Auramine: Human health tier II assessment

13 February 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-	492-80-8
Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, monohydrochloride	2465-27-2
Benzenesulfonic acid, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine]	32783-54-3
Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, sulfate	52497-46-8
[1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)azo]-, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:2)	72939-51-6
Sulfuric acid, monododecyl ester, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:1)	84030-53-5
Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, mononitrate	84255-15-2
Benzenesulfonic acid, mono-C10-14-alkyl derivatives, compounds with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine]	84418-51-9
Ferrate(4-), hexakis(cyano-C)-, 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine], copper(1+) salts	103818-83-3

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or

for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

Auramine base (CAS No. 492-80-8) and auramine-based compounds including three simple salts (hydrochloride, CAS No. 2465-27-2; sulfate, CAS No. 52497-46-8 and nitrate, CAS No. 84255-15-2), are grouped together with five more complex salts of auramine in this assessment, as most of them are mainly used in dyes and pigments for various purposes. The main hazard driving the risk from these chemicals is their potential for carcinogenicity due to the presence of auramine base (IARC, 2010).

Auramine is a cationic dye that is insoluble in water, but soluble in ethanol and diethyl ether (IARC, 2010). Auramine-based compounds and salts are commonly manufactured to have a specific solubility in various solvents. The hydrochloride salt (CAS No. 2465-27-2) is readily soluble in water, but only moderately soluble in polar solvents such as alcohols and lacquers (US Patent Office, 1961). The benzenesulfonic acid salt (CAS No. 84418-51-9) is soluble in alcohols as well as in mixtures of alcohols and water (US Patent Office, 1964). The sulfuric acid, monododecyl ester, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:1) (CAS No. 84030-53-5) consists of auramine with the anion lauryl sulfate (CAS No. 151-41-7), which is known for its surfactant and solubilising properties (Lu & Chen, 2003).

While there can be variations between the chemicals in this group for acute toxicity and local effects, precautions to avoid exposure to carcinogenic auramine base should limit the risk associated with these endpoints.

Import, Manufacture and Use

Australian

No specific Australian industrial use, import, or manufacturing information has been identified for any of these chemicals.

Only the following non-industrial use has been identified for benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, monohydrochloride (CAS No. 2465-27-2) (trade name: auramine O):

- biological stain (Therapeutic Goods Administration—TGA).

International

Auramine production has been discontinued in Europe and the USA and it is now manufactured only in India and China (IARC, 2010).

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening Information Dataset Initial Assessment Report (OECD SIAR); Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary; the International Agency for Research on Cancer (IARC); and eChemPortal: OECD High Production Volume chemical program (OECD HPV); the US Environmental Protection Agency's Aggregated Computational Toxicology Resource (ACToR), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Auramine and its salts/derivatives have reported commercial use in:

- ballpoint pen pastes, oils and waxes;
- dyes for paper (including in carbon paper);
- flexographic printing;
- offset printing;
- dyes for textiles;
- colouring agent for smoke in military applications;
- inking ribbons; and
- fireworks.

The following non-industrial uses have been identified for auramine and auramine hydrochloride as:

- disinfectant and antiseptic agents;
- colouring agents in pharmacological products; and
- food colourants (except in EU member countries)

No specific international use, importation, or manufacturing information has been identified for:

- sulfuric acid, monododecyl ester, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:1) (CAS No. 84030-53-5),
- benzenesulfonic acid, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (CAS No. 32783-54-3),
- [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)azo]-, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:2) (CAS No. 72939-51-6) and
- ferrate(4-), hexakis(cyano-C)-, 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine], copper(1+) salts (CAS No. 103818-83-3).

Auramine was used as a component of a specific hair product for men (Brillantine) in the 1930s (IARC, 2010).

Restrictions

Australian

No known restrictions have been identified.

International

Four of these chemicals (auramine, CAS No. 492-80-8; auramine hydrochloride, CAS No. 2465-27-2; auramine sulfate, CAS No. 52497-46-8; and auramine nitrate, CAS No. 84255-15-2) are listed on the following (Galleria Chemica):

- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products; and
- China list of banned substances for use in cosmetics.

Three of these chemicals (auramine, CAS No. 492-80-8; auramine hydrochloride, CAS No. 2465-27-2 and auramine nitrate, CAS No. 84255-15-2) are also listed on the following (Galleria Chemica):

- Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products; and
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain.

Existing Worker Health and Safety Controls

Hazard Classification

Auramine and its salts are classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- Carc. Cat. 3; R40 (carcinogenicity)
- Xn; R22 (acute toxicity)

- Xi; R36 (irritation).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standard is identified (Galleria Chemica):

- time weighted average (TWA) of 0.08 mg/m^3 in Germany for auramine and its salts and for auramine in Switzerland.

Health Hazard Information

The main hazard driving the risk from these chemicals is carcinogenicity, due to the presence of the auramine base. Auramine base is reported to be unstable in water and is therefore sold in powder form. It hydrolyses rapidly in dilute aqueous solutions to form 4,4'-bis(dimethylamino)benzophenone (CAS No. 90-94-8; also known as Michler's ketone) (US Patent Office, 1968). The hydrolysis product, Michler's ketone, is a Category 2 carcinogen and a Category 3 mutagen (HSIS, SWA). It is used as an intermediate to synthesise auramine derivatives (IARC, 2010).

When no toxicity data are available for the specific auramine compounds assessed in this report, data on the auramine base are considered suitable to use to derive toxicity end points for those compounds.

Toxicokinetics

After administering 20 mg/kg bw of labelled auramine orally to rats, 74.5 % and 17.4 % of the applied radioactivity was excreted in the faeces and in urine, respectively, with 70 % excreted within 24 hours and about 97–98 % within 48 hours (MAK, 2012).

Following an intravenous injection of auramine in rats, up to 90 % of the administered dose was recovered in urine and bile, with biliary excretion being dominant. The chemical was reported to be actively metabolised with only 9 % of the urinary radioactivity being an unchanged auramine. Following intraduodenal injection, only 1.6 % was excreted unchanged, showing a first pass effect (MAK, 2012).

Chromatographic analysis of metabolites following oral administration of auramine at 20 or 100 mg/kg bw in rats showed complete metabolism into three different polarity groups of substances:

1. demethylated auramine derivatives;
2. demethylated derivatives of Michler's ketone (CAS No. 90-94-8) and other hydrolysis products of auramine; and
3. an unidentified group of intermediate polarity (MAK, 2012).

Acute Toxicity

Oral

Auramine and its salts are classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). The available data on auramine and its hydrochloride salt support this classification for all chemicals considered in this group assessment.

The median lethal dose (LD50) values in rats have been reported as 1100 mg/kg bw for auramine and 1490 mg/kg bw for auramine hydrochloride (MAK, 2012). A LD50 of 3000 mg/kg bw for auramine was found in rats (details not available, RTECS).

Oral LD50 values of 480 mg/kg bw in mice and 150 mg/kg bw in cats and other domestic mammals were reported for auramine hydrochloride (RTECS). As the values given by RTECS were derived from studies conducted prior to test guidelines, these were not used in the hazard classification.

No data are available for other auramine compounds.

Dermal

Only limited data are available. In the absence of more reliable information, the available data were not considered sufficient to warrant a hazard classification.

A dermal LD50 of 300 mg/kg bw in mice was reported for auramine hydrochloride (1964 study, details not available; RTECS).

Inhalation

No data are available for any of the chemicals in this group.

Corrosion / Irritation

Skin Irritation

Only limited information on auramine hydrochloride is available.

The shaved dorsal skin of white rabbits rubbed with a suspension of auramine hydrochloride in distilled water (dose/concentration not available), showed no skin irritation (MAK, 2012).

Eye Irritation

Auramine and its salts are classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). Only limited information is available. However, based on the available data on auramine hydrochloride and observations in humans with auramine, the chemicals in this group are considered to be potential eye irritants. Therefore, the existing hazard classification should be applied to all chemicals in this group.

Auramine hydrochloride (100 mg) applied to the rabbit eye caused severe irritation (scores not available), but the effects were reversible within eight days (MAK, 2012).

Observation in humans

Auramine is reported to be injurious to human eyes (HSBD). Details are not available.

Sensitisation

Skin Sensitisation

No data are available for any of the chemicals in this group.

Repeated Dose Toxicity

Oral

Studies are available for auramine and auramine hydrochloride. Based on the available data, the chemicals in this group are not considered to cause severe health effects from repeated oral exposure. Chronic liver effects were only observed at doses around 180 mg/kg bw/d. Liver tumours observed from long-term exposure to the chemicals are considered in the **Carcinogenicity** section.

In a nine-month study, Wistar rats (n = 15 per sex/dose) were administered purified auramine (99 %) at 0, 300, 500, 1000, 1500 or 2000 mg/kg diet (equivalent to 0, 15, 25, 50, 75 and 100 mg/kg bw/d approximately, according to EFSA, 2012). Every three months, five animals per group were euthanised for haematological and clinical observations. A dose-dependent reduction in food consumption and delayed body weight gain were observed in treated animals. The plasma alanine aminotransferase (ALT) activity was increased from ~45 mg/kg bw/d after three months. A dose-dependent increase in the relative liver weight was observed from the 1000 mg/kg diet. After three months on the 2000 mg/kg diet (equivalent to 180 mg/kg bw/d according to EFSA, 2012), chronic liver effects were reported including cirrhosis, adenofibrosis, bile duct proliferation and severe metaplastic changes. These effects were observed at a later stage in animals that received 1500 mg/kg in the diet. Foci of modified hepatocytes were observed after three months at high doses (~135 and 180 mg/kg bw/d), and after nine months at low doses (~15 and 25 mg/kg bw/d) (EFSA, 2012; MAK, 2012).

Auramine hydrochloride (purity 87 %) was administered in the diet of Sprague Dawley (SD) rats at concentrations of 0, 100, or 400 ppm for 28 days (n = 10 per sex/dose); 0, 50, 100, or 200 ppm for 90 days with a 21-month recovery period (n = 10 per sex/dose); or 0, 50, 100, or 200 ppm for two years (n = 20 per sex/dose) (Kirsch et al., 1978 cited in MAK, 2012).

In the 28-day study, the only effects reported were delayed body weight gain and increased relative liver weights in male rats at 400 ppm (approximately 48 mg/kg bw/d according to EFSA, 2012).

Increased relative liver weights in males were observed at 100 and 200 ppm (equivalent to 9 and 18 mg/kg bw/d, respectively according to EFSA, 2012) in the 90-day study. No other systemic toxicity effects were reported in the 28-day and 90-day studies. A no observed adverse effect level (NOAEL) was not determined.

No haematological or clinical changes were observed in the two-year study. At 200 ppm 10/20 females had liver tumours (see **Carcinogenicity**) and the authors determined the no effect concentration based on carcinogenicity as 100 ppm, equivalent to a NOAEL of 5 mg/kg bw/d (Kirsch et al., 1978).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Purified auramine powder may not be mutagenic. However, auramine base is unstable in water and therefore commercial auramine (purity 87–98 % according to MAK, 2012) could be genotoxic due to the presence of its hydrolysis product, Michler's ketone. Michler's ketone is a Category 3 mutagenic substance (R68—Possible risk of irreversible effect) (HSIS, SWA). The chemicals in this group are not recommended for classification as Category 3 mutagens on this basis, as the content of Michler's ketone in these chemicals could vary significantly.

In vitro and in vivo genotoxicity studies indicated mixed results for auramine, possibly due to the varying degree of purity (IARC, 2010), including the amount of Michler's ketone present in the test sample. Results of DNA strand break assays and sister chromatid exchange (SCE) assays listed below on auramine, purified auramine and Michler's ketone suggest that commercial auramine is mutagenic because of the presence of Michler's ketone (Parodi et al., 1982, cited in MAK, 2012).

The following in vitro studies results are available for auramine (IARC, 2010; MAK, 2012):

- commercial form of the chemical produced mostly negative results in bacterial gene mutation assays with *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535, TA1537, TA1538 and YG10, up to 2000 µg/plate, with or without metabolic activation. However, some strains showed positive results with metabolic activation only: TA98 (from 250 µg/plate), TA1535 (from 250 µg/plate), TA1538 (from 33 µg/plate) and YG10 (from 150 µg/plate);
- negative results in two bacterial gene mutation tests with *Escherichia coli*, with or without metabolic activation at 40 µg/plate;
- in gene mutation tests without metabolic activation in *Saccharomyces cerevisiae*, the chemical induced depletions (from 1200 µg/mL), gene conversion (from 75 µg/mL) and aneuploidy (abnormal number of chromosomes) from 250 µg/mL;
- induction of gene mutations in Chinese hamster lung V79 cells at the *Hprt* locus, only with metabolic activation at 401–1069 µg/mL;
- negative results for induction of gene mutations at the *Tk* locus in mouse lymphoma L5178Y cells at 45 to 332 µg/mL, with or without metabolic activation;
- two positive micronucleus tests in Syrian hamster embryo cells, but negative in primary rat hepatocytes (only limited details available); and
- increased chromosome aberrations in Chinese hamster ovary (CHO) cells at 20 µM when incubated for five hours.

The following in vivo studies are available for auramine (MAK, 2012):

- in a host-mediated assay with *S. typhimurium* G46, no evidence of mutagenicity was found in CFLP male rats following oral administration of the chemical at 0, 1000, 2000 or 4000 mg/kg;
- weakly positive results were observed in mice in a host-mediated assay with *S. cerevisiae* following oral administration of the chemical at 660 mg/kg;
- micronucleus tests showed negative results in CD1 mice that received two intraperitoneal (i.p.) injections of the chemical at 13, 26 or 52 mg/kg, in B6C3F1 mice that received two i.p. injections at 82.4 mg/kg and in mice following oral administration of the chemical at 1000, 2000 or 4000 mg/kg;
- in DNA strand break assays, auramine caused DNA fragmentation when administered as a single i.p. dose of 15, 30 or 60 mg to SD rats or i.p. dose of 30 mg/kg in Swiss CD mice; in contrast, purified auramine tested under the same conditions gave negative results in rats and Michler's ketone tested at i.p. doses of 7.5 and 15 mg/kg in rats induced DNA fragmentation in liver cells;
- commercial auramine was mutagenic in SCE assays in Swiss mice (i.p. injections of 7.5 or 15 mg/kg); although purified auramine at 15 mg/kg was not mutagenic, and the same dose of Michler's ketone or commercial auramine tested in parallel induced a clear increase in SCE; and
- in a dominant lethal test, auramine (90 % dyestuff) was found negative in mice at an i.p. dose of 21.5 mg/kg.

Carcinogenicity

Auramine and its salts are classified as hazardous (Category 3 carcinogenic substance) with the risk phrase ‘Limited evidence of carcinogenic effect’ (Xn; R40) in HSIS (Safe Work Australia). The hydrolysis product of auramine, Michler's ketone, is used as an intermediate to produce auramine derivatives and is a Category 2 carcinogen (R45—May cause cancer) (HSIS). The available data for auramine and Michler's ketone support a Category 3 classification for carcinogenicity of auramine, its salts and other auramine-based substances considered in this report.

The International Agency for Research on Cancer (IARC, 2012) concluded that 'Auramine production is carcinogenic to humans (Group 1)' based on sufficient evidence of bladder cancer in humans. The evidence on humans was based on an old epidemiological study conducted in workers manufacturing auramine in the British chemical industry between 1910 and 1952 (IARC, 2010). However, two other epidemiological studies did not show increased risk of bladder cancer or carcinogenic effects from auramine exposure in 191 workers employed in manufacturing auramine during 1932–1976, and in 79 workers exposed to auramine (IARC, 2010; MAK, 2012).

IARC (2010) concluded that 'Auramine is possibly carcinogenic to humans (Group 2B)', based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity based on animal testing; and that 'Michler's ketone is possibly carcinogenic to humans (Group 2B)', based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity based on animal testing.

In a two-year study, SD rats (n = 20 per sex/dose) were administered auramine (purity: 87 %) in the diet at 0, 50, 100 or 200 ppm. The number of females with benign tumours or malignant tumours was significantly higher than the number of males similarly affected (details not available). At 200 ppm, 10/20 females had

liver tumours (hepatocellular adenomas and one hepatocellular carcinoma) (Kirsch et al., 1978 cited in MAK, 2012), but the tumour incidence was not statistically significant (MAK, 2012).

In a 52-week study, mice (n = 15 per sex) were administered a diet containing 0.1 % auramine (estimated total intake = 728 mg/animal). Nineteen mice died during the study. Seven mice (23 %) developed hepatomas and 11 (37 %) had lymphomas, compared with no hepatomas and 8 % with lymphomas in the control group. One animal also developed a subcutaneous sarcoma (Bonser et al., 1956 cited in IARC, 2010).

In rodent studies, it was concluded that oral exposure to auramine was carcinogenic and induced hepatomas and fibrosarcomas by subcutaneous injection (Williams & Bonser, 1962). Male Wistar rats (n = 24) were administered 0.1 % commercial auramine in the diet for 87 weeks, or injected daily with a 2.5 % suspension of commercial auramine in arachis oil, subcutaneously, for 21 weeks. Results showed that 97 % of rats administered auramine in the diet developed hepatomas (from small single or multiple foci to large masses occupying much of the liver substance) compared with none in the control group. After subcutaneous injection (estimated total intake = 110–120 mg/animal), 55 % rats exhibited fibrosarcomas, 15 % hepatomas, and three intestinal carcinomas were reported. Thirty (15/sex) albino mice (stock mice) and 27 (12 male and 15 female) CBA mice were administered auramine in the diet at 0.1 and 0.2 %, respectively for 52 weeks. Both male and female stock mice developed hepatomas (30 % and 57 %, respectively) compared with none in the control group. In CBA mice, 58 % of males and 73 % of females developed tumours, compared with 11 % and 5 % in the control male and female groups, respectively (IARC, 2010).

Michler's ketone was reported to be carcinogenic in rats and mice (NCI, 1979). A carcinogenicity study was conducted in B6C3F1 mice (n = 50) administered Michler's ketone in the diet at 1250 or 2500 ppm for 78 weeks. Females exhibited an increase in the indicence of hepatocellular carcinomas compared with the control group (33 % and 56 % in low and high dose groups, respectively). The incidence of haemangiosarcomas in males was increased significantly (10 % and 40 % in low and high dose groups, respectively) (NCI, 1979; IARC, 2010). In the same study, Fischer 344 (F344) rats were administered Michler's ketone in the diet (250 and 500 ppm for males and 500 and 1000 ppm for females) for 78 weeks. Incidences of hepatocellular carcinomas in males were 18 % and 80 % for low and high doses, respectively and in females 87 % and 90 % for low and high doses, respectively, compared with zero incidence in the control groups (NCI, 1979; IARC, 2010).

Reproductive and Developmental Toxicity

No data are available for the chemicals in this group.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are systemic long-term effects (carcinogenicity).

The chemicals in this group can also cause systemic acute effects (acute toxicity from oral exposure) and local effects (eye irritation).

No data are available for skin sensitisation, or reproductive and developmental toxicity. Human data collected over previous decades showed no evidence of skin sensitisation following exposure to auramine or its salts.

