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Safety Assessment of Amino Acid Alkyl Amides as Used in Cosmetics

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Abstract

The Cosmetic Ingredient Review Expert Panel (Panel) reviewed the product use, formulation, and safety data of 115 amino acid alkyl amides, which function as skin and hair conditioning agents and as surfactants—cleansing agents in personal care products. Safety test data on dermal irritation and sensitization for the ingredients with the highest use concentrations, lauroyl lysine and sodium lauroyl glutamate, were reviewed and determined to adequately support the safe use of the ingredients in this report. The Panel concluded that amino acid alkyl amides are safe in the present practices of use and concentration in cosmetics, when formulated to be nonirritating.

Keywords

amino acid alkyl amides, safety, cosmetics

Introduction

This safety assessment summarizes the available data relevant to assessing the safety of 115 amino acid alkyl amides as used in cosmetics. These ingredients mainly function as skin and hair conditioning agents and as surfactants—cleansing agents in personal care products. The list of ingredients in this report is found in Table 1.

By and large, the ingredients in this report will not rapidly dissociate (beyond zwitterion formation) in the presence of water, but action by amidases is the most likely first step of metabolism if dermal penetration occurs. The relative exposure, hence, would also include amino acids and fatty acids. The Cosmetic Ingredient Review Expert Panel (Panel) previously has reviewed the safety of α-amino acids and animal- and plant-derived amino acids and concluded that these ingredients are safe for use as cosmetic ingredients.[1,2] The Panel also reviewed the following fatty acid constituents and concluded that these fatty acids are safe for use as cosmetic ingredients: coconut acid, olive acid, sunflower seed acid, palm acid, acetic acid, lauric acid, oleic acid, palmitic acid, stearic acid, and myristic acid.[3-9] The Panel concluded that malic acid was safe for use as a pH adjuster, but the data were insufficient to determine safety for any other functions.[10] The maximum concentrations of use along with summaries of the data included in those existing safety assessments are provided in Table 2.

Chemistry

The amino acid alkyl amides in this report are comprised of amino acids acylated with acids or acid chlorides at the amino acid nitrogen to form amides (except for lauroyl lysine, which is formed by acylation at the epsilon nitrogen). For example, capryloyl glycine is the *N*-acylation product of glycine with caprylic acid chloride.

A likely metabolic pathway for these ingredients includes reactions catalyzed by amidases, should the ingredients penetrate the skin. The net result would be the release of the amino acid (glycine in the example above) and a fatty acid (caprylic acid in the example). The definitions of the amino acid alkyl amides can be found in Table 1, and the structures can be found in Table 3.

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Table 1. Definitions and Functions of the Amino Acid Alkyl Amides in This Safety Assessment.[20,69,a]

Ingredient CAS No.	Definition	Function
Acetyl arginine 210545-23-6	Acetyl arginine is the substituted amino acid that conforms to the formula. *Acetyl arginine is the amide formed from the reaction of acetic acid chloride and arginine.*	Humectants; skin conditioning agents—emollient
Acetyl cysteine 616-91-1	Acetyl cysteine is the organic compound that conforms to the formula. *Acetyl cysteine is the amide formed from the reaction of acetic acid chloride and cysteine.*	Antioxidants; skin conditioning agents—misc
Acetyl glutamic acid 1188-37-0	Acetyl glutamic acid is the substituted amino acid that conforms to the formula. *Acetyl glutamic acid is the amide formed from the reaction of acetic acid chloride and glutamic acid.*	Skin conditioning agents—misc
Acetyl glutamine 2490-97-3 35305-74-9	Acetyl glutamine is the organic compound that conforms to the formula. *Acetyl glutamine is the amide formed from the reaction of acetic acid chloride and glutamine.*	Skin conditioning agents—misc
Acetyl histidine 39145-52-3	Acetyl histidine is the organic compound that conforms to the formula. *Acetyl histidine is the amide formed from the reaction of acetic acid chloride and histidine.*	Skin conditioning agents—emollient; skin conditioning agents—humectant
Acetyl methionine 1115-47-5 65-82-7	Acetyl methionine is the substituted amino acid that conforms to the formula. *Acetyl methionine is the amide formed from the reaction of acetic acid chloride and methionine.*	Skin conditioning agents—misc
Acetyl proline 68-95-1	Acetyl proline is the substituted amino acid that conforms to the formula. *Acetyl proline is the amide formed from the reaction of acetic acid chloride and proline.*	Skin conditioning agents—emollient
Acetyl tyrosine 537-55-3	Acetyl tyrosine is the organic compound that conforms to the formula. *Acetyl tyrosine is the amide formed from the reaction of acetic acid chloride and tyrosine.*	Skin conditioning agents—misc
Capryloyl collagen amino acids	Capryloyl collagen amino acid is the condensation product of caprylic acid chloride with collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents
Capryloyl glycine 14246-53-8	Capryloyl glycine is the acylation product of glycine with caprylic acid chloride.	Hair conditioning agents; surfactants—cleansing agents
Capryloyl gold of pleasure amino acids	Capryloyl gold of pleasure amino acid is the condensation product of caprylic acid chloride and the amino acids derived from the complete hydrolysis of the protein fraction obtained from the seeds of *Camelina sativa*.	Cosmetic biocides; deodorant agents
Capryloyl keratin amino acids	Capryloyl keratin amino acid is the condensation product of caprylic acid chloride with keratin amino acids.	Hair conditioning agents; surfactants—cleansing agents
Capryloyl pea amino acids	Capryloyl pea amino acid is the product obtained by the condensation of caprylic acid chloride and pea amino acids.	Hair conditioning agents; skin conditioning agents—misc
Capryloyl quinoa amino acids	Capryloyl quinoa amino acid is the condensation product of caprylic acid chloride and amino acids obtained from the complete hydrolysis of the protein obtained from the seeds of *Chenopodium quinoa*.	Hair conditioning agents; skin conditioning agents—misc
Capryloyl silk amino acids	Capryloyl silk amino acid is the product obtained by the condensation of caprylic acid chloride with silk amino acids.	Hair conditioning agents; surfactants—cleansing agents
Cocoyl glutamic acid	Cocoyl glutamic acid is the coconut acid amide of glutamic acid that conforms to the formula.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Dipalmitoyl cystine 17627-10-0	Dipalmitoyl cystine is the product obtained by acylation of cystine with palmitoyl chloride.	Hair conditioning agents
Dipotassium capryloyl glutamate	Dipotassium capryloyl glutamate is the organic compound that conforms to the formula. *Dipotassium capryloyl glutamate is the dipotassium salt of the amide formed from the reaction of capryloyl chloride and glutamic acid.*	Deodorant agents; surfactants—cleansing agents
Dipotassium undecylenoyl glutamate	Dipotassium undecylenoyl glutamate is the substituted amino acid that conforms to the formula. *Dipotassium undecylenoyl glutamate is the dipotassium salt of the amide formed from the reaction of undecenoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition	Function
Disodium capryloyl glutamate	Disodium capryloyl glutamate is the organic compound that conforms to the formula. *Disodium capryloyl glutamate is the disodium salt of the amide formed from the reaction of capryloyl chloride and glutamic acid.*	Deodorant agents; surfactants—cleansing agents
Disodium cocoyl glutamate 68187-30-4	Disodium cocoyl glutamate is the disodium salt of the coconut acid amide of glutamic acid. It conforms generally to the formula.	Surfactants—cleansing agents
Disodium hydrogenated tallow glutamate	Disodium hydrogenated tallