United States
Environmental Protection
Agency

Office of Pesticide Programs (TS-766C)
Washington, DC 20460

EPA Pesticide Fact Sheet

Name of Chemical: Arsenic acid
Reason for Issuance: Registration Standard
Date Issued: September, 1986
Fact Sheet Number: 91

1. DESCRIPTION OF CHEMICAL

Chemical Names: Arsenic acid, Orthoarsenic acid
Common Name: Arsenic acid
Trade Names: Desiccant L-10®, Hi Yield® H-10, Poly Brand Desiccant, Hi Yield® Synergized H-10®
EPA Shaughnessy Code: 006801
Chemical Abstracts Service (CAS) Number: 7778-39-4
Pesticide Types: Desiccant, Wood preservative
Chemical Family: Inorganic arsenicals
U. S. and Foreign Producers: Pennwalt Corporation
Voluntary Purchasing Corporation

2. USE PATTERNS AND FORMULATIONS

Application Sites: Terrestrial crop use on machine and stripper harvested cotton as a desiccant; Non-food use on seed crop okra (Arizona only) as a desiccant.

Types of formulations: 75% soluble concentrate formulation intermediate, also used as end use product.

Types and Methods of Application: Foliar spray (single application at least 4 and 10 days prior to harvest of cotton and okra, respectively.)

Application Rates: Cotton — 2.94 to 4.42 pounds active per acre

Okra — 4.42 pounds active per acre

(Note: 1 quart of 75% liquid = about 2.94 pounds active ingredient)

Usual Carriers: Water

3. SCIENCE FINDINGS

Science summary: Arsenic acid is a form of inorganic arsenic. Such compounds are acutely toxic to humans by ingestion. Inorganic arsenical compounds have been classified as Class A oncogens, demonstrating positive oncogenic effects based on sufficient human epidemiological evidence. The weight of evidence indicates that inorganical arsenical compounds are also mutagens. Although there is teratogenic and fetotoxic potential based on intravenous and intraperitoneal routes of exposure, there is insufficient evidence by the oral route to confirm arsenic acid's teratogenic or fetotoxic effects. Neurotoxic effects have been demonstrated after acute, subchronic and chronic exposures. The metabolism of arsenical compounds in humans is well-documented, but animal studies are not adequate to determine no observed effect levels (NOELs) and acceptable daily intakes (ADIs).

The environmental fate of arsenic acid is not well documented. Studies to demonstrate its fate must take into account the fact that inorganic arsenicals are natural constituents of the soil, and that the forms of inorganic arsenic may change depending on environmental conditions. Based on very limited data, arsenic acid is not predicted to leach significantly. Although elevated levels of arsenic have been found in groundwater in Texas, the source of the arsenic cannot be determined; non-pesticide sources may have been the cause.

Arsenic acid is moderately toxic to birds, slightly toxic to fish and moderately toxic to aquatic invertebrate species.

Chemical Characteristics:

Physical state - Aqueous solution
Oxidation state - pentavalent (As^{+5})
Color - Pale yellow to pale green
Odor - None
Boiling point - Not available
Specific gravity - 1.884 at 20°C
Solubility - Readily soluble in water, forming various As salts
Stability - Most stable under conditions favoring oxidation and at high pH; under reduction conditions or low pH, pentavalent form may convert to trivalent arsenic

Unusual handling characteristics: Reacts with fabric, galvanized metals, black iron and certain other metals resulting in deterioration, corrosion, or liberation of toxic gases (e.g., hydrogen, arsine).

Forms of inorganic arsenic referenced in the Registration Standard

Arsenic acid - H_3AsO_4, containing arsenic in a +5 oxidation form
Sodium arsenate (Na_3AsO_4) - the sodium salt of arsenic acid, also +5
Arsenic trioxide (As_2O_3) - an oxide of arsenic, containing arsenic in a +3 oxidation form
Sodium arsenite ($NaAsO_2$) - a sodium compound related to arsenic trioxide, also +3

Toxicological Characteristics:

Acute toxicity. Although arsenic is known to be highly toxic by ingestion, few animal studies are available on the active ingredient, or on the formulated products of arsenic acid. Moreover, the toxicity of arsenic compounds may vary widely depending on the type of formulation and the form of inorganic arsenic in the product.

