1-Octadecyl- and hydrogenated tallow alkyl- amines: Human health tier II assessment

04 July 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
1-Octadecanamine	124-30-1
Amines, hydrogenated tallow alkyl	61788-45-2

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 chemicals in this group are structurally related primary amines with a linear aliphatic chain with an average chain length of 18 carbon atoms. Hydrogenated tallow alkyl amines (CAS No. 61788-45-2) is derived from fatty acids and is comprised of a mixture of alkyl amines where the carbon chain length varies between 12 and 18 carbon atoms (even numbers only), with a low percentage of unsaturation of the alkyl chain.

Commercially, high purity alkyl amines are isolated by fractional distillation of fatty alkyl amines products. Alkyl amines are derived from natural sources and are usually converted through the catalytic hydrogenation of nitrile intermediates. The carbon chain distribution of the naturally derived chemicals will vary depending on the method of production and the source of the precursor chemicals. The typical composition of the fatty amine is:

- Hydrogenated tallow amines (CAS No. 61788-45-2) (C12: 1 %, C14: 4 %, C16: 30.5 %, C18: 62 %, incl. unsat. C18: <5 %);

The alkyl amines in this group are strongly basic and the primary amine is the most relevant property for consideration of the toxicity of any endpoint.

Saturated and unsaturated primary fatty alkyl amines have similar effects for systemic toxicity (repeated dose, reproductive/developmental toxicity) and genotoxicity – data from similar (NICNAS) chemicals have been 'read-across' to the chemicals in this assessment according to the principles of read-across (OECD 2014).

Import, Manufacture and Use

Australian

Hydrogenated tallow alkyl amines (CAS No. 61788-45-2) has identified domestic use in cleaning and washing agents at 60–100 % concentration.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; 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).

The chemicals in this group are reported in the CosIng database with the identified cosmetic function of antistatic agent. The chemical 1-octadecanamine (CAS No. 124-30-1) is included in the US Personal Care Products Council INCI dictionary with the identified cosmetic function of antistatic agent with a low reported frequency of use (5) (ed. Bailey, 2011).

Hydrogenated tallow alkyl amines (CAS No. 61788-45-2) has reported domestic use as a surfactant and in surface treatment.

The chemicals in this group have reported commercial use as:

- lubricants and additives; and
- anti-adhesive agents.

Restrictions

Australian

The chemicals in this group are listed in the *Poisons Standard* (Standard for the Uniform Scheduling of Medicines and Poisons 2014 SUSMP) in Schedule 5 as follows:

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

Schedule 5 chemicals are labelled with 'Caution'. These are 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.

International

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

EU Cosmetics Regulation 1223/2009 Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down;

Monoalkylamines, monoalkanolamines and their salts.

- maximum secondary amines content in the finished product: 0.5 %.
- minimum raw material purity: 99 %.
- maximum secondary amine content in the raw materials: 0.5 % (applies).
- maximum nitrosamine content: 50 µg/kg.
- should not be used with nitrosating systems and should be kept in nitrite-free environments.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals in this group are not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica) for 1-octadecanamine (CAS No. 124-30-1):

An exposure limit (TWA) of 0.14–1 mg/m^3 in different countries such as Latvia, Russia and the USA.

Health Hazard Information

Toxicokinetics

Toxicokinetic data available for analogue chemicals assessed as *Primary aliphatic (C12-22) and fatty amines* (NICNAS) are reported below.

The chemicals in this group have average molecular weights of 270 Da and a calculated log Pow > 7. The vapour pressure is expected to be low and they are insoluble in water. The oral and inhalation bioavailability is expected to be low. Diffusion across the gastrointestinal and respiratory tracts is possible. Following absorption, on average 80 % of the chemicals are expected to be exhaled as carbon dioxide within 24 h.

Following dermal exposure of hairless HR/DE mice to the analogue 1-dodecanamine (CAS No. 124-22-1) in squalane at concentrations of 0.5, 5, and 50 %, after 24 hours up to 5 % was absorbed at the highest dose. At the 5 and 0.5 % dilutions, 28 % and 57 % respectively were dermally absorbed. Dermal absorption by penetration through damaged skin is possible due to the corrosive properties of the chemicals in this group.

