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SECOND DRAFT

Information Profiles on Potential Occupational Hazards: Aminoazobenzenes

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16. Abstract (Limit: 200 words) Information profiles were prepared for the following aminoazobenzenes: deemed to be of significance due to the fact that they each had an annual production volume in the range of at least the thousands of pounds: 4-aminoazobenzene (60093), 4-aminoazobenzene-3,4'-disulfonic-acid (101508), 4-aminoazobenzene-3,4'-disulfonic-acid-disodium-salt (2706287), 4-aminoazobenzene-hydrochloride (3457985), 4'-aminoazobenzene-4-sulfonic-acid (104234), 4'-aminoazobenzene-4-sulfonic-acid-sodium-salt (2491716), ortho-aminoazotoluene (97563), ortho-aminoazotoluene-hydrochloride (2298137), C.I.-Disperse-Orange-3 (730405), C.I.-Disperse-Red-1 (2872528), C.I.-Disperse-Red-5 (3769571), C.I.-Disperse-Red-17 (3179893), C.I.-Disperse-Yellow-3 (2832408), chrysodine (532821), 2,4-diaminoazobenzene (495545), and N,N,-diethylaminoazobenzene (2481949). Information suggested that these compounds were only mildly toxic following acute exposure. Organ damage was noted in the liver, kidneys, and spleen following subchronic or chronic exposure to N,N-diethylaminoazobenzene, 4-aminoazobenzene, and ortho-aminoazotoluene. After metabolic activation in the Ames assay, positive findings were obtained for 4-aminoazobenzene, chrysodine and ortho-animoazotoluene. Cell transformation assays gave positive results for 4-aminoazobenzene and 4-aminoazobenzene-4-sulfonic-acid. Aminoazobenzenes, 4-aminoazobenzenes, chrysodine and ortho-aminoazotoluene have tested positively in carcinogenicity studies using laboratory mice. Ortho-aminoazotoluene crossed the placenta and increased tumor incidence in the F1 generation.

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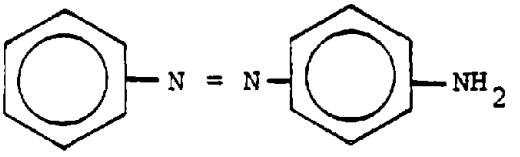
I. SCOPE OF DOCUMENT AND SUMMARY OF MAJOR FINDINGS

A. CLASS IDENTIFICATION

The aminoazobenzenes have been identified as the compounds having the basic general structure as follows:



The hydrogen atoms attached to the amino group or to the aromatic rings may be replaced by other functional groups such as nitro, methyl, chloro, sulfonic acid, amino, ethyl, or other common functional groups.

The appendix contains a listing of all the aminoazobenzenes identified from the above definition.

B. CHEMICALS TO BE ADDRESSED

Individual profiles have been prepared for the following aminoazobenzenes:

4-Aminoazobenzene
4-Aminoazobenzene-3,4'-disulfonic acid
4-Aminoazobenzene-3,4'-disulfonic acid, disodium salt
4-Aminoazobenzene hydrochloride
4'-Aminoazobenzene-4-sulfonic acid
4'-Aminoazobenzene-4-sulfonic acid, sodium salt
ortho-Aminoazotoluene
ortho-Aminoazotoluene hydrochloride
C.I. Disperse Orange 3
C.I. Disperse Red 1
C.I. Disperse Red 5
C.I. Disperse Red 17
C.I. Disperse Yellow 3
Chrysoidine
2,4-Diaminoazobenzene
N,N-Diethylaminoazobenzene

Individual profiles were prepared for each aminoazobenzene identified as having an annual production volume in, at least, the thousands of pounds. This

criterion was used to insure that the individual aminoazobenzenes were not produced primarily for research or laboratory applications.

The only major commercial use identified for all of the aminoazobenzenes was as a dyestuff or dye intermediate. In this application, small volumes of an aminoazobenzene (dye) may have some commercial significance. For example, in industry, the 100% active dye chemical is commonly "cut" to commercial strengths by additions of sodium sulfate, non-dusting agents, surfactants, dextrins, and other inert ingredients. The actual dye content of the commercial product may be as low as 25%. Also, a specific aminoazobenzene (dye) may have only one or two specialized commercial applications. Therefore, some of the aminoazobenzenes from the Appendix which are not profiled individually may have some commercial significance.

C. SUMMARY OF BIOLOGICAL ACTIVITY

There is little information on the toxicity of the aminoazobenzenes. The information that is available would indicate that compounds of this group are only moderately toxic following acute exposure. With the few chemicals examined by either subchronic or chronic exposure, N,N-diethylaminoazobenzene, 4-aminoazobenzene, and ortho-aminoazotoluene, organ damage was observed in the liver, kidneys, and spleen. The only reports of human experience with aminoazobenzenes relates to case studies of allergic eczema in individuals exposed to C.I. Disperse Yellow 3 in nylon stockings. Similar allergic responses have been observed with 4-aminoazobenzene-3,4'-disulfonic acid following sensitization of guinea pigs.

Most of the aminoazobenzenes have not been studied for mutagenic or carcinogenic activity. Of the compounds assayed for mutagenic activity, both N,N-diethylaminoazobenzene and ortho-aminoazotoluene hydrochloride have given negative results. The other compounds tested, 4-aminoazobenzene, chrysoidine

and ortho-aminoazotoluene, have been positive in the Ames assay after metabolic activation. Also, both 4-aminoazobenzene, and 4'-aminoazobenzene-4-sulfonic acid have been shown to be positive in cell transformation assays.

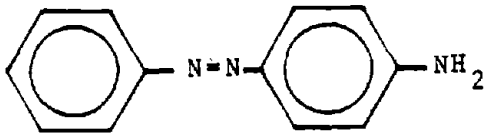
The aminoazobenzenes, 4-aminoazobenzenes, chrysoidine and ortho-aminoazotoluene have been shown to be carcinogens in laboratory rodents. Ortho-aminoazotoluene has been shown to cross the placenta and increase the tumor incidence in the F_1 generation. The dye C.I. Disperse Yellow 3 was possibly carcinogenic in mice, however, the study was inadequate to allow for a definitive determination. Of the compounds tested for carcinogenicity, only N,N-diethylaminoazobenzene has been determined to be non-carcinogenic in rats and mice. The limited data available and the fact that the mutagenicity data indicates that metabolic activation is required makes it impossible to predict the carcinogenic potential of the aminoazobenzenes that have not been assayed in either short term or long term bioassays.

II. INFORMATION PROFILES

A. 4-AMINOAZOBENZENE

1. Chemical Name: 4-Aminoazobenzene

2. Chemical Structure:



3. Synonyms: Aminoazobenzol
p-Aminodiphenylimide
Aniline Yellow
4-Benzeneazoaniline
C.I. 11000
C.I. Solvent Yellow 1
Organol Yellow
p-(Phenylazo)aniline

4. Chemical Abstracts Service (CAS) Number: 60-09-3

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

BY8225000

6. Chemical and Physical Properties:

Description:	yellow to brownish-tan crystals
Molecular Weight:	197.26
Boiling Point:	>360°C
Melting Point:	126-128°C
Vapor Pressure:	---
Solubility:	slightly soluble in water; soluble in ethanol, benzene, chloroform, and ether
Specific Gravity:	---
Stability:	---

7. Production

The following figures for production volumes of aminoazobenzene and its hydrochloride are available (USITC, 1976, 1975):

Year	Production in Thousands of Pounds
1974	329
1973	462

Reported importation in recent years is as follows (USITC, 1980a, 1977a, 1978a):

Year	Importation in Thousands of Pounds
1979	189.816
1977	174.163
1976	41.225

Data available from the U.S. EPA (1980) regarding producers of 4-aminoazobenzene and production volumes are presented in Table 1.

8. Use

4-Aminoazobenzene is used in dyeing and in the production of dye intermediates (The Merck Index, 1976). It reportedly is used as a dye for lacquers, varnishes, wax products, oil stains, and styrene resins and as an intermediate in the manufacture of acid yellow, diazo dyes, and indulines. According to U.S. industrial sources, 4-aminoazobenzene is not used in foods, drugs, or cosmetics (IARC, 1975a).

9. Manufacturers and Distributors

SRI International (1980) lists American Cyanamid Co. (Bound Brook, NJ) as a manufacturer, while USITC (1978b) lists American Cyanamid and Atlantic Chemical (Nutley, NJ) as manufacturers. American Cyanamid, however, no longer manufacturers aminoazobenzene (Gerko, written communication, 1980).

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers Guide Issue, 1980; Chem Sources--USA, 1980):

Anachemia Chem.	Gallard-Schlesinger Chem.
Atlantic Chem.	ICN/K and K
Atomergic Chemetals	Lachat Chem.
Bio-Clinical Lab.	MCB Reagents
Crompton and Knowles	Mobay Chem.
Eastern Chem.	Orlex Chem.
EM Lab.	Tridom Chem.
Fisher Sci.	TransWorld Chem.

Table 1. Producers of 4-Aminoazobenzene and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Eastman Kodak Rochester, NY	Manufacturer	none
Alliance Chemical Inc. Newark, NJ	Manufacturer	none
The Harshaw Chemical Co. Lowell, NC	Manufactuer	1-10 thousand lb
GAF Corp. New York City, NY	Importer	1-10 thousand lb
Mobay Chemical Corp. Pittsburg, PA	Importer	confidential

10. Manufacturing Processes

4-Aminoazobenzene is produced by diazotization of aniline with sodium nitrite and hydrochloric acid (Hydro and Willard, 1959; The Merck Index, 1976).

This type of reaction is commonly carried out in a well-stirred batch tank for the reactor (Steadman et al., 1977). An aqueous medium is used whenever possible (Bannister et al., 1979). The reaction begins by introducing aniline, hydrochloric acid, and ice into the reactor. The temperature must be kept cool to prevent decomposition of the diazonium salts that are produced. To the resulting solution or suspension, a solution of sodium nitrate is rapidly injected, which forms nitrous acid and thereby begins the azo coupling of the aniline compound. Tests are conducted to determine when the degree of azo coupling is sufficient.

When the reaction is complete, sodium carbonate is added to the reactor to neutralize excess hydrochloric acid. The dye can now be precipitated from solution by addition of sodium chloride. The precipitated aminoazobenzene can be recovered by filter presses and dried in tray driers. Figure 1 outlines the manufacturing operations.

11. Impurities or Additives

The manufacture and testing of 4-aminoazobenzene do not conform to rigid chemical specifications, and its composition varies in order to meet customer shade and intensity requirements (IARC, 1975a).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 250 workers are potentially exposed to 4-aminoazobenzene.

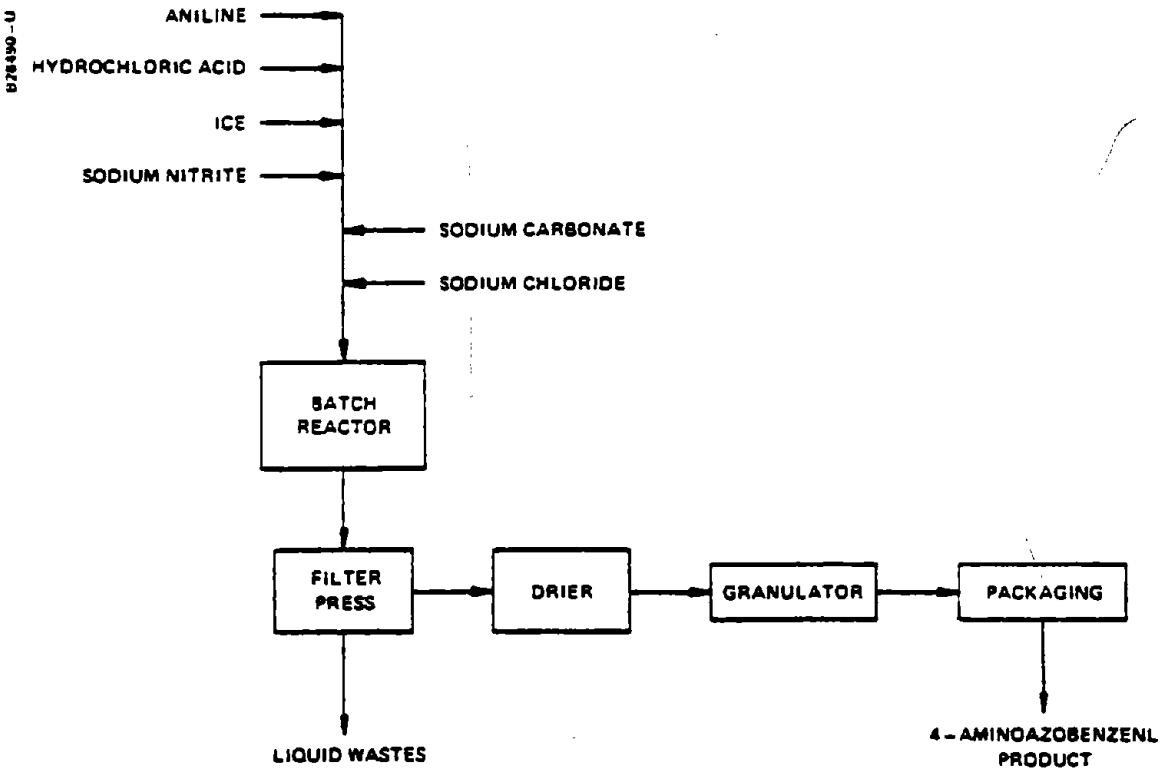


Figure 1. Manufacture of 4-Aminoazobenzene

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4-aminoazobenzene were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

An LDLo value of 200 mg/kg has been reported for 4-aminoazobenzene administered intraperitoneally to mice (NIOSH, 1979). Simmon et al. (1979) determined that the LD50 of 4-aminoazobenzene in mice was 483 mg/kg. Lin et al (1972) demonstrated that 4-aminoazobenzene formed methemoglobin in a dose-dependent manner in rats following intraperitoneal administration. At the highest dose tested, 60 mg/kg, 66.6% of the total hemoglobin was converted to methemoglobin in 1 hour; this value fell to 44.5% by 4 hours.

