White phosphorus; CASRN 7723-14-0

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 White phosphorus

File First On-Line 08/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	08/01/1990
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 — White phosphorus
CASRN — 7723-14-0
Last Revised — 08/01/1990

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Parturition mortality; forelimb hair loss **Reproductive Rat Study** **Condray, 1985**	NOAEL: 0.015 mg/kg/day LOAEL: 0.075 mg/kg/day	1000	1	2E-5 mg/kg/day

*Conversion Factors: None

I.A.2. Principal and Supporting Studies (Oral RfD)

Condray, J.R. 1985. Elemental yellow phosphorus one-generation reproduction study in rats. IR-82-215; IRD No. 401-189. Monsanto Company, St. Louis, MO.

Elemental yellow (white) phosphorus in corn oil was administered orally by gavage to groups of 15 males and 30 female Sprague-Dawley rats at doses of 0, 0.005, 0.015, or 0.075 mg/kg/day beginning at 80 days prior to mating and continuing through weaning of two complete reproductive cycles. A mortality rate of 53%, reported in the high-dose females, was attributed to difficulty during parturition, with 13 of 16 deaths occurring on days 21 or 22 of gestation. No specific cause was determined but this finding is uncommon during rat reproduction studies and may be attributed to white phosphorus administration. Hair loss was evident on the forelimbs of this group. A slight but not significant decrease in mean number of viable pups in the F1a litter was reported with a concomitant increase in mean number of dead pups. A similar trend was observed in the F1b litter. All other findings were comparable to controls.

Mean body weight of the high dose males was lower than controls beginning at 15 weeks of treatment, while body weights of the males receiving the two remaining test doses were slightly, but not significantly, lower than controls throughout the study. The NOAEL was 0.015 mg/kg/day and the LOAEL was 0.075 mg/kg/day for effects of white phosphorus on parturition.

White phosphorus was incorporated into the diets of young female albino rats (6 to 10/group) and fed at median doses of 0.0032, 0.018, or 0.072 mg/kg/day for 22 weeks and to 10 older male rats at a median dose of 0.0027 mg/kg/day for 25 weeks (Sollmann, 1925). Half of the animals from each female rat group were removed from the test diet during the later part of the experiment and they were observed in the same manner as the animals that continued to receive the test diet. A zero dose concurrent control group was not included in the experiment; however, the results from this study were compared to "normal growth curves" determined by the author and others in 13 previous investigations using a total of 72 rats.

The 0.072 mg/kg/day group (i.e., the high-dose group) exhibited 30% (3/10) mortality and a marked and progressive weight loss. Upon termination of the experiment the final weight of the animals was 41% below normal. No recovery was evident when the test diet was removed from a part of the test group after 10 weeks, but the progressive weight loss was checked. There was 50% (3/6) mortality for the 0.018 mg/kg/day group and growth was below normal resulting in a final weight 15% less than normal. When the test diet was removed from several animals in this dose group their growth returned to normal. There was a check in growth at 15 weeks and an overall mortality of 33% (2/6) for the 0.0032 mg/kg/day animals. There was no definite growth effect prior to 15 weeks. When animals from this group were removed from the diet their weights increased to levels greater than normal.

The male rats that received 0.0027 mg/kg/day demonstrated greater weight gain than normal while remaining on the test diet. They had a 10% (1/10) mortality; however, no other treatment related effects or toxicity signs were reported. The median dose of 0.0027 was considered the NOAEL from this study based upon body weight gain.

White phosphorous was administered daily to young rabbits (15-17) by oral insertion of a tablet containing 0.6 mg white phosphorus (equivalent to approximately 0.3 mg/kg/day for a 2 kg rabbit) for a period of 13 to 117 days (Adams and Sarnat, 1940). Fourteen young rats received white phosphorus in cod liver oil in the diet at a concentration of 0.01% for 22 to 57 days (equivalent mg/kg/day doses could not be estimated from available data). Treated rabbits exhibited a decrease in weight gain as well as in the average daily growth of the tibial diaphysis (0.27 mm vs 0.36 mm in controls). A retardation of the normal tubulation process was reported when white phosphorus was administered to rats for 4 weeks or longer. Histological examination of rabbit long bones revealed a narrowing of the epiphyseal cartilage plate, reduction in number of cartilage cells/column, increased density in metaphyseal zone along with a greater number of trabeculae containing increased amounts of calcified cartilage matrix. In some cases, the hemopoietic marrow of the bone was replaced with loose fibrous tissue. Examination of the teeth revealed zones of abnormal dentin corresponding to periods of white phosphorus ingestion, but changes were considered non- specific.

