Benzenamine, 4-chloro-2-methyl- and its hydrochloride: Human health tier II assessment

04 July 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Benzenamine, 4-chloro-2-methyl-	95-69-2
Benzenamine, 4-chloro-2-methyl-, hydrochloride	3165-93-3

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

The chemical, benzenamine, 4-chloro-2-methyl, hydrochloride (CAS No. 3165-93-3) is a salt resulting from benzenamine, 4-chloro-2-methyl- (CAS No. 95-69-2; referred to as the parent base in this report) reacting with one molecule of hydrochloric acid. Therefore, these two chemicals are considered together in this assessment report. The speciation of these chemicals in biological fluids is pH-dependent, but independent of the original form.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified. The use of the chemicals are restricted in Australia (see **Restrictions**: Australian).

International

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; 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).

Whilst the chemicals are not directly included in domestic products as an ingredient, the parent base has been detected in finger paints at concentrations between 0.3–0.6 ng/g dry paint as an impurity (Garrigos, 2000; IARC, 2010).

The chemicals have reported site-limited use including as intermediates in producing:

- azo dyes for cotton, silk, acetate and nylon; and
- pigments such as Pigment Red 7 and Pigment Yellow 49.

The chemical, 4-chloro-2-methylbenzenamine, also has reported site-limited use as a laboratory analytical agent such as an immunohistochemical stain.

Restrictions

Australian

The chemicals are listed in The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons—SUSMP) (SUSMP, 2013) in Schedule 7.

Schedule 7 chemicals are described as 'Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply' (SUSMP). Schedule 7 chemicals are labelled with 'Dangerous Poison'. Products for domestic use must not include poisons listed in Schedule 7.

International

The chemicals are listed in the Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist") under the entry 'Toluidines, their isomers, salts and halogenated and sulfonated derivatives'.

The chemical, CAS No. 95-69-2, is restricted under Annex XVII to REACH Regulations. ‘The chemical cannot be used in substances and preparations placed on the market for sale to the general public in individual concentrations ≥ 0.1 % ' (European Parliament and Council 1999; European Parliament and Council 2006; European Parliament and Council 2008).

The parent base is not allowed to be detectable in finger paints under European Standard EN 71-7:2002.

The chemicals are also listed on the following (Galleria Chemica):

- Japan Poisonous and Deleterious Substances Control Law—Cabinet Order (Article Poisonous Substances);
- Chile List of Dangerous Substances; and
- United Arab Emirates Restricted Chemicals.

Existing Worker Health and Safety Controls

Hazard Classification

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

- R45 Carc. Cat. 2 (carcinogenicity);
- R68 Muta. Cat. 3 (mutagenicity); and

- T; R23/24/25 (acute toxicity).

Exposure Standards

Australian

No specific exposure standards are available. *Guidance on the Interpretation of Workplace Exposure Standards for Airborne Contaminants* provides advice that 'exposure to carcinogens should be eliminated or minimised so far as is reasonably practicable' (Safe Work Australia).

International

The chemical CAS No. 95-69-2 has an exposure limit (OEL) of 12 mg/m^3 in Switzerland (IARC, 2010).

Health Hazard Information

The chemical, CAS No. 95-69-2, is mainly used to manufacture azo dyes. It is included in the European Union list of aromatic amines with carcinogenic potential. It is also known as a powerful producer of methaemoglobin and Heinz bodies, and causes toxic haemolytic anaemia. In addition, the chemical has a direct action on the bladder, which leads to irritation (NTP, 2011; Wiley VCH).

Toxicokinetics

Experimental studies in rats and mice indicated that the parent base is rapidly eliminated (within 72 hours) primarily through urinary excretion.

Unlike other aromatic amines, N-acetylation does not appear to be an important metabolic step. Following oral administration of ^{14}C-4-chloro-o-toluidine in Sprague Dawley (SD) rats, the urinary metabolites identified (in addition to the parent base) were 5-chloroanthranilic acid, 4-chloro-2-methylacetanilide and small levels of unidentified ethyl acetate-soluble substances. The results from the in vitro analysis on rat liver microsomes showed conversion of the chemical to symmetrical azo derivatives by peroxidases. These microsomal metabolites include 5-chloro-2-N-hydroxyaminotoluene and 4,4'-dichloro-2,2'-dimethyl-azobenzene (Hill et al., 1979). However, these metabolites have not been observed in vivo (Wiley VCH; IARC, 2000; NTP, 2011).