Public Risk Characterisation

No domestic uses were identified for these chemicals. Consumers might be exposed to low concentrations of the chemicals in ball point pen pastes, but exposure is expected to be minimal. Similarly, consumer exposure to the chemicals is expected to be minimal from their use in carbon paper and inking ribbons.

Occupational Risk Characterisation

Given the critical systemic long-term, systemic acute and local health effects, these chemicals might pose an unreasonable risk to workers unless adequate control measures to minimise dermal and ocular exposure to the chemicals are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

Based on the available data, the hazard classification in HSIS for auramine and its salts is considered appropriate and needs to be applied to all the chemicals in this group.

NICNAS Recommendation

For auramine and its simple salts, current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Further risk management is required for other auramine compounds in this group. Sufficient information is available to recommend that risks for workplace health and safety be managed through changes to classification and labelling for these remaining chemicals in this group.

Assessment of the chemicals is considered to be sufficient provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Work Health and Safety

Auramine and its salts are classified as hazardous with the risk phrases provided below (HSIS, SWA). Other chemicals in this group are recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)	Harmful if swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)	Suspected of causing cancer - Cat. 2 (H351)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from dermal and ocular exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- health monitoring for any worker who is at risk of exposure to the chemicals if valid techniques are available to monitor the effect on the worker's health;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals— Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemicals has not been undertaken as part of this assessment.

References

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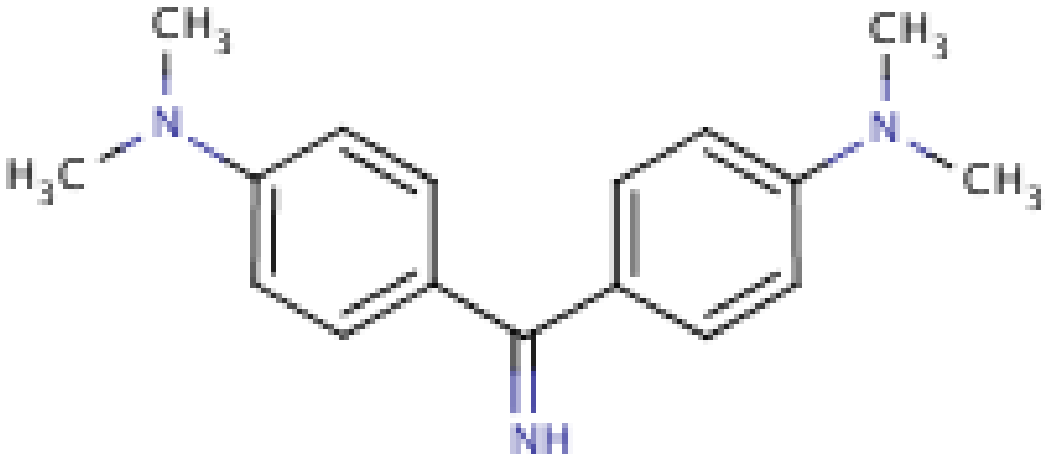
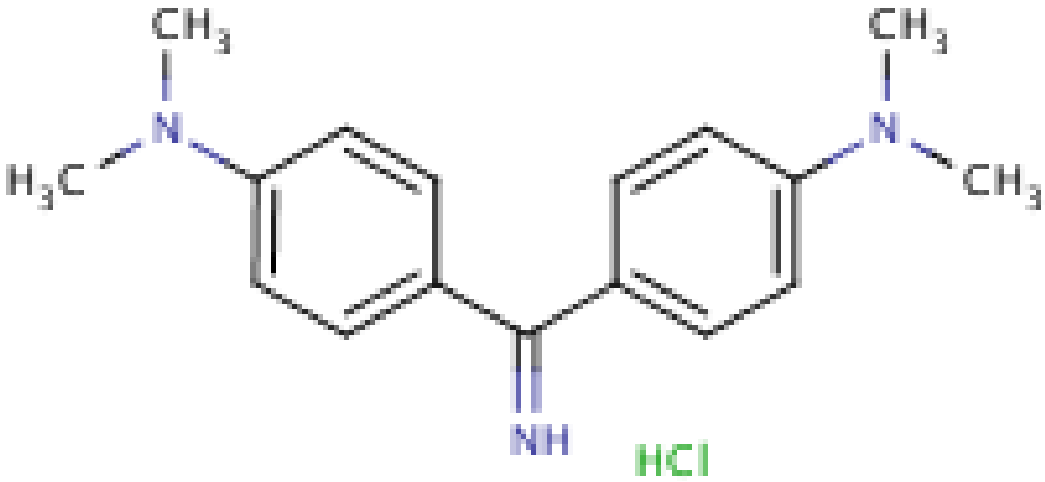
Last Update 13 February 2015