A solution of white phosphorus in peanut oil was incorporated into stock diets and fed to groups of domestic male and female rats (6/group) at doses of 0, 0.2, 0.4, 0.8, and 1.6 mg/kg/day over their lifetime (approximately 420 days average duration) (Fleming et al., 1942). While mortality decreased with decreasing dose of white phosphorus, background mortality of controls was reported to be higher than in groups receiving the lower doses of white phosphorus. Retardation of weight gain was reported and those animals fed the larger doses also exhibited a definite loss of appetite. All treated animals showed changes in the bone consisting of a thickening of the epiphyseal line and extension of the trabeculae into the shaft. No other changes related to ingestion of white phosphorus were seen. A NOAEL/LOAEL could not be determined.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — This uncertainty factor includes a factor of 10 for interspecies diversity, 10 for intraspecies diversity, and 10 for incomplete reproductive/ developmental data and a less than adequate lifetime study.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

In humans, white phosphorus toxicity is associated with its use in matches during the 1830s and later in fireworks and rodent poisons. The reported acute effects of white phosphorus are conflicting; however, chronic effects of white phosphorus on the bone are widely known. Acute effects have been reported from cases of accidental or intentional (suicidal) ingestion sometimes in combination with other substances such as alcohol. The reports indicate that acute ingestion affects the liver, kidney, hematopoietic system, brain, intestines, circulatory system and the myocardium resulting in electrocardiographic changes (Davidson et al., 1987). Deaths usually occurred within the first 24 hours. A minimum lethal dose of 1 mg/kg has been reported, and in a child, death has occurred after the consumption of as little as 3 mg (Brewer and Haggerty, 1958; Dacre and Rosenblatt, 1974; Davidson et al., 1987). The white phosphorus doses reported in the acute poisoning cases were estimated, therefore exact dose-response relationships cannot be determined.

Chronic exposure to white phosphorus in man has been associated with a progressive necrotic disease of the jaw bones known as "phossy jaw" (Davidson et al., 1987). Cases of this disease have been observed among workers in the phosphorus match industry (white phosphorus is no longer used for this purpose), firecracker manufacture, and white phosphorus production. The disease often takes years to develop and its pathogenesis currently is uncertain. The most widely held theory is that the phosphorus enters the jaw directly, reacts with the mouth flora, and subsequent infection develops followed by the disease. Even though several investigators report

the occurrence of this disease in workers, dose information either is lacking entirely or a surrogate exposure measure, i.e., exposure time, is reported.

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Low
RfD — Low

On its merits an RfD based on the Condray (1985) study has low confidence. The study does not provide unequivocal evidence of an adverse effect from white phosphorus exposure at the doses tested. The mortality in female rats during parturition was considered by the author to be related to white phosphorus exposure. However, the exact nature of the deaths was not examined as to conclusively implicate white phosphorus. The study also lacked adequate assessment of developmental indices.

The supporting studies indicate significant white phosphorus-related body weight and/or bone changes, but they have design deficiencies that lower the confidence in the reported observations. The investigation by Sollmann (1925) did not use concurrent controls, treatment groups differed by sex, and judging from the initial weight at the beginning of the study, the test animals appeared to be from different age groups. The studies by Adams and Sarnat (1940) and Fleming et al. (1942) both suggest white phosphorus-induced bone growth retardation; however, the numbers of animals in the dose groups were small and in some cases the exact dose of the test compound administered could not be determined.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — None

Agency Work Group Review — 05/17/1990

Verification Date — 05/17/1990

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for white phosphorus conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

I.A.7. EPA Contacts (Oral RfD)

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).

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

Substance Name — White phosphorus
CASRN — 7723-14-0

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — White phosphorus
CASRN — 7723-14-0
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 — D; not classifiable as to human carcinogenicity

Basis — Based on no data in humans or animals

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

None.

II.A.4. Supporting Data for Carcinogenicity

Groups of 6 to 10 male and female rats received subcutaneous injections of elemental phosphorus in vegetable oil solutions at 0.5-3.2 mg/kg/day in two injections/week for life. A control group received injections of oil alone (Fleming et al., 1942). The range of the average group survival was 3.2 to 610 days. No evidence of treatment-related lesions was noted. This study, however, was not designed as a carcinogenicity bioassay, and is further limited by the use of a small number of animals. In addition, the maximum tolerated dose was not achieved.

Mutagenicity testing with several strains of Salmonella typhimurium did not result in a significant increase in the number of revertant colonies with or without metabolic activation (Ellis et al., 1978).

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

None.

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

None.

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1990

The 1990 Health Advisory for White Phosphorus has received Agency Review.

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

Agency Work Group Review — 06/15/1990

Verification Date — 06/15/1990

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for white phosphorus conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

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 — White phosphorus
CASRN — 7723-14-0

VI.A. Oral RfD References

Adams, C.O. and B.G. Sarnat. 1940. Effects of yellow phosphorus and arsenic trioxide on growing bones and growing teeth. Arch. Pathol. 30: 1192-1201.

Brewer, E. and R.J. Haggerty. 1958. Toxic Hazards * Rat Poisons. II - Phosphorus. N. Eng. J. Med. 258(3): 147-148.

Condray, J.R. 1985. Elemental yellow phosphorus one-generation reproduction study in rats. IR-82-215; IRD No. 401-189. Monsanto Company, St. Louis, MO.

Dacre, J.C. and D.H. Rosenblatt. 1974. Mammalian toxicology and toxicity to aquatic organisms of four important types of waterborne munitions pollutants - An extensive literature evaluation. Technical Report No. 7403. U.S. Army Medical Bioengineering Research and Development Laboratory, Aberdeen Proving Ground, Ft. Detrick, Frederick, MD. NTIS AD778-725.

Davidson, K.A., P.S. Hovatter and C.F. Sigmon. 1987. Water quality criteria for white phosphorus. Final Report ORNL - 6336. Oak Ridge National Laboratory. AD-A186613.

Fleming, R.B.L., J.W. Miller and V.R. Swayne, Jr. 1942. Some recent observations on phosphorus toxicology. J. Ind. Hyg. Toxicol. 24(6): 154-158.

Sollmann, T. 1925. Studies of chronic intoxications on albino rats. VIII. Yellow phosphorus. J. Pharmacol. Exp. Therap. 24: 119-122.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Ellis, H.V., III, J.R. Hodgson, S.W. Hwang, et al. 1978. Mammalian toxicity of munitions compounds Phase I: Acute oral toxicity, primary skin and eye irritation, dermal sensitization, disposition and metabolism, and Ames tests of additional compounds. Progress report No. 6, prepared by Midwest Research Institute and submitted to U.S. Army Medical Bioengineering Research and Development Laboratory, Environmental Protection Research Division, Fort Detrick, Frederick, MD. December 8, 1978.

Fleming, R.B.L., J.W. Miller and V.R. Swayne, Jr. 1942. Some recent observations on phosphorus toxicology. J. Ind. Hyg. Toxicol. 24(6): 154-158.

U.S. EPA. 1990. Health Advisory for White Phosphorus. Office of Drinking Water, Washington, DC. (Draft)

VII. Revision History

Substance Name — White phosphorus
CASRN — 7723-14-0

Date	Section	Description
08/01/1990	I.A.	Oral RfD summary on-line
12/01/1990	II.	Carcinogen assessment on-line
10/28/2003	I.A.6, II.D.2	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — White phosphorus
CASRN — 7723-14-0
Last Revised — 08/01/1990

- 7723-14-0
- BONIDE BLUE DEATH RAT KILLER
- CASWELL NO. 663
- COMMON SENSE COCKROACH AND RAT PREPARATIONS
- EPA PESTICIDE CHEMICAL CODE 066502

- EXOLIT LPKN 275
- EXOLIT VPK-N 361
- FOSFORO BIANCO [ITALIAN]
- FOSFORO BLANCO [SPANISH]
- FOSFORO [SPANISH]
- GELBER PHOSPHOR [GERMAN]
- HSDB 1169
- PHOSPHORE BLANC [FRENCH]
- PHOSPHORE BLANC [FRENCH]
- PHOSPHORE [FRENCH]
- PHOSPHOROUS (WHITE)
- PHOSPHORUS
- PHOSPHORUS-31
- PHOSPHORUS (RED)
- PHOSPHORUS, RED
- PHOSPHORUS WHITE
- PHOSPHORUS, WHITE
- RAT-NIP
- RED PHOSPHORUS
- TETRAFOSFOR [DUTCH]
- TETRAPHOSPHOR [GERMAN]
- UN 1338
- UN 1381
- UN 2447
- WEISS PHOSPHOR [GERMAN]
- WHITE PHOSPHORUS
- YELLOW PHOSPHORUS