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

Kirby (1947) maintained 16 rats on a low-protein diet containing 4-aminoazobenzene (the dose schedule is presented in the Carcinogenicity section). One animal at the time of natural death had an enlarged spleen and periportal cirrhosis of the liver, and a number of animals had cholangiectases. In 7 rats that received 4-aminoazobenzene and a normal diet, occasional fatty degeneration of the liver was noted.

In a study of 29 mice injected with 4-aminoazobenzene and maintained on a restricted diet (the dose schedule is presented in the Carcinogenicity section), Kirby (1945) observed liver necrosis and acute toxic nephritis in many of the animals. In 7 mice that received 4-aminoazobenzene and

an adequate diet, toxic nephritis usually was observed. No signs of liver cirrhosis, however, were detected in either group of mice.

(4) Carcinogenicity

The carcinogenicity of 4-aminoazobenzene has been reviewed by an IARC Working Group (IARC, 1975), by Miller and Miller (1953), and by Terayama (1967).

Kirby (1947) studied the chronic effects of 4-aminoazobenzene on rats fed two types of diet--one containing adequate protein and boiled potato and the other restricted in protein and containing rice starch. These results were also reported by Kirby and Peacock (1947). A group of 16 male rats were fed a diet (adequate in protein) containing 0.3% 4-aminoazobenzene for 20 weeks, after which the composition was changed to 0.5% for 10 weeks, 1.0% for 15 weeks, and 0.2% for the remainder of the experiment until the animals died. The total amount of 4-aminoazobenzene consumed during the lifetime of these rats ranged from 20 to 36 g. Of the 16 rats, 7 developed liver tumors; 5 hepatomas and 2 liver cell carcinomas were identified. In the second study, a group of 8 male and 7 female rats were fed the protein-restricted diet containing 0.25% 4-aminoazobenzene for 20 weeks, after which the diet was changed to 0.15% for 8 weeks, 0.1% for 44 weeks, and 0.08% for the remainder of the experiment until the animals died. In this study, no proliferative changes were observed in the livers of any of the animals.

In a limited study, Odashima and Hashimoto (1968) fed 32 male Donryu rats diets containing 0.8% 4-aminoazobenzene for 60 weeks. At the end of 60 weeks, the 18 surviving animals were killed. Only one tumor--a fibrosarcoma--was detected. The short duration of this study has been noted by the IARC Working Group (IARC, 1975).

Fare (1966) painted the dorsal skin of 6 male rats twice weekly with a 0.2% solution of 4-aminoazobenzene in acetone for a mean time of 123 weeks (the life of the animals). All 6 rats developed skin tumors; 4 squamous cell carcinomas, 8 basal cell carcinomas, 2 anaplastic carcinomas, 1 squamous cell papilloma, and 3 miscellaneous tumors were identified histologically. No proliferative changes were noted in the livers.

Kirby (1945) administered 4-aminoazobenzene as a 3% solution in arachis oil by subcutaneous injection of 0.25 ml once every 2 weeks to 29 stock mice. The animals in this study were maintained on a protein-restricted diet. After 48 days, half the mice had died and the dose was reduced to 2%. Of the surviving animals, 8 lived for more than 100 days and 3 lived for more than 300 days. No tumors were observed either locally at the site of injection or in any other body organ. Moreover, no tumors were noted in 7 mice that received the same treatment while maintained on a normal diet. In a similar study, Poirier et al. (1967) subcutaneously injected 20 male CD rats with 2.3 mg 4-aminoazobenzene in 0.2 ml tricaprylin. The rats were injected twice weekly for 12 weeks, followed by an 11-month observation period. No tumors were detected in these animals.

No increase in tumor incidence was observed in 20 rats following intraperitoneal administration of 4-aminoazobenzene (Sato et al., 1966). Weanling female Charles River rats were injected 3 times weekly with 100 mg/kg 4-aminoazobenzene for 6 injections, followed by an additional injection of 75 mg/kg. This dose of 4-aminoazobenzene killed 16 of the animals prior to 12 months, at which time the study was terminated. The IARC Working Group noted the short duration of the study (IARC, 1975).

(5) Mutagenicity

Extensive mutagenicity assays have been performed using 4-aminoazobenzene (see Table 2). There have been conflicting results using the reverse mutation assay of Ames with Anderson and Styles (1978) and McCann et al. (1975) obtaining a positive mutagenic response, Simmon (1979b) obtaining a marginally positive response, and Rosenkranz and Poirier (1979) demonstrating no mutagenic activity. The reason for these differences in the Ames assay was not apparent from the experimental details reported in the articles.

Poiley et al. (1979) reported positive results in a cell transformation assay, while three other investigators could demonstrate no transforming activity with 4-aminoazobenzene. Poiley et al. (1979) employed a higher concentration of the compound and hepatocyte feeder cells to provide metabolic activation.

The other assay systems described in Table 2 showed no genotoxic effect attributable to 4-aminoazobenzene.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

Sato et al. (1966) injected 4-aminoazobenzene intraperitoneally into male rats and hamsters and female mice. The metabolites N-acetyl-4-aminoazobenzene and its N-hydroxy-, 3-hydroxy-, and 4'-hydroxy derivatives were detected in the urine. Not all the metabolites were detected for each species and all represented only a minor fraction (<1%) of the dose excreted. The N-hydroxy-N-acetyl-4-aminoazobenzene was administered to rats either in the diet or by intraperitoneal injection in a limited 12-month study.

Table 2. *In Vitro* Mutagenicity and Cell Transformation Assays of 4-Aminoazobezene

Type of Assay	Organism	Strain	With Mammalian Metabolic Activation	Dose	Results[a]	Reference
Reverse mutation	*S. typhimurium*	TA1535	Yes and No	250 µg/plate	-	Rosenkranz and Poirier, 1979
		TA1538	Yes and No	250 µg/plate	-	
Reverse mutation	*S. typhimurium*	TA1535	Yes	500 µg/plate	+	Anderson and Styles, 1978
		TA1538	Yes	100 µg/plate	+	
		TA98	Yes	500 µg/plate	+	
		TA100	Yes	20 µg/plate	+	
Reverse mutation	*S. typhimurium*	TA98	Yes	100 µg/plate	+	McCann *et al.*, 1975
Reverse mutation (liquid incubation)	*S. typhimurium*	TA1535	Yes	125 µg/plate	-	Simmon, 1979a
		TA1536	Yes	125 µg/plate	-	
		TA1537	Yes	125 µg/plate	-	
		TA1538	Yes	125 µg/plate	+[b]	
		TA98	Yes	125 µg/plate	+[b]	
		TA100	Yes	125 µg/plate	+[b]	
Host-mediated	*S. typhimurium*	TA1530	Mouse	125 mg/kg	+[b]	Simmon *et al.*, 1979
		TA1538	Mouse	125 mg/kg	-	
Mitotic, recombination	*S. cerevisiae*	D3	Yes and No	1 mg/ml	-	Simmon, 1979b
Host-mediated	*S. cerevisiae*	D3	Mouse	500 mg/kg	-	Simmon *et al.*, 1979
DNA modifying activity	*E. coli*	pol A	Yes	25 µg/ml	-	Rosenkranz and Poirer, 1979
Unscheduled DNA synthesis	Rat liver primary cell cultures	NA[c]	No	2.4 µg/ml	-	Williams, 1977

Table 2. *In Vitro* Mutagenicity and Cell Transformation Assays of 4-Aminoazobenzene (Cont'd)

Type of Assay	Organism	Strain	With Mammalian Metabolic Activation	Dose	Results[a]	Reference
Unscheduled DNA synthesis	Human cells	Epithelial	No	400 µg/ml	-	Lake *et al.*, 1978
Cell transformation	Rat embryo cells infected with Rausch Leukemia Virus	NA	No	10 µg/ml	-	Freeman *et al.*, 1973
Cell transformation	Mouse embryo cells infected with AKR Leukemia Virus	NA	No	0.1 µg/ml	-	Rhim *et al.*, 1974
Cell transformation	BHK cells, clone 13	NA	No	25 µg/ml	-	Ashby *et al.*, 1978
Cell transformation	Hamster cells	NA	Hepatocyte feeder cells	31.6 µg/ml	+	Polley *et al.*, 1979
X chromosome lethal	*Drosphila*	NA	NA	unknown	-	Demerec, 1948

[a] "" = negative response; "+" = positive response.

[b] Colony number did not exceed 2x the control value (many investigators have set the minimum number of colonies for a positive response at 2x the control value).

[c] NA = not applicable.

At autopsy, the animals were examined for gross tumors. Although this metabolite was toxic (it killed 12 of the 16 animals prior to 12 months), no tumors were detected. Levine and Finkelstein (1978) have preliminary evidence that the hydroxylation of 4-aminoazobenzene may be the rate-limiting step in the biliary excretion of 4-aminoazobenzene while conjugation of the hydroxylated metabolite occurs rapidly.

b. Human Studies

No information was found in the literature searched.

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of 4-aminoazobenzene were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 4-aminoazobenzene were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

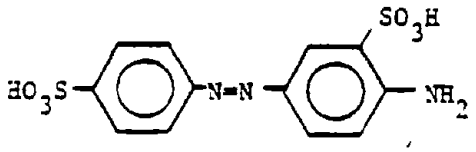
18. Other Pertinent Data

No other information that would aid in the assessment of 4-aminoazobenzene as an occupational hazard was found in the literature searched.

B. 4-AMINOAZOBENZENE-3,4'-DISULFONIC ACID

1. Chemical Name: 4-Aminoazobenzene-3,4'-disulfonic acid

2. Chemical Structure:



3. Synonyms: 6-Amino-3,4'-azodi (benzenesulfonic acid)
Benzenesulfonic acid, 6-amino-3,4'-azodi
Benzenesulfonic acid, 2-amino-5-[(4-sulfophenyl)azo]-

4. Chemical Abstracts Service (CAS) Number: 101-50-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	bright violet needles
Molecular Weight:	357.35
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	soluble in hot water
Specific Gravity:	---
Stability:	---

7. Production

Data available from the U.S. EPA (1980) regarding producers of 4-aminoazobenzene-3,4'-disulfonic acid and production volumes are presented in Table 3.

Table 3. Producers of 4-Aminoazobenzene-3,4'-disulfonic acid and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Toms River Chemical Corp. Toms River, NJ	Manufacturer/ Produced Site Limited	confidential
Mobay Chemical Corp. Pittsburgh, PA	Importer	confidential
Sandoz Colors and Chemicals East Hanover, NJ	Importer	confidential
Plant Site Not on File	---	0.1-1.0 million lb

Recent importation of 4-aminoazobenzene-3,4'-disulfonic acid has been reported as follows (USITC, 1980a, 1979a, 1978a, 1977a):

Year	Import in Thousands of Pounds
1979	108.299
1978	41.375
1977	7.545
1976	17.474

8. Use

4-Aminoazobenzene-3,4'-disulfonic acid is used in the synthesis of dyes and in wool dyeing (Hawley, 1977).

9. Manufacturers and Distributors

Producers listed by the U.S. EPA (1980) are presented in Table 3.

SRI International (1980) and USITC (1980a) do not list aminoazobenzene-disulfonic acid.

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources--USA, 1980):

Aceto Chem.	Crompton and Knowles
Atlantic Chem.	ICN/K and K
Chemcentral/Pittsburgh	Orlex Chem.
	Pfaltz and Bauer

10. Manufacturing Processes

4-Aminoazobenzene-3,4'-disulfonic acid is derived by heating either aminoazobenzene hydrochloride or aminoazobenzene-monosulfonic acid with fuming sulfuric acid (Rose and Rose, 1956). The reaction products will require neutralization, washing, drying, and finishing.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 4-aminoazobenzene-3,4'-disulfonic acid.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4-aminoazobenzene-3,4'-disulfonic acid were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

It has been noted in the Czechoslovakian literature that 4-aminoazobenzene-3,4'-disulfonic acid is not highly toxic (rat oral LD50 of (5 g/kg), and that instillation of 500 mg was severely irritating to the eyes of rabbits after 24 hours (Marhold, 1972).

Allergic reactions developed in 2 of 18 guinea pigs sensitized with p-phenylenediamine after a challenge with 4-aminoazobenzene-3,4'-disulfonic acid (Sulser and Schwarz, 1962).

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of 4-aminoazobenzene-3,4'-disulfonic acid were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 4-aminoazobenzene-3,4'-disulfonic acid were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

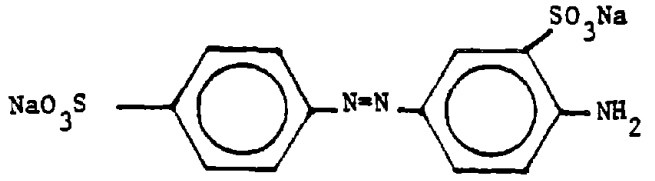
18. Other Pertinent Data

No other information that would aid in the assessment of 4-aminoazobenzene-3,4'-disulfonic acid as an occupational hazard was found in the literature searched.

