Safety Assessment of Alkyl Amide MIPA ingredients as Used in Cosmetics

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All interested persons are provided 60 days from the above release date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.

The 2019 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Alice Akinsulie, Scientific Analyst/Writer.

1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢
cirinfo@cir-safety.org

INTRODUCTION

This scientific literature review is the initial step in preparing a safety assessment of the 13 ingredients listed below that are mixtures comprising isopropanolamides of fatty acids. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook (*wINCI; *Dictionary*), all but a few of these ingredients are reported to function in cosmetics as a surfactant or viscosity increasing agent (Table 1.).[1] The ingredients included in this safety assessment are:

Lauramide MIPA
Cocamide MIPA
Coconut Oil MIPA Amides
Hydroxyethyl Stearamide-MIPA
Isostearamide MIPA
Linoleamide MIPA
Myristamide MIPA
Oleamide MIPA
Palmamide MIPA
Palm Kernelamide MIPA
Ricinoleamide MIPA
Stearamide MIPA
MIPA- Myristate

The rationale for this grouping of alkyl amide MIPA ingredients stems from the fact that each of the ingredients in this report is a mixture of isopropanolamides of a simple carboxylic acid. These ingredients are classic surfactants and viscosity increasing agents. Diisopropanolamine, triisopropanolamine, and isopropanolamine are structurally similar to the ingredients currently under review, and are mixed aliphatic amines of isopropyl alcohol. An earlier safety assessment by the Cosmetic Ingredient Review (CIR) Expert Panel addressed the safety of diisopropanolamine, triisopropanolamine, isopropanolamine, and mixed isopropanolamine, and concluded that these ingredients are "safe as cosmetic ingredients in the present practices of use and concentration. The Panel also concluded that those ingredients should not be used in products containing *N*-nitrosating agents."[2] Several acids that are components of the alkyl amide MIPA ingredients have also been reviewed.[3-8] The conclusions of these reviews are provided in Table 2.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Much of the data on Oleamide MIPA included in this safety assessment were obtained from robust summaries of data submitted to the European Chemical Agency (ECHA) by companies as part of the REACH chemical registration process.[9] When appropriate, information from these summary documents has been included in this report, and is cited to these sources.

CHEMISTRY

Definition and Structure

The definitions and structures of the alkyl amide MIPA ingredients included in this report are provided in Table 1. The available fatty acid compositions for the oils that are components of ingredients in this report are found in Table 3.

Monoisopropanolamine (MIPA) is a member of the chemical class called monoalkanolamines. The ingredients reviewed in this report are the fatty amides resulting from the amidation of fatty acids with MIPA.

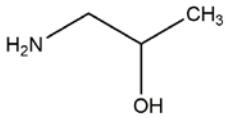


Figure 1. MIPA

Figure 2. Alkylamide MIPA ingredients (generic) and an example (Lauramide MIPA)

However, two ingredients in this group deviate from this structure pattern (Figures 3 and 4). One is further substituted at MIPA, while the other is the MIPA salt of a fatty acid. Specifically, Hydroxyethyl Stearamide-MIPA is substituted with 2-ethanol. MIPA-Myristate, on the other hand, is the MIPA salt of myristic acid. MIPA-Myristate would be the direct esterase metabolite of Myristamide MIPA.

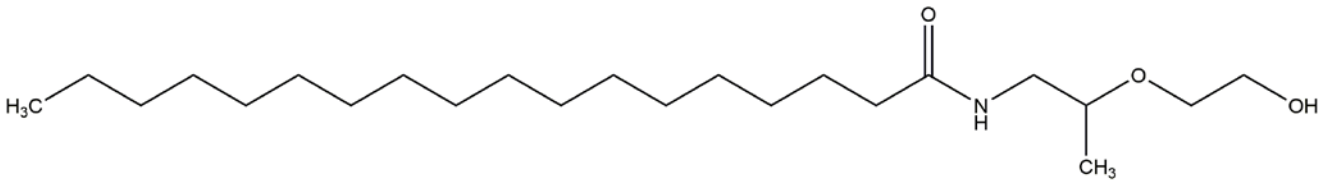


Figure 3. Hydroxyethyl Stearamide-MIPA

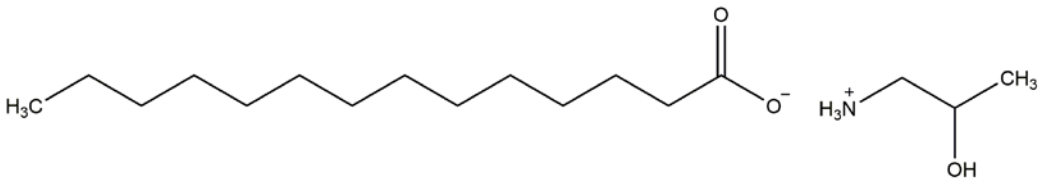


Figure 4. MIPA-Myristate

Physical and Chemical Properties

Experimental boiling point, density, vapor pressure, solubility, and log K_{ow} values were available for Lauramide, Myristamide, Oleamide, Lauramide, Ricinoleamide, and Stearamide MIPA. The available physical and chemical properties of many of the amides in this report are provided in Table 4.

