2-Chloroaniline and its hydrochloride: Human health tier II assessment

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Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Benzenamine, 2-chloro-, hydrochloride	137-04-2
Benzenamine, 2-chloro-	95-51-2

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

The chemical, 2-chloroaniline, hydrochloride (CAS No 137-04-2) is a salt resulting from 2-chloroaniline (CAS No 95-51-2) reacting with a single molecule of hydrochloric acid. The chemicals are also referred to as salt and parent base, respectively, in this report. The parent base and its salt have been grouped together for assessment due to their similar toxicological properties and uses.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

The chemicals have reported international site-limited uses as intermediate for petroleum solvents, rubber chemicals, pigments, pesticides, fungicides and dyes identified through the following sources: the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossier for 2-chloroaniline (REACH), Galleria Chemica, Government of Canada (2016), the United States (US) National Toxicology Program Technical Report for 2-chloroaniline (NTP), the US Environmental Protection Agency (EPA) Chemical and Product Categories (CPCat) database, the US National Library of Medicine Occupational Health Database (HazMap), and Hazardous Substances Data Bank (HSDB).

Restrictions

Australian

This chemicals are not directly listed in the *Poisons Standard*—the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). However, the chemicals fall under the scope of the following group entry in Schedule 5:

'AMINES for use as curing agents for epoxy resins except when separately specified in these Schedules' (SUSMP).

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.' (SUSMP). Schedule 5 chemicals are labelled with 'Caution'.

International

The chemicals are listed in Health Canada’s Cosmetic Ingredient Hotlist (under 'Aniline (CAS RN 62-53-3), its salts and its halogenated and sulfonated derivatives') (Galleria Chemica).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are classified as hazardous, with the following hazard categories and hazard statements for human health in the Hazardous Chemical Information System (HCIS) (Safe Work Australia) under ‘Chloroanilines, with exception of those specified elsewhere in HCIS’:

- Acute toxicity – category 3; H301 (Toxic if swallowed); H311 (Toxic in contact with skin); H331 (Toxic if inhaled); and
- Specific target organ toxicity (repeated exposure) – category 2; H373 (May cause damage to organs through prolonged or repeated exposure).

Exposure Standards

Australian

The chemicals fall under the scope of the following group entry 'aniline & homologues' (Safe Work Australia):

Time Weighted Average (TWA) of 7.6 mg/m3 for 8 hours.

International

The following exposure standards are mainly identified for group of chemicals under 'aniline & homologues' (Galleria Chemica):

A TWA of 0.5-19 mg/m3 for 8 hours in countries such as Bulgaria, Belgium, Egypt, Korea, New Zealand, South Africa, India, United States of America (USA) and Poland.

Health Hazard Information

Toxicokinetics

In a non-guideline toxicokinetics study, male Fischer 344 (F344)rats were injected with 0.5 or 1 mmol/kg bw of the radiolabelled hydrochloride salt intraperitoneally (i.p). Tissue distribution and faecal and urinary radioactivity output were determined 3 and 24

hours post-dosing. The parent base accumulated mainly in the liver (compared to total dose) but also in kidneys. It was primarily excreted in urine (53 %), with less than 1 % excretion in the faeces within 24 h post dosing in the high dose group (REACH).

In another non-guideline study, Doe rabbits (sex and number not specified) were exposed (route not specified) to the parent base at a single dose of 0.1 g/kg bw. The unmetabolised parent base (9 % of applied dose), 4-amino-3-chlorophenol and traces of 2-amino-3-chlorophenol were identified as metabolites in urine (REACH).

Biotransformation of the parent base was assessed in male F344 rats following i.p. injection of 1 mmol/kg bw of ^{14}C-labelled chemical. During 24 hours, majority of radioactivity was eliminated via the urine (53 % of the administered radioactivity), and only <1 % of radioactivity appeared in faeces. The major biotransformation pathways of 2-chloroaniline were para-hydroxylation and sulfate conjugation. The major urinary metabolite, comprising 31.6 % of total urinary radioactivity, was 4-amino-3-chlorophenyl sulfate. The para-hydroxylated metabolite, 4-amino-3-chlorophenol (10.8 %), and its O-glucuronide conjugate (3.7 %) were also detected in urine. The direct conjugates of the parent base, the N-sulfate and N-glucuronide, comprised 18.6 and 8.6 %, respectively, of the metabolites excreted in the urine. The parent base accounted for 16.9 % of urinary radioactivity. Minor metabolites present in urine were N-acetylated products (HSDB).

The chemical 2-chloroaniline is absorbed through the intact skin (HSDB).

Acute Toxicity

Oral

The chemicals are classified as hazardous with hazard category 'Acute toxicity category 3' and hazard statement ‘Toxic if swallowed’ (H301) in HCIS (Safe Work Australia). The reported median lethal dose (LD50) values for the parent base support this classification. Observed sub-lethal effects include acute symptoms of methaemoglobinaemia (cyanosis), fatigue, dyspnoea, and muscle weakness.

In a non-guideline study similar to the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 401 (Acute Oral Toxicity), male Wistar rats received oral (gavage) dose of 0.5, 0.7, 0.9, 1, 1.6 mL/kg bw of parent base (n=10 rats/dose). The LD50 was 1016 mg/kg bw as calculated by the method of Fink and Hund (1965). Clinical signs included sedation, convulsion and chromodacryorrhea (red tears due to release of red pigment from the Harderian gland) (REACH).

In a non-guideline study, mice (no other details available) were administered 2-chloroaniline orally (gavage). The reported LD50 was 256 mg/kg bw. Clinical signs of toxicity included methaemoglobinaemia (REACH).

Dermal

The chemicals are classified as hazardous with hazard category 'Acute toxicity category 3' and hazard statement ‘Toxic in contact with skin’ (H311) in HCIS (Safe Work Australia). The reported LD50 values for the parent base support this classification. Observed sub-lethal effects include acute symptoms including methaemoglobinaemia (cyanosis), tremors and eye irritation.

In an OECD TG 402 (Acute dermal toxicity) study, Wistar rats (n=5/sex/dose) were treated (occlusive) with 100, 500 or 2000 mg/kg bw of 2-chloroaniline for 24 hours. The LD50 was calculated to be 1000 mg/kg bw. Mortality was observed only in the highest dose level with 9 out of 10 animals euthanised 6 hours post-application due to their moribund condition. The clinical signs of toxicity at two highest doses included tremors, laboured breathing, cyanosis, poor condition and almost no motor activity. Pathophysiological changes were only evident at the highest dose level and included severe cyanosis (methaemoglobin formation) and dark liquid in the thoracal cavity (REACH).

In a non-guideline study, rabbits were treated with a single dose of 200 mg/kg bw of 2-chloroaniline for 48 hours. The chemical was rubbed into the shaved dorsal skin. The LD50 was >200 mg/kg bw (REACH). No other details were provided.

Inhalation

The chemicals are classified as hazardous with hazard category 'Acute toxicity category 3' and hazard statement ‘Toxic if inhaled’ (H331) in HCIS (Safe Work Australia). The reported median lethal concentration (LC50) values for the parent base support this classification. Observed sub-lethal effects include methaemoglobinaemia (cyanosis), tremors, and eye irritation.

In an OECD TG 403 (Acute inhalation toxicity) study, Wistar rats (n=5/dose/sex) were exposed to 2-chloroaniline vapour at 0.371, 0.745 or 1.156 mg/L or aerosol at 2.642 or 4.406 mg/L (maximal attainable dose) via nose or head only for four hours. The LC50 was >4.406 mg/L air/4 hour. Clinical signs included: tremor, reduced motor activity and in the highest dose group serous secretion from the nose, indicating an irritating effect to the respiratory system (REACH).