Chemical Identities

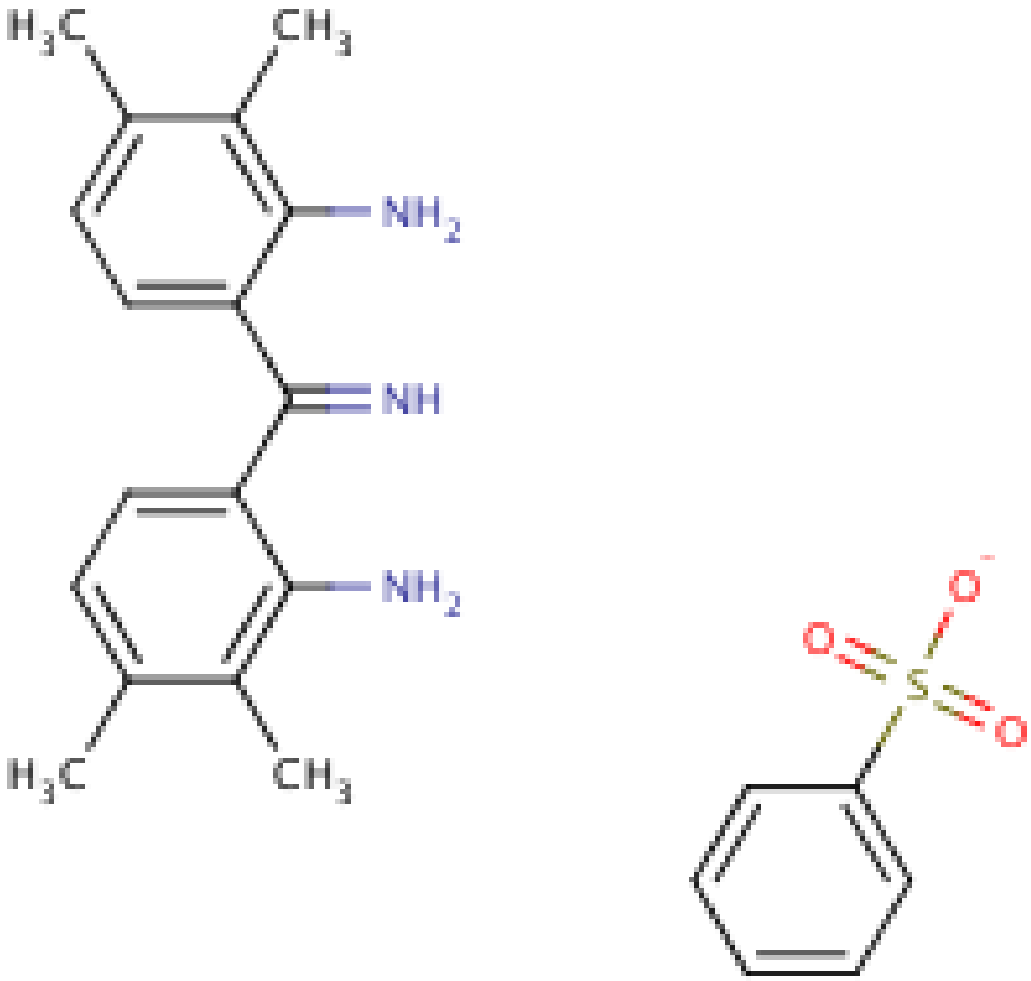
Chemical Name in the Inventory and Synonyms	**Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-** auramine 4,4'-dimethylaminobenzophenonimide 4,4-(iminocarbonyl)bis(N,N-dimethylaniline) 4,4'-carbonimidoylbis(N,N-dimethylbenzenamine) C.I. Solvent Yellow 34
CAS Number	492-80-8
Structural Formula	

	
Molecular Formula	C17H21N3
Molecular Weight	267.374

Chemical Name in the Inventory and Synonyms	**Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, monohydrochloride** auramine hydrochloride C.I. Basic Yellow 2 4,4'-(imidocarbonyl)bis(N,N-dimethylamine), monohydrochloride 1,1-bis(p-dimethylaminophenyl)methylenimine hydrochloride aniline, 4,4'-(imidocarbonyl)bis(N,N-dimethyl-, hydrochloride
CAS Number	2465-27-2
Structural Formula	