Method of Manufacture

Method of manufacture data were not found in the published literature, and unpublished data were not submitted.

Impurities

Impurities data were not found in the published literature, and unpublished data were not submitted.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2018 VCRP survey data, Lauramide MIPA has the highest frequency of use, with a total of 410 formulations.[10] Lauramide MIPA is most commonly used in bath soaps and detergents (381 formulations). Cocamide MIPA is reported to have is reported to have 279 uses, 271 of which are in rinse-off formulations. The results of the concentration of use survey conducted in 2017 by the Council indicate that Cocamide MIPA has the highest maximum concentration of use, and is used at up to 12% in hair bleaches.[11] The next highest reported maximum concentration of use is 4.8% Lauramide MIPA in bath soaps and detergents. Oleamide MIPA was reported to be used at up to 0.4% in face and neck products. Although Oleamide MIPA only had uses reported as hair dyes and colors in the VCRP, only use in face and neck products was reported in the concentration of use survey. The use information for the alkyl amide MIPA ingredients is provided in Table 5.

The alkyl amide MIPA ingredients are primarily used in rinse-off formulations, with a few leave-on formulations. Most of the reported uses are in some type of hair or skin cleansing formulation. The highest concentrations of use reported for products resulting in leave-on and rinse-off dermal exposure are 1% Cocamide MIPA in body and hand preparations and 4.8% Lauramide MIPA in bath soaps and detergents, respectively. Additionally, uses were reported in the VCRP for Isostearamide MIPA, but no concentrations of use were reported in the industry survey. The ingredients not in use, according to both the 2018 VCRP data and the industry survey, are listed in Table 6.

A few of the ingredients included in this safety assessment are reported to be used in products that come into contact with mucous membranes. For example, Lauramide MIPA is used in bath soaps and detergents at up to 4.8%, and Cocamide MIPA is used in bath soaps and detergents at up to 4%.[11]

The alkyl amide ingredients named in the report are listed in the European Union inventory of cosmetic ingredients, however they have no restrictions. Monoalkanolamines are listed by the European Commission in Annex III Part 1: the list of substances which cosmetic products must not contain, except subject to the restrictions and conditions laid down.[12] These ingredients are allowed a maximum secondary amine content of 0.5% in finished product; are not to be used with nitrosating agents; must have a minimum purity of 99%; the maximum secondary amine content of 0.5% is allowed for raw materials; maximum nitrosamine content allowed is 50 µg/kg; and the chemicals must be kept in nitrite-free containers.

Non-Cosmetic

In the US, MIPA is allowed as an indirect food additive as a component of adhesives [21 CFR 175.105] and as a defoaming agent used in the manufacture of paper and paperboard. [21CFR176.210]

TOXICOKINETIC STUDIES

Toxicokinetics studies were not found in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Dermal

Oleamide MIPA

The acute dermal toxicity of Oleamide MIPA was determined using five female and five male Sprague-Dawley rats.[9] Rats were dermally administered 2000 mg/kg of Oleamide MIPA. The application site was covered by a semiocclusive dressing for 24 hours. Each animal was observed for 15 days after treatment. Slight erythema was noted in both male and female rats; however, no deaths occurred during the study and no clinical signs indicative of systemic toxicity were observed in any animals. The dermal LD_{50} of the test article was higher than 2000 mg/kg in rats.

