Fatty amines, di(long chain)alkyl: Human health tier II assessment

30 June 2017

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
1-Octadecanamine, N-octadecyl-	112-99-2
1-Hexadecanamine, N-hexadecyl-	16724-63-3
1-Tetradecanamine, N-tetradecyl-	17361-44-3
9-Octadecen-1-amine, N-9-octadecenyl-, (Z,Z)-	40165-68-2
1-Docosanamine, N-docosyl-	53171-44-1
Amines, dicoco alkyl	61789-76-2
Amines, bis(hydrogenated tallow alkyl)	61789-79-5
Amines, di-C14-18-alkyl	68037-98-9
Amines, di-C12-18-alkyl	68153-95-7
Amines, disoya alkyl	68783-23-3
Amines, ditallow alkyl	68783-24-4

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 secondary amines with two linear aliphatic chains.

The chemicals in this group can have an alkyl chain between 12 and 22 carbon atoms. Some of the chemicals are derived from fatty acids and are comprised of mixtures where the carbon chain varies between 12 and 18 atoms (even numbers only). The individual components may also have unsaturation of the alkyl chain.

Commercially, high purity alkyl amines are isolated by fractional distillation of fatty alkyl amine products.

Alkyl amines are derived from fatty acids from natural sources and converted through 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. Data regarding the typical composition of chemicals similar to those in this group are limited to the following fatty amines (NICNASa; NICNASb; Lawrence, 2004):

- soya alkyl amines (C16: 16 %, C18: 78 %, incl. unsat. C18: >60 %
- cocoamine (<C12: 15.5 %, C12: 50 %, C14: 18 %, C16: 8 %, C18: 8.5 %, incl. unsat. C18: <10 %);
- tallow alkylamines (C12: 1 %, C14: 3 %, C16: 32 %, C18: 61.5 %, incl. unsat. C18: >40 %); and
- hydrogenated tallow amines (C12: 1 %, C14: 4 %, C16: 30.5 %, C18: 62 %, incl. unsat. C18: <5 %).

An increasing percentage of unsaturation of the alkyl chains decreases the melting point of the chemical while the reactivity is expected to increase. The secondary amine functional group is strongly basic and is the most relevant functional group for consideration of the toxicity for any endpoint.

Import, Manufacture and Use

Australian

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

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary and the US Household Products Database.

The following chemicals have reported cosmetic use: N-hexadecyl 1-hexadecanamine (listed on the EU, Chilean and Canadian inventories of cosmetic ingredients), disoya alkyl amines, dicoco alkyl amines and bis(hydrogenated tallow alkyl) amines. The latter chemical has a low reported frequency of use (4) in cosmetic products (ed. Bailey 2011).

Dicoco alkyl amines, bis(hydrogenated tallow alkyl) amines and disoya alkyl amines function as antistatic agents. Dicoco alkyl amines are also used as emollients, emulsifiers and hair conditioners.

Bis(hydrogenated tallow alkyl) amines has reported domestic use as a surface active agent.

Commercial uses are reported for the following:

- as corrosion inhibitors (di-C14-18-alkyl amines, di-C12-18-alkyl amines, and ditallow alkyl amines);
- when hydrophobing silica (di-C14-18-alkyl amines and di-C12-18-alkyl amines);
- as an asphalt emulsifier (ditallow alkyl amines; and
- as lubricants and additives (N-9-octadecenyl-(Z,Z)-9-octadecen-1-amine).

Site limited uses are reported for the following:

- as an intermediate in the manufacturing of chemicals and chemical products (N-octadecyl-1-octadecanamine and N-9-octadecenyl-, (Z,Z)-9-octadecen-1-amine); and
- in ore flotation (ditallow alkyl amines).

Restrictions

Australian

The chemicals in this group are listed in the *Poisons Standard—Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedule 5 as follows (SUSMP, 2017):

'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.

This restriction does not affect other uses.

International

No known restrictions have been identified.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

The chemicals in this group are metabolised to substances that are naturally present in humans and do not cause systemic toxicity. Therefore, toxicity is confined to the potential for irritation or corrosion arising from the amine functionality.

Only one of the chemicals in this group has data regarding corrosion/irritation, di-C12-18-alkyl amines, which is corrosive. Regarding the rest of the chemicals, two opposing factors need to be considered in relation to predicting irritation potential using suitable analogue chemicals with data, the number of alkyl chains attached to the nitrogen and the length of those chains (OECD, 2014). Generally, primary amines (one alkyl chain attached) are more irritating than secondary amines (which have two alkyl chains attached), which are more irritating compared to tertiary amines (with three alkyl chains). The potential for irritation also decreases as the chain length increases (alkyl chain length = 12 indicates high reactivity). Although primary fatty amines with shorter alkyl chains are corrosive, their activity decreases and they are only found to be irritating when the chain length becomes long enough, as in N-octadecanamine (NICNASb).

Although secondary amines are generally more irritating compared to tertiary amines, substituting a methyl group on the dialkyl methyl amines with hydrogen is not expected to outweigh the impact of having two long chains attached to the nitrogen, which tend to reduce irritating properties. As a result, reading across from the non-irritating long chain dialkyl methyl amines (NICNASc) and the long chain primary amines (NICNASb) to the long chain dialkyl amines in this group, most of these chemicals are expected, at worst, to be irritating.

The chemical di-C12-18-alkyl amines is corrosive as a result of the shorter chain lengths being attached to the nitrogen. Note that both the primary amine C12-18-alkyl amines and tertiary amine C12-18-alkyldimethyl amines are very corrosive (NICNASb; REACH). The

other chemical in this group with short alkyl chains, dicoco alkylamine with 15.5 % <C12, is expected to be corrosive similarly to di-C12-18 alkyl amines.

Acute Toxicity

Oral

The chemicals di-C14-18-alkyl amines and di-C12-18-alkyl amines had low toxicity in animal tests following oral exposure. The median lethal dose (LD50) in rats is >10000 mg/kg bw.

Male albino rats were administered di-C14-18-alkyl amines at dose levels of 464, 1000, 2150, 4640 and 10000 mg/kg bw as a single oral dose (n = 5/group). As the highest dose would have exceeded the capacity of the rat's stomach, this was administered as a split-dose, with one half being administered in the morning and the second half within four or five hours. Signs of toxicity noted at the highest dose included depression, depressed righting and placement reflexes, ataxia, rapid or shallow respiration, mucoid diarrhoea and oily, unkempt fur. All animals appeared normal from the fifth or sixth day after dosing throughout the rest of the study period. The LD50 was >10000 mg/kg bw (USEPA, 1971).

Wistar rats (n = 5/sex) were administered di-C12-18-alkyl amines as a single oral dose of 2000 mg/kg bw. Clinical signs included piloerection, curved position, non-coordinated behaviour and non-regular breathing. The LD50 was >2000 mg/kg bw (REACH).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Corrosivity

Data are only available for one chemical, di-C12-18-alkyl amines. This chemical is corrosive and warrants classification. Di coco alkyl amines, which has a similar or shorter chain length distribution, should be classified likewise (see **Recommendation** section).

In a skin irritation study performed in accordance with OECD TG 404 and good laboratory practice (GLP), di-C12-18-alkyl amines was applied to the intact skin of six New Zealand White (NZW) rabbits (sex unspecified) and covered with a semiocclusive patch for three minutes and also for four hours. After three minutes of exposure, the following observations were made: slight to clear erythema after one hour, slight erythema and oedema after 1–7 days, redness of the skin in one animal after 14 days. Overall the skin was reported to be 'dry, rough and whitened and alopecic' (missing hair). After four hours of exposure, the following observations were made: severe erythema and slight oedema after one hour to 14 days and, one animal had a scar after 21 days. Overall the skin was rough, dry, swollen, whitened and hardened (REACH).