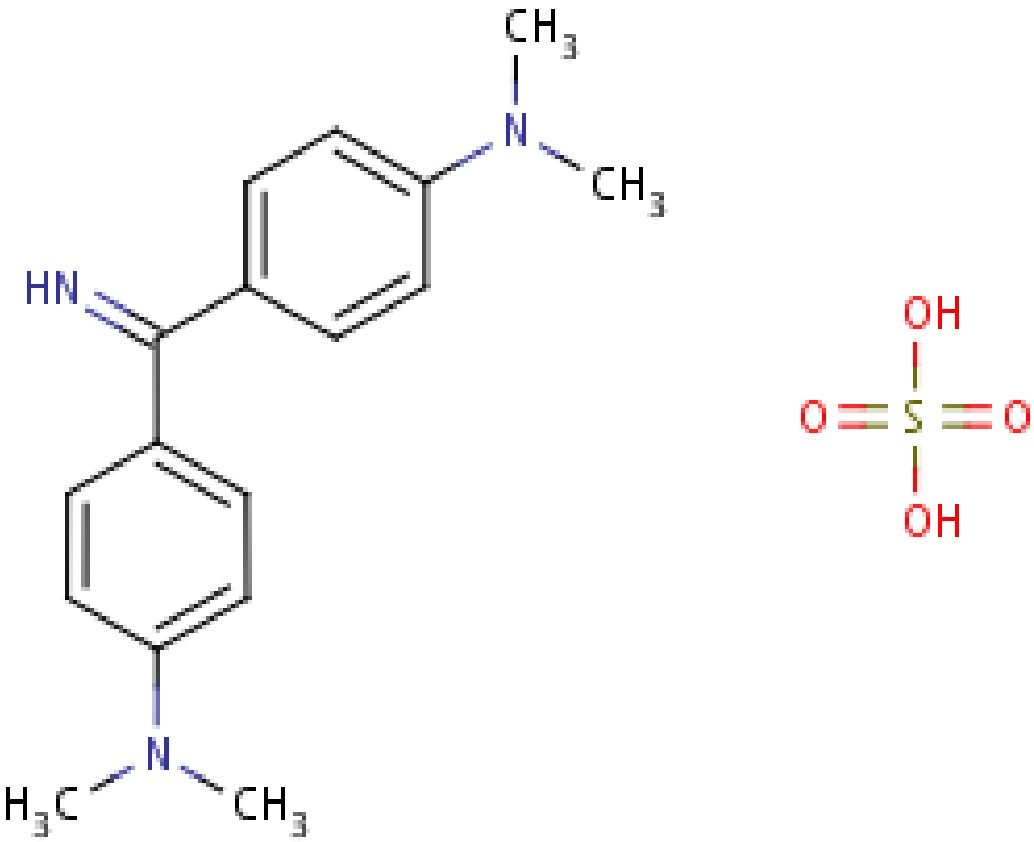
	
Molecular Formula	C17H21N3.ClH
Molecular Weight	303.835

Chemical Name in the Inventory and Synonyms	**Benzenesulfonic acid, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine]** benzenesulfonic acid, compound with C.I. Basic Yellow 2 benzenamine, 4,4'-carbonimidoylbis(N,N-dimethyl-, benzenesulfonate benzenamine, 4,4'-carbonimidoylbis(N,N-dimethyl-, benzenesulfonate (1:?) benzenesulphonic acid, compound with p,p'-carbonimidoylbis(N,N-dimethylaniline)
CAS Number	32783-54-3
Structural Formula	



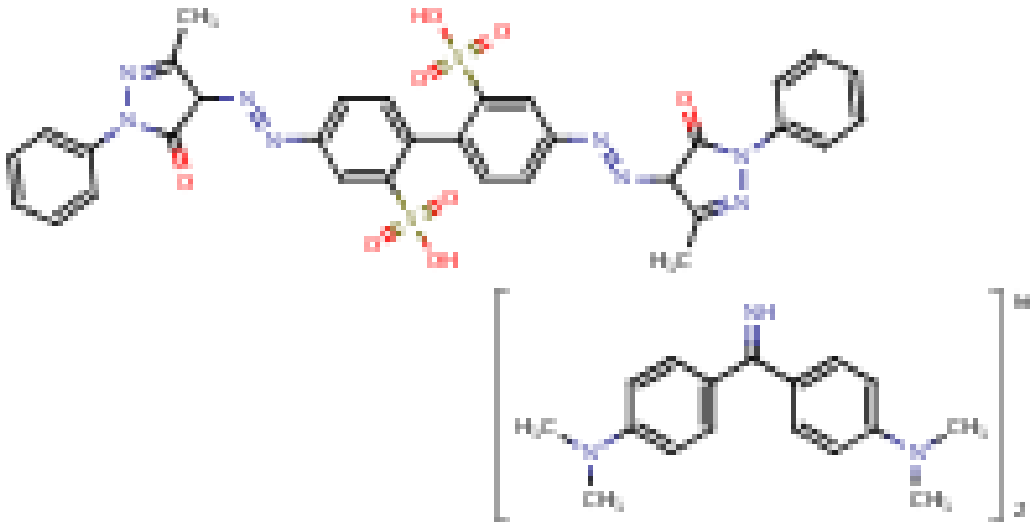
Molecular Formula	C17H21N3.xC6H6O3S
Molecular Weight	424.542

Chemical Name in the Inventory and Synonyms	**Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, sulfate** auramine sulfate 4,4'-carboimidoyl bis(N,N-dimethyl benzenamine, sulfate 4,4'-carbonimidoylbis(N,N-dimethylbenzenoamineaniline) sulfate
CAS Number	52497-46-8
Structural Formula	