In a human study reported in EU RAR (2008), [11C]-1-octananamine (CAS No. 768306-69-0) was applied intravenously to human volunteers. Although the alkyl chain is significantly shorter than in the chemicals in this group, the amine functional group is the same and metabolism is expected to be similar. The chemical was rapidly distributed to the lungs (65–70 %, decreasing to 16–19 % within 30 min). Oxidation with monoamineoxidases was rapid with deaminated metabolites (95 %) in the blood within 2 minutes. Deaminated metabolites accumulated in the liver, and exhaled carbon dioxide (10–13 % of the dose) accounted for the majority of the dose, while excretion through urine was 1–2 % of the dose.

Acute Toxicity

Oral

Hydrogenated tallow alkyl amines (CAS No. 61788-45-2) and 1-octadecanamine (CAS No. 124-30-1) had low acute oral toxicity in rats with median lethal doses (LD50s) greater than 2000 mg/kg bw.

Dermal

Based on the analogue data available the chemicals in this group had low acute toxicity in animal tests following dermal exposure.

In studies reported in EU RAR (2008), the analogue cocoamine (CAS No. 61788-46-3) had low acute toxicity in animal tests following dermal exposure in GLP-compliant studies similar to OECD TG 402. The LD50 in rats was greater than 2000 mg/kg bw, and in rabbits greater than 1600 mg/kg bw (the maximum dose tested). Observed sub-lethal effects in the rat study included hunched posture, abnormal gait, lethargy, and decreased respiratory rate. Dermal reactions at the application site were observed in rats and rabbits, including well-defined moderate to severe oedema. Hard scabs, beet red lesions and hard necrotic skin were observed with both species.

Inhalation

Based on the analogue data available for the chemicals in this group following acute inhalation exposure, a hazard classification is not warranted. However, there are sufficient data to support hazard classification as an aspiration hazard.

The analogue cocoamine (CAS No. 61788-46-3) had low acute toxicity in an animal test following a one-hour inhalation exposure. The median lethal concentration (LC50) in rats could not be determined because the vapour concentration used in the study was not high enough to rule out systemic effects at the maximum concentration for which a classification can be determined.

In a range finding inhalation study (1 hour whole body exposure) reported in EU RAR (2008) in male Sprague Dawley (SD) rats, the analogue cocoamine (CAS No. 61788-46-3) caused local effects at concentrations of 0.096 and 0.099 mg/L but was not systemically toxic. There were no deaths, although all the animals were hypoactive after 10 minutes. After 30 minutes, several animals showed signs of irritation and exhibited nasal discharge. At the end of the exposure, all animals showed mild to severe irritation around the muzzle and fur discoloration. Evaluation of selected tissues following gross necropsy showed slight peribronchial lymphoid hyperplasia in the lung and minimal focal interstitial nephritis. The study authors were of the opinion that the findings were not treatment related.

In ECHA RAC (2011), the kinematic viscosity of hydrogenated tallow alkyl amine (CAS No.61788-45-2), was reported as 6.3 mm^2/s at 60 °C. This is within the threshold value of 20.5 mm^2/s at 40 °C for classification as an aspiration hazard and similar to other chemicals of this type (NICNAS). The opinion of the committee was that the measurement at 60 °C was ‘very low and cannot exceed the threshold value for classification even if the measure was made at 40 °C’. The primary consideration for chemicals in this group for this endpoint is the long linear hydrocarbon group which significantly influences the physicochemical properties.

The clinical symptoms observed in the many of the acute oral toxicity (laboured breathing, rattling noise) and repeated oral toxicity (severe lung damage) studies (see **Repeated dose toxicity** section), both by gavage and in the diet, support the classification of the chemicals in this group as an aspiration hazard. Additionally, there is not sufficient uncertainty to attribute the clinical observations to gavage errors leading to accidental aspiration of the chemicals into the lungs rather than the effect of the chemical.

Corrosion / Irritation

Skin Irritation

The chemicals in this group are irritating to skin. The available data warrant hazard classification.