Oral

Oleamide MIPA

An acute oral toxicity study was performed according to Organization for Economic Cooperation and Development (OECD) test guideline (TG) 423.[9] Oleamide MIPA in corn oil was administered once by gavage to two groups of three female Sprague-Dawley rats at a dosage-volume of 10 mL/kg. All animals were observed for 15 days after treatment. All animals survived until study termination. There were no macroscopic post-mortem observations. No evidence of toxicity was observed. The oral LD_{50} of the test article was > 2000 mg/kg.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Oleamide MIPA

In an oral developmental toxicity study performed in accord with OECD TG 414, Oleamide MIPA diluted in corn oil was administered by gavage to groups of mated female Sprague-Dawley rats (20 mated females/dose) at dose levels of 0, 100, 300, and 1000 mg/kg bw/day from days 6 to 19 of gestation.[9] On day 20 of gestation, all mated females were killed and necropsied, and all fetuses were examined. The clinical signs (increased salivation and chromodacryorrhoea) observed were at low incidence and were not attributed to a toxicological effect of the test article. The test article did not induce any relevant changes in fetuses examined at skeletal and visceral examination. There was a statistically significant lower placenta weight in the group receiving 100 mg/kg of the test substance. This was low in amplitude and was not attributed to a toxicological effect of the test substance. The NOAEL for embryo fetal development was 1000 mg/kg bw/day.

In an oral reproductive study, Oleamide MIPA in corn oil was administered daily by gavage to groups of 10 male and female Sprague-Dawley rats.[9] In males, the test article was administered 2 weeks before mating, during the mating period, and until sacrificed (at least 5 weeks in total). Females were treated 2 weeks before mating, during the mating period (1 week), during pregnancy, during lactation until day 5 post-partum (inclusive) and until sacrificed. Animals were treated at dose-levels of 0, 100, 300, or 1000 mg/kg/day. A constant dosage-volume of 5 mL/kg/day was used. At 100 mg/kg/day, the only finding was ptyalism in most test animals. At 300 mg/kg/day, ptyalism, hypoactivity, loud breathing, piloerection and/or round back was also noted with comparable incidence. At 1000 mg/kg/day, the main clinical sign noted was ptyalism in all test animals. Hypoactivity, loud breathing, piloerection and/or round back were also recorded transiently in a few animals. No effects in the study were considered

to be adverse. The NOAEL for parental toxicity, reproductive performance (mating and fertility) and toxic effects on progeny was 1000 mg/kg/day.

GENOTOXICITY

In Vitro

In an Ames test to examine the mutagenic activity of Oleamide MIPA, five *Salmonella typhimurium* strains, TA1535, TA1537, TA98, TA100, and TA102, were tested with and without metabolic activation, in three or four independent assays.[9] In the mutagenic assay without metabolic activation, 50 - 5000 µg/plate were tested in strains TA1535, TA1537 and TA98. In strain TA100, 15 - 5000 µg/plate were tested. In strain TA100, 5 - 5000 µg/plate were tested. In another assay with metabolic activation, Oleamide MIPA was tested at doses of 1.5 - 500 µg/plate in strain TA1535. Strain TA100 was tested at doses of 15 - 5000 µg/plate. And in strain TA102, doses of 5 - 5000 µg/plate were tested. Under these experimental conditions, no mutagenic activity was revealed.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not found in the published literature, and unpublished data were not provided.

OTHER RELEVANT STUDIES

Effect on Cell Proliferation and Apoptosis

Oleamide MIPA

To determine whether repeated oral administration of Oleamide MIPA induced cell proliferation and/or apoptosis in rats, a GLP compliant study was performed in accord to OECD TG 408.[9] Oleamide MIPA diluted in corn oil was administered by gavage to groups of male and female Sprague-Dawley rats (10/sex/dose) at the dose levels of 0, 100, 300, 1000 mg/kg bw/day for 13 weeks (at constant administration volume of 5 mL/kg bw). Six animals treated with the test article were found dead between day 59 and day 91. In the males treated at 100 mg/kg and killed early on day 77, there was a mild periacinar hepatocytic hypertrophy and minimal sternal lipid hyperplasia. At 300 mg/kg, two male rats were found dead on day 88 and 59. At 1000 mg/kg, 2 male rats were found dead on day 59 and day 80, and one female was found dead on day 91. In decedent animals, no lesions at histopathology examination suggested the cause of death. In other animals treated at 100 mg/kg, there were no microscopic changes. In surviving animals treated with 300 mg/kg, there were slight clinical signs including higher hepatic plasma enzyme activity not accompanied by microscopic changes. There was no mortality in the control group. The no-observed-adverse-effect-level (NOAEL) was not determined in males. In females, the NOAEL corresponds to 300 mg/kg.

DERMAL IRRITATION AND SENSITIZATION

Irritation

In Vitro

The primary skin irritation potential of Oleamide MIPA was evaluated using the Episkin™ reconstructed human epidermis model based on OECD TG 439.[9] The test material (undiluted Oleamide MIPA) was applied to skin (10 mg). Oleamide MIPA was considered to be non-irritant to skin.