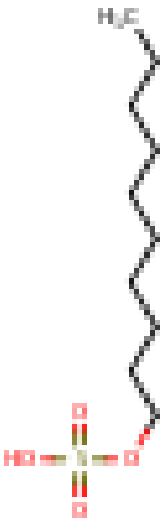
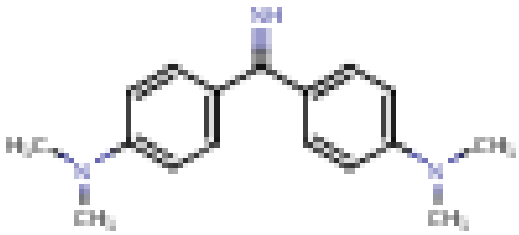
Molecular Formula	C17H21N3.xH2O4S
Molecular Weight	459.498

Chemical Name in the Inventory and Synonyms	**[1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)azo]-, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:2)** (1,1'-biphenyl)-2,2'-disulfonic acid, 4,4'-bis(2-(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)diazenyl)-, compd. with 4,4'-carbonimidoylbis(N,N-dimethylbenzenamine) (1:2) 4,4'-bis((4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)azo)(1,1'-biphenyl)-2,2'-disulphonic acid, compound with 4,4'-carbonimidoylbis(N,N-dimethylphenylamine) (1:2)
CAS Number	72939-51-6
Structural Formula	

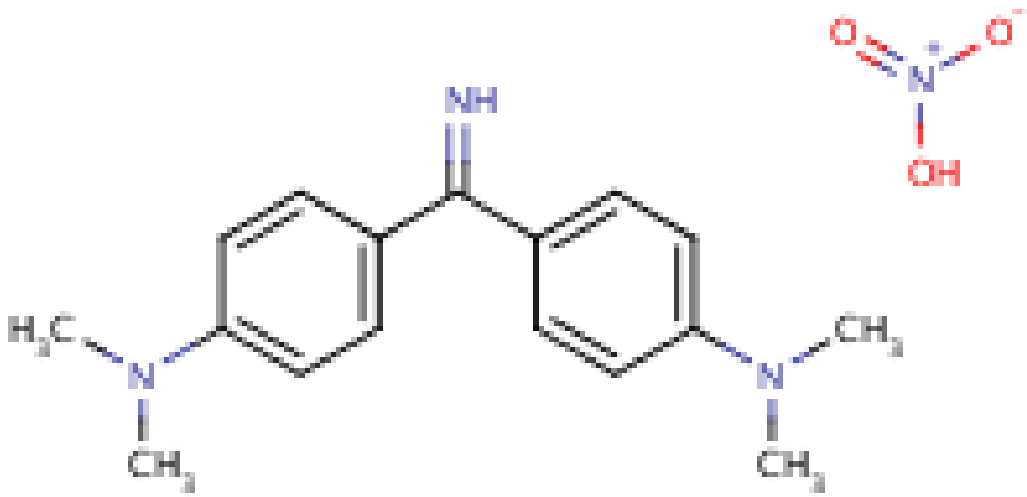


Molecular Formula	C32H26N8O8S2.2C17H21N3
Molecular Weight	1249.49

Chemical Name in the Inventory and Synonyms	**Sulfuric acid, monododecyl ester, compound with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine] (1:1)** benzenamine, 4,4-carbonimidoylbis[N,N-dimethyl-, compound with sulfuric acid monododecyl ester (1:1) decyl hydrogen sulphate, compound with 4,4'-carbonimidoylbis(N,N-dimethylaniline) (1:1) auramine lauryl sulfate
CAS Number	84030-53-5
Structural Formula	

	 
Molecular Formula	C17H21N3.C12H26O4S
Molecular Weight	505.72

Chemical Name in the Inventory and Synonyms	**Benzenamine, 4,4'-carbonimidoylbis[N,N-dimethyl-, mononitrate** auramine nitrate 4,4'-carbonimidoylbis(N,N-dimethylaniline) nitrate benzenamine, 4,4'-carbonimidoylbis(N,N-dimethyl-, nitrate (1:1)
CAS Number	84255-15-2
Structural Formula	



Molecular Formula	C17H21N3.HNO3
Molecular Weight	330.38

Chemical Name in the Inventory and Synonyms	**Benzenesulfonic acid, mono-C10-14-alkyl derivatives, compounds with 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine]**
CAS Number	84418-51-9
Structural Formula	**No Structural Diagram Available**

Molecular Formula	C17H21N3.C6H6O3S
Molecular Weight	

Chemical Name in the Inventory and Synonyms	**Ferrate(4-), hexakis(cyano-C)-, 4,4'-carbonimidoylbis[N,N-dimethylbenzenamine], copper(1+) salts**
CAS Number	103818-83-3
Structural Formula	**No Structural Diagram Available**
Molecular Formula	Unspecified
Molecular Weight	

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