EU RAR (2008) reported five studies performed in accordance with OECD TG 404 and three studies similar to OECD TG 404. Hydrogenated tallow alkylamines (CAS No. 61788-45-2) produced slight to well-defined erythema and slight to moderate oedema after 24 hours on intact New Zealand White rabbit skin. Hyperkeratinisation was observed in one animal in one study,

brown skin discolouration in all three animals in another study, and desquamation in 5/6 animals in another study. In all studies, the exposed areas were free of irritation after 21 days.

In ECHA RAC (2011), 1-octadecanamine (CAS No. 124-30-1) was irritating to intact rabbit skin when applied for four hours in three studies performed in accordance with OECD TG 404, and was corrosive in three non-guideline compliant studies. In the most detailed study (to OECD TG 404) the chemical on intact rabbit skin produced pronounced erythema and slight to moderate oedema. The average scores for erythema were 3.0/3.0/3.0, and for oedema, 2.7/1.3/1.3, at the 24, 48 and 72 hour time-points. Desquamation and dried, brittle, crusty, and cracked skin were observed over time. Effects were reversible in one rabbit by 14 days and the remaining two rabbits by 28 days. In another study conducted in accordance with OECD TG 404, the scores for erythema were 2.0/1.7/1.7 and oedema, 2.3/1.7/1.3 at the 24, 48 and 72 hour time-points. Erythema had cleared by day 10 and oedema by day 9. The three studies where the authors classified the chemical as corrosive to the skin were not reliable for classification as insufficient details were reported on the experimental conditions and clinical observations.

Eye Irritation

Studies were reported for the chemicals in this group in EU RAR (2008) and ECHA RAC (2011). The results showed that the chemicals may cause damage to the eyes. The available data warrant hazard classification.

In an eye irritation study conducted to OECD TG 405 in New Zealand White rabbits, hydrogenated tallow alkyl amines (CAS No. 61788-45-2) caused irreversible eye damage. There were pronounced redness of the conjunctivae and chemosis, corneal opacity and moderate iris lesions observed throughout the observation period. The average scores for iris/cornea density/conjunctivae (redness)/conjunctivae (chemosis) were reported as 1.0/3.3/3.0/3.1. The effects on the iris were reversible between days 14 and 21. The other effects were not reversed within 21 days.

In an eye irritation study conducted in accordance with OECD TG 405 in one New Zealand White rabbit, 1-octadecanamine (CAS No. 124-30-1) caused irreversible eye damage. One hour after application of the chemical there were pronounced redness of the conjuctivae and chemosis, iris and corneal lesions, and a clear colourless to whitish-slimy discharge. The study was terminated after seven days due to progressive vascularisation of the eye.

Sensitisation

Skin Sensitisation

There are no reliable human or animal data available. For primary aliphatic (C12-22) and fatty amines (NICNAS) the content of unsaturated alkyl chains and the chain length are of primary consideration for evaluating the differences with respect to sensitising potential. The available data do not warrant hazard classification.

In a study reported in EU RAR (2008), hydrogenated tallow alkyl amines (CAS No. 61788-45-2) did not induce skin sensitisation in an unreliable non-GLP compliant guinea pig maximisation test (GPMT). An unsuitable vehicle was selected and the reported nominal concentrations were not technically achievable.

In a study reported in EU RAR (2008), the analogue cocoamine (CAS No. 61788-46-3) was found to equivocally induce dermal sensitisation when tested similarly to OECD TG 406. Although GLP compliant the recommended number of test animals was not used. This chemical includes unsaturated components and components with shorter chain lengths, and thus may be expected to be a worst case example.

Repeated Dose Toxicity

Oral

Nine repeated dose toxicity studies with rats and dogs were reported in EU RAR (2008) and ECHA RAC (2011) for the chemicals in this group and analogue chemicals (NICNAS). In oral gavage and dietary studies in rats and dogs ranging between

14 days and 2 years, no observed adverse effect levels (NOAELs) of 3–10 mg/kg bw/day were reported. Based on the weight of evidence for the data available for the chemicals in this group and analogue chemicals (NICNAS), the chemicals may cause damage to health from repeated oral exposure.

