Chrysene; CASRN 218-01-9

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR Chrysene

File First On-Line 12/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	12/01/1990

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Chrysene
CASRN — 218-01-9

Not available at this time.

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Chrysene
CASRN — 218-01-9

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Chrysene
CASRN — 218-01-9
Last Revised — 12/01/1990

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — B2; probable human carcinogen

Basis — No human data and sufficient data from animal bioassays. Chrysene produced carcinomas and malignant lymphoma in mice after intraperitoneal injection and skin carcinomas in mice following dermal exposure. Chrysene produced chromosomal abnormalities in hamsters and mouse germ cells after gavage exposure, positive responses in bacterial gene mutation assays and transformed mammalian cells exposed in culture.

II.A.2. Human Carcinogenicity Data

None. Although there are no human data that specifically link exposure to chrysene to human cancers, chrysene is a component of mixtures that have been associated with human cancer. These include coal tar, soots, coke oven emissions and cigarette smoke (U.S. EPA, 1984, 1990; IARC, 1983, 1984).

II.A.3. Animal Carcinogenicity Data

Sufficient. Intraperitoneal chrysene injections in male mice caused an increased incidence of liver tumors (Wislocki et al., 1986; Buening et al., 1979) and increased incidences of malignant lymphoma and lung tumors (Wislocki et al., 1986). In mouse skinpainting assays chrysene tested positive in both initiation and complete carcinogen studies (Wynder and Hoffman, 1959).

On days 1, 8, and 15 of age, groups of male (28 to 35/group) and female (24 to 34/group) CD-1 mice received intraperitoneal injections of chrysene in dimethyl sulfoxide (DMSO) (total dose = 0, 160 ug or 640 ug/mouse) (Wislocki et al., 1986). The low-dose and high-dose experiments were initiated 10 weeks apart and had separate concurrent vehicle controls. Tumors were evaluated in animals that died spontaneously after weaning and in all remaining animals at 1 year after exposure. A statistically significant increase in the incidence of liver adenomas or carcinomas occurred in treated male mice relative to their respective controls: 10/35 (29%) and 5/45 (11%) in the low-dose mice and controls, respectively; and 14/34 (41%) and 2/28 (7%) in the high-dose mice and controls, respectively. The majority of the liver tumors in the high-dose males were carcinomas and the incidence was statistically significantly greater than in its respective control group, whereas the majority of tumors in the low-dose males were adenomas. Liver adenonas, but no carcinomas were observed in the control groups. In female mice no tumors were observed. The incidence of lung adenomas or carcinomas in the low-dose male mice was 6/35 (17%) (one of which was a carcinoma) and 4/45 (9%) (two of which were carcinomas) in their control group. The incidence of lung adenomas was statistically elevated in high-dose males 7/34 (21%) when compared with their control group (1/28, 4%). The incidence of malignant lymphoma was significantly elevated (3/35, 9%) in low-dose males relative to the controls (0/45), but not in the high-dose males (1/34) relative to their controls (1/28). In females, there was no statistically significant increase in lung tumors or lymphoma. This is generally regarded as a short-term exposure study with a less-than-lifetime (1 year) experiment.

Male and female Swiss Webster BLU/Ha(ICR) mice received intraperitoneal injections of chrysene in DMSO (total dose = 320 ug/mouse) or DMSO alone on days 1, 8 and 15 after birth (Buening et al., 1979). Mice were killed at 38- 42 weeks of age. The incidences of lung tumors in the treated group appeared to be elevated (5/24 (21%) and 1/11 (9%) in males and females, respectively), although not statistically significantly, when compared with the control groups (2/21 (10%) and 7/38 (18%) in males and females, respectively). The incidence of hepatic tumors in the treated males was statistically significantly greater (6/24, 25%) than in control

males (0/21), whereas no hepatic tumors were found in the females. In a replication of this study, lung tumor incidence was not increased; however, the incidence of hepatic tumors in treated male mice was significantly elevated (6/27, 22%) over the incidence in the control group (0/52) (Chang et al., 1983). No liver tumors were reported in the females. These studies are regarded as short-term exposure, less-than-lifetime experiments.

Chrysene has been tested for complete carcinogenic activity and initiating activity in mouse skin painting assays. It was shown to be a complete carcinogen (Wynder and Hoffmann, 1959). Chrysene has produced positive results for initiating activity in several mouse strains (C3H, ICR/Ha Swiss, Ha/ICR/Mil Swiss, CD-1, Sencar) when applied in combination with various promoting agents (decahydronaphthalene, croton oil, TPA) producing skin papillomas and carcinomas (Van Duuren et al., 1966; Scribner, 1973; Horton and Christian, 1974; Hecht et al., 1974; Levin et al., 1978; Wood et al., 1979, 1980; Slaga et al., 1980; Rice et al., 1985).

II.A.4. Supporting Data for Carcinogenicity

Chrysene produced positive results in tests for reverse mutation in three strains of Salmonella typhimurium and positive results for forward mutation in one strain (McCann et al., 1975; Tokiwa et al., 1977; Wood et al., 1977; LaVoie et al., 1979; Dunkel and Simmon, 1980; Sakai et al., 1985; Kaden et al., 1979).

Chromosomal effects were observed in Chinese hamster cells, mouse oocytes and hamster spermatogonia following gavage doses of 450 or 900 mg/kg (Basler et al., 1977; Roszinsky-Kocher et al., 1979). Positive results were obtained (10 ug/mL) in tests for cell transformation in Syrian hamster embryo cells and negative results in mouse prostrate C3HG23 cells (Marquardt and Heidelberger, 1972; Pienta et al., 1977).

Current theories on mechanisms of metabolic activation of polycyclic aromatic hydrocarbons are consistent with a carcinogenic potential for chrysene. Chrysene has a "bay-region" in structure (Jerina et al., 1978). It is metabolized by mixed function oxidases to reactive "bay-region" diol epoxides (Nordqvist et al., 1981; Vyas et al., 1982) that are mutagenic in bacteria and tumorigenic in mouse skin painting assays and when injected into newborn mice (Levin et al., 1978; Wood et al., 1977, 1979; Slaga et al., 1980; Chang et al., 1983).

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

Not available.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

Not available.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1984, 1990

The 1990 Drinking Water Criteria Document for Polychlorinated Aromatic Hydrocarbons has received Agency and external review.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 02/07/1990, 08/05/1993, 09/21/1993, 02/02/1994

Verification Date — 02/07/1990

II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Chrysene
CASRN — 218-01-9

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — Chrysene
CASRN — 218-01-9

Date	Section	Description
12/01/1990	II.	Carcinogen assessment on-line

VIII. Synonyms

Substance Name — Chrysene
CASRN — 218-01-9
Last Revised — 12/01/1990

- 218-01-9
- Chrysene
- BENZ(a)PHENANTHRENE
- BENZO(a)PHENANTHRENE
- Chrysene
- HSDB 2810
- NSC 6175
- RCRA WASTE NUMBER U050
- 1,2-BENZOPHENANTHRENE
- 1,2-BENZPHENANTHRENE
- 1,2,5,6-DIBENZONAPHTHALENE