

GHS Classification

ID211

CAS 101-77-9

Physical Hazards

4,4'-Methylenedianiline

Date Classified: Jul. 24, 2006 (Environmental Hazards: Mar. 31, 2006)

Reference Manual: GHS Classification Manual (Feb. 10, 2006)

Hazard class	Classification	symbol	signal word	hazard statement	Rational for the classification
1 Explosives	Not applicable	—	—	—	Containing no chemical groups with explosive properties
2 Flammable gases	Not applicable	—	—	—	Classified as "solid" according to GHS definition
3 Flammable aerosols	Not applicable	—	—	—	Not aerosol products
4 Oxidizing gases	Not applicable	—	—	—	Classified as "solid" according to GHS definition
5 Gases under pressure	Not applicable	—	—	—	Classified as "solid" according to GHS definition
6 Flammable liquids	Not applicable	—	—	—	Classified as "solid" according to GHS definition
7 Flammable solids	Not classified	—	—	—	Classified as "flammable" by ICSC (2004). Classified into Division 6.1 (UN#2651) (UN Recommendations on the Transport of Dangerous Goods).
8 Self-reactive substances and mixtures	Not applicable	—	—	—	Containing no chemical groups with explosive or self-reactive properties
9 Pyrophoric liquids	Not applicable	—	—	—	Classified as "solid" according to GHS definition
10 Pyrophoric solids	Not classified	—	—	—	Classified into Division 6.1 (UN#2651) (UN Recommendations on the Transport of Dangerous Goods)
11 Self-heating substances and mixtures	Classification not possible	—	—	—	Test methods applicable to liquid substances are not available (melting point: 91.5-92degC (ICSC, 2004), test temperature: 140degC).
12 Substances and mixtures, which in contact with water, emit flammable gases	Not applicable	—	—	—	Containing no metals or metalloids (B, Si, P, Ge, As, Se, Sn, Sb, Te, Bi, Po, At)
13 Oxidizing liquids	Not applicable	—	—	—	Classified as "solid" according to GHS definition
14 Oxidizing solids	Not applicable	—	—	—	Organic compounds containing no oxygen, fluorine and chlorine
15 Organic peroxides	Not applicable	—	—	—	Organic compounds containing no "-O-O-" structure
16 Corrosive to metals	Classification not possible	—	—	—	Test methods applicable to solid substances are not available

Health Hazards

Hazard class	Classification	symbol	signal word	hazard statement	Rational for the classification
1 Acute toxicity (oral)	Category 4	Exclamation mark	Warning	Harmful if swallowed	Based on the LD50 value of 335mg/kg calculated from the testing data of rat LD50 (oral route) of 264mg/kg (MOE Risk Assessment vol. 2 (2003)), 355mg/kg, 475mg/kg, 547mg/kg and 830mg/kg (DFGOT vol.7 (1996)).
1 Acute toxicity (dermal)	Category 3	Skull and crossbones	Danger	Toxic in contact with skin	Based on the rat LD50 (dermal route) value of 1,000mg/kg (SIDS (2002)).
1 Acute toxicity (inhalation: gas)	Not applicable	—	—	—	Due to the fact that the substance is "solid" according to the GHS definition and inhalation of its gas is not expected.
1 Acute toxicity (inhalation: dust, mist)	Classification not possible	—	—	—	No data available
1 Acute toxicity (inhalation: dust, mist)	Classification not possible	—	—	—	Insufficient data available
2 Skin corrosion / irritation	Category 3	—	Warning	Causes mild skin irritation	Based on the description in the report on rabbit skin irritation tests (SIDS (2002)): "The substance produced slight irritation of the skin" (though exposure duration is not presented).
3 Serious eye damage / eye irritation	Category 2A	Exclamation mark	Warning	Causes serious eye irritation	Based on the description in the report on rabbit eye irritation tests (SIDS (2002)): "The substance produced mild to moderate irritation of the eye."
4 Respiratory/skin sensitization	Respiratory sensitization: Classification not possible Skin sensitization: Category 1	(Respiratory sensitization) — (Skin sensitization) Exclamation mark	(Respiratory sensitization) — (Skin sensitization) Warning	(Respiratory sensitization) — (Skin sensitization) May cause an allergic skin reaction	Respiratory sensitization: The substance is considered to cause no skin sensitization, based on the results of respiratory sensitization studies in guinea pigs (CERI Hazard Data 97-11 (2002)). However, the test methods are not detailed enough and the available data are insufficient to determine the presence or absence of skin sensitization. Skin sensitization: Due to the fact that the substance is classified as a "Skin Sensitizing Substance" by the ad hoc committee of the Japanese Society of Occupational Allergy. Also based on four cases of sensitization reported in human epidemiological studies (CERI Hazard Data 97-11 (2002) and MOE Risk Assessment vol. 2 (2003)).
5 Germ cell mutagenicity	Category 2	Health hazard	Warning	Suspected of causing genetic defects	Based on the absence of data on multi-generation mutagenicity tests, germ cell mutagenicity tests in vivo and germ cell genotoxicity tests in vivo, and positive data on somatic cell mutagenicity tests in vivo (micronucleus tests, chromosome aberration tests), described in NTP DB (Access on Mar., 2006), EU-RAR No.9 (2001), SIDS (2002) and ATSDR (1998).
6 Carcinogenicity	Category 2	Health hazard	Warning	Suspected of causing cancer	Due to the fact that the substance is classified as Category A3 by ACGIH (2001) and Group 2B by IARC (1987).
7 Toxic to reproduction	Category 2	Health hazard	Warning	Suspected of damaging fertility or the unborn child	Based on the evidence of adverse effects on fetuses at doses causing maternal toxicity, described in DFGOT vol.7 (1996).