In a study similar to OECD TG 403, Crl:CD male rats (n=10/dose) were exposed to 2-chloroaniline aerosol at 1.6, 2.4, 2.8, 4.0, 4.3 or 4.4 mg/L for four hours. The calculated LC50 was 4.2 mg/L air. Mortality was observed in two animals in the 4.0 mg/L dose group, four animals in the 4.3 mg/L dose group, and nine animals in the highest dose group. Clinical observations included cyanosis, fine tremors, slight to severe corneal opacity, prostration and semi-prostration, pallor, stained and wet perineal area, head alopecia, reddish-brown nasal, mouth and eye discharges, and tachypnoea (REACH).

In a study similar to OECD TG 403, ChR-CD male rats (6/dose) were exposed to 2-chloroaniline aerosol at 3.5, 4.4, 6.0, 6.6, 6.7 or 14.3 mg/L for four hours. The LC50 was 6.1 mg/L air. Mortality was observed in two rats dosed at 4.4 mg/L air, in three rats dosed at 6.0 and 6.6 mg/L, and in all rats dosed at 6.7 and 14.3 mg/L. Clinical observations included inactivity, irregular respiration, exophthalmos, lacrimation and tremors. Clinical observations post-exposure included loss of hair, paleness, unkemptness and initial weight loss. Gross necropsy revealed large, heavy and dark red spleens and active blood formation (REACH).

Observation in humans

Exposure to chloroanilines in general has been associated with methaemoglobinaemia, with potential liver and kidney damage, in humans (NTP).

Humans are much more sensitive to chemical causation of methaemoglobin than rats (NRC, 2000).

Corrosion / Irritation

Skin Irritation

Based on the available data, the chemical is considered to be, at most, a slight skin irritant.

In an OECD TG 404 (Acute dermal irritation / corrosion) study, New Zealand White (NZW) rabbits (n=3; sex not specified) were dermally exposed to 0.5 mL of 2-chloroaniline under a semiocclusive patch for four hours. Erythema was observed in all rabbits at 24 hours but was reversible within 14 days. Slight oedema was reported at 24 hours but was reversed by 48 hours (REACH).

Eye Irritation

Based on the available data, the chemical may be moderately irritating to the eye. Effects are not considered sufficient to warrant hazard classification.

In an eye irritation study performed according to EU Method B.5 (Acute toxicity: eye irritation / corrosion), NZW rabbits (n=3; sex not specified) were treated with 0.5 mL of 2-chloroaniline (neat). At 24 hours, the average scores for chemosis, conjunctivitis, iritis and corneal opacity were 0.7, 2, 1, and 1, respectively. All effects were reversible within 7 days (REACH).

In an eye irritation study similar to EU Method B.5 (Acute toxicity: Eye irritation / corrosion), rabbits (n=2; sex and strain not specified) were treated with 2-chloroaniline (neat; no washing) and observed for seven days. Moderate irritation and corneal damage were reported (REACH).

In a non-guideline eye irritation study, rabbits (n=2; sex and strain not specified), were treated with 0.01 mL of 2-chloroaniline (neat) into right eye. The treated eye of one rabbit was washed with tap water after 20 seconds exposure, while the eye of the

second rabbit was not washed. Irritation of conjunctivae, cornea and iris were reported with corneal clouding persisting even after 28 days in non-washed eye. The effects were reversible within 14 days in the washed eye (REACH).

Sensitisation

Skin Sensitisation

Based on the available data on the parent base, the chemicals are not expected to be skin sensitisers.

In a guinea pig maximisation test performed according to OECD TG 406 (Skin sensitisation), Bor:DHPW male guinea pigs (n=20 males for test group and 10 for control groups) were intradermally induced with 5 % of 2-chloroaniline in propylene glycol (w/v) followed by topical treatment using occulusive patches with 0.5 mL neat 2-chloroaniline. A challenge phase was conducted with semiocclusive patch with 0.5 mL of neat 2-chloroaniline for 24 hours. On challenge, reactions were not observed in the control or in the test group (REACH).

Repeated Dose Toxicity

Oral

The chemicals are classified as hazardous with hazard category 'Specific target organ toxicity (repeated exposure) – category 2' and hazard statement 'May cause damage to organs through prolonged or repeated exposure' (H373). Based on the treatment related effects reported in repeated dose toxicity studies and due to the potential for chloroanilines to induce haematological changes via all routes (see **Acute toxicity** section), the classification is warranted for the chemicals.