Oral (rat) - 40-100 mg/kg. Rats are not a good test species, however, since, alone among animal test species, they retain arsenic in their bodies without significant excretion. Humans are known to be more sensitive to acute arsenic effects than rats.

Dermal - Undetermined

Inhalation - Undetermined

Eye and Skin Irritation - Undetermined

Dermal Sensitization - Undetermined

Chronic toxicity.

Oncogenicity: Arsenic compounds, including arsenic acid, have been classified as Class A oncogens. Epidemiological studies on workers in copper smelting and pesticide manufacturing, and on populations exposed to excess levels of arsenic in well water in Taiwan are the basis for this classification. Inhalation exposure leads to lung cancers, and ingestion exposure has shown a correlation with development of skin cancers.

The lifetime inhalation oncogenic risks to workers from the cotton use have been estimated at negligible for applicators, and 10^{-4} to 10^{-5} for mixer/loaders.

Dermal and oral oncogenic risks have not been calculated because the risk models are still undergoing Agency review. Completion of this review is expected in late 1986 or early 1987.

Mutagenicity: The sodium salt of arsenic acid (sodium arsenate) and the sodium salt of arsenous acid (a related form of arsenic) have been found to be mutagenic, that is, to interact with DNA to cause heritable effects. Numerous assays have been conducted on cells in vitro. Other observed effects include interference with DNA repair mechanisms, direct toxicity to mammalian gonads, and positive effects in microbial systems. Other evidence suggests that similar effects may occur in vivo. Sodium arsenite is a more potent mutagen than sodium arsenate.

Teratogenicity/fetotoxicity: Sodium arsenate has been shown to produce teratogenic or fetotoxic effects in hamsters (15-25 mg/kg intravenously); mice (40-45 mg/kg intraperitoneally); and rats (20-50 mg/kg interperitoneally). Similar results have been obtained with sodium arsenite at lower dosages. These results have not been demonstrated using an oral route of exposure, or have been found only at dosages that also cause significant maternal mortality. Because the effects have been shown only using routes of exposure that are not likely to occur with pesticide use, and because the studies were not adequate to establish no-observed effect levels (NOELs) the Agency will require an oral teratogenicity study in two species other than the rat.

Reproductive effects: No data that meet Agency standards are available. A reproduction study on a species other than the rat will be required.

Neurotoxicity: Subchronic and chronic exposure to arsenic compounds causes peripheral and central nervous system neuropathy, the effects of which vary from slight to severe depending on the level and duration of exposure.

Other subchronic and chronic effects: Inorganic arsenic compounds have been observed to cause cardiovascular, skin, blood, and liver and kidney effects in humans. The same effects have been observed in experimental animals. The NOEL for blood effects in dogs is 50 ppm (1.25 mg/kg). The NOEL for liver effects in rats of arsenites is 62.5 ppm and of arsenates is 125 ppm.

Metabolism: The metabolism of inorganic arsenic compounds in animals is well known. The pentavalent form, such as arsenic acid, is metabolized by reduction into the trivalent form, followed by transformation into organic forms which are excreted within several days via the urine. All mammals exhibit this metabolism except rats, which retain arsenic in their bodies for up to 90 days.

Physiological and Behavioral Characteristics: Mechanism of Pesticide Action -- Protein denaturation and enzyme inactivation, resulting in desiccation of plant foliage and stems

Environmental Characteristics: Few data are available on the environmental fate of arsenic acid. Arsenic is a naturally occurring compound that is ubiquitous and exists in different forms (species) depending on environmental conditions. Arsenic acid rapidly dissolves in water. The arsenic moiety of the residue cannot be distinguished from natural arsenic in the soil. Special environmental fate data are required to be submitted. Studies on environmental fate of arsenic acid must be designed to differentiate between natural and pesticide sources of arsenic.

Groundwater concerns: Arsenic has been detected in groundwater underlying areas of arsenic acid use. However, the source of this contamination cannot be determined. Limited information currently available suggests that arsenic acid will not leach significantly. Additional data are required to further evaluate leaching potential.