Skin Irritation

There are no irritation/corrosion data available for the remainder of the chemicals in this group. However, hazard classification is recommended based on reading across from similar chemicals in accordance with the OECD Guideline on Grouping of Chemicals (OECD, 2014) (see **Recommendation** section).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are likely to be local effects only. Based on the limited data available and reading across from data on dialkyl methylamines (NICNASc) and the long chain primary amines (NICNASb), the chemicals are considered to be irritating to the skin provided that the alkyl groups do not include shorter chain lengths, such as di-C12-18-alkyl amines, which was corrosive.

Public Risk Characterisation

Although use in cosmetic products in Australia is not known, international information indicates that the chemicals in this group are not likely to be widely available for cosmetic use. Bis(hydrogenated tallow alkyl)methyl amines has been identified as an antistatic, hair conditioning, surfactant or emulsifying agent in cosmetics. Limited information suggests that N-hexadecyl 1-hexadecanamine may also have cosmetic use. Cosmetic products are not likely to have extreme pH levels and thus public exposure to high concentrations of these chemicals in free base form are not expected from cosmetic use. 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

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 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.

During product formulation, dermal and ocular and inhalation exposure to these chemicals might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure at lower concentrations could 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.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

Assessment of these chemical are 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, 2017).

Work Health and Safety

The chemicals in this group 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.

Should empirical data become available indicating that a lower (or higher) classification is appropriate for any of the chemicals in this assessment, this may be used to amend the default classification.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia). The corrosivity classification (H314) applies to di-C12-18 alkyl amines and dicoco alkyl amines only. The rest of the chemicals should be classified for irritation (H315), unless sufficient empirical data are available to show this classification is not required.

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]
Irritation / Corrosivity	Not Applicable	Causes skin irritation - Cat. 2 (H315) Causes severe skin burns and eye damage - Cat. 1 (H314)

[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 chemicals should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular or inhalation exposure 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 local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- 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.

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.

CosIng. Cosmetic Ingredients and Substances. Accessed June 2017 at **http://ec.europa.eu/growth/tools-databases/cosing/**

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Last Update 30 June 2017

Chemical Identities

Chemical Name in the Inventory and Synonyms	**1-Octadecanamine, N-octadecyl-** distearylamine

CAS Number	112-99-2
Structural Formula	
Molecular Formula	C36H75N
Molecular Weight	522.00

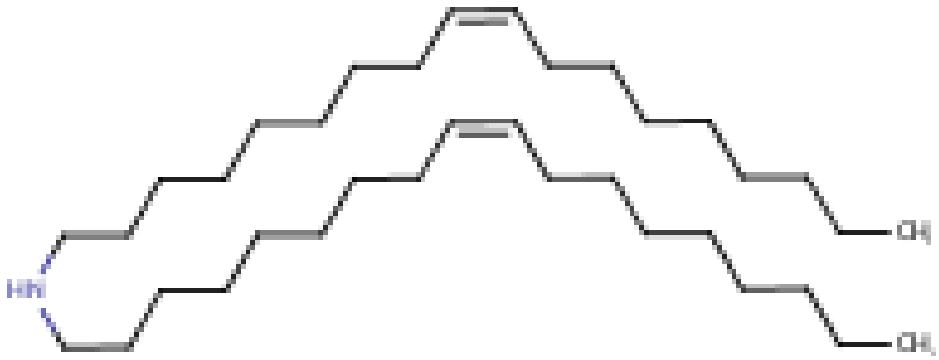
Chemical Name in the Inventory and Synonyms	**1-Hexadecanamine, N-hexadecyl-** dipalmitylamine dipalmitamine
CAS Number	16724-63-3
Structural Formula	

	
Molecular Formula	C32H67N
Molecular Weight	465.88

Chemical Name in the Inventory and Synonyms	**1-Tetradecanamine, N-tetradecyl-** dimyristylamine ditetradecylamine
CAS Number	17361-44-3
Structural Formula	