Sensitization

Animal

The sensitization potential of Oleamide MIPA was evaluated in a guinea pig maximization study.[9] The test group consisted of 10 male and 10 female Dunkin Hartley guinea pigs, and a group of 5 males and 5 females was used as the control group. For the test group, 10% Oleamide MIPA in corn oil was used for intradermal induction (day 1), and 75% Oleamide MIPA in ethanol/water was applied for the topical induction with an occlusive dressing for 48 hours (day 8). On day 22, challenge consisted of a topical application of 50% Oleamide MIPA to the right flank and acetone to the left flank held in place by an occlusive dressing for 24 hours. The control group was administered vehicle only. Oleamide MIPA induced delayed contact hypersensitivity in more than 30% of the animals.

OCULAR IRRITATION STUDIES

Animal

Three male New Zealand White rabbits were used to determine the ocular irritation potential of Oleamide MIPA.[9] A dosage volume of 0.1 mL of undiluted test article was instilled into the conjunctival sac of the left eye of each rabbit, and the eyes were not rinsed. The right eye remained untreated and served as control. The mean scores (calculated using the 24, 48, and 72-h scores for each animal) for the conjunctiva ranged from 0.3 - 1.0 for redness and 0 - 0.3 for chemosis. Corneal opacity and iridial inflammation were not observed. The test substance was non-irritant when administered by ocular route to rabbits.

SUMMARY

This is a safety assessment of 13 alkyl amide MIPA ingredients as used in cosmetics. These ingredients consist of a fatty acids amidated with MIPA. The ingredients in this report are primarily reported to function as surfactants or viscosity increasing agents.

Four of the 13 ingredients included in this assessment are reported to be in use. Lauramide MIPA has the highest reported frequency of use (410 formulations), and Cocamide MIPA has the second greatest reported number of uses (279). The alkyl amide MIPA ingredients are primarily used in rinse-off formulations, and most of these reported uses are in some type of hair or skin cleansing formulations. Cocamide MIPA has the highest concentration of use, at 12% in hair bleaches. Lauramide MIPA has the next highest reported concentration of use; it is used at 4.8% in bath soaps and detergents. The highest concentrations of use reported for products resulting in leave-on dermal exposure is 1% Cocamide MIPA in body and hand preparations. In Europe, monoalkanolamines are on the list of substances which must not form part of the composition of cosmetic products, except subject to restrictions and conditions laid down. These restrictions include a maximum secondary amines contaminant content of 0.5% in finished products, a maximum secondary amines content of 0.5% in raw materials, and a maximum nitrosamine content of 50 μg/kg.

In an acute dermal toxicity study in five female and five male Sprague-Dawley rats, a single dermal application of 2000 mg/kg of Oleamide MIPA resulted in an LD_{50} > 2000 mg/kg bw. No deaths occurred during the study and no clinical signs of systemic toxicity were observed in any animals.

In an acute oral toxicity study, two groups of three female Sprague-Dawley rats were administered 2000 mg/kg Oleamide MIPA in corn oil by gavage to two groups of three female Sprague-Dawley rats at a dosage-volume of 10 mL/kg. All animals were observed for 15 days after treatment. No evidence of toxicity was observed. The oral LD_{50} of the test article was less than 2000 mg/kg.

A developmental toxicity test was performed with groups of 20 female rats that were dosed with 0, 100, 300, or 1000 mg/kg/day Oleamide MIPA in corn oil from days 6 to19 of gestation. The test article did not induce any relevant changes in fetuses examined at skeletal and visceral examination. There was a statistically significant lower placenta weight in the group receiving 100 mg/kg of the test substance. This was low in amplitude and was not attributed to a toxicological effect of the test substance. The NOAEL was considered to be 1000 mg/kg/day.

The reproductive toxicity of Oleamide MIPA was evaluated in groups of 10 male and female Sprague-Dawley rats at dose levels of 0, 100, 300, or 1000 mg/kg/day. In males, test article was administered 2 weeks before mating, during the mating period, and until sacrificed (at least 5 weeks in total). Females were treated 2 weeks before mating, during mating (1 week), during gestation, during lactation until day 5 post-partum (inclusive) and until sacrificed. No treatment-related, adverse effects were observed. The NOAEL for parental toxicity, reproductive performance (mating and fertility), and toxic effects on progeny was 1000 mg/kg/day.