Ecological Characteristics:

Avian acute toxicity:	No data available
Avian dietary toxicity:	Mallard duck - 1606 ppm Bobwhite quail - 168 ppm
Freshwater fish toxicity:	Bluegill sunfish - 66.8 ppm Rainbow trout - 53.1 ppm
Aquatic invertebrates:	Daphnia magna - 6.5 ppm

Based on limited data, the Agency characterizes arsenic acid as moderately toxic to birds by ingestion in the diet. Arsenic acid is slightly toxic to fish and moderately toxic to aquatic invertebrates.

Endangered Species: Cotton desiccant use may pose a potential hazard to the Attwater's Greater Prairie Chicken in three Texas counties (Victoria, Refugio, and Fort Bend). The Agency has referred arsenic acid to the Office of Endangered Species, U.S. Department of Interior, for review as part of a group of cotton pesticides, and will require labeling to protect this endangered species.

Tolerance Assessment

A tolerance of 4.0 ppm in cottonseed oil has been established for arsenic acid, expressed as arsenic trioxide (As_2O_3) (40 CFR 180.180). The use on okra seed crop is a non-food use for which no tolerance is required.

Because the metabolism and chronic effects of inorganic arsenic in humans are well-known, the Agency is not requiring the submission of chronic feeding studies on arsenic acid per se. For regulatory purposes, and until teratogenicity and reproduction studies are submitted, the Agency has calculated a provisional acceptable daily intake (PADI) based upon studies using sodium arsenate.

Based upon a dog study having a NOEL of 50 ppm (1.25 mg/kg of actual arsenic) and a safety factor of 100, the PADI is 0.0165 mg/kg/day of As_2O_3, and the maximum permissible intake for a 60 kg person is 0.99 mg/day.

Available residue data indicate that the maximum residue that will theoretically occur in cottonseed from use of arsenic acid is 0.009 mg/day. The maximum residue therefore uses 0.009/0.99 of the maximum permissible intake, or 0.9%.

Reported Pesticide Incidents

In the period from 1966-1981, 8 incidents were reported to the Agency concerning arsenic acid related to its cotton use. Among these, one involved one human fatality and two persons hospitalized, three involved cattle, and four involved crop damage from spray drift of arsenic acid from nearby areas.

4. SUMMARY OF REGULATORY POSITION AND RATIONALE

—Arsenic acid is currently ungoing Agency Special Review, based upon its oncogenic and teratogenic effects. Products will remain registered until the conclusion of this review. New uses, however, will not be accepted.

--Arsenic acid products will be restricted to use by certified applicators, because of its acute toxicity and oncogenicity.

—Use restrictions based upon groundwater concerns are not warranted at the present time.

—Reentry intervals are not required because use as a desiccant does not lead to significant exposure to field workers.

—Protective clothing is specified for mixer/loaders and applicators, because of the acidic properties of arsenic acid, and its potential oncogenic risks to mixer/loaders and applicators.

—Endangered species labeling statements are required because of potential hazard to the Attwater's Greater Prairie Chicken in Texas. An avian residue monitoring study is required to determine actual levels of arsenic acid in avian feed items.

—Tolerances will be reassessed based upon residue and metabolism studies to be submitted. A rotational crop restriction may be needed if followup crops take up arsenic acid residues from the soil.

5. SUMMARY OF MAJOR DATA GAPS

Product chemistry data - arsenic acid	Feb. 1987
Residue chemistry data - arsenic acid	Feb. 1988
—Plant and animal metabolism	
—Analytical methodology for residues	
—Magnitude of residues in cotton	
Environmental fate studies	
—Metabolism in soil	Dec. 1988
—Leaching	Aug. 1987
—Laboratory volatility	Aug. 1987
—Soil dissipation	Dec. 1988
—Rotational crop studies	Dec. 1989
Toxicology studies	
—Acute toxicity	Feb. 1987
—Teratology (rabbit and mouse or hamster)	Dec. 1987
—Reproduction (rodent other than rat)	Dec. 1989
—Dermal penetration	Aug. 1987
—Glove permeability	Feb. 1987

Ecological effects studies

--Avian acute toxicity	May 1987
--Residue monitoring study on avian food items	Dec. 1987
--Aquatic invertebrate early life stage	Dec. 1987

6. CONTACT PERSON AT EPA

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