In a 13-week oral toxicity study similar to OECD TG 408 (Repeated dose 90-day oral toxicity in rodents), Fischer 344 rats and B6C3F1 mice (n=10/sex/dose) were treated orally (gavage) with 10, 20, 40, 80 and 160 mg/kg bw/day of 2-chloroaniline (in water with 0.1 N HCl) once per day, 5 days per week for 13 weeks plus two days. No treatment related deaths were reported in either species. Significant reduction in body weight was reported in male rats at the highest dose, but not in female rats or in mice. Clinical signs of toxicity included transient tremors (highest dose only) and dose related increase of methaemoglobin levels in all animals. Methaemoglobin formation and the accompanying hemolytic anaemia, extramedullary haematopoiesis, and Heinz body formation were indicative of erythrocyte toxicity induced by 2-chloroaniline. The lowest observed adverse effect level (LOAEL) was reported at 10 mg/kg bw/day (NTP).

Overall, the haematotoxicity findings were similar to those for other chloroaniline isomers (i.e. 4-chloroaniline; NICNAS); however, 2-chloroaniline was of lower potency (NTP).

Dermal

The chemicals are classified as hazardous with hazard category 'Specific target organ toxicity (repeated exposure) – category 2' and hazard statement 'May cause damage to organs through prolonged or repeated exposure' (H373). No data are available for the chemicals. However, since the acute toxicity study showed bioavailability of the chemical via dermal route and haematological symptoms (see **Acute Toxicity: Dermal** section), the classification is warranted for the chemicals.

Inhalation

The chemicals are classified as hazardous with hazard category 'Specific target organ toxicity (repeated exposure) – category 2' and hazard statement 'Causes damage to organs' (H372). Based on the treatment related effects reported in repeated dose toxicity studies and due to the potential for chloroanilines to induce haematological changes via all routes (see **Acute toxicity** section), the classification is warranted for the chemicals.

In an OECD TG 412 study (Repeated dose inhalation toxicity: 28/14-day), male and female Wistar rats (n=10/sex/dose) were exposed to 2-chloroaniline vapour at 0, 39, 217 and 886 mg/m^3 (7, 41 and 169 ppm), head only for 6 hours per day, 5 days per week for 28 days. No mortality was observed. Cyanosis was observed in females of the mid-dose group and males and females of the high-dose group. Dose-dependent increase in spleen weight and significant increase in liver weight at the highest dose were observed. The primary toxic effect reported was destruction of erythrocytes, evident already at the lowest dose of 39 mg/m^3 (0.039 mg/L). A no observed effect concentration (NOEC) of 6.4 mg/m^3 (0.0064 mg/L) was extrapolated for male and female rats (REACH).

In a non-guideline subchronic inhalation toxicity study, rats (n=6; sex and strain not specified) were exposed (head only) to 2-chloroaniline vapours at 1.23 mg/L (237 ppm, v/v; 1230 mg/m^3) for 4 hours per day, 5 days per week for 14 days. No mortalities were reported. Clinical signs of toxicity included inactivity, irregular respiration, exophthalmos (bulging of the eye), intermittent tremors and hyperactivity (observed in 1 rat only). Necropsy revealed a large and heavy spleen in 2/3 rats sacrificed after the 10th exposure and in 2/3 rats sacrificed after a 14-day recovery period. The body weight was not affected.

In a dose-finding inhalation toxicity study (OECD TG 412), male and female Wistar rats (n=10/sex/dose) were exposed (head only) to 2-chloroaniline at 55, 379 and 868 mg/m^3 for 6 hours per day for 5 days. Clinical signs of toxicity included cyanosis, tremor, and impairment of reflexes in the high-dose groups. Haematological findings including increased Heinz bodies and reduced haemoglobin (females only) were reported for low-dose groups while increased methaemoglobin (1.3-3.3 %) and decreased erythrocytes and haematocrit were reported for higher dose groups. The primary toxic effect was damage to the erythrocytes evident at the lowest dose tested (REACH).