8	Specific target organs/systemic toxicity following single exposure	Category 1 (liver, kidneys, heart, central nervous system, optic organ)	Health hazard	Danger	Causes damage to organs (liver, kidneys, heart, central nervous system, optic organ)	Based on the human evidence including "influenza-like symptoms with fever, jaundice," "blurred vision progressed to a significant decrease in vision; hepatic toxicity was observed," "hepatic toxicity, progression of albuminuria/hematuria," "myalgia and arthralgia" (ATSDR (1998)), "hepatitis observed in 3 days," "hepatitis," "acute hepatic symptoms," "severe pain above the navel, jaundice, electrocardiographic abnormalities suggesting cardiac muscle damage" (EU-RAR No.9 (2001)), and the evidence from animal studies including "necrosis and hemorrhage of the hepatocyte/bile duct" (ATSDR (1998)), "liver and kidney damage," "exophthalmos, hunchback position, rough fur," "indifference, chromodacryorrhea, jaundice" (EU-RAR No. 9 (2001)), "atrophy of the nucleus of rod/cone/outer nuclear layer of the retina" (CERI Hazard Data 97-11 (1998)). The effects on experimental animals were observed at dosing levels within the guidance value ranges for Category 1.
9	Specific target organs/systemic toxicity following repeated exposure	Category 1 (liver, heart) Category 2 (thyroid gland, kidneys, blood system)	Health hazard	Danger Warning	Causes damage to organs through prolonged or repeated exposure (liver, heart) May cause damage to organs through prolonged or repeated exposure (thyroid gland, kidneys, blood system)	Based on the human evidence: "A man exhibited hepatic toxicity following accidental ingestion of a solution containing 4,4'-methylenedianiline, potassium carbonate and gammabutyrolactone; elevated transaminase and bilirubinemia were detected at clinical examination performed 2 days after exposure. Though the solution contain other substances, the clinical findings were consistent with those reported by Kopelman et al., which were considered to be 4,4'-methylenedianiline-induced toxic effects," "echocardiography revealed evidence of decreased septal motion and hypofunction of the left ventricle" (ATSDR (1998)), "11 patients had jaundice," "exposure to MDA caused hepatitis" (EU-RAR No.9 (2001)). Also based on the evidence from animal studies including "hyperplasia of the bile duct," "hyperplasia of the thyroid gland" (ATSDR (1998)), "anemia, hyperplasia of the small bile duct, hypertrophy of the thyroid gland follicular epitheliocytes, nephrocalcinosis," "hepatic parenchyma was replaced by the proliferative bile duct, leading to portal cirrhosis" (EU-RAR No.9 (2001)). The effects on experimental animals were observed at dosing levels within the guidance value ranges for Category 2.
10	Aspiration hazard	Classification not possible	—	—	—	No data available

Environmental Hazards

Hazard class	Classification	symbol	signal word	hazard statement	Rational for the classification
11 Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning	Very toxic to aquatic life	It was classified into Category 1 from 48 hours EC50=0.105mg/L of the crustacea (Daphnia magna) (CERI Hazard Data, 1997).
11 Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning	Very toxic to aquatic life with long lasting effects	Although acute toxicity is Category 1 and bio-accumulation is low (BCF=15(Existing Chemical Safety Inspections Data,)), since there was no rapidly degrading (the decomposition by BOD: 0%(Existing Chemical Safety Inspections Data)), it was classified into Category 1.