The genotoxic potential of Oleamide MIPA was evaluated by means of an Ames test in five *S. typhimurium* strains (TA1535, TA1537, TA98, TA100, and TA102) tested either in presence or in absence of metabolic activation. Oleamide MIPA, evaluated at doses of 5-5000 μg/plate, was not mutagenic.

In 13-wk oral toxicity study, 4 groups of 10 male and 10 female Sprague-Dawley rats were administered 0, 100, 300, and 1000 mg/kg bw/day Oleamide MIPA in corn oil by gavage at 5 mL/kg bw. Oleamide MIPA induced mortality, low food consumption, and low body weight gain in males. There were no changes in cell proliferation and apoptosis attributed to the test article. The NOAEL was determined to be 300 mg/kg bw/day in females; a NOAEL was not determined for males.

The dermal irritation potential of undiluted Oleamide MIPA was evaluated in vitro using the Episkin™ reconstructed human epidermis model . Oleamide MIPA was determined to be a non-irritant to skin. In a guinea pig maximization test, Oleamide MIPA induced delayed contact hypersensitivity in more than 30% of the 20 test animals.

Undiluted Oleamide MIPA was not irritating to rabbit eyes.

INFORMATION SOUGHT

The CIR is seeking the following information on all ingredients that comprise the alkyl amide MIPA family for use in the resulting safety assessment. Specifically, the following would strengthen this safety assessment.

1. Methods of manufacture
2. Impurities data
3. Dermal absorption data; if absorbed, systemic data may be needed
4. Dermal irritation and sensitization data at concentrations of use
5. Any other data relevant to the determination of safety of these ingredients as used in cosmetics

TABLES

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1], CIR Staff

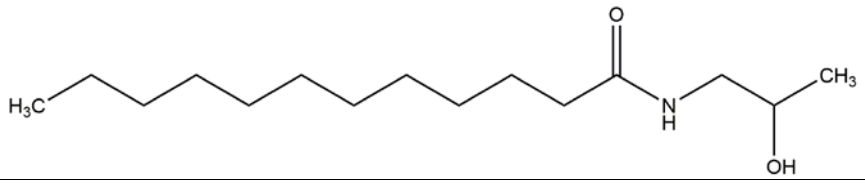
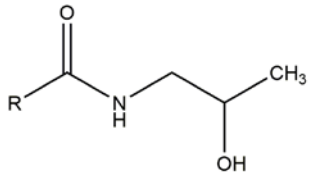
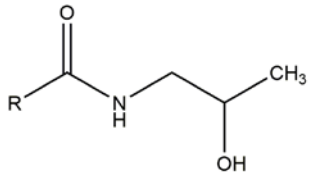
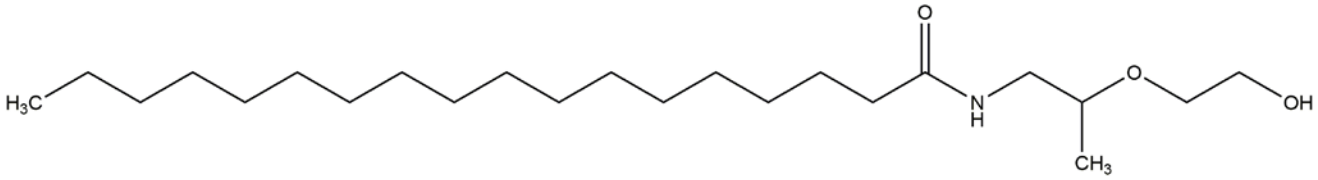
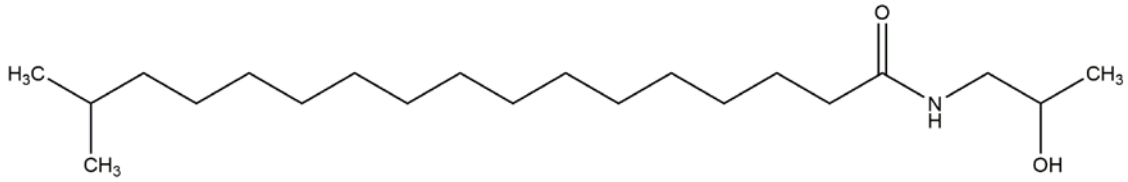
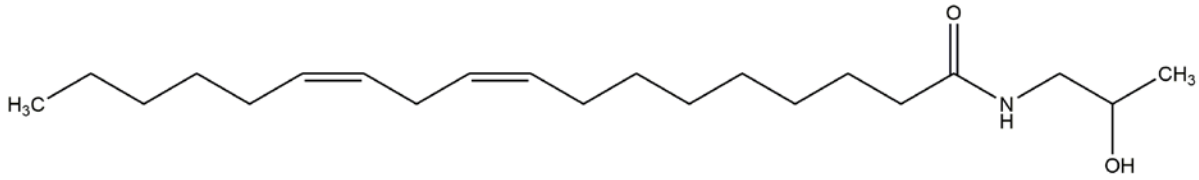
Ingredient & CAS No.	Definition & Example Structure	Function(s)
Lauramide MIPA 142-54-1	Lauramide MIPA is a mixture of isopropanolamides of lauric acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
Cocamide MIPA 68333-82-4	Cocamide MIPA is a mixture of isopropanolamides of coconut acid.  wherein RC(O)- represents the fatty acid residues derived from coconut acid.	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
Coconut Oil MIPA Amides 68333-82-4	Coconut Oil MIPA Amides is the mixture of amides produced by the transamidation of *Cocos nucifera* (coconut) oil with isopropanolamine.  wherein RC(O)- represents the fatty acid residues derived from coconut oil.	Viscosity Increasing Agents - Nonaqueous
Hydroxyethyl Stearamide-MIPA	Hydroxyethyl Stearamide-MIPA is the substituted isopropanolamide. 	Opacifying Agents; Viscosity Increasing Agents - Aqueous
Isostearamide MIPA 152848-22-1	Isostearamide MIPA is a mixture of isopropanolamides of isostearic acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents – Aqueous
Linoleamide MIPA	Linoleamide MIPA is a mixture of isopropanolamides of linoleic acid 	Hair Conditioning Agents; Surfactants - Foam Boosters; Viscosity Increasing Agents – Aqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1], CIR Staff