Accumulation of the chemicals in the tissues is low. However, binding of the chemicals to proteins, DNA and RNA, particularly in rat and mice liver, were observed following oral or intraperitoneal (i.p.) administration. The metabolism of the chemicals and level of binding appear to be species dependent. The level of covalent binding to liver DNA was reported to be higher in mice, but the binding to liver RNA and protein was higher in the rats. In some studies (in vitro), mouse liver fractions and, to a lesser extent, rat liver fractions incubated with the chemical 4-chloro-2-methylbenzenamine, formed reactive metabolites that bound to the DNA of calf thymus. The binding of the chemicals to haemoglobin was also observed in rats and mice following its oral intake, where higher levels of binding was seen in rats (Wiley VCH; IARC, 2010).

Futhermore, administration of the chemical 4-chloro-2-methylbenzenamine to male SD rats induced production of enzymes involved in xenobiotic metabolism including cytochrome P-450 isozymes (CYP1A1 and 1A2), ethoxycoumarin-O-deethylase, gluthathione S-transferase and epoxide hydrolase. Additionally, this study also reported a chemically-induced elevation of the levels of ethoxyresorufin-O-deethylase (EROD), a measure of aryl hydrocarbon receptor (AHR) agonism, following exposure to the chemical (Leslie et al., 1988; IARC, 2000).

Acute Toxicity

Oral

The chemicals are classified as hazardous with the risk phrase ‘Toxic if swallowed’ (T; R25) in HSIS (Safe Work Australia). While the available data do not support this classification, in the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend this classification.

Rats (Tif:RAC/f) exposed orally to the chemicals for 24 hours caused dose-dependent cyanosis, exophthalmos (protruding eyeballs), lacrimation and secretion from the Harderian gland, shortness of breath, loss of consciousness, reduced mandible mobility and death with median lethal dose (LD50) of 860 and1000 mg/kg bw for the hydrochloride and parent base respectively. The chemicals also induced ruffled fur, prostration and muscle spasms. In addition, histopathological findings showed marked changes in the gastrointestinal tract, livers, kidneys and spleens observed during autopsy. In C57BL/6J mice, oral administration of the parent base at 160 mg/kg bw resulted in delayed body weight gain (Wiley VCH).

Dermal

The chemical is classified as hazardous with the risk phrase ‘Toxic in contact with skin’ (T; R24) in HSIS (Safe Work Australia). While the available data do not support this classification, in the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend this classification.

In rats (Tif:RAC/f), the LD50 was reported to be 1800 and >2150 for the parent base and hydrochloride salt respectively. Reported signs of toxicity after 24 hours of exposure in rats include cyanosis, exophthalmos (protruding eyeballs), lacrimation and secretion from the Harderian gland, dyspnoea (shortness of breath), loss of consciousness and reduced mandible mobility. In cats, dermal exposure to the parent base (935 mg/kg bw) on shaved skin for three and five days resulted in apathy, dyspnoea and death (Wiley VCH).

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Toxic by inhalation’ (T; R23) in HSIS (Safe Work Australia). Limited data are available to evaluate this classification.

Inhalation exposure of cats to the chemical at concentration ranges 0.1–5 mg/L air (duration not specified) induced irritation of the nasal mucosa and conjuctiva, pathological changes in the deep airways, tracheitis and large volumes of mucus from the lungs. During autopsy, pulmonary oedema was identified in the animals that died (number and doses not specified) (Wiley VCH).

Observation in humans

Toxic effects have been observed in workers using the chemicals, even after a single exposure. These include blood in the urine (haematuria), inflammation of the bladder (cystitis), painful urination (dysuria), reduced bladder capacity and generalised pain in the lower abdomen (IARC, 2000; Wiley VCH).

Corrosion / Irritation

Skin Irritation

Limited data are available.

No signs of irritation were reported in rats following occlusive application of the parent base at doses of 500, 1000 or 2000 mg/kg. In cats, no dermal irritation was observed in another 12-day study (Wiley VCH). However, exposure to the the chemical 4-chloro-o-toluidine hydrochloride has been suggested to cause skin irritation in humans (NJ Department of Health, 2004).

Eye Irritation

No data are available.