C. 4-AMINOAZOBENZENE-3,4'-DISULFONIC ACID, DISODIUM SALT

1. Chemical Name: 4-Aminoazobenzene-3,4'-disulfonic acid, disodium salt

2. Chemical Structure:



3. Synonyms: Acid Yellow 9
4-Aminoazobenzene-3,4'-disulfonate
6-Amino-3,4-azodibenzenesulfonic acid, disodium salt
Benzenesulfonic acid, 2-amino-5-[(4-sulfophenyl)azo]-, disodium
C.I. 13015
C.I. Acid Yellow 9
C.I. Food Yellow 2
Disulfonate p-phenylazoanile
Fast Yellow AB

4. Chemical Abstract Service (CAS) Number: 2706-28-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	red-yellow crystals
Molecular Weight:	401.31
Boiling Point:	---
Melting Point:	---
Vapor Pressure	---
Solubility:	soluble in water; slightly soluble in ethanol and Cellosolve
Specific Gravity:	---
Stability:	---

7. Production

The only production data available from the U.S. EPA (1980) is that the Harshaw Chemical Co. (Lowell, N.C.) produced between 0 and 1000 pounds in 1977 for captive consumption.

4-Aminoazobenzene-3,4'-disulfonic acid, disodium salt (Acid Yellow 9) is produced as an intermediate in the synthesis of 4-aminoazobenzene-3,4'-disulfonic acid (The Colour Index, 1956); the production volume of this compound in 1978 may have been on the order of 100 thousand pounds (see profile for 4-aminoazobenzene-3,4'-disulfonic acid).

8. Use

Acid Yellow 9 is used an an intermediate in the manufacture of disazo and trisazo dyes in addition to being used as an acid dye (The Colour Index, 1956).

9. Manufacturers and Distributors

Acid Yellow 9 is manufactured by Toms River Chemical Corp., in Toms River, NJ (USITC, 1980a) and by the Harshaw Chemical Co. in Lowell, N.C. (U.S. EPA, 1980).

The Aceto Chemical Co. is a distributor (Chem Sources--USA, 1980).

10. Manufacturing Processes

4-Aminoazobenzene-3,4'-disulfonic acid is derived by heating either aminoazobenzene hydrochloride or aminoazobenzene monosulfonic acid with fuming sulfuric acid (Rose and Rose, 1956); neutralization of the reaction products yields the disodium salt which can be washed and dried. Subsequent acidification of the disodium salt (Acid Yellow 9) yields the product 4-aminoazobenzene-3,4'-disulfonic acid.

11. Impurities or Additives

Many commercial dyes are "cut" to commercial strength by additions of sodium sulfate, non-dusting agents, surfactants, dextrins, and other inert ingredients. The actual dye content of the final product may be as low 25%.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 88 workers are potentially exposed to 4-aminoazobenzene-3,4'-disulfonic acid, disodium salt.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4-aminoazobenzene-3,4'-disulfonic acid, disodium salt were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

No information was found in the literature searched.

(2) Subchronic Exposures

A single subchronic toxicity study was found in the literature searched. Søndergaard et al. (1977) treated 2 male and 2 female pigs by gavage with Fast Yellow AB (4-aminoazobenzene-3,4'-disulfonic acid, disodium salt). A mixture containing 87.4% dye was administered at a dose of 1 g/kg/day for the first 21 days followed by 1.5 g/kg/day for the remainder of the study. Blood was obtained on days 5, 19, and 68 of treatment and examined for changes in hemoglobin, hemiglobin, packed cell volume, total erythrocyte count, Heinz Body counts, reticulocyte counts, cell volume, and serum lactic dehydrogenase levels. At the termination of the study autopsies were performed and histologic examination made of the kidneys, spleen, liver, hepatic and renal lymph nodes, and the bone marrow. There was no significant effect of treatment on any of the investigated parameters.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

Scheline and Longberg (1965) investigated the absorption, excretion, and metabolism of acid yellow (4-aminoazobenzene-3,4'-disulfonic acid, disodium salt) in the rat. When 2 mg/rat of acid yellow was administered to 7 rats by intraperitoneal injection, 87% of the dose was recovered as unchanged compound in the urine. When the dye was administered by gavage at a dose of 100 mg/rat, only 2.6, 0.0, and 0.12% of the unchanged compound appeared in the urine, feces, and bile, respectively. Ryan and Wright (1961) observed a 10% biliary excretion of Fast Yellow following intravenous administration of the compound to rats. The reduction products of acid yellow, sulfanilic acid and p-phenylnediamine sulfonic acid, were isolated by Scheline and Longberg (1965) in large quantities from the urine and feces of animals treated by gavage. Since these compounds were not found after intraperitoneal injection of acid yellow, it was suggested that the reduction occurred by the gut flora rather than the azo reductase system of the rat. Preliminary studies confirmed the capability of bacteria isolated from rat feces to form sulfanilic acid and p-phenylenediamine sulfonic acid from acid yellow.

b. Human Studies

No information was found in the literature searched regarding human studies of 4-aminoazobenzene-3,4'-disulfonic acid, disodium salt.

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of 4-aminoazobenzene-3,4'-disulfonic acid, disodium salt were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 4-aminoazobenzene-3,4'-disulfonic acid, disodium salt were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

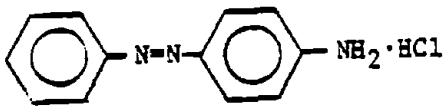
18. Other Pertinent Data

No other information that would aid in the assessment of 4-aminoazobenzene-3,4'-disulfonic acid, disodium salt as an occupational hazard was found in the literature searched.

D. 4-AMINOAZOBENZENE HYDROCHLORIDE

1. Chemical Name: 4-Aminoazobenzene Hydrochloride

2. Chemical Structure:



3. Synonyms: p-(Phenylazo)aniline hydrochloride
p-Aminoazobenzene hydrochloride
Benzamine, 4-(phenylazo)-, monochloride

4. Chemical Abstracts Service (CAS) Number: 3457-98-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

BY8235000

6. Chemical and Physical Properties:

Description:	steel-blue crystals
Molecular Weight:	233.72
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	slightly soluble in water; soluble in alcohol
Specific Gravity:	---
Stability:	---

7. Production

The following information regarding production volumes of aminoazobenzene and its hydrochloride is available (USITC, 1976, 1975):

Year	Production in Thousands of Pounds
1974	329
1973	462

In 1978, 2,608 thousand pounds were reported imported (USITC, 1979).

Data available from the U.S. EPA (1980) regarding producers of 4-aminoazobenzene hydrochloride and production volumes are presented in Table 4.

8. Use

4-Aminoazobenzene hydrochloride is used in dyes, coloring lacquers, and intermediates (Hawley, 1977).

9. Manufacturers and Distributors

SRI International (1980) lists American Cyanamid Co. (Bound Brook, NJ) as a manufacturer, while USITC (1978b) lists American Cyanamid and Atlantic Chemical (Nutley, NJ) as manufacturers. American Cyanamid, however, no longer makes this compound (Gerko, written communication, 1980).

Producers listed by the U.S. EPA (1980) are shown in Table 4.

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources--USA, 1980):

Crompton and Knowles Corp.	Pfaltz and Bauer
ICN/K and K	TransWorld Chem.
Orlex Chem.	Tridom Chem.

10. Manufacturing Processes

4-Aminoazobenzene hydrochloride can be produced by passing dry HCl gas into a solution of aminoazobenzene and purifying by crystallization (Hawley, 1977). It also may be possible to separate the hydrochloride for isolation during production of aminoazobenzene. Production methods for aminoazobenzene are discussed in the profile for that compound.

11. Impurities or Additives

The following are the properties of commercial aminoazobenzene hydrochloride (American Cyanimid, n.d.):

Table 4. Producers of 4-Aminoazobenzene Hydrochloride and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Atlantic Chemical Corp. Nutley, NJ	Manufacturer	10-100 thousand lb
E.I. du Pont deNemours and Co. Deepwater, NJ	Manufacturer	zero
Chemtronics Inc. Swannanda, NC	Manufacturer	10-100 thousand lb
American Cyanamid Bound Brook, NJ	Importer	confidential
Plant Site Not on File	---	zero

Description: A steel blue or purplish-blue paste.

	Specifications	Typical Analysis
Real Content (Dry basis)	96.0% min.	97-100%
Water	50% max.	16-35%

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 4-Aminoazobenzene hydrochloride.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4-aminoazobenzene hydrochloride were not found in the literature searched.

14. Biological Effects

No information was found in the literature searched regarding the biological effects of 4-aminoazobenzene hydrochloride, except a single oral LD50 value for rats of 1250 mg 4-aminoazobenzene hydrochloride per kg body weight (NIOSH, 1979).

15. Ongoing Studies

No current toxicological or environmental studies of 4-aminoazobenzene hydrochloride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 4-aminoazobenzene hydrochloride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

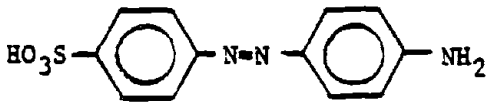
18. Other Pertinent Data

No other information that would aid in the assessment of 4-amino-azobenzene hydrochloride as an occupational hazard was found in the literature searched.

E. 4'-AMINOAZOBENZENE-4-SULFONIC ACID

1. Chemical Name: 4'-Aminoazobenzene-4-sulfonic acid

2. Chemical Structure:



3. Synonyms: p-[(p-Aminophenyl]azo1benzenesulfonic acid
Aminoazobenzene-p-sulfonic acid
4'-Amino-4-sulfoazobenzene
([4-Anilinoazo]benzene-4-sulfonic acid)
(4-[4'-Sulfophenylazo]aniline)
Benzenesulfonic acid, 4-[(4-aminophenyl)azo]
C.I. 13011 (free acid)

4. Chemical Abstracts Service (CAS) Number: 104-23-4

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	yellowish-white, microscopic needles
Molecular Weight:	277.32
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	barely soluble
Specific Gravity:	---
Stability:	---

7. Production

Reported production of 4'-aminoazobenzene-4-sulfonic acid in recent years is as follows (USITC, 1980b, 1979b, 1978b, 1977b, 1977c, 1976):

Year	Production in Thousands of Pounds
1979	302
1978	316
1977	277
1976	411
1975	178
1974	434

Reported importation in recent years is as follows (USITC, 1980a, 1979a, 1978a, 1977a):

Year	Importation in Thousands of Pounds
1979	59.009
1978	92.057
1977	192.062
1976	187.510

Data available from the U.S. EPA (1980) regarding producers of 4'-aminoazobenzene-4-sulfonic acid and production volumes are presented in Table 5.

8. Use

4'-Aminoazobenzene-4-sulfonic acid is used in dyestuff manufacture (Hawley, 1977).

9. Manufacturers and Distributors

SRI International (1980) lists the following manufacturers:

American Cyanamid Co.	Bound Brook, NJ
Atlantic Chemical Corp.	Nutley, NJ
BASF Wyandotte Corp.	Rensselaer, NY
Toms River Chemical Corp.	Toms River, NJ

USITC (1980b) lists American Cyanamid, Toms River, and du Pont as manufacturers. American Cyanamid, however, no longer manufacturers this compound (Gerko, written communication, 1980). Producers reported by the U.S. EPA (1980) are shown in Table 5.

Table 5. Producers of 4'-Aminoazobenzene-4-sulfonic acid and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Mobay Chemical Corp.		
Bayonne, NJ	Manufacturer	confidential
Pittsburgh, PA	Importer	confidential
Toms River Chemical Corp.		
Toms River, NJ	Manufacturer/ Produced Site Limited	confidential
Drake Chemical Inc.		
Lock Haven, PA	Manufacturer	confidential
American Cyanamid Co.		
Bound Brook, NJ	Importer/ Produced Site Limited	confidential
GAF Corp.		
New York, NY	Importer	10-100 thousand lb
Plant Site Not on File	---	10-100 thousand lb

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources--USA, 1980):

Aceto Chem.	Mobay Chem.
Atlantic Chem.	Montedison USA
Crompton and Knowles	Orlex Chem.
	Sandoz Colors and Chem.

10. Manufacturing Processes

4'-Aminoazobenzene-4-sulfonic acid is made by sulfonating aminoazobenzene (Hawley, 1977). The process operations may be similar to those for aminoazobenzene with the addition of a sulfonation step (see profile for 4-Aminoazobenzene).

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 4'-aminoazobenzene-4-sulfonic acid.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4'-aminoazobenzene-4-sulfonic acid were not found in the literature searched.

14. Biological Effects

No information was found in the literature searched regarding the biological effects of 4'-aminoazobenzene-4-sulfonic acid, except a positive *in vitro* cell transformation assay (Ashby *et al.*, 1978). The compound was tested at 25 mg 4'-aminoazobenzene-4-sulfonic acid per ml.

15. Ongoing Studies

No current toxicological or environmental studies of 4'-aminoazobenzene-4-sulfonic acid were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 4'-aminoazobenzene-4-sulfonic acid were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

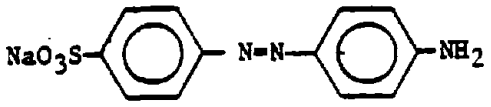
18. Other Pertinent Data

No other information that would aid in the assessment of 4'-aminoazobenzene-4-sulfonic acid as an occupational hazard was found in the literature searched.