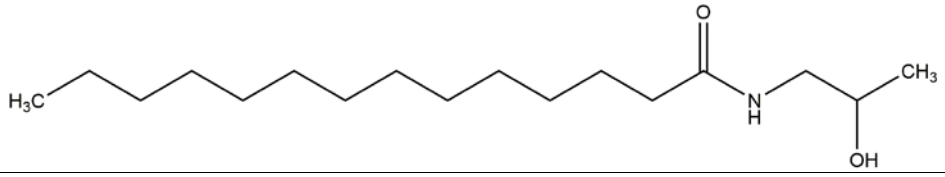
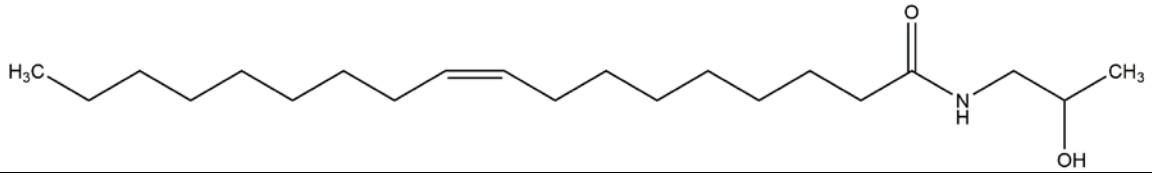
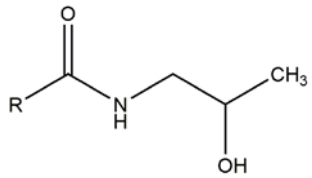
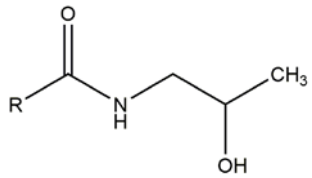
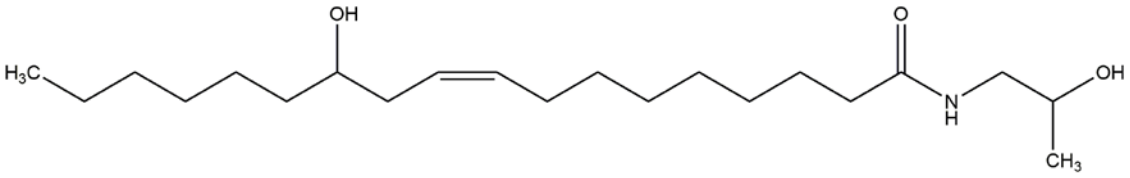
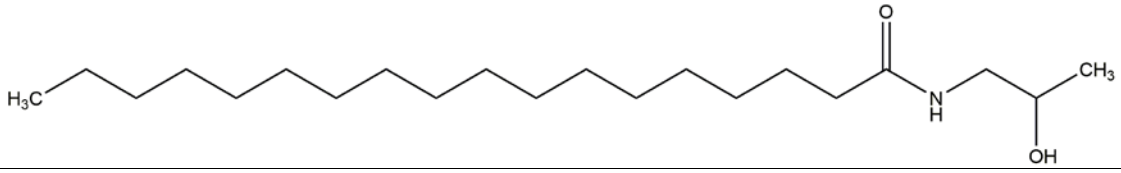
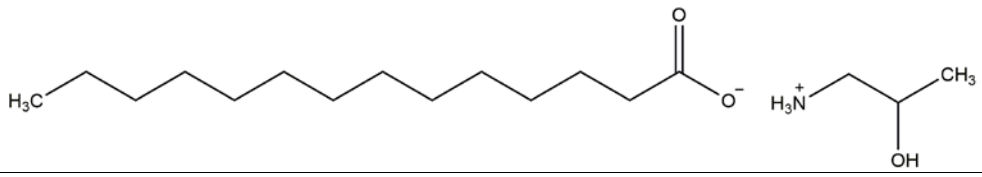
Ingredient & CAS No.	Definition & Example Structure	Function(s)
Myristamide MIPA 10525-14-1	Myristamide MIPA is a mixture of isopropanolamides of myristic acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents – Aqueous
Oleamide MIPA 111-05-7	Oleamide MIPA is a mixture of isopropanolamides of oleic acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
Palmamide MIPA	Palmamide MIPA is a mixture of isopropanolamides of the fatty acids derived from *Elaeis guineensis* (palm) oil.  wherein RC(O)- represents the fatty acid residues derived from *Elaeis guineensis* (palm) oil.	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
Palm Kernelamide MIPA	Palm Kernelamide MIPA is a mixture of isopropanolamides of the fatty acids derived from *Elaeis guineensis* (palm) kernel oil.  wherein RC(O)- represents the fatty acid residues derived from *Elaeis guineensis* (palm) kernel oil.	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
Ricinoleamide MIPA 40986-29-6	Ricinoleamide MIPA is a mixture of isopropanolamides of ricinoleic acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
Stearamide MIPA 35627-96-4	Stearamide MIPA is a mixture of isopropanolamides of stearic acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous
MIPA-Myristate	MIPA-Myristate is the salt of monoisopropanolamine and myristic acid. 	Surfactants - Foam Boosters; Viscosity Increasing Agents - Aqueous