Sensitisation

Skin Sensitisation

No data are available. The chemical does not contain a structural alert for skin sensitisation (OECD Toolbox).

Repeated Dose Toxicity

Oral

The chronic oral toxicity of the hydrochloride salt of the chemical has been investigated in Tif:RAI rats and Tif:NMRI mice. Pathological changes were observed in all treated animals following the exposure to the chemical at doses of 0, 750, 1500, 3000 or 6000 mg/kg in the diet for 60 days. These include the following:

- dose-dependent delay in body weight gain;
- toxic haemolytic anaemia with an increase in immature red blood cells (reticulocytes);
- polychromatophilia (presence of excessive red blood cells);
- formation of Heinz bodies;
- methaemoglobinaemia (abnormal amount of methaemoglobin); and
- reduced levels of haemoglobin, haematocrit and erythrocyte counts.

Moreover, a reduced level of protein in the blood was also observed in animals treated with 3000 and 6000 mg/kg of the chemical. In male rats, an increased incidence of haematuria was observed at the top dose (6000 mg/kg diet). Effects of the chemical exposure were also noted in other tissues such as the liver, spleen and bladder. Observations during the autopsy of the treated mice and rats include dose-dependent enlargement of the liver and spleen with mild to moderate vacuolation of the hepatocytes. Proliferation of the transitional epithelium of the bladder and hyperaemia were also noted in the bladder (Wiley VCH).

Using approximate diet conversion factors, the lowest observed adverse effect level (LOAEL) for this study is 75 mg/kg bw/day and 150 mg/kg bw/day in rats and mice respectively (Derelanko & Auletta, 2014).

Additionally, mice (B6C3F1) exposed orally to the parent base at doses ≥1250 ppm (females) and ≥3750 ppm (males) in the diet resulted in a high incidence of haemosiderin deposit in the renal tubular epithelium. This observation was more prominent in mice with haemangiosarcoma (IARC, 2000).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

The chemical is classified as hazardous (Category 3 mutagenic substance) with the risk phrase 'Possible risk of irreversible effects' (Xn; R68) in HSIS (Safe Work Australia). The available data support this classification.

Generally the chemicals were negative in bacterial mutagenicity tests. However, the chemicals gave positive results in strains of *Salmonella typhimurium* TA100 and TA98 (with metabolic activation) and TA1535 (without metabolic activation) at doses of 200, 250 and 375 µg/plate.

Positive results have been obtained in several in vitro tests in mammalian systems, including:

- unscheduled DNA synthesis in rat primary hepatocytes;
- DNA strand breaks, cross-links or related damage in Chinese hamster V79 lung cells;
- chromosomal aberration (CA) test in Chinese hamster ovary (CHO) cells with and/or without activation;
- sister chromatid exchange (SCE) in CHO cells with and/or without metabolic activation (IARC, 2000; Wiley VCH); and
- transformation of BALB/c 3T3 mouse cells.

However, the parent-base tested negative in both SCE and and CA tests in human lymphocytes in vitro.

The hydrochloride salt of the chemical was positive in a mouse spot test, but negative in a heritable translocation assay in vivo (IARC, 2000). DNA breakage was detected by a single-cell gel electrophoresis (Comet assay) in mouse liver, urinary bladder, lung, and brain and in rat liver and kidney following in vivo exposure to the chemical.

Carcinogenicity

The chemical is classified as hazardous (Category 2 carcinogenic substance) with the risk phrase 'May cause cancer' (T; R45) in HSIS (Safe Work Australia). The available data support this classification.

The carcinogenic potential of the chemicals has been evaluated in several long-term feeding studies in various strains of rats and mice. The most commonly observed cancer-related effects in these studies are benign or malignant blood vessel tumours (haemangioma, haemangiosarcoma or a combination) observed in the spleen and adipose tissues in mice. In these studies, mice showed greater sensitivity to the carcinogenic effects of the chemical than rats, with no increased incidence of tumours observed in the latter (IARC, 2000; IARC, 2010; NTP, 2011).