F. 4'-AMINOAZOBENZENE-4-SULFONIC ACID, SODIUM SALT

1. Chemical Name: 4'-Aminoazobenzene-4-sulfonic acid, sodium salt

2. Chemical Structure:



3. Synonyms: Benzenesulfonic acid, 4 [(4 aminophenyl)azo]-, monosodium
p-[(p-Aminophenyl)azo]benzenesulfonic acid, sodium salt
4'-Amino-4-sulfoazobenzene, sodium salt
4'-Aminoazobenzene-4-sodium sulfonate
[4-Anilinoazo]benzene-4-sulfonic acid, sodium salt
(4-[4'-Sulfophenylazo]aniline), sodium salt
C.I. 13011

4. Chemical Abstracts Service (CAS) Number: 2491-71-6

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	solid
Molecular Weight:	299.30
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	---
Stability:	---

7. Production

Data available from the U.S. EPA (1980) regarding producers of 4'-aminoazobenzene-4-sulfonic acid, sodium salt and production volumes are presented in Table 6.

Table 6. Producers of 4'-Aminoazobenzene-4-sulfonic acid, sodium salt and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Toms River Chemical Co. Toms River, NJ	Manufacturer/ Produced Site Limited	confidential
The Harshaw Lowell, NC	Manufacturer/ Produced Site Limited	0-1000 lb
E.I. du Pont deNemours and Co. Deepwater, NJ	Manufacturer	0.1-1.0 million lb
Aceto Chemical Co. Flushing, NY	Importer	10-100 thousand lb
Montedison USA New York, NY	Importer	confidential
GAF Corp. New York, NY	Importer	10-100 thousand lb

Reported import in recent years is as follows (USITC, 1980a, 1979a, 1978a, 1977a):

Year	Import in (thousands of pounds)
1979	98.526
1978	127.501
1977	36.987
1976	201.822

8. Use

4'-Aminoazobenzene-4-sulfonic acid, sodium salt is used in dyestuff production.

9. Manufacturers and Distributors

Producers listed by the U.S. EPA (1980) are presented in Table 6.

SRI International (1980) and USITC (1980) do not have listings for aminoazobenzene sulfonic acid, sodium salt.

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources--USA, 1980):

Aceto Chem.	ICN/K and K
Orlex Chem.	Pfaltz and Bauer
	TransWorld Chem.

10. Manufacturing Processes

4'-Aminoazobenzene-4-sulfonic acid is made by sulfonating aminoazobenzene (Hawley, 1977). The sodium salt may be prepared by simple neutralization with a sodium compound.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 4'-aminoazobenzene-4-sulfonic acid, sodium salt.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4'-aminoazobenzene-4-sulfonic acid, sodium salt were not found in the literature searched.

14. Biological Effects

No information was found in the literature searched regarding the biological effects of the sodium salt of 4'-aminoazobenzene-4-sulfonic acid.

15. Ongoing Studies

No current toxicological or environmental studies of 4'-aminoazobenzene-4-sulfonic acid, sodium salt were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for the sodium salt of 4'-aminoazobenzene-4-sulfonic acid were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

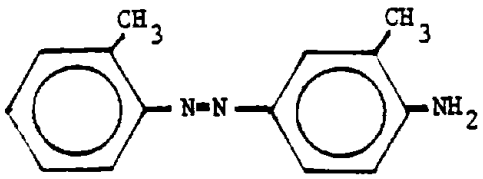
18. Other Pertinent Data

No other information that would aid in the assessment of the sodium salt of 4'-aminoazobenzene-4-sulfonic acid as an occupational hazard was found in the literature searched.

G. ORTHO-AMINOAZOTOLUENE

1. Chemical Name: ortho-Aminoazotoluene

2. Chemical Structure:



3. Synonyms: o-AAT
5-(o-tolylazo)-2-aminotoluene
o-Aminoazotoluol
2-Amino-5-azotoluene
4-Amino-2'3-dimethylazobenzene
Benzenamine, 2-methyl-4-[(2-methylphenyl)azo]-
Butter Yellow
C.I. 11160
C.I. Solvent Yellow 3
2',3-Dimethyl-4-aminoazobenzene
Fast Oil Yellow
Fast Yellow AT
Fat Yellow B
Garnet GBC salt
Hidaco Oil Yellow
Oil Yellow
Organol Yellow 2T
Somalia Yellow R
Sudan Yellow RRA
Toluazotoluidine
o-Toluidine, 4-(o-tolylazo)
Waxakol Yellow NL

4. Chemical Abstract Service (CAS) Number: 97-56-3

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

XY8800000

6. Chemical and Physical Properties:

Description:	golden crystals to reddish-brown crystals
Molecular Weight:	225.32
Boiling Point:	---
Melting Point:	101-102°C
Vapor Pressure	---
Solubility:	practically insoluble in water; soluble in ethanol, ether, chloroform, acetone, cellosolve, and toluene

Specific Gravity: ---

Stability: ---

7. Production

Data available from the U.S. EPA (1980) regarding producers of o-aminoazotoluene and production volumes are presented in Table 7.

Production in the most recent years is as follows (USITC, 1976, 1975):

Year	Production (in thousands of pounds)
1974	264
1973	453

8. Use

o-Aminoazotoluene is used to color oils, fats, and waxes (IARC, 1975b) and as a dyestuff intermediate (Snell and Snell, 1962). Other uses cited include applications in medicine (Hawley, 1977) and as an intermediate to produce toluene-2,5-diamine (Thirtle, 1968).

9. Manufacturers and Distributors

SRI International (1980) lists American Cyanamid Co. (Bound Brook, NJ) as a manufacturer; USITC (1980a) lists Passaic Color and Chemical as a manufacturer of Solvent Yellow 3. Producers listed by the U.S. EPA (1980) are shown in Table 7.

In addition to the manufacturers, the distributors include (Chem Sources--USA, 1980):

Atlantic Chem.
Chemical Dynamics Corp.
MCB Reagents
Pfaltz and Bauer
Pfister Chem. (listed as a producer)
Reliable Chem.
TransWorld Chem.

Table 7. Producers of o-Aminoazotoluene and Production Ranges (U.S. EPA, 1980)

Producers	Type of Production	1977 Production Range
Passaic Color and Chemical Co. Patterson, NJ	Manufacturer Produced Site Limited	10-100 thousand lb
Eastman Kodak Rochester, NY	Manufacturer	zero
Alliance Chemical Inc. Newark, NJ	Manufacturer	10-100 thousand lb
Hilton-Davis Chemical Co. Cincinnati, OH	Manufacturer	zero
GAF Corp. Rensselaer, NY	Manufacturer Produced Site Limited	zero
Blackman-Ulmer Chemical Div. Augusta, GA	Manufacturer	10-100 thousand lb.
E.I. du Pont de Nemours and Co. Deepwater, NJ	Manufacturer	zero
Crescent Chemical Co. Hauppauge, NY	Importer Small Manufacturer	confidential
Mobay Chemical Corp. Pittsburgh, PA	Importer	confidential

10. Manufacturing Processes

o-Aminoazotoluene is prepared by solution of ortho-toluidine in cold hydrochloric acid and treatment with sodium nitrite solution (Snell and Snell, 1962; Hawley, 1977). The manufacturing operations will be similar to those for 4-aminoazobenzene (see profile on 4-aminoazobenzene for this description).

11. Impurities or Additives

The manufacture of o-aminoazotoluene does not conform to rigid chemical specifications and its composition varies in order to meet customer shade and intensity requirements (IARC, 1975b).

12. Occupational Exposures

The National Occupational Hazard Survey indicates that 3811 workers are potentially exposed to o-aminoazotoluene.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to o-aminoazotoluene were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

Little information is available on the acute toxic effects of o-aminoazotoluene except for the range finding studies of Andervont (1950). These studies were designed to determine the maximum tolerated dose of ortho-aminoazotoluene in mice for experiments in chemical carcinogenesis. A summary of these studies is presented in Table 8.

(2) Subchronic Exposures

No information was found in the literature searched.

Table 8. Acute Toxicity of o-Aminoazotoluene in Mice (Andervont, 1950)

Strain	Route[a]	dose (mg/mouse)	Observation
C	gavage	40 mg	all animals died within 2 days
C	gavage	30 mg	all animals died within 2 days
C	gavage	20 mg	all animals died within 1 week
C	gavage	10 mg	all animals survived
C	gavage	10 mg, 3 times in 1 week	1 of 3 males died
C	gavage	10 mg, 4 times in 1 week	1 of 4 females died
A	gavage	20 mg	all animals died within 3 days (females)
A	gavage	10 mg	all animals survived (females)
A	gavage	10 mg, 3 times in 1 week	3 of 4 females died
A	gavage	10 mg, 5 times in 4 weeks	all animals survived (females)
C	subcutaneous	60 mg	all animals died within 2 days
C	subcutaneous	40 mg	all animals died within 1 week
C	subcutaneous	30 mg	3 of 4 females, and all males died within 1 month
C	subcutaneous	20 mg	all animals survived
C	subcutaneous	10 mg	all animals survived
C	subcutaneous	10 mg, 3 times in 1 week	all males survived
C	subcutaneous	10 mg, 4 times in 1 week	all females survived
A	subcutaneous	10 mg	all animals survived (females)
A	subcutaneous	10 mg, 5 times in 4 weeks	all animals survived (females)

[a]The ortho-aminoazotoluene was disolved in olive oil (Andervont, 1950).

(3) Chronic Exposures

Liver necrosis and regenerative changes were observed in rats fed a diet containing 0.06% o-aminoazotoluene for 400 to 435 days (Crabtree, 1949).

(4) Carcinogenicity

o-Aminoazotoluene has been used for many years in the study of chemical carcinogenesis. A survey of the animal species in which o-aminoazotoluene has produced tumors is presented in Table 9. Tumors have been observed in a variety of organs including the bladder, cecum, mammary gland, and lungs, however, liver has been the most extensively studied. Although these studies were designed to investigate the mechanism of chemical carcinogenesis and not to determine the carcinogenicity of ortho-aminoazotoluene, the observed large increases in tumor incidence is good evidence that o-aminoazotoluene is an animal carcinogen and potentially a human carcinogen.

Studies in mice have indicated that o-aminoaztoluene may be more carcinogenic in females than in males. Andervont and Gray (1942) administered 10 mg of o-aminoazotoluene each month for 10 months to mice of strains A, C, and C57 Black by subcutaneous injection. In each case the incidence of hepatic chance was 100% in the females, whereas an incidence of 45, 8, and 9% occurred respectively in the male mice of strains A, C, and C57 Black. Andervont et al. (1944) obtained similar results with strain C mice following ingestion of a diet containing 0.03% o-aminoazotoluene for 223 days. In this study, 13 of 19 females developed hepatomas, while only 1 of 17 males had a tumor. Shelton (1955) suggested that this sex-related difference may be related to sex hormones since female strain A mice treated with stilbestrol had a shorter latency time for the induction of o-aminoazotoluene induced liver tumors. Also, Lawson (1968) demonstrated that radioactively labelled o-aminoazotoluene

Table 9. Carcinogenicity of ortho-Aminoazotoluene

Species	Strain	Sex[a]	Number of Animals[c]	Route of Administration	Dose	Duration of Treatment or Observation	Tumor Incidences[c]	Tumor Incidences in Control	Tumor Type or Tumor Rate	Reference
Rats	52	M+F (15 each)	30	diet	0.06% (w/w)	400-435 days	8/27	0/24	liver[b]	Crabtree, 1949
Rats	Sprague-Dawley	F	20	gavage (in sesame oil)	150 mg/rat (single dose)	180 days	0/20	NR	mammary gland[b]	Griswold et al., 1966
Mice	Simpson	M+F (20 each)	40	diet	0.06% (w/w)	400-435 days	10/12	0/18	liver[b]	Crabtree, 1949
Mice	C	M+F (12 each)	24	diet	0.06% (w/w)[d]	183 days over a 218 day period	18/24 21/24 13/24	NR NR NR	hepatoma pulmonary hemangio-endothelioma	Andervont et al., 1944
Mice	C	M (17) F (19)	36	diet	0.03% (w/w)	223 days	14/36 26/36 9/36	NR NR NR	hepatoma pulmonary hemangio-endothelioma	Andervant et al., 1944
Mice	A	F	9[f]	diet	0.05% (w/w)	30 days, observed for 90 days	44%	0/20	liver tumors[b]	Shelton, 1955
			11[f]			60 days, observed for 60 days	82%			
			10[f]			90 days, observed for 30 days	80%			
			12[f]			120 days	83%			
			24			88 days, observed for 27 days	29%			
			12[f]			70 days, observed for 21 days	100%			
Mice	A	M	14	11 subcutaneous injection	10 mg/injection	≈300 days 3 mice killed every 3 months	11/14	NR	pulmonary tumors[b] pulmonary tumors[b]	Andervont, 1959
	I		20	11 subcutaneous injection	10 mg/injection	365 days	2/18	NR	pulmonary tumors[b]	
	C_3H		10				0/9	NR	pulmonary tumors[b]	
	Y		15				1/12	NR	pulmonary tumors[b]	
	C		14				12/14	NR	pulmonary tumors[b]	
	A		10				7/10	NR	pulmonary tumors[b]	

Table 9. Carcinogenicity of ortho-Aminoazotoluene (Cont.)