Genotoxicity

Based on the weight of evidence from available in vitro and in vivo genotoxicity studies for the parent base, the chemicals have genotoxic potential. The information available is not sufficient for classification. While generally negative results are reported for reverse mutations in *Salmonella typhimurium*, positive results were observed in several clastogenicity assays in vitro. In vivo micronuclus tests were mainly negative although few positive results were reported at the higher doses.

In vitro studies

Positive results were obtained in the following in vitro assays for the parent base (REACH):

- in vitro mammalian cell gene mutation assay (hypoxanthine-guanine phosphoribosyl transferase) in Chinese hamster lung fibroblasts (V79) at 0 to 0.6 µg/mL;
- in vitro mammalian cell gene mutation assay (lymphoma assay) in L5178Y cells (similar to OECD TG 476) with S9 metabolic activation at 31.25 to 700 µg/mL; and
- bacterial DNA damage or repair test (similar to EPA OPPTS 870.5500) in *Escherichia coli* without metabolic activation at 0.5 µg/mL (separation of cytotoxicity and genotoxicity unclear).

Negative results were obtained in the following in vitro assays for the parent base (REACH):

- Ames assays (OECD TG 471) with TA92, TA94, TA100, TA1535, TA1537, TA97 and TA98 strains of *S. typhimurium* with and without S9 metabolic activation and up to a maximum dose of 3000-3333 µg/plate;
- Umu-test genotoxicity assay (non-guideline) with and without S9 metabolic activation at 100 µg/mL;
- in vitro mammalian chromosome aberration (CA) test in Chinese hamster lung (CHL) cells at 250 µg/mL;
- in vitro cell transformation assay in Syrian hamster embryo (SHE) cells; and
- in vitro mammalian cell unscheduled DNA synthesis test (similar to EU Method B.18) in male ACI rat primary hepatocytes at 127 µg/mL to 127 ng/mL.

In vivo studies

A weak clastogenic effect was reported for the parent base in the following in vivo micronucleus tests (OECD TG 474) (REACH):

- NMRI male and female mice (n=5/sex/dose) received a single oral dose of 500, 1000 or 1500 mg/kg bw. Biologically important and statistically significant variations in incidence of micronucleated polychromatic erythrocytes between the negative control and the highest dose of 1500 mg/kg bw were reported; and

- NMRI male and female mice (n=5/sex per timepoint of 24h, 48h, 72h) received a single oral dose of 1000 mg/kg bw.

Negative results were obtained for the parent base in the following in vivo micronucleus tests similar to OECD TG 474. In general, the negative studies were performed on the lower doses (REACH):

- male rats (n=5/dose) were treated with single i.p. injection of 200, 400 or 550 mg/kg bw/day for three consecutive days. No increases in the frequency of micronucleated bone marrow cells from the femur were reported;

- male and female ICR mice received a single i.p. injection of 0, 20, 70, 200 mg/kg bw of 2-chloroaniline. No statistically significant increases in the frequency of micronucleated polychromatic erythrocytes were observed;

- male B6C3F1 mice received a single i.p. injection of 125, 250, 500, 750 or 1000 mg/kg bw of 2-chloroaniline. A positive trend was reported in frequency of micronucleated polychromatic erythrocytes, but the test was considered to be negative; and

- male and female B6C3F1 mice were treated orally (gavage) with 0, 1, 2, 4, 8 and 16 mg/mL of 2-chloroaniline (in water containing 0.1 N HCl) once per day, 5 days per week for 13 weeks. No statistically significant increases in the frequency of micronucleated polychromatic erythrocytes were observed.

Carcinogenicity

Based on the available information, the chemicals are not expected to be potent carcinogens. However, the carcinogenic potential of these chemicals cannot be ruled out, and should be reviewed if further information becomes available.

No experimental carcinogenicity data are available for the chemicals. The parent base is suggested to have carcinogenicity concern (Bruschweiler et al., 2014).