High incidence rates of haemangiosarcoma and the combination of haemangiomas and haemangiosarcomas were observed following dietary administration of the hydrochloride salt of the chemical to B6C3F1 mice for 99 weeks. In this study, male mice were given 0, 3750, and 15000 mg/kg, while females were exposed to 0, 1250, and 5000 mg/kg of the chemical. The incidence of tumours was >70% in the high dose males, and low and high dose females. In addition to tumours, a dose-dependent delay in body weight gain and increase in the number of deaths occurring in treated animals were observed compared with controls. Similar findings were noted in Ham/ICR and CD-1 mice with exposure to the hydrochloride salt at doses between 750–4000 mg/kg/diet for 18 months. The incidence of tumours (haemangiomas and haemangiosarcomas) was >60% in animals exposed to the chemical. These were more prominent in areas such as the spleen, and in the subperitoneal and subcutaneous adipose tissues (IARC 2000; IARC, 2010; NTP, 2011).

In humans, epidemiological studies on the carcinogenicity of the chemical are limited. However, the available data indicate a high relative risk for urinary bladder cancer in individuals exposed to the chemical, in particular, workers in the dye and synthetic chemical industries (NTP, 2011). Several cases of urinary bladder tumours were identified in workers who were irregularly exposed to the chemical for an average of 18 years through production of the insecticide, chlordimeform. The occurrence of brain tumour was also reported in 1/7 workers with urinary bladder cancer. Co-exposure to other aromatic amines that may cause bladder cancer could not be ruled out as a confounding factor (IARC, 2000; NTP, 2011).

The International Agency for Research on Cancer (IARC) has reviewed and subsequently concluded that it is 'probably carcinogenic to humans' (Group 2A) (IARC, 2010). The chemical is also listed in the National Toxicology Program (NTP) *Report on carcinogens* as 'reasonably anticipated to be human carcinogens' (NTP, 2011).

Reproductive and Developmental Toxicity

The chemical does not show specific reproductive or developmental toxicity.

Risk Characterisation

Critical Health Effects

The chemicals are both genotoxic and carcinogenic in animals and are reasonably anticipated to be carcinogens in humans. Exposure to the chemical also causes systemic acute effects through oral, dermal, and inhalation exposure.

Public Risk Characterisation

The chemicals are currently listed on Schedule 7 of the SUSMP and therefore cannot be included in domestic products. These current controls are considered adequate to minimise the risk to public health posed by products containing the chemical.

However, chemicals may be present in small quantities as an impurity in some consumer products containing dyes and pigments manufactured from the chemical. The parent base has been detected in finger paints at concentrations between 0.3–0.6 ng/g dry paint as an impurity (see **International use** section). The public may also be exposed to these chemicals as a result of their release from these dyes. The risk to the public from this route of exposure will be considered in the IMAP assessment of dyes based on the chemicals.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure of workers to the chemicals may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemical at lower concentrations may also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemical are implemented. The chemical 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.

Guidance on the interpretation of workplace exposure standards for airborne contaminants provides advice that 'exposure to carcinogens should be eliminated or minimised so far as is reasonably practicable' (Safe Work Australia).

Based on the available data, the hazard classification in HSIS is considered appropriate.

NICNAS Recommendation

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. No further assessment is required.

However, the chemicals may be used to manufacture dyes and pigments. Recommendations for additional regulatory controls may be required to limit exposure to the chemicals as a result of the release from these dyes. This will be considered in the IMAP assessment of dyes based on the chemicals.

Regulatory Control

Public Health

The Schedule 7 entry in the SUSMP provides special precautionary measures to be taken during manufacturing, handling and using; and restriction on the availability, possession and storage or use of the chemical. This is considered adequate to mitigate potential risk of public exposure of the chemical from domestic articles such as finger paints and textile dyes.

Work Health and Safety

The chemicals 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	Toxic if swallowed (T; R25)* Toxic in contact with skin (T; R24)* Toxic by inhalation (T; R23)*	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
Genotoxicity	Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68)*	Suspected of causing genetic defects - Cat. 2 (H341)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)*	May cause cancer - Cat. 1B (H350)

[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 oral, dermal, ocular 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 which may 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 chemical if valid techniques are available to monitor the effect on the worker's health;

- air monitoring to ensure control measures in place are working effectively and continue to do so;
- 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 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 chemical 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

ChemIDPlus Advanced. Accessed April 2014 at **http://chem.sis.nlm.nih.gov/chemidplus/**

Derelanko and Auletta (2014). Approximate conversion factors (pppm to mg/kg/day) in Handbook of Toxicology, Third Edition, p84. Boca Raton: Taylor and Francis.