The available data clearly demonstrated local effects through erosion of the gastrointestinal mucosa. One study was performed in accordance with OECD TG407 while the other studies were non-guideline studies mostly conducted pre-GLP.

No standard studies are available for hydrogenated tallow alkyl amines (CAS No. 61788-45-2). In one study reported in EU RAR (2008), stearic acid (a metabolite of hydrogenated tallow alkyl amine) was fed to SD rats in the diet for 206 days at a dose of ~200 mg/kg bw/day. Two out of five females died spontaneously (no further details). There was reduced weight gain in both sexes with animal condition reported as 'anorexic'. Tissues showed severe pulmonary infection including tracheobronchitis, lobular pneumonia and lipoid histiocytic response. Histopathological changes in other organs were not observed.

In a comparative study on hypolipidaemic activity, 1-tetradecanamine (CAS No. 2016-42-4),1-hexadecanamine (CAS No. 143-27-1), 1-octadecanamine (CAS No. 124-30-1), and components of hydrogenated tallow alkyl amines (CAS No. 61788-45-3), were administered by gavage to SD rats at dosages of 0, 8, or 20 mg/kg bw/day for 14 days. There was a significant reduction in food consumption and reduced concentrations of cholesterol and triglycerides in serum. There were significantly reduced concentrations of triglycerides and phospholipids in faeces. No other histopathological data were reported.

In three studies, SD rats were fed diets containing 1-octadecanamine (CAS No. 124-30-1) at concentrations ranging from 20 to 300 ppm (1.20–138 mg/kg bw/day in females; 1.05–88 mg/kg bw/day in males) for 209 days or 2 years. In the 209 day rat study, the survival rates were 20 % (males) and 80 % (females), while in the 2 year study the rates were 17–33 % (both sexes). There was reduced daily feed intake and weight loss or reduced weight gain observed in all studies. Common histopathological changes observed included accumulated histiocytes in the mucosa of the small intestine and mesenteric lymph nodes, and enlarged lymph nodes with necrosis and fibrosis. There were varying degrees of pulmonary infection and multiple organ inflammation. In rats, the NOAEL was determined to be 10 mg/kg bw/day.

In one study, dogs were fed diets of 1-octadecanamine (CAS No. 124-30-1) at dosages of 0, 0.6, 3 or 15 mg/kg bw/day for 1 year (5 days/week). One out of three of the dogs in the high dose group died prematurely. There was reduced weight gain in the high dose group and two animals had lesions of the mesenteric lymph nodes filled with pale histiocytes. In dogs, the NOAEL was determined to be 3 mg/kg bw/day.

In a 28-day gavage study in SD rats, performed according to OECD TG 407 (except for specific neurofunction investigations), the analogue tallow alkylamines (CAS No. 61790-33-8) was administered at dosages of 0, 12.5, 50 or 150 mg/kg bw/day. A lowest observed adverse effect level (LOAEL) of 12.5 mg/kg bw/day was reported. At the mid dose one female died at day 11, and at the high dose two males and three females died between day 8 and day 27. There was a dose related body weight decrease and reduced food consumption. In the high dose group, there were statistically significant changes in absolute and relative weights (usually decreases) for all organs. The predominant toxic effects in this study were dilation and mucosal erosion of the gastrointestinal tract associated with poor health status and unscheduled deaths. There was accumulation of the chemical in histiocytes in the mesenteric lymph nodes and intestinal submucosa. At the low dose there was slight histiocytic vacuolation in mesenteric lymph nodes and small intestines, and therefore a NOAEL could not be derived. Effects observed at higher concentrations included immunosuppresion in lymphoid tissues, adrenal and mucosal hyperplasia, leukocytosis, and liver toxicity.

Dermal

Limited data are available for 1-octadecanamine (CAS No. 124-30-1) and the analogue chemical (Z)-octadec-9-enylamine (CAS No. 112-90-3) (EU RAR 2008). Irritant effects were reported at all doses tested. The available data do not warrant hazard classification for systemic effects.