In general, there is evidence that methaemoglobin-producing anilines may have non-genotoxic mechanism for the induction of haemangio- and fibrosarcomas in the spleen of rats (US EPA, 1988). This is supported by findings in a related chemical, the isomeric 4-chloroaniline (CAS No 106-47-8) which is classified for Carcinogenicity - category 1B with a hazard statement of ‘May cause cancer’ (Safe Work Australia). The chemical 4-chloroaniline produces spleen and liver neoplasms in rats and mice, respectively (NICNAS). Whether the mechanism of carcinogenesis induced by 4-chloroaniline is mediated through genotoxic or non-genotoxic mechanisms is not understood (WHO, 2003).

Compared to 4-chloroaniline with the strongest potential to bind to haemoglobin, the binding of 2-chloroaniline is lower. The order of potency for methaemoglobin formation for the chloroaniline isomers in rats and mice is p-chloroaniline (4-chloroaniline) > m-chloroaniline (3-chloroaniline; CAS No 108-42-9) > 2-chloroaniline (Hejtmancik et al., 2002). Similarly, 4-chloroaniline was consistently mutagenic in various genotoxicity assays (NICNAS), while the findings in 2-chloroaniline indicated potential for genotoxicity, but were inconsistent (see **Genotoxicity** section).

Reproductive and Developmental Toxicity

Based on the available data, the chemicals are not expected to be developmentally toxic. Developmental effects were only observed secondary to maternal toxicity. No data are available to assess the reproductive toxicity of the chemicals.

In an OECD TG 414 (Prenatal developmental toxicity) study, Bor:WISW (SPF Cpb) female rats were orally (gavage) treated with 10, 50, or 250 mg/kg bw/day of the parent base (in 5 mL/kg polyethylene glycol) from day 6 to 15 of pregnancy. The experiment was terminated on day 20 of pregnancy (a day before expected delivery). No mortality was observed in the dams. Clinical signs of toxicity including tremor, reduced food intake and reduced body weight gain were observed in dams from the highest dose group. Increased spleen weights were reported in dams from the 50 and 250 mg/kg bw/day groups. Significant increase of late resorptions, decrease in number of viable pups/ litter and increase in number of spontaneous malformations were reported at the highest dose of 250 mg/kg bw/day. The maternal and foetal NOAELs were 10 and 50 mg/kg bw/day, respectively (REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation for the chemicals include systemic acute and chronic effects (acute and chronic toxicity from oral, dermal and inhalation exposure). Additionally, the carcinogenic potential of these chemicals cannot be ruled out, and should be reviewed if further information becomes available.

Public Risk Characterisation

The chemicals could be used as intermediates in the manufacture of dyes and pigments (see **Import, Manufacture and Use** section) which may be used in tattoo inks and textile dyes, and it may then be regenerated by reductive cleavage of the azo dyes. The chemical 2-chloroaniline was indicated as a potential aromatic amine cleavage product of concern from azo dyes (Bruschweiler et al., 2014). As such, further regulatory controls for public health may be determined as part of a Tier III assessment for ‘Azo dyes that cleave to aromatic amines of potential toxicological concern’.

Occupational Risk Characterisation

Given the critical health effects (acute and chronic toxicity, eye irritation and skin sensitisation), the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise 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 the appropriate controls.

NICNAS Recommendation

The chemicals are recommended for a Tier III assessment as part of the assessment of 'Azo dyes that cleave to aromatic amines of potential toxicological concern' (NICNAS).

Regulatory Control

Public Health

The need for regulatory control for public health will be determined as part of the Tier III assessment.

Work Health and Safety

The chemicals are recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Toxic if swallowed - Cat. 3 (H301)* Toxic in contact with skin - Cat. 3 (H311)* Toxic if inhaled - Cat. 3 (H331)*
Repeat Dose Toxicity	Not Applicable	May cause damage to organs through prolonged or repeated exposure - Cat. 2 (H373)*

[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 consumers

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, and inhalation exposure to the chemical 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 chemical is used. Examples of control measures that could minimise the risk include, but are not limited to:

· using closed systems or isolating operations;

· using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;

· 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 chemical.