European Parliament and Council 1999. Directive 1999/45/EC, Official Journal of the European Union, Publications Office of the European Union, Luxembourg. Accessed May 2014 at **http://www.biosafety.be/PDF/1999_45.pdf**.

European Parliament and Council 2006. Annex XII: Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles. Regulation (EC) No 1907/2006, Accessed May 2014 at **http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2006R1907:20130701:EN:PDF#page=234**.

European Parliament and Council 2008. Annex 1 to Directive 67/548/EEC, Regulation (EC) No 1272/2008, Official Journal of the European Union, Publications Office of the European Union, Luxembourg. Accessed May 2014 at **http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L:2014:163:FULL&from=EN**.

Galleria Chemica. Accessed May 2014 at **https://jr.chemwatch.net/galleria/**

Garrigos M, Reche F, Pernia K, Jimenez A 2000. Optimization of parameters for the analysis of aromatic amines in finger-paints. Journal of Chromatography A, 896 pp.291-298

Hill D, Shih TW, Struck R 1979. Macromolecular binding and metabolism of the carcinogen 4-chloro-2-methylaniline. Cancer Research 39 pp. 2528-2531

International Agency for Research on Cancer (IARC) 2000. Volume 77-IARC monographs on the evaluation of carcinogenic risks to humans. Some industrial chemicals. Accessed April 2014 at **http://monographs.iarc.fr/ENG/Monographs/vol77/**

International Agency for Research on Cancer (IARC) 2010. Volume 99-IARC monographs on the evaluation of carcinogenic risks to humans. Some aromatic amines, organic dyes, and related exposures. Accessed April 2014 at **http://monographs.iarc.fr/ENG/Monographs/vol99/mono99.pdf**

Leslie C, Reidy G, Murray M, Stacey N 1988. Induction of xenobiotic biotransformation by the insecticide chlordimeform, a metabolite 4-chloro-o-toluidine and a structurally related chemical o-toluidine. Biochemical Pharmacology 37(13) pp. 2529-2535

New Jersey Department of Health and Senior Services (2004). Hazardous substance fact sheet for 4-chloro-o-toluidine hydrochloride (CAS Number 3165-93-3). Accessed May 2014 at **http://nj.gov/health/eoh/rtkweb/documents/fs/0397.pdf**

NTP 2011. NTP Report on the Carcinogens, Twelfth Edition. p-Chloro-o-toluidine and its hydrochloride (CAS Nos 95-69-2 and 3165-93-3). Accessed April 2014 at **http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/chlorotoluidine.pdf#search=p-chloro-o-toluidine**

OECD QSAR Toolbox version 3.1. **http://www.oecd.org/chemicalsafety/assessmentofchemicals/theoecdqsartoolbox.htm**

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed April 2014 at **http://hsis.safeworkaustralia.gov.au/HazardousSubstance**

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2013. Accessed April 2014 at **http://www.comlaw.gov.au/Details/F2013L01607/Download**

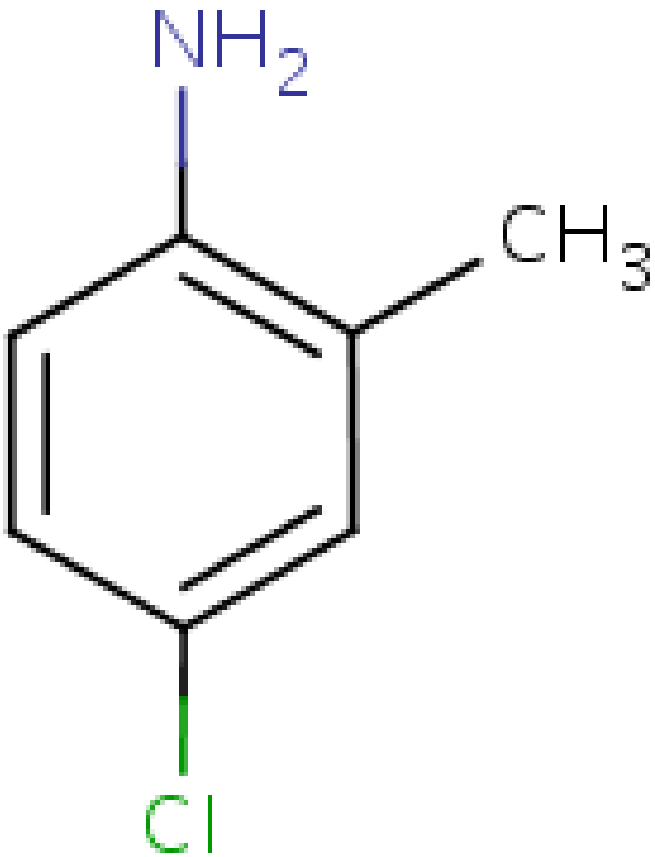
US Department of Health and Human Services, Household Products Database (HHPD), health and safety information on household products. Accessed April 2014 at **http://householdproducts.nlm.nih.gov/**