	
Molecular Formula	C28H59N
Molecular Weight	409.77

Chemical Name in the Inventory and Synonyms	**9-Octadecen-1-amine, N-9-octadecenyl-, (Z,Z)-** dioleylamine
CAS Number	40165-68-2
Structural Formula	

	
Molecular Formula	C36H71N
Molecular Weight	517.96

Chemical Name in the Inventory and Synonyms	**1-Docosanamine, N-docosyl-** dibehenylamine didocosylamine
CAS Number	53171-44-1
Structural Formula	

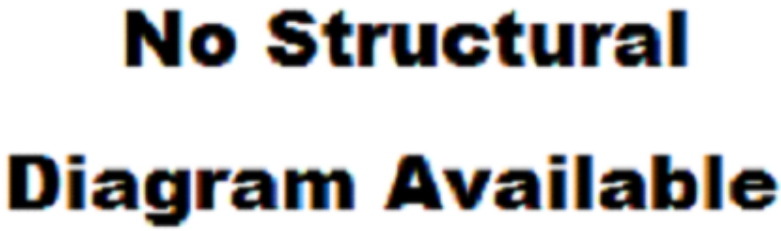
	
Molecular Formula	C44H91N
Molecular Weight	634.20

Chemical Name in the Inventory and Synonyms	**Amines, dicoco alkyl** dicocoalkylamine
CAS Number	61789-76-2
Structural Formula	**No Structural Diagram Available**

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Amines, bis(hydrogenated tallow alkyl)** di-H-tallow amines
CAS Number	61789-79-5
Structural Formula	**No Structural Diagram Available**
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Amines, di-C14-18-alkyl** (C14-18) dialkylamine
CAS Number	68037-98-9
Structural Formula	

	
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Amines, di-C12-18-alkyl** (C12-18) dialkylamine
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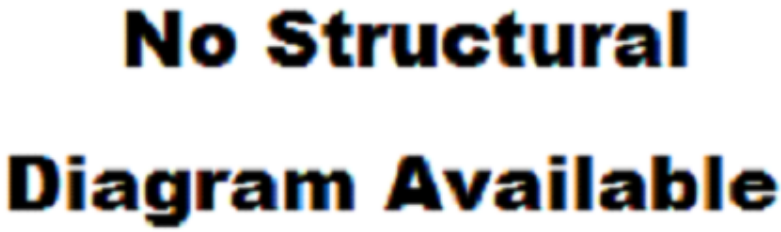
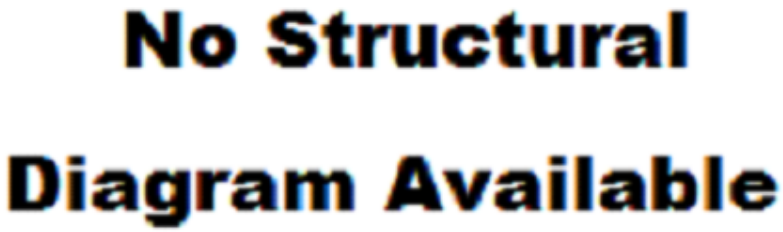
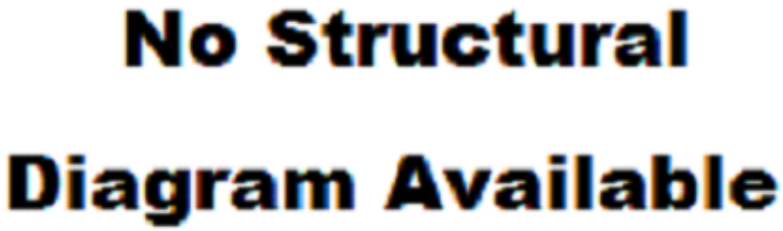
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Amines, disoya alkyl** disoybean oil alkylamine disoy alkyl amines

CAS Number	68783-23-3
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Amines, ditallow alkyl** di(tallowalkyl)amine
CAS Number	68783-24-4
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	Unspecified

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