Species	Strain	Sex[a]	Number of Animals[c]	Route of Administration	Dose	Duration of Treatment or Observation	Tumor Incidences[d]	Tumor Incidences in Control	Tumor Type or Tumor Rate	Reference
Mice	C57	F	30	subcutaneous injection	10 mg	3 injections in 2 months; at	43%	NR	subcutaneous	Law, 1941
	Dba	F	30	subcutaneous injection	10 mg	4 months a 5 mg pellet was implanted	0%	NR	fibrosarcoma	
Mice	C	NR	10	subcutaneous injection	2.5 mg/wk	11 months	8/10	NR	subcutaneous sarcoma	Turner and Milliken, 1942
Mice	C	M (38) F (50)	88	subcutaneous injection	10 mg/mouse	7 injections in 8 months	40/88	NR	hemangio-endothelioma[b]	Andervont, 1950
Mice	A/Ha	M	60	subcutaneous implant	10 mg/mouse	8 implants in 8 months	19/60	NR	andenocarcinoma of the cecum	Kaledin et al., 1978
Mice	CBA	M (47) F (47)	94	gavage in oil	12 mg/mouse total	observed until death	84%	40%	liver tumors	Kolasnichanko et al., 1978
Mice	C_{57}xIF	M,F	52	bladder implant	2 mg/mouse	40 weeks	17.3%	4.5%	bladder tumors[b]	Claysen et al., 1968
Hamsters	Syrian Yellow	M (25) F (15)	40	diet	1000 ppm	49 weeks	80% 79%	0 1	bladder tumors liver tumors	Tomatis, 1981
Dog		M,F		diet	5 mg/kg/day	30-62 months	2/4 2/4	NR NR	bladder tumors liver tumors	Nelson and Woodward, 1953

[a]The numbers in parentheses indicate the number of animals of each sex.

[b]This was the only organ examined.

[c]Number of animals at the start of the study.

[d]Tumor incidence represents number of tumor bearing animals over the number of animals examined.

[e]The exact dose was unclear in the paper.

[f]The animals were simultaneously treated with stilbestrol.

covalently bound more extensively to macromolecules of the liver of female mice than to the liver of male C57 mice. At least in mice, o-aminoazotoluene is a more potent carcinogen in females.

Gel'shtein (1961) and Golub' et al. (1975) have observed an increase in tumors in the offspring of mice treated with ortho-aminoazotoluene. Golub' et al. (1975) gave BALB/c mice 4 to 5 subcutaneous injections (24 mg/0.2 ml of sunflower oil) during the last week of pregnancy. During the life span of the progency, there was an increase in the incidence of total tumors to 58.5% as compared to an incidence of 6% for the control. Gel'shtein (1961) observed similar results after treating C3HA mice with o-aminoazotoluene by skin painting. The increased incidence of tumors in the first generation was observed even when the treatment of the dams was ceased prior to giving birth. The authors noted that exposure of the pups may have occurred during nursing, however, studies using embyronic organic culture indicates that o-aminoazotoluene can cross the placenta. Shabad et al. (1972) and Popova (1977) administered ortho-aminoaztoluene to mice during the last week of pregnancy, and the embryos from these treated animals were used to obtain liver and kidney for the preparation of organ cultures. In cultures prepared from embryos of exposed dams, an increase in tissue survival time was observed alone with some hyperplastic growth. It was concluded that o-aminoazotoluene had crossed the placenta and altered the growth potential of the embryonic tissue.

(5) Mutagenicity

ortho-Aminoazotoluene has been tested in a variety of mutagenicity assays, and the results are presented in Table 10. The most extensively used test system, the Ames assay using Salmonella typhimurium, has demonstrated that o-aminoazotoluene was mutagenic to strains TA100, TA98, and

Table 10. *In Vitro* Mutagenicity and Chromosomal Aberration Assays of *o*-Aminoazotoluene

Type of Assay	Organism	Strain	With Mammalian Metabolic Activation	Dose	Results[a]	Reference
Reverse mutation	*S. typhimurium*	TA100	yes	20 µg/plate	+	McCann *et al.*, 1975
		TA98	yes	20 µg/plate	+	
		TA1538	yes	20 µg/plate	+	
Reverse mutation	*S. typhimurium*	TA1535	yes	25 µg/plate	-	Simmon, 1979a
		TA1536	yes	25 µg/plate	-	
		TA1537	yes	25 µg/plate	-	
		TA1538	yes	25 µg/plate	+	
		TA98	yes	25 µg/plate	+	
		TA100	yes	25 µg/plate	+	
Reverse mutation	*S. typhimurium*	TA98	yes	50 µg/plate	+	Kawajiri *et al.*, 1980
Reverse mutation	*S. typhimurium*	TA100	yes[b]	50 µg/plate	+	Müller *et al.*, 1980
Reverse mutation	*S. typhimurium*	TA1535	yes and no	250 µg/plate	-	Rosenkranz and Poirier, 1979
		TA1538	yes	50 µg/plate	+	
		TA1538	no	250 µg/plate	-	
Reverse mutation (liquid incubation)	*S. typhimurium*	TA98	yes	32-322 µg/ml	+	Yahagi *et al.*, 1975
		TA98	no	32-322 µg/ml	-	
		TA100	yes	32-322 µg/ml	+	
		TA100	no	32-322 µg/ml	-	
DNA-modifying activity	*E. coli*	pol A$^-$	yes	25 µg/ml	+	Rosenkranz and Poirier, 1979
DNA-modifying activity (spot test)	*E. coli*	rec$^-$	yes and no	1 µg/well	+	Ichenotsubo *et al.*, 1977

Table 10. *In Vitro* Mutagenicity and Chromosomal Aberration Assays of o-Aminoazotoluene (Cont'd)

Type of Assay	Organism	Strain	With Mammalian Metabolic Activation	Dose	Results[a]	Reference
Forward mutation	*E. coli*	B/n	no	210 µg/ml	+	Scherr *et al.*, 1954
Forward mutation	*Neurospora*	NA	no	0.1%	+	Barratt and Yatum 1958
Mitotic, recombination	*S. cerevisiae*	D3	yes and no	10 µg/ml	-	Simmons, 1979b
Host-mediated	*S. typhimurium*	TA1530 TA1538	mouse mouse	125 mg/kg 1250 mg/kg	-- --	Simmons *et al.*, 1979
Host-mediated	*S. cerevisiae*	D3	mouse	1250 mg/kg	--	Simmons *et al.*, 1979
Chromosomal aberration	Chinese hamster cells	--	yes	0.03 mg/ml	--	Matsuoka *et al.*, 1979
Chromosomal aberration	Chinese hamster cells	--	no	0.015 mg/ml	--	Ishadate and and Odashima, 1977

[a] - = negative response; + = positive response

[b] the S-9 which gave positive results was prepared from Aroclor pretreated mice, rats, Chinese hamsters, mini pig, and Rhesus monkey. S-9 prepared from baboons gave only a slightly positive response and the S-9 from dogs gave negative results.

TA1538 in the presence of a liver metabolic activation system. No mutagenic response was observed with strains TA1535, TA1536, and TA1537, and there was no positive response in the absence of a metabolic activation system. Muller et al. (1980) demonstrated that microsomal enzymes derived from the livers of a number of species (mice, rats, Chinese hamsters, dogs, mini pigs, rhesus monkeys, and baboons) were capable of providing metabolic activation for o-aminoazotoluene. There was some species variation, however, since microsomes from baboons produced only a slight increase in the number of revertant colonies, and preparations from dog liver were ineffective in activating the compound. o-Aminoazotoluene was also positive in growth inhibition tests with pol A^- and rec^- strains of Escherichia coli (Table 10).

Other in vitro assays using yeast and mammalian cells in culture to detect genotoxicity gave generally negative results with o-aminoazotoluene (Table 10). The only study that gave slightly positive results was an early investigation by Barratt and Tatum (1958). In this study the yeast Neurospora was exposed to o-aminoazotluene at 0.1%, and following exposure evaluated for both biochemical (nutritional) mutants and total mutants (both biochemical and morphological mutants). The treatment produced no increase in biochemical mutants, but did show an increase of 1.6 times in total mutants. The overall negative results in these assays and in the the host-mediated assays (Table 10) may be the result of differences in the end-points or the activation system.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

The only reproductive studies have been concerned with the carcinogenicity of o-aminoazotoluene and are discussed under Section 4.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of o-aminoazotoluene were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for o-aminoazotoluene were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

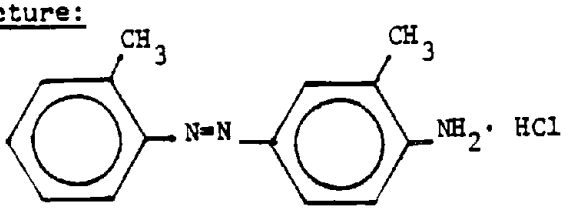
18. Other Pertinent Data

No other information that would aid in the assessment of o-aminoazotoluene as an occupational hazard was found in the literature searched.

H. ORTHO-AMINOAZOTOLUENE HYDROCHLORIDE

1. Chemical Name: ortho-Aminoazotoluene hydrochloride

2. Chemical Structure:



3. Synonyms: Benzeneamine,2-methyl-4-[(2methylphenyl)azo]-, hydrochloride
C.I. 37210
C.I. Solvent Yellow 3, monohydrochloride
Fast Garnet GBC
4-(o-Tolylazo)-o-toluidine hydrochloride

4. Chemical Abstract Service (CAS) Number: 2298-13-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	solid
Molecular Weight:	261.78
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	---
Specific Gravity:	---
Stability:	---

7. Production

Data available from the U.S. EPA (1980) regarding producers of o-aminoazotoluene hydrochloride and production volumes are presented in Table 11.

8. Use

o-Aminoazotoluene hydrochloride is used as a dye and in dyestuff production.

Table 11. Producers of o-Aminoazotoluene Hydrochloride and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Alliance Chemical Inc. Newark, NJ	Manufacturer	none
Atlantic Chemical Corp. Nutley, NJ	Manufacturer Produced Site Limited	10-100 thousand lb
Crescent Chemical Hauppauge, NY	Importer	confidential

9. Manufacturers and Distributors

Data available from the U.S. EPA (1980) regarding producers of o-aminoazotoluene hydrochloride and production volumes are presented in Table 11.

10. Manufacturing Processes

The commercial process was not available from the literature searched; however, the process is likely to be similar to the process used to produced o-aminoazotoluene (see o-aminoazotoluene profile).

11. Additives or Impurities

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to o-aminoazotoluene hydrochloride.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to o-aminoazotoluene hydrochlorde were not found in the literature searched.

14. Biological Effects

The only information found in the literature searched was a mutagenicity assay (Brown et al., 1978). The standard plate incorporation assay of Ames was used with Salmonella typhimurium strains TA1535, TA100, TA1537, TA1538, and TA98. o-Aminoazotoluene hydrochloride was tested at 100 µg/plate, both with and without a mammalian microsomal activating system prepared from the livers of Aroclor 1254 pretreated rats. No mutagenic activity was observed in any of the tester strains. With strain TA1538 in the presence of the activation system there was an increase in the number of revertant colonies,

however, this increase did not meet the criteria of exceeding twice the background number for a positive response.

15. Ongoing Studies

No current toxicological or environmental studies of o-aminoazotoluene hydrochloride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for o-aminoazotoluene hydrochloride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

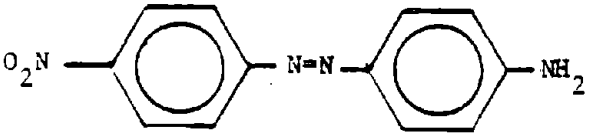
18. Other Pertinent Data

No other information that would aid in the assessment of o-aminoazotoluene hydrochloride as an occupational hazard was found in the literature searched.

I. C.I. DISPERSE ORANGE 3

1. Chemical Name: C.I. Disperse Orange 3

2. Chemical Structure:



3. Synonyms: Benzenamine, 4-[(4-nitrophenyl)azo]-
C.I. 11005
4'-Nitro-4-aminoazobenzene

4. Chemical Abstract Service (CAS) Number: 730-40-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	orange solid
Molecular Weight:	210.24
Boiling Point:	---
Melting Point:	210-212°C
Vapor Pressure:	---
Solubility:	soluble in ethanol, acetone, cellosolve, and toluene
Specific Gravity:	---
Stability:	---

7. Production

U.S. Production of C.I. Disperse Orange 3 in recent years is as follows (USITC, 1980b, 1979b, 1978b, 1977b):

Year	Production (in thousands of pounds)
1979	115
1978	47
1977	134
1976	106

Data available from the U.S. EPA (1980) regarding producers of C.I. Disperse Orange 3 and production volumes are presented in Table 12.

8. Use

C.I. Disperse Orange 3 is used in dyestuff.

9. Manufacturers and Distributors

C.I. Disperse Orange 3 is commercially manufactuered by (USITC, 1980b):

American Color and Chem.
Atlantic Chemical
Crompton and Knowles
Toms River Chemical

Other manufacturers cited by the U.S. EPA (1980) are listed in Table 12.

10. Manufacturing Processes

C.I. Disperse Orange 3 is synthesized by diazotising p-niotro-aniline into anilinomethanesulfonic acid, then removing the methane sulfonic acid group by hydrolysis with boiling aqueous caustic soda (The Colour Index, 1956).

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 1765 workers are potentially exposed to C.I. Disperse Orange 3.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to C.I. Disperse Orange 3 were not found in the literature searched.

14. Biological Effects

No information on the biological effects of C.I. Disperse Orange 3 was found in the literature searched.