The chemical 1-octadecanamine (CAS No. 124-30-1) was applied dermally to mice at dosages of 0, 1.5 or 15 g/kg bw/day on alternate days over 6 days. Substantial hyperplasia of the epidermis with an increase in cholesterol content was observed at 1.5 mg/kg bw. Severe hyperplasia with 5-fold increase in weight per cm^2 and absence of sebaceous glands and hair follicles were observed at the highest dose.

The analogue (Z)-octadec-9-enylamine (CAS No. 112-90-3) was applied dermally to male and female SD rats at dosages of 0, 12.5, 62.5, or 125 mg/kg bw day for 14 days (applied 5/7 days). Due to excessive tissue destruction in the 62.5 and 125 mg/kg

groups, the study was discontinued on day 9 and the animals humanely sacrificed. Moderate to severe erythema was observed in the animals in the 12.5 and 62.5 mg/kg groups, which progressed to sloughing of the skin in some instances. Females were more sensitive to the irritant effects of the chemical than males. The LOAEL for local dermal effects was reported as 12.5 mg/kg bw/day. A NOAEL for systemic toxicity from dermal exposure could not be derived due to lack of histopathological data.

Inhalation

No data are available.

Genotoxicity

Limited data are available on the chemicals in this group. However, the available data on the analogue chemicals (NICNAS) suggest that the chemicals in this group are unlikely to be genotoxic based on negative results in several in vitro (bacterial gene mutation, mouse lymphoma assay, HPRT gene mutation test) and in vivo (bone marrow micronucleus test, chromosomal aberration) tests for gene mutation and clastogenicity.

In general, strong strain specific cytotoxicity was observed in in vitro studies reported in EU RAR (2008), likely due to the high basicity of the chemicals. In most experiments, cytotoxicity was observed at lower concentrations in experiments without metabolic activation than experiments with metabolic activation. Precipitation at higher doses was observed in some experiments.

Negative results were reported in bacterial reverse mutation tests for mutagenicity to *Salmonella typhimurium* (strains included TA97, TA98, TA100, TA1535, TA1537, TA1538) and/or *Escherichia coli* (strain WP2uvrA) for 1-octadecanamine (CAS No. 124-30-1) and the analogue chemicals, 1-hexadecanamine (CAS No. 143-27-1), (Z)-octadec-9-enylamine (CAS No. 112-90-3), tallow alkylamines (CAS No. 61790-33-8) and cocoamine (CAS No. 61788-46-3), with and without metabolic activation.

Negative results were also reported for the analogue (Z)-octadec-9-enylamine (CAS No. 112-90-3) in mouse lymphoma cells in accordance with OECD TG 476, and Chinese hamster ovary cells, although the cells were unable to form clones at higher concentrations.

The analogue tallow alkylamines (CAS No. 61790-33-8) did not induce in vivo chromosomal damage in SD rat bone marrow cells after an acute oral dose of 2000 mg/kg bw. Signs of toxicity included piloerection, hunched posture, hypoactivity and shallow breathing in all animals. One male animal died at 48 hours after exposure.

The analogue (Z)-octadec-9-enylamine (CAS No. 112-90-3) did not induce in vivo chromosomal damage in mouse bone marrow cells after an acute oral dose up to 5000 mg/kg bw. Clinical signs of toxicity were observed at all doses but were not described in the report.

Carcinogenicity

The limited data available for the chemicals in this group and analogue chemicals (NICNAS) do not warrant hazard classification for carcinogenicity.

In a pre-GLP study reported in EU RAR (2008), 1-octadecanamine (CAS No. 124-30-1) was not considered likely to have carcinogenic effects in studies where SD rats were given the chemical in diet at concentrations of 20, 100, 200 or 500 ppm for 2 years (mg/kg bw equivalents not reported). The survival rate was 17–33 % in all groups including the control group. No treatment related differences in incidence and type of tumours compared to controls were reported.

Reproductive and Developmental Toxicity

The data available for the chemicals in this group and the analogue chemicals (NICNAS) are not sufficient for hazard classification. Based on the available data, the reproductive/developmental effects observed were secondary to maternal toxicity.

There are no reliable data available on reproductive toxicity for 1-octadecanamine (CAS No. 124-30-1). In a chronic toxicity study in rats and dogs fed the chemical in the diet for 2 years, there were no reported effects on male or female gonads (EU RAR 2008).