Wiley VCH. 4-Chloro-o-toluidine and its hydrochloride, vol 6, completed 22.9.1992. Accessed April 2014 at **http://onlinelibrary.wiley.com/doi/10.1002/3527600418.mb9569e0006/pdf**

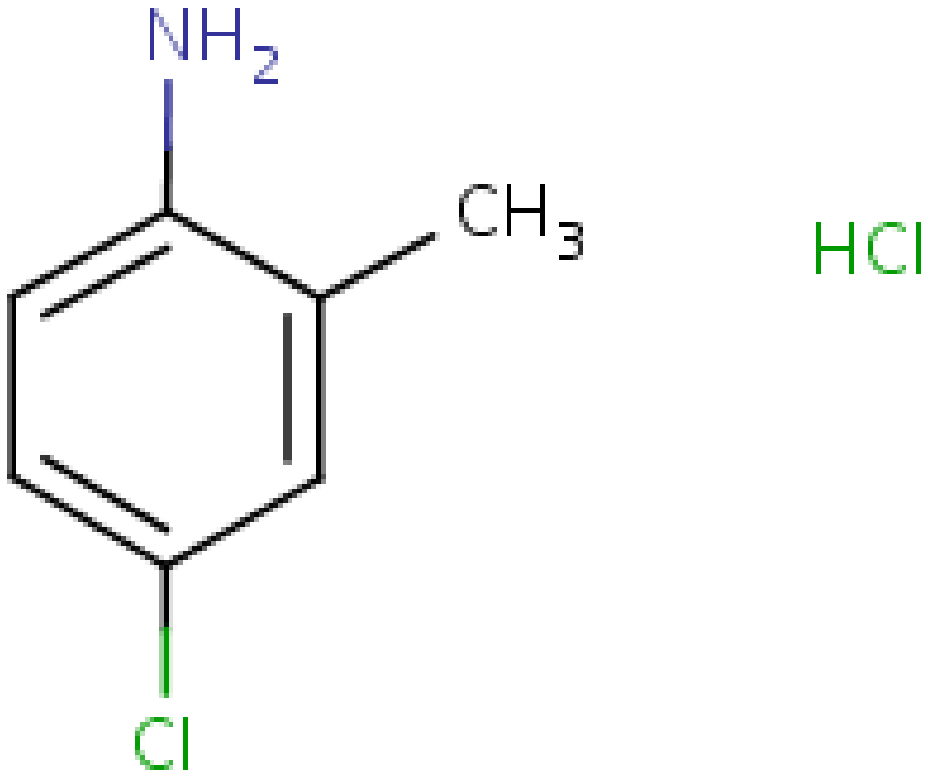
Last Update 04 July 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Benzenamine, 4-chloro-2-methyl-** 4-chloro-2-methylbenzeneamine 4-chloro-o-toluidine Brentamine Fast Red TR Base 4-chloro-2-methylaniline 4-chloro-2-methylaniline
CAS Number	95-69-2
Structural Formula	

	
Molecular Formula	C7H8ClN
Molecular Weight	141.6

Chemical Name in the Inventory and Synonyms	**Benzenamine, 4-chloro-2-methyl-, hydrochloride** 4-chloro-o-toluidine hydrochloride 4-chloro-2-methylaniline hydrochloride 4-chloro-o-toluidine hydrochloride 2-amino-5-chlorotoluene hydrochloride C.I. Azoic Diazo Component 11
CAS Number	3165-93-3
Structural Formula	

	
Molecular Formula	C7H8ClN.ClH
Molecular Weight	178.06

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