. (1986) suggest that phenanthrene's inactivity is probably not related to failure to penetrate the intestinal mucosa where, at least in male Sprague-Dawley rats, the compound appeared to be more or less quantitatively absorbed.

The use of other protocols has pointed to the largely benign nature of phenanthrene in experimental systems. Thus, the compound appears to be negative in the Ames test, even in circumstances where its reactive metabolite, phenanthrene 9,10 oxide, itself brings about gene reversion in *Salmonella typhimurium* strains TA98, TA100, TA1537 and TA1538 (Bucker et al. 1979). However, when Bucker et al. (1979) included the epoxide hydratase inhibitor, 1,1,1-trichloropropene 2,3-oxide in the culture medium, they observed the formation of histidine-independent colonies, which suggests that phenanthrene is normally inactive in this system because its active metabolite normally cannot accumulate. More recent studies have shown phenanthrene to be weakly positive in TA100, but ineffective in TA98 (Bos et al. 1988).

In the battery of experiments aimed at researching the ability of PAHs to induce or initiate skin tumors in mice, phenanthrene has been found to be inactive under most experimental conditions and does not behave like a complete carcinogen (Faust et al. 1993; ATSDR 1995).

Results from these studies indicate that phenanthrene is relatively benign. Given the lack of noticeable toxic effects of the compound a meaningful TRV cannot be derived. Phenanthrene may be regarded as a part of the overall issue of the toxic effects of multiple PAHs on wildlife.

2.4 Summary of Avian Toxicology

Toxicological data for the effects of phenanthrene on avian species was not located. Ecotoxicological research on the effects of this compound in birds is recommended.

2.5 Amphibian Toxicology

Toxicological data on the effects of phenanthrene on amphibian species was not located. Ecotoxicological research on the effects of this compound on amphibians is recommended.

2.6 Reptilian Toxicology

Toxicological data on the effects of phenanthrene on reptilian species was not located. Ecotoxicological research on the effects of this compound on reptiles is recommended.

3. RECOMMENDED TOXICITY REFERENCE VALUES

3.1 Toxicity Reference Values for Mammals

3.1.1 TRVs for ingestion Exposures for the Class Mammalia

At this time it is not possible to derive a TRV for the oral route of exposure for phenanthrene. No studies have shown toxicological effects of phenanthrene ingestion.

3.1.2 TRVs for Inhalation Exposures for the Class Mammalia

Not available at this time

3.1.3 TRVs for Dermal Exposures for the Class Mammalia

There is limited data suggesting that phenanthrene will not induce tumors when applied dermally (Roe and Grant 1964). Given these results and the lack of other suitable studies, it is not possible to derive a TRV for dermal exposure at this time.

3.2 Toxicity Reference Values for Amphibians

Not available at this time.

3.3 Toxicity Reference Values for Reptiles

Not available at this time.

4. IMPORTANT RESEARCH NEEDS

The limited data available on the toxicity of phenanthrene reflects the need for more research concerning the oral, dermal and inhalation routes of exposure. In particular, chronic studies on mammals are necessary considering the limited data now available. Adequate characterization of the toxicity of phenanthrene is required before a reliable TRV can be derived. WTA documents on compounds, having scant information on which to base a TRV, still form a part of the overall risk management process, not only by identifying research needs but by helping to prioritize the allocation of finite resources in research.

5. References

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U.S. EPA. 2001. Integrated Risk Information System. Online. Office of Health and Environmental Assessment, National Center for Environmental Assessment, Cincinnati, OH.

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APPENDIX A

LITERATURE REVIEW

The following files were searched in Dialog:

File 155 MEDLINE; File 156, TOXLINE, File 5 BIOSIS, File 10 AGRICOLA, File 203 AGRIS, File 399 Chemical Abstracts, File 337 CHEMTOX, File 77 Conference Papers Index, File 35 Dissertation Abstracts, File 40 ENVIRONLINE, File 68 Environmental Bibliography, File 76 Life Sciences Collection, File 41 Pollution Abstracts, File 185 Zoological Record, File 6 NTIS, File 50 CAB, File 144 PASCAL, File 34 SCISEARCH.

The search strategy for **Amphibians & Reptiles**:

- Chemical name, synonyms, CAS numbers
- AND (amphibi? or frog or frogs or salamander? or newt or newts or toad? or reptil? or crocodil? or alligator? or caiman? snake? or lizard? or turtle? or tortoise? or terrapin?)
- RD (reduce duplicates)

The search strategy for **Birds:**

- Chemical name, synonyms, CAS numbers
- And chicken? or duck or duckling? or ducks or mallard? or quail? or (japanese()quail?) or coturnix or (gallus()domesticus) or platyrhyn? or anas or aves or avian or bird? or (song()bird?) or bobwhite? or (water()bird) or (water()fowl)
- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))
- RD

The search strategy for **Laboratory Mammals:**

- Chemical name, synonyms, CAS numbers
- AND (rat or rats or mice or mouse or hamster? or (guinea()pig?) or rabbit? or monkey?)
- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))
- NOT (human? or culture? or subcutaneous or vitro or gene or inject? or tumo? or inhalation or carcin? or cancer?)/ti,de
- RD

The search strategy for **Wild Mammals:**

- Chemical name, synonyms, CAS numbers

- And(didelphidae or opossum? or soricidae or shrew? Or talpidae or armadillo? or dasypodidae or ochotonidae or leporidae)or canidae or ursidae or procyonidae or mustelidae or felidae or cat or cats or dog or dogs or bear or bears or weasel? or skunk? or marten or martens or badger? or ferret? or mink? Or aplodontidae or beaver? or sciuridae or geomyidae or heteromyidae or castoridae or equidae or suidae or dicotylidae or cervidae or antilocapridae or bovidae arvicolinae or mycocastoridae or dipodidae or erethizontidae or sigmodon? or (harvest()mice) or (harvest()mouse) or microtus or peromyscus or reithrodontomys or onychomys or vole or voles or lemming?

- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))

- RD

All abstracts from the DIALOG search were reviewed and encoded in ProCite. When the search retrieved an appreciable number of hits, *keywords in context* were reviewed to minimize costs before any abstracts were downloaded (Tier 1). However, when only a limited number of studies were identified by the search, the abstracts were downloaded at the time of the search (Tier 2).

As noted in Section 2.1, 157 hits on phenanthrene were obtained in the initial search, of which 22 were retrieved for this survey.