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 help meet 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 these chemicals has not been undertaken as part of this assessment.

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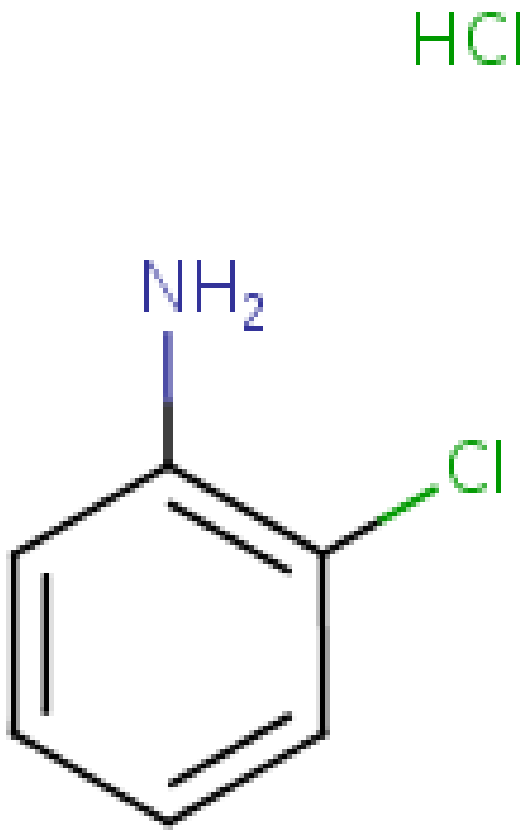
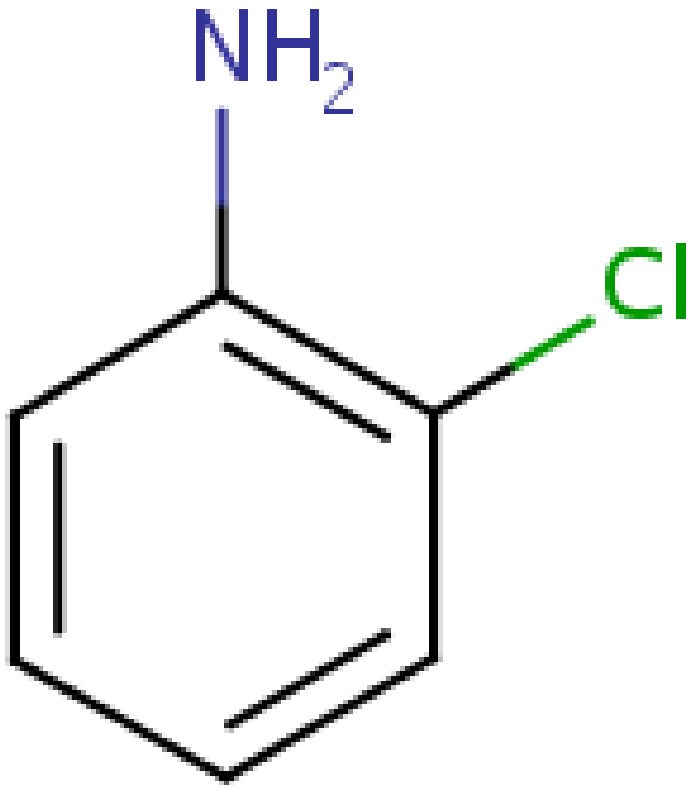
Last Update 30 June 2017

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Benzenamine, 2-chloro-, hydrochloride** C.I. 37000 C.I. azoic diazo component 44 2-chloroanilinium chloride
CAS Number	137-04-2
Structural Formula	
Molecular Formula	C6H6ClN.ClH
Molecular Weight	164.03

Chemical Name in the Inventory and Synonyms	**Benzenamine, 2-chloro-** 2-chloroaniline 1-amino-2-chlorobenzene

	o-chloroaniline fast yellow GC base
CAS Number	95-51-2
Structural Formula	
Molecular Formula	C6H6ClN
Molecular Weight	127.57

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