Table 2. CIR Conclusions of Components of the Alkyl Amide MIPA Ingredients that were Previously Reviewed

Ingredients	Conclusion	Assessment Publication Status	Reference
Isostearic Acid	Safe as used	published in 1983; re-review published in 2005 – not reopened	[3,6]
Lauric Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[4,7]
Myristic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened; included in expanded report with salts and esters published in 2010	[4,5,7]
Oleic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[4,7]
Ricinoleic Acid	Safe as used	published in 2007	[8]
Stearic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[4,7]

Table 3. Fatty acid composition (%) of component plant-derived fatty acid oils

Fatty Acids	Cocos Nucifera (Coconut) Oil[13]	Elaeis Guineensis (Palm) Oil[14]	Elaeis Guineensis (Palm) Kernel Oil[14]
Caproic (C6)	0-1		0.3
Caprylic (C8)	5-9		4.4
Capric (C10)	6-10		3.7
Lauric (C12)	44-52	0.2	48.3
Myristic (C14)	13-19	1.1	15.6
Palmitic (C16)	8-11	44	
Palmitoleic (C16:1)	0-1	0.1	7.8
Stearic (C18)	1-3	4.5	2
Oleic (C18:1)	5-8	39.2	15.1
Linoleic (C18:2)	Trace-2.5	10.1	2.7
Linolenic (C18:3)		0.4	
Arachidic (C20)		0.4	
Others			0.2