In a reproductive/developmental toxicity screening study conducted in accordance with OECD TG 421, SD rats were exposed to the analogue tallow alkylamines (CAS No. 61790-33-8) at dosages of 0, 12.5, 50 or 150 mg/kg bw/day by gavage. Males were treated for 28 days while females were treated from the beginning of the study until day 3 of lactation. In the high dose group, 6/10 males and 5/10 females died between day 9 and day 25. In the mid-dose group, one male and one female died on day 13 and day 24, respectively. Statistically significant body weight loss was observed in the high dose group, and reduced body weight gain in the mid-dose group. A statistically significant lower absolute and relative weights of epididymides and statistically significant higher relative weight of testes was observed at the highest dose. However, histopathology of the testes and epididymides did not show treatment related changes. In the high dose group, there was moderately increased frequency of atrophic corpora lutea in the ovaries compared to controls; this was considered a secondary effect to the decrease in body weight gain (EU RAR 2008).

Impairment of reproductive performance was observed at the highest dose (increased pre-coital interval, only one female pregnant but with only implantation sites and no live pups). No dose-dependent or statistically significant differences in reproductive performance (including mating, fertility, gestational indices and pup viability and growth) compared with controls were reported for the low- and mid-dosages. Pre-implantation loss was not evaluated in the study. Based on the results, a reported NOAEL of 12.5 mg/kg bw/day was determined for both parental and reproductive toxicity.

In prenatal developmental toxicity studies reported in ECHA RAC (2011) the analogue (Z)-octadec-9-enylamine (CAS No. 112-90-3) was administered by gavage to rats (up to 250 mg/kg bw/day) and rabbits (up to 150 mg/kg bw/day) in range-finding studies. Clinical signs of toxicity, body weight loss and reduced weight gain were observed at all dose levels, while treatment related mortalities were observed at the higher doses. For the main studies, the dosages administered to rats were 10, 40 or 80 mg/kg bw/day and administered to rabbits were 3, 10 or 30 mg/kg bw/day.

In the rat study, all animals survived to scheduled sacrifice. General irritant effects including rales, salivation and unkempt appearance were observed at the mid and high doses. Pronounced toxicity was observed at the high dose including emaciation, rough coat, and dark red material around the eyes, nose and/or mouth. There was dose dependent body weight loss, or reduced weight gain observed at the mid and high doses. There were no statistically significant differences in reproductive parameters (number of corpora lutea, implantation sites, viable foetuses, foetal sex and foetal weight) when compared with controls. There were no reported indications of effects on embryotoxic, foetotoxic or teratogenic potential. In rats, the NOAELs were determined to be 10 mg/kg bw/day for maternal toxicity and =80 mg/kg bw/day for developmental toxicity.

In the rabbit study, two females died in the high dose group and one female at each of the treated groups aborted prior to scheduled sacrifice. Clinical signs of toxicity including rales and laboured breathing at the mid dose, and emaciation, few or no faeces, and irritation of the snout area at the high dose were observed. There was dose dependent body weight loss, or reduced weight gain observed at the mid and high doses. There were no statistically significant differences in reproductive parameters (number of corpora lutea, implantation sites, viable foetuses, foetal sex and foetal weight) when compared with controls. There were no reported indications of embryotoxic, foetotoxic or teratogenic potential. In rabbits NOAELs were determined to be 3 mg/kg bw/day for maternal toxicity and =30 mg/kg bw/day for developmental toxicity.

In an oral 28-day study in rats with the analogue (Z)-octadec-9-enylamine (CAS No. 112-90-3), histopathological examination of the testes, epididymides, seminal vesicles, ovaries (including oviducts), and uteri did not show chemical-related effects up to a dose of 50 mg/kg bw/day (EU RAR 2008).

Risk Characterisation

Critical Health Effects

The toxicity data for the chemicals in this group showed severe local effects including eye damage. Effects in dermal studies were also consistent with skin irritation. The chemicals are also aspiration hazards in the pure form. The chemical may also cause harmful effects following repeated exposure through ingestion.