Table 12. Producers of C.I. Disperse Orange 3 and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Fabricolor Mfg. Corp. Paterson, NJ	Manufacturer	none
Atlantic Chemical Co. Nutley, NJ	Manufacturer	10-100 thousand lb
Toms River Chemical Co. Toms River, NJ	Manufacturer	confidential
Sandoz Colors and Chem. East Hanover, NJ	Manufacturer	none
The Harshaw Lowell, NC	Manufacturer	10-100 thousand lb
GAF Corp. Rensselaer, NY	Manufacturer	1-10 thousand lb
BASF Wyandotte Parsippany, NJ	Importer	none
Montedison USA New York City, NY	Importer	under 1000 lb
Carey Industries Danbury, CT	Importer	none

15. Ongoing Studies

No current toxicological or environmental studies of C.I. Disperse Orange 3 were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for C.I. Disperse Orange 3 were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

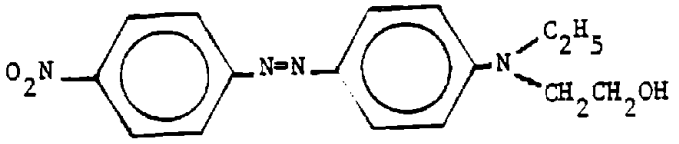
18. Other Pertinent Data

No other information that would aid in the assessment of C.I. Disperse Orange 3 as an occupational hazard was found in the literature searched.

J. C.I. DISPERSE RED 1

1. Chemical Name: C.I. Disperse Red 1

2. Chemical Structure:



3. Synonyms: CI 11110
Ethanol, 2-[ethyl[4-[(4-nitrophenyl)azo] phenyl] amino] -

4. Chemical Abstract Service (CAS) Number: 2872-52-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	red solid
Molecular Weight:	314.34
Boiling Point:	---
Melting Point:	160°C
Vapor Pressure:	---
Solubility:	soluble in acetone, ethanol, and benzene
Specific Gravity:	---
Stability:	---

7. Production

U.S. Production in recent years is as follows:

Year	Production (in thousands of pounds)
1979	526
1978	383
1977	345
1976	399

Data available from the U.S. EPA (1980) regarding producers of C.I. Disperse Red 1 and production volumes are presented in Table 13.

Table 13. Producers of C.I. Disperse Red 1 and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Tennessee Eastman Kingsport, TN	Manufacturer	under 1000 lb
Atlantic Chemical Co. Nutley, NJ	Manufacturer	10-100 thousand lb
Toms River Chemical Co. Toms River, NJ	Manufacturer	confidential
Sandoz Colors and Chem. East Hanover, NJ	Manufacturer	none
The Harshaw Lowell, NC	Manufacturer	10-100 thousand lb
GAF Corp. Rensselaer, NY	Manufacturer	1-10 thousand lb
E.I. du Pont de Nemours Deepwater, NJ	Manufacturer	10-100 thousand lb
Yorkshire Dyes Gastonia, NC	Importer	confidential
BASF Wyandotte Parsippany, NJ	Importer	none

8. Use

C.I. Disperse Red 1 is used in dyestuffs.

9. Manufacturers and Distributors

Commercial manufacturers include (USITC, 1980b):

American Color and Chem.	Crompton and Knowles
Atlantic Chem.	du Pont
BASF Wyandotte	Tennessee Eastman
	Toms River Chem.

10. Manufacturing Processes

C.I. Disperse Red 1 is synthesized by diazotising p-nitroaniline into 2(N-ethylanilino)ethanol (The Colour Index, 1965).

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 2637 workers are potentially exposed to C.I. Disperse Red 1.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to C.I. Disperse Red 1 were not found in the literature searched.

14. Biological Effects

No information on the biological effects of C.I. Disperse Red 1 was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of C.I. Disperse Red 1 were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for C.I. Disperse Red 1 were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

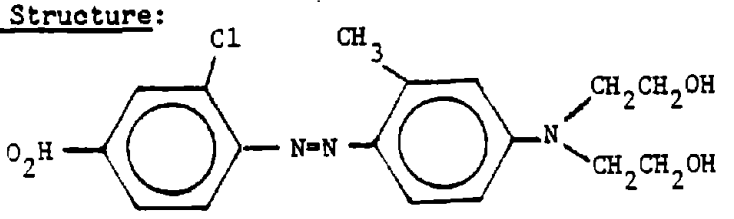
18. Other Pertinent Data

No other information that would aid in the assessment of C.I. Disperse Red 1 as an occupational hazard was found in the literature searched.

K. C.I. DISPERSE RED 5

1. Chemical Name: C.I. Disperse Red 5

2. Chemical Structure:



3. Synonyms: C.I. 11215
Ethanol, 2,2'-[[4-[(2-chloro-4-nitrophenyl)azo]-3-methylphenyl]iminio]bis-

4. Chemical Abstract Service (CAS) Number: 3769-57-1

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not Listed

6. Chemical and Physical Properties:

Description:	bluish-red solid
Molecular Weight:	315.34
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	very soluble in ethanol and cellosolve; soluble in acetone; slightly soluble in benzene and CCl_4
Specific Gravity:	---
Stability:	---

7. Production

U.S. production in recent years is as follows (USITC, 1979b, 1978b, 1977b):

Year	Production (in thousands of pounds)
1978	80
1977	67
1976	106

Data available from the U.S. EPA (1980) regarding producers of C.I. Disperse Red 5 and production volumes are presented in Table 14.

8. Use

C.I. Disperse Red 5 is used in dyestuffs.

9. Manufacturers and Distributors

Commercial manufacturers include (USITC, 1980b):

- American Color and Chemical
- Crompton and Knowles

See also Table 14.

10. Manufacturing Processes

C.I. Disperse Red 5 is synthesized by diazotising 2-chloro-4-nitroaniline into 2,2'-(m-tolylimino)diethanol (The Colour Index, 1956).

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 1925 workers are potentially exposed to C.I. Disperse Red 5.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to C.I. Disperse Red 5 were not found in the literature searched.

14. Biological Effects

No information on the biological effects of C.I. Disperse Red 5 was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of C.I. Disperse Red 5 were found.

Table 14. Producers of C.I. Disperse Red 5 and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
The Harshaw Lowell, NC	Manufacturer	10-100 thousand lb
GAF Corp. Rensselaer, NY	Manufacturer	none
Plant Site Noton File	Manufacturer	confidential
Instel Corp. New York City, NY	Importer	under 1000 lb
BASF Wyandotte Parsippany, NJ	Importer	none
Sandoz Color and Chem. East Hanover, NJ	Importer	none

16. Exposure Standards

No recommended or promulgated occupational exposure standards for C.I. Disperse Red 5 were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

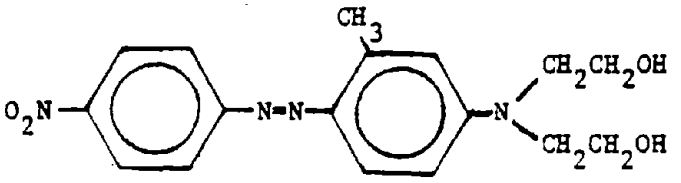
18. Other Pertinent Data

No other information that would aid in the assessment of C.I. Disperse Red 5 as an occupational hazard was found in the literature searched.

L. C.I. DISPERSE RED 17

1. Chemical Name: C.I. Disperse Red 17

2. Chemical Structure:



3. Synonyms: C.I. 11210
Ethanol, 2,2'-[[3-methyl-4-[(4-nitrophenyl)azo] phenyl] imino] bis-

4. Chemical Abstract Service (CAS) Number: 3179-89-3

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	red solid
Molecular Weight:	344.36
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	soluble in ethanol and acetone
Specific Gravity:	---
Stability:	---

7. Production

U.S. production in recent years is as follows (USITC, 1980b, 1979b, 1978b, 1977b):

Year	Production (in thousands of pounds)
1979	233
1978	170
1977	202
1976	358

In 1979, only 250 pounds were reported imported (USITC, 1980a).

Data available from the U.S. EPA (1980) regarding producers of C.I. Disperse Red 17 and production volumes are presented in Table 15.

8. Use

C.I. Disperse Red 17 is used in dyestuffs.

9. Manufacturers and Distributors

Commercial manufacturers include (USITC, 1980b):

American Color and Chemical
Atlantic Chemical
BASF Wyandotte
Crompton and Knowles
Tennessee Eastman
Toms River Chemical

10. Manufacturing Processes

C.I. Disperse Red 17 is synthesized by diazotising p-nitroaniline into 2,2'-(m-tolylimino)diethanol (The Colour Index, 1956).

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 1440 workers are potentially exposed to C.I. Disperse Red 17.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to C.I. Disperse Red 17 were not found in the literature searched.

14. Biological Effects

No information on the biological effects of C.I. Disperse Red 17 was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of C.I. Disperse Red 17 were found.

Table 15. Producers of C.I. Disperse Orange 3 and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Fabricolor Mfg. Corp. Paterson, NJ	Manufacturer	none
Tennessee Eastman Kingsport, TN	Manufacturer	1-10 thousand lb
Atlantic Chemical Co. Nutley, NJ	Manufacturer	10-100 thousand lb
Toms River Chemical Co. Toms River, NJ	Manufacturer	confidential
The Harshaw Lowell, NC	Manufacturer	under 1000 lb
GAF Corp. Rensselaer, NY	Manufacturer	1-10 thousand lb
BASF Wyandotte Parsippany, NJ	Importer	none
Montedison USA New York City, NY	Importer	under 1000 lb
Carey Industries Danbury, CT	Importer	none

16. Exposure Standards

No recommended or promulgated occupational exposure standards for C.I. Disperse Red 17 were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

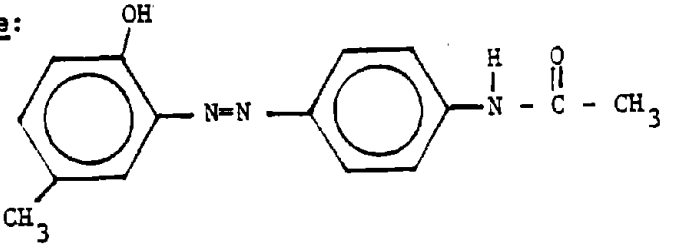
18. Other Pertinent Data

No other information that would aid in the assessment of C.I. Disperse Red 17 as an occupational hazard was found in the literature searched.

M. C.I. DISPERSE YELLOW 3

1. Chemical Name: C.I. Disperse Yellow 3

2. Chemical Structure:



3. Synonyms: A list of synonyms are presented in Table 16.

4. Chemical Abstract Service (CAS) Number: 2832-40-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

AC3650000

6. Chemical and Physical Properties:

Description:	solid
Molecular Weight:	269.33
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility:	soluble in acetone, ethanol and benzene
Specific Gravity:	---
Stability:	---

7. Production

U.S. production of Disperse Yellow 3 in recent years is as follows (USITC, 1980b, 1977b, 1977c):

Year	Production (in millions of pounds)
1979	3.218
1978	---
1977	---
1976	1.161
1975	3.125

Table 16. Synonyms for C.I. Disperse Yellow 3

Acetamine Yellow CG
Acetate Fast Yellow G
Acetoquinone Light Yellow
Acetoquinone Light Yellow 4JLZ
N-Acetyl-2'-hydroxy-5'-methyl-aminoazobenzene
Altco Sperse Fast Yellow GFN New
Amacel Yellow G
Artisil Yellow G
Artisil Yellow 2GN
Artisil Direct Yellow G
Calcosyn Yellow GC
Calcosyn Yellow GCN
Celliton Discharge Yellow GL
Celliton Fast Yellow G
Celliton Fast Yellow GA
Celliton Fast Yellow GA-CF
Celliton Yellow G
Celutate Yellow GH
C.I. 11855
C.I. 3/11855
Cibacete Yellow GBA
Cibacet Yellow 2GC
Cibacet Yellow GBA
C.I. Disperse Yellow 3
Cilla Fast Yellow G
Diacelliton Fast Yellow G
Disperse Yellow 3
Disperse Yellow G
Disperse Yellow Z
Disperse Fast Yellow G
Dispersol Printing Yellow G
Durgacet Yellow G
Durosperse Yellow G
Estone Yellow GN
Esteroquinone Light Yellow 4JL
Fenacet Fast Yellow G
Fenacet Yellow G
Genacron Yellow G
Hispacet Fast Yellow G
Hisperse Yellow G
N-(4[(2-Hydroxy-5-methylphenyl)azo]phenyl]acetamide
4'-((6-Hydroxy-m-tolylazo)acetanilide
Interchem Acetate Yellow G
Interchem Hisperse Yellow GH
Intraperse Yellow GBA
Kayalon Fast Yellow G
KCA Acetate Fast Yellow G
Microsetile Yellow GR
Miketon Fast Yellow G
Nacelean Fast Yellow CG
NCI-C53781 Novalon Yellow 2GN
Nylogquinone Light Yellow 4JL
Nyloquinone Yellow 4J
Ostacet Yellow P2G
Palacet Yellow GN
Palanil Yellow G
Pamacel Yellow G-3
Perliton Yellow G
Reliton Yellow C
Safaritone Yellow G
Samaron Yellow PA3
Serinyl Hosiery Yellow GD
Serisol Fast Yellow GD
Setacyl Yellow G
Setacyl Yellow 2GN
Setacyl Yellow P-2GL
Silotras Yellow TSG
Supracet Fast Yellow G
Synten Yellow 2G
Synton Yellow 2G
Terasil Yellow GBA
Extra Terasil Yellow 2GC
Tertranese Yellow N-2GL
Tuladisperse Fast Yellow 2G
Vonteryl Yellow G
Vonteryl Yellow R
Yellow Reliton G
Yellow Z

Import in recent years is reported as follows (USITC, 1980a, 1979a, 1978a, 1977a).

Year	Import (in thousands of pounds)
1979	24.631
1978	144.842
1977	1.984
1976	1.551

Data available from the U.S. EPA (1980) regarding producers of C.I. Disperse Yellow 3 and production volumes are presented in Table 17.