Table 4. Physical and Chemical Properties

Property	Value	Reference
	Lauramide MIPA	
Molecular Weight (g/mol)	257.418	[15]
Density/Specific Gravity (@ 20ºC)	0.919 ± 0.06	[16]
Melting Point (ºC)	65 – 66	[16]
Boiling Point (ºC)	418.3 ± 28.0	[16]
Disassociation constants pKa (@25ºC)	14.56 ± 0.20	[16]
	Hydroxyethyl Stearamide-MIPA	
Molecular Weight (g/mol)	385.6	[17]
	Isostearamide MIPA	
Molecular Weight (g/mol)	341.58	[18]
	Linoleamide MIPA	
Molecular Weight (g/mol)	337.6	[17]
	Myristamide MIPA	
Molecular Weight (g/mol)	285.472	[19]
Molecular Volume (mL/mol)	312.9 ± 3.0	[16]
Formula Weight	303.5	[17]
Density (@ 20ºC)	0.912 ± 0.06	[16]
Vapor Pressure (@ 25ºC)	9.44×10^{-10}	[16]
Melting Point (ºC)	70 – 72	[16]
Boiling Point (ºC)	444.1 ± 28.0	[16]
Disassociation constants pKa (@25ºC)	14.56±0.20	[16]
	Oleamide MIPA	
Physical Form	Paste	[9]
Color	Beige	[9]
Odor	Strong	[9]
Molecular Weight (g/mol)	339.564	[20]
Density/Specific Gravity (g/mL @ 25ºC)	0.883, 0.891	[9]

Table 4. Physical and Chemical Properties

Property	Value	Reference
Vapor pressure (25ºC)	0	[9]
Melting Point (ºC)	35.9 - 41.7	[9]
Boiling Point (ºC)	503.6 ± 43.0	[16]
Water Solubility (mg/L)	1	[9]
log K_{ow}	6.39	[9]
	Ricinoleamide MIPA	
Molecular Weight (g/mol)	355.56	[16]
Molecular Volume (mL/mol)	370.4 ± 3.0	[16]
Density (@ 20ºC)	0.959 ± 0.06	[16]
Vapor pressure (@ 25ºC)	5.15×10^{-14}	[16]
Boiling Point (ºC)	542.1 ± 40.0	[16]
Disassociation constants pKa (@25ºC)	14.51 ± 0.10	[16]
	Stearamide MIPA	
Molecular Weight (g/mol)	341.57	[16]
Molecular Volume (mL/mol)	378.9 ± 3.0	[16]
Density (@ 20ºC)	0.901 ± 0.06	[16]
Vapor pressure (@ 25ºC)	8.03×10^{-12}	[16]
Boiling Point (ºC)	493.8 ± 28.0	[16]
Disassociation constants pKa (@25ºC)	14.56 ± 0.20	[16]

Table 5. Frequency and concentration of use data for alkyl amide MIPA ingredients

	# of Uses[10]	Max Conc of Use (%)[11]	# of Uses[10]	Max Conc of Use (%)[11]	# of Uses[10]	Max Conc of Use (%)[11]
	Cocamide MIPA		**Isostearamide MIPA**		**Lauramide MIPA**	
Totals*	**279**	**0.1 - 12**	**9**	**NR**	**410**	**2 - 4.8**
Duration of Use						
Leave-On	*7*	*0.12 - 1*	*NR*	*NR*	*2*	*NR*
Rinse-Off	*271*	*0.1 - 12*	*9*	*NR*	*406*	*2 - 4.8*
Diluted for (Bath) Use	*1*	*1.5 - 2*	*NR*	*NR*	*2*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	3[a]	0.12[b]	NR	NR	1	NR
Incidental Inhalation-Powder	NR	1[c]	NR	NR	NR	NR
Dermal Contact	133	0.1 - 4	2	NR	405	3 - 4.8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	128	0.12 - 3.7	7	NR	5	2
Hair-Coloring	18	12	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	120	1.1 - 4	NR	NR	399	4.8
Baby Products	NR	NR	NR	NR	NR	NR

	Oleamide MIPA			
Totals*	**51**	**0.4**		
Duration of Use				
Leave-On	*NR*	*0.4*		
Rinse Off	*51*	*NR*		
Diluted for (Bath) Use	*NR*	*NR*		
Exposure Type				
Eye Area	NR	NR		
Incidental Ingestion	NR	NR		
Incidental Inhalation-Spray	NR	NR		
Incidental Inhalation-Powder	NR	0.4[c]		
Dermal Contact	NR	0.4		
Deodorant (underarm)	NR	NR		
Hair - Non-Coloring	NR	NR		
Hair-Coloring	51	NR		
Nail	NR	NR		
Mucous Membrane	NR	NR		
Baby Products	NR	NR		

NR = Not reported.

† Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a.] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[b.] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.

[c.] It is possible these products may be powders, but it is not specified whether the reported uses are powders.

Table 6. Ingredients not reported to be in use (according to VCRP and Council survey data)[10,11]

Coconut Oil MIPA Amides
Hydroxyethyl Stearamide MIPA
Linoleamide MIPA
Myristamide MIPA
Palmamide MIPA
Palm Kernelamide MIPA
Ricinoleamide MIPA
Stearamide MIPA
MIPA-Myristate

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