Public Risk Characterisation

Although use in cosmetic products in Australia is not known, international information indicate that the chemicals in this group are not likely to be widely available for cosmetic use. When the chemicals are used as an antistatic agent in cosmetics (CosIng) the products are not likely to have extreme pH levels and thus public exposure to high concentrations of the chemicals are not expected from cosmetic use. The general public may be exposed to the chemicals through dermal and/or inhalation routes when using domestic products containing these chemicals. However, based on limited US information derived from the National Library of Medicine (NLM) Household Products Database, the concentration in these products is not considered to be sufficiently high to cause irritation effects. Therefore, the risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

Hydrogenated tallow alkyl amines (CAS No. 61788-45-2) has identified use in domestic products from 60–100 % concentration. The chemical is formulated in a solid block for pre-wash applications where dermal exposure is expected to be infrequent and of short duration. A pH < 11 is expected for the chemical in formulated products. A significant proportion of the chemical will be protonated when used in such products and given these buffering conditions a high level of irritation is not expected. Therefore, the risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

Occupational Risk Characterisation

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

Given the critical health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation 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.

The data available support an amendment to the hazard classification in HSIS (refer to **Recommendation** section).

NICNAS Recommendation

The assessment of the chemicals is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP).

Work Health and Safety

The 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.

In the absence of specific data on all the chemicals, data have been read-across (OECD 2014) from the chemicals in this group for which data was available. Should empirical data become available indicating that a lower (or higher) classification is appropriate for these chemicals, this may be used to amend the default classification.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful: may cause lung damage if swallowed (Xn; R65)	May be fatal if swallowed and enters airways - Aspi. Cat. 1 (H304)
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41) Irritating to skin (Xi; R38)	Causes serious eye damage - Cat. 1 (H318) Causes skin irritation - Cat. 2 (H315)
Repeat Dose Toxicity	Harmful: Danger of serious damage to health by prolonged exposure if swallowed (Xn; R48/22)	May cause damage to organs through prolonged or repeated exposure through the oral route - 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 industry

Control measures

Control measures to minimise the risk from oral, 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 chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- 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

Bailey, JE (ed.) 2011, Compilation of Ingredients Used in Cosmetics in the United States (CIUCUS), 1st Edition, Personal Care Products Council, Washington, D.C.

European Chemical Agency Committee for Risk Assessment (ECHA RAC) 2011 Annex 1 Background document to the Opinion proposing harmonised classification and labelling at Community level of amines, coco alkyl (CAS No. 61788-46-3) (Document Number: ECHA/RAC/CLH-O-0000002195-77-01/A1). Accessed June 2014 at **http://echa.europa.eu/opinions-of-the-committee-for-risk-assessment-on-proposals**-for-harmonised-classification-and-labelling

European Union Risk Assessment Report (EU RAR) 2008. Summary report for primary alkyl amines. Accessed February 2014 at **http://esis.jrc.ec.europa.eu/**

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

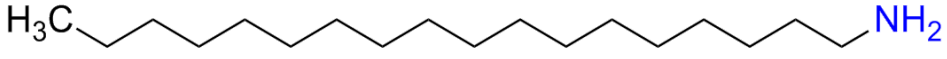
National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for Primary aliphatic (C12-22) and fatty amines. Available at **http://www.nicnas.gov.au**

OECD (2014). Guidance on Grouping of Chemicals, Second Edition. Environment Directorate. Joint meeting of the Chemicals Committee and the Working party on Chemicals, Pesticides and Biotechnology. Series on Testing& Assessment No. 194. Accessed April 2014 at **http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en**

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**

Last Update 04 July 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**1-Octadecanamine** n-octadecylamine stearylamine 1-?octadecylamine 1-?aminooctadecane
CAS Number	124-30-1
Structural Formula	

Molecular Formula	C18H39N
Molecular Weight	269.51

Chemical Name in the Inventory and Synonyms	**Amines, hydrogenated tallow alkyl** hydrogenated tallow alkyl amines tallow amine (hard)
CAS Number	61788-45-2
Structural Formula	**No Structural Diagram Available**
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Share this page