8. Use

C.I. Disperse Yellow 3 is reportedly used for dyeing textiles, sheepskins and furs, for coloring polymethyl methacrylate and nylon, and in the surface-dyeing of cellulose acetate (IARC, 1975c).

9. Manufacturers and Distributors

Disperse Yellow 3 is manufactured commercially by (USITC, 1980b):

American Color and Chemical Corp.
Crompton and Knowles Corp.
du Pont
Toms River Chemical Corp.

Other manufacturers are cited by the U.S. EPA, 1980 (see Table 17).

10. Manufacturing Processes

C.I. Disperse Yellow 3 has been prepared by coupling diazotised 4-acetamidoaniline with p-cresol, but it is not known whether this method is used for commercial production (IARC, 1975c).

11. Impurities or Additives

According to U.S. industrial sources, C.I. Disperse Yellow 3 is not used in foods, drugs and cosmetics; thus, its manufacture and testing do not conform to rigid chemical specifications, and its composition varies in order to meet customer shade and intensity requirements (IARC, 1975c).

Table 17. Producers of C.I. Disperse Yellow 3 and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Fabricolor Mfg. Corp. Paterson, NJ	Manufacturer	none
du Pont Puerto Rico Manati, PR	Manufacturer	0.1-1.0 million lb
Mobay Chemical Corp. Bayonne, NJ	Manufacturer	confidential
Atlantic Chemical Co. Nutley, NJ	Manufacturer	confidential
Toms River Chemical Co. Toms River, NJ	Manufacturer	confidential
Sandoz Colors and Chem. East Hanover, NJ	Manufacturer	none
The Harshaw Lowell, NC	Manufacturer	0.1-1.0 million lb
GAF Corp. Rensselaer, NY	Manufacturer	10-100 thousand lb
E.I. du Pont de Nemours Deepwater, NJ	Manufacturer	none
Intsel Corp. New York City, NY	Importer	under 1000 lb
Ugine Kuhlmann of America Paramus, NJ	Importer	confidential
Binney and Smith, Inc. Easton, PA	Importer	under 1000 lb
Yorkshire Dyes Inc. Gaston, NC	Importer	confidential

Table 17. Producers of C.I. Disperse Yellow 3 and Production Ranges (U.S. EPA, 1980) (Cont'd)

Producer	Type of Production	1977 Production Range
BASF Wyandotte Parsippany, NJ	Importer	none
Montedison USA New York City, NY	Importer	under 1000 lb
Carey Industries Danbury, CT	Importer	none
ICI Americas Wilmington, DE	Importer	confidential

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 3929 workers are potentially exposed to C.I. Disperse Yellow 3.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to C.I. Disperse Yellow 3 were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

No information was found in the literature searched.

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

The potential for C.I. Disperse Yellow 3 to be a carcinogen was reviewed by IARC (1975). It was concluded that the data from a single study by Boyland et al. (1964) was insufficient to determine whether this compound was tumorogenic. Boyland et al., (1964) implanted cholesterol pellets containing C.I. Disperse Yellow 3 into the bladders of stock bred mice, and examined the animals that survived for 25 weeks for bladder tumors. In the 25 mice that survived, there was 1 papilloma and 6 carcinomas of the bladder for a total tumor incidence of 33%. The total tumor incidence in control mice was 12%, however, there was a discrepancy in the nomenclature used to describe the test compound. The compound was referred to as both Celliton Yellow, a trade name for C.I. Disperse Yellow 3, and as 4-acetamino-2'-hydroxy-6'-methylazobenzene. In C.I. Disperse Yellow 3 the methyl group is in the 5'

position and not the 6'. It cannot be determined with certainty whether C.I. Disperse Yellow 3 was used in this study.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Dobkevitch and Baer (1947) tested 8 human subjects affected with stocking dermatitis for allergic sensitivity to C.I. Disperse Yellow 3. Of the 8 subjects, 6 had positive patch tests, 1 a possible positive test, and 1 a negative test. It was concluded that C.I. Disperse Yellow 3 could produce allergic contact dermatitis.

Foussereau et al. (1972) reported on 10 similar cases of allergic eczema produced by nylon stockings. In 8 of the patients that were tested a clearly allergic reaction was elicited with Disperse Yellow 3.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

C.I. Disperse Yellow 3 is undergoing a carcinogenicity bioassay in a feeding study employing both rats and mice (NTP, 1981).

16. Exposure Standards

No recommended or promulgated occupational standards for C.I. Disperse Yellow 3 were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

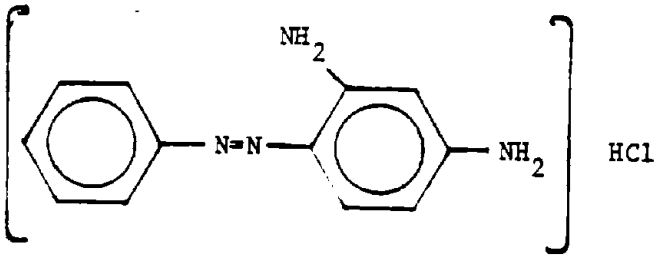
18. Other Pertinent Data

No other information that would aid in the assessment of C.I. Disperse Yellow 3 as an occupational hazard was found in the literature searched.

N. CHRYSOIDINE

1. Chemical Name: Chrysoidine

2. Chemical Structure:



3. Synonyms: Synonyms for chrysoidine are presented in Table 18.

4. Chemical Abstract Service (CAS) Number: 532-82-1

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

ST3380000

6. Chemical and Physical Properties:

Description:	Reddish-brown crystals or large black shiny crystals with a green luster
Molecular Weight:	248.71
Boiling Point:	---
Melting Point:	118-118.5°C
Vapor Pressure:	---
Solubility:	At 15°C: in water, 5.5%; in ethanol, 4.75%; in cellosolve, 6.0%; in ethylene glycol, 9.5%; in xylene, 0.005%; slightly soluble in acetone; practically insoluble in benzene
Specific Gravity:	---
Stability:	---

7. Production

U.S. production of chrysoidine in recent years is as follows (USITC, 1980b, 1979b, 1978b, 1977b):

Year	Production (in millions of pounds)
1979	0.605
1978	0.614
1977	0.486
1976	0.488

Table 18. Synonyms for Chrysoidine

Astra Chrysoidine R
2-Amino-4-aminoazobenzene hydrochloride
Brasilazina Orange Y
Brilliant Oil Orange Y Base
Calcozine Chrysoidine Y
Calcozine Orange YS
Chrysoidin
Chrysoidine
Chrysoidine A
Chrysoidine B
Chrysoidine C Crystals
Chyrsoidine Crystals
Chrysoidine G
Chrysoidine GN
Chrysoidine GS
Chrysoidine HR
Chrysoidine (II)
Chrysoidine J
Chrysoidine M
Chrysoidine Orange
Chrysoidine PRL
Chrysoidine PRR
Chrysoidine SL
Chrysoidine Special (Biological stain and indicator)
Chrysoidine SS
Chrysodidine Y
Chrysodidine Y Base New
Chrysoidine Y Crystals
Chrysoidine Y EX
Chrysoidine YGH
Chrysoidine YL
Chrysodidine YN
Chrysodidine Y Special
Chrysoidin FB
Chrysoidin Y
Chrysoidin YN
C.I. 11270
C.I. Basic Orange 2
C.I. Basic Orange 3
C.I. Basic Orange 2 Monohydrochloride
C.I. Solvent Orange 3
2,4-Diaminoazobenzene hydrochloride
Diazocard Chrysoidine G
Elcozine Chrysoidine Y
Leather Orange Hr
Nippon Kagaku Chrysoidine
4-(Phenylazo)-1,3-benzenediamine monohydrochloride
4-Phenylazo-m-phenylenediamine hydrochloride
4-(Phenylzao)-m-phenylendiamine monohydrochloride
m-Phenylenediamine,4-(phenylazo)-, hydrochloride
Pure Chrysoidine YBH
Pure Chrysoidine YD
Pyracryl Orange Y
Sugal Chrysoidine
Tertophene Brown CG

Data available from the U.S. EPA (1980) regarding producers of chrysoidine and production volumes are presented in Table 19.

8. Use

Chrysodine is used as a colorant and orange dye for cotton and silk (Hawley, 1977) and for textiles, paper, leather, inks, wood, and biological stains (IARC, 1975d). Derivatives are used as antiseptics and as a disinfectant in the treatment of throat infections (IARC, 1975d).

9. Manufacturers and Distributors

Chrysoidine is commercially manufactured by (USITC, 1980b):

American Cyanamid
Atlantic Chemical Corp.
BASF Wyandotte
du Pont
Passaic Color and Chemical
Toms River Chemical

Distributors include Chem Soruces--USA, 1980):

Anachemia Chem.
Atomergic Chemetals
Chem Services
Gallard-Schlesinger
Lachat Chem.
MCB Reagents
Mide Chem.
Monomer-Polymer Dujac
Pfaltz and Bauer
Polysciences
TransWorld Chem.
Tridom Chem.

10. Manufacturing Processes

Chrysoidine can be synthesized by coupling diazotised aniline with meta-phenylenediamine, but it is not known whether this is the method used for commercial production (IARC, 1975d).

11. Impurities or Additives

According to U.S. industrial sources, since chrysoidine is not used in foods, drugs, or cosmetics, its manufacture and testing do not conform to rigid chemical specifications, and its composition varies in order to meet customer shade and intensity requirements (IARC, 1975d).

Table 19. Producers of Chrysoidine and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Passaic Color and Chemical Co. Patterson, NJ	Manufacturer Produced Site Limited	10-100 thousand lb
Atlantic Chemical Co. Nutley, NJ	Manufacturer	10-100 thousand lb
Toms River Chemical Co. Toms River, NJ	Manufacturer	confidential
E.I. du Pont de Nemours Deepwater, NJ	Manufacturer Produced Site Limited	10-100 thousand lb
Ugine Kuhlmann of America Paramus, NJ	Importer	confidential
L and R Dyestuff Corp. Parsippany, NJ	Importer	none
BASF Wyandotte Parsippany, NJ	Importer	none
American Hoechst Bridgewater, NJ	Importer	none

12. Occupational Exposures

The National Occupational Hazard Survey indicates that 3312 workers are potentially exposed to chrysoidine.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to chrysoidine were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

No information was found in the literature searched.

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

The carcinogenicity studies on chrysoidine have been reviewed by the International Agency for Research on Cancer (IARC, 1975), and it was concluded that chrysoidine was carcinogenic in mice. Albert (1956) maintained 120 C57BL mice (60 animals of each sex) for 13 months on a diet containing 2000 mg chrysoidine/kg. The mice were observed until natural death. The incidence of liver tumors was 75/104 in the treated animals relative to 3/104 in the controls. The liver tumors consisted of 25 adenomas and 50 adenocarcinomas. Also the incidence of leukemias and reticulum-cell sarcomas was increased in the treated animals.

In rats, tumors were not observed to increase after ingestion of a diet containing 1000 mg/kg chrysoidine for 51-366 days (Maruya, 1939). Only 10 animals were used, however, in this study.

(5) Mutagenicity

Chrysoidine has been assayed for mutagenic activity in one strain (TA1538) of Salmonella typhimurium (Garner and Nutman, 1977). A positive mutagenic response was observed at both 50 and 100 µg/plate in the presence of an enzyme activation system derived from the livers of phenobarbitone treated rats. In the absence of liver enzymes, no mutagenic activity was observed.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of chrysoidine were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for chrysoidine were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

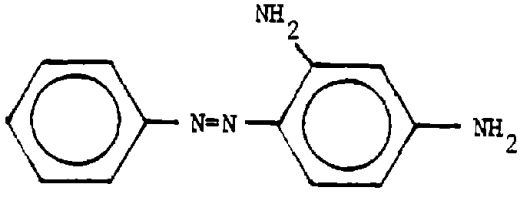
18. Other Pertinent Data

No other information that would aid in the assessment of chrysoidine as an occupational hazard was found in the literature searched.

O. 2,4-DIAMINOAZOBENZENE

1. Chemical Name: 2,4-Diaminoazobenzene

2. Chemical Structure:



3. Synonyms: 2-Amino-4-aminoazobenzene
1,3-Benzenediamine, 4-(phenylazo)-
Diaminoazobenzene
4-Phenylazo-1,3-phenylenediamine
m-Phenylenediamine, 4-(phenylazo)-

4. Chemical Abstract Service (CAS) Number: 495-54-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

ST3325000

6. Chemical and Physical Properties

Description:	solid
Molecular Weight:	212.28
Boiling Point:	---
Melting Point:	---
Vapor Pressure	---
Solubility:	---
Specific Gravity:	---
Stability:	---

7. Production

Data available from the U.S. EPA (1980) regarding producers of 2,4-diaminoazobenzene and production volumes are presented in Table 20.

8. Use

2,4-Diaminoazobenzene is chemically similar to chrysoidine; chrysoidine is the hydrochloride of 2-amino-4-aminoazobenzene. See chrysoidine profile for uses.

Table 20. Producers of 2,4-Diaminoazobenzene and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Passaic Color and Chemical Co. Patterson, NJ	Manufacturer Produced Site Limited	10-100 thousand lb
R and L Dyestuff Corp. Parsippany, NJ	Importer	none
BASF Wyandotte Parsippany, NJ	Importer	none
Atlantic Chemical Co. Nutley, NJ	Manufacturer	confidential
GAF Corp. Rensselaer, NY	Manufacturer	none

9. Manufacturers and Distributors

Data available from the U.S. EPA (1980) regarding producers of 2,4-diaminoazobenzene and production volumes are presented in Table 20.

10. Manufacturing Process

No information was found in the literature searched.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 759 workers are potentially exposed to 2,4-diaminoazobenzene.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 2,4-diaminoazobenzene were not found in the literature searched.

14. Biological Effects

No information on the biological effects of 2,4-diaminoazobenzene was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of 2,4-diaminoazobenzene were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 2,4-diaminoazobenzene were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

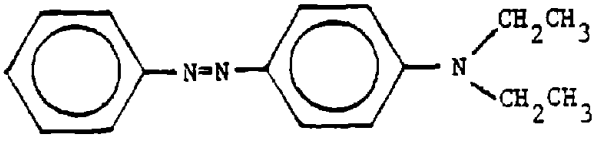
18. Other Pertinent Data

No other information that would aid in the assessment of 2,4-diaminoazobenzene as an occupational hazard was found in the literature searched.

P. N,N-DIETHYLAMINOAZOBENZENE

1. Chemical Name: N,N-Diethylaminoazobenzene

2. Chemical Structure:



3. Synonyms: Benzenamine, N,N-diethyl-4-(phenylazo)-
C.I. Solvent Yellow 56
4-Phenylazo-N,N-diethylaniline

4. Chemical Abstract Service (CAS) Number: 2481-94-9

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

Not listed

6. Chemical and Physical Properties:

Description:	solid
Molecular Weight:	253.35
Boiling Point:	---
Melting Point:	---
Vapor Pressure:	---
Solubility	---
Specific Gravity:	---
Stability:	---

7. Production

Data available from the U.S. EPA (1980) regarding producers of N,N-diethylaminoazobenzene and production volumes are presented in Table 21.

8. Use

N,N-Diethylaminoazobenzene is used in dyes and dyestuffs.

9. Manufacturers and Distributors

Data available from the U.S. EPA (1980) regarding producers of N,N-diethylaminoazobenzene and production volumes are presented in Table 21.

Table 21. Producers of N,N-Diethylaminoazobenzene and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Passaic Color and Chemical Co. Patterson, NJ	Manufacturer Produced Site Limited	1-10 thousand lb
Ugine Kuhlmann of America Paramus, NJ	Importer	confidential
BASF Wyandotte Parsippany, NJ	Importer	under 1000 lb
American Cyanamid Co. Bound Brook, NJ	Importer	confidential
Mobil Oil Co. New York City, NY	Importer	under 1000 lb

10. Manufacturing Processes

No information was found in the literature searched.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 35 workers are potentially exposed to N,N-diethylaminoazobenzene.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to N,N-diethylaminoazobenzene were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The only information found in the literature searched was a carcinogenicity study by Kirby (1947). Stock mice (36 males and 34 females) received subcutaneous injections of 0.25 ml of a 3% solution of N,N-diethylaminoazobenzene in arachis oil. Of the mice treated, 11 males and 13 females died within the first week. Necrosis of the kidney was observed in some of the short lived mice.

(2) Subchronic Exposures

No information was found in the literature searched regarding the biological effects of N,N-diethylaminoazobenzene.

(3) Chronic Exposures

Kirby (1947) exposed 9 male and 10 female rats to N,N-diethylaminoazobenzene in a low protein diet for the lifespan of the animals. The dose schedule is given in the carcinogenicity section. At the time of

autopsy there was no proliferative or degenerative changes in the liver, however, the kidneys of 4 animals and the spleen of 3 showed fibrosis. Stock mice were also treated with N,N-diethylaminoazobenzene by subcutaneous injection and examined at death for pathologic changes. The dose schedule for the mice is also given in the section on carcinogenicity. Some liver changes were observed including one male mouse with hyperplasia, and fatty degeneration in 13 female mice. In 6 mice surviving 30 to 622 days there was cystic dilation of the kidney tubules, and 1 mouse with degenerative changes in the spleen.

(4) Carcinogenicity

The carcinogenicity of N,N-diethylaminoazobenzene has been reveiwed by Miller and Miller (1953) in a paper considering the mechanism of azo dye carcinogenisis.

Kirby (1947) fed 9 male and 10 female Wistar rats a low protein diet containing N,N-diethylaminoazobenzene at a level of 0.1% for 6 weeks, 0.08% for 6 weeks, 0.06% for 4 weeks and 0.05% for the rest of the duration of the study. The longest survival time was 635 days for a male rat with 12 animals surviving over 400 days. No tumors were detected in the livers of the treated rats. Kirby (1947) also treated 27 male and 23 female stock mice by subcutaneous injection with N,N-diethylaminoazobenzene. The maximum amount of N,N-diethylaminoazobenzene received (only 4 mice) was 55 mg/mouse in 10 injections. The mice died between 1 and 622 days after the first injection. A similar study was done with 18 male and 26 female CBA mice. The maximum dose received was 42.5 mg/mouse. The mice did not have in either study, higher than expected tumor incidences in the liver, kidney, or spleen. Kirby (1947) concluded that N,N-diethylaminoazobenzene was not a carcinogen in rats and mice.

Sagiura et al. (1945) fed 10 Sherman stock rats (150 g at the start of the study) a diet containing N,N-diethylaminoazobenzene for

88-511 days. The average daily intake of test compound was 4.8 mg. At death, the animals were examined for liver tumors. No tumors were observed in the 10 experimental animals either by gross observation or microscopic examination.

(5) Mutagenicity

The results of mutagenicity and cell transformation assays of N,N-diethylaminoazobenzene are presented in Table 22. Most of the studies demonstrated that N,N-diethylaminoazobenzene was not mutagenic to bacteria and yeast either in the presence or absence of a mammalian metabolic activation system. Only the study by Søderlund et al. (1980) indicated a slight positive response in the Ames assay with S. typhimurium strain TA98. This positive result (2.5 times background) was achieved only with high levels of S-9 in the assay system. The other positive result was in a cell transformation assay (Ashly et al., 1978). The reason for the positive result in the cell transformation assay and the generally negative results in the microbial systems is not apparent.

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

Golub (1972) administered 24 mg of N,N-diethylaminoazobenzene subcutaneously to pregnant BALB/c mice 4 to 5 times during the last week of gestation. After treatment, explants of fetal kidney were made. The explants from N,N-diethylaminoazobenzene treated mice had a better survival rate, 82%, as compared to the 48% survival for the control explants. Morphologic differences including foci of proliferation were present in the experimental explants at an increased frequency. Although no speculation was made about the

Table 22. *In Vitro* Mutagenicity and Cell Transformation Assays of N,N-diethylaminoazobenzene

Type of Assay	Organism	Strain	With Mammalian Metabolic Activation	Dose	Results	Reference
Reverse mutation	*S. typhimurium*	TA1535	yes and no	1000 µg/plate	-	Simmon, 1979a
		TA1537	yes and no	1000 µg/plate	-	
		TA1538	yes and no	1000 µg/plate	-	
Reverse mutation	*S. typhimurium*	TA100	yes	500 µg/plate	-	McCann *et al.*, 1975
		TA98	yes	500 µg/plate	-	
Reverse mutation	*S. typhimurium*	TA98	yes	100 µg/plate	±	Spolerlund *et al.*, 1980
Reverse mutation	*S. typhimurium*	TA1535	yes and no	250 µg/plate	-	Rosenkranz and Poirier, 1979
		TA1538	yes and no	250 µg/plate	-	
Mitotic recombination	*S. cerevisiae*	D3	yes and no	0.1% w/v	-	Simmon, 1979b
Cell transformation	BHK_{21}	C13	yes	25 µg/ml	+	Ashly *et al.*, 1978
DNA-modifying activity	*E. coli*	pol A^-	yes	25 µg/ml	-	Rosenkranz and Poirier, 1979

significance of the proliferative changes, it was suggested that this evidence supports the theory of transplacental transfer of N,N-diethylaminoazobenzene in mice.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of N,N-diethylaminoazobenzene were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for N,N-diethylaminoazobenzene were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

18. Other Pertinent Data

No other information that would aid in the assessment of N,N-diethylaminoazobenzene as an occupational hazard was found in the literature searched.

APPENDIX - AMINOAZOBENZENES

The following list includes all of the aminoazobenzenes considered under the class definition. The compounds in the list were identified primarily from the following sources: U.S. EPA TSCA list and U.S. EPA (1980), USITC (1980a,b), The Colour Index, SRI International (1980), Chem Sources--USA (1980), Kirk-Othmer's Encyclopedia of Chemical Technology, The Merck Index (1976), and Hawley (1977).

CAS numbers are given, when available, to aid in the identification as these types of compounds can be named by a variety of synonyms.

	CAS No.
4-Aminoazobenzene	60-09-3
4-Aminoazobenzene-4'-carboxylic acid	6925-48-0
4-Aminoazobenzene-3,4'-disulfonic acid	101-50-8
p-Aminoazobenzenedisulfonic acid	61916-43-6
4-Aminoazobenzene-3,4'-disulfonic acid, disodium salt	2706-28-7
p-Aminoazobenzenedisulfonic acid, monosodium	61950-37-6
4-Aminoazobenzene hydrochloride	3457-98-5
4-Aminoazobenzene-4'-sulfonic acid	104-23-4
4-Aminoazobenzene-4'-sulfonic acid, sodium salt	2491-71-6
4-Aminoazobenzene-3'-sulfonic acid	102-23-8
ortho-Aminoazotoluene	97-56-3
para-Aminoazotoluene	41576-40-3
ortho-Aminoazotoluene diazonium salt	---
ortho-Aminoazotoluene disulfonic acid	---
ortho-Aminoazotoluene hydrochloride	2298-13-7
ortho-Aminoazotoluene-4'-sulfonic acid	120-68-3
4-Aminoazotoluene-4'-sulfonic acid	---
Aminoazoxylene hydrochloride	---
Benzenamine, 4-[(4-chlorophenyl)azo]-N,N-diemthyl-	2491-76-1
Benzenamine, 2-methoxy-4-[(2-methoxyphenyl)azo]-*	2615-05-6
Benzenamine, 2-methoxy-4-[(4-methoxyphenyl)azo]-	17210-48-9
Benzenamine, 2-methoxy-5-methyl-4-[(4-methylphenyl)azo]-	6369-01-3
Benzenamine, 2-methoxy-5-methyl-4-[(4-nitrophenyl)azo]-	2475-43-6
Benzenamine, 2-methoxy-4-(phenylazo)-	3544-23-8
Benzenamine, 2 (or 3)-methyl-4-[(4-methylphenyl)azo]-	41576-40-3

	CAS No.
C.I. Disperse Black 2*	6232-57-1
C.I. Disperse Black 3	539-17-3
C.I. Disperse Black 4	6054-50-8
C.I. Disperse Black 7	6054-51-9
C.I. Disperse Orange 1	2581-69-3
C.I. Disperse Orange 3	730-40-5
C.I. Disperse Orange 5*	6232-56-0
C.I. Disperse Orange 7	6492-50-8
C.I. Disperse Red 1	2872-52-8
C.I. Disperse Red 2	3769-58-2
C.I. Disperse Red 5	3769-57-1
C.I. Disperse Red 7*	4540-00-5
C.I. Disperse Red 13*	3180-81-2
C.I. Disperse Red 16	6253-14-1
C.I. Disperse Red 17	3179-89-3
C.I. Disperse Red 19*	2734-52-3
C.I. Disperse Red 31	2475-43-6
C.I. Disperse Red 32	3084-21-7
C.I. Disperse Red 41	6373-90-6
C.I. Disperse Violet 12	3266-98-6
C.I. Disperse Violet 13	6374-02-3
C.I. Disperse Yellow 3	2832-40-8
C.I. Mordant Brown 4	6247-27-4
C.I. Mordant Brown 12	6364-36-9
C.I. Mordant Brown 48	6232-53-7
C.I. Solvent Yellow 2	60-11-7
C.I. 11015	6373-87-1
C.I. 11030	1591-56-9
C.I. 11060	6373-96-2
C.I. 11070	6373-95-1
C.I. 11125	6373-99-5
C.I. 11180*	2581-69-3
C.I. 11200	6374-03-4
C.I. 11205	4665-65-0
C.I. 11230	6054-58-6
C.I. 11245	6364-31-4
C.I. 11275	6364-34-7
C.I. 11280	6364-35-8
C.I. 11310	6416-58-6
C.I. 11325	6416-59-7
Chrysoidine	532-82-1

	CAS No.
Diacetylaminoazobenzene	83-63-6
2,4-Diaminoazobenzene	495-54-5
4,4'-Diaminoazobenzene	538-41-0
2,4-Diaminoazobenzene hydrochloride citrate	5909-04-6
p-Diaminoazobenzene hydrochloride	5893-95-8
2,4-Diaminoazobenzene monothiocyanate	16484-81-4
2,4-Diaminoazobenzene-4-sulfonamide hydrochloride	140-14-7
N,N-Diethylaminoazobenzene	2481-94-9
2,4'-Dimethyl-4-aminoazobenzene	3398-09-2
4-Dimethylaminoazobenzene-4'-arsonic acid	---
4-Dimethylaminoazobenzene-4'-arsonic acid, hydrochloride	---
p-(Dimethylamino)azobenzene-o-carboxylic acid	493-52-7
4-N,N-Dimethylaminoazo-4'-isothiocyanate	---
4-Dimethylaminoazobenzene-4'-sulfonyl chloride	---
4-(Methylamino)azobenzene	621-90-9
3-Methyl-4'-(dimethylamino)azobenzene	55-80-1
2'-Methyl-4-dimethylaminoazobenzene	---
4'-Methyl-4-dimethylaminoazobenzene	---

*These aminoazobenzenes were not profiled individually; however, limited data available from the U.S. EPA (1980) and USITC (1980a,b) indicates that they may have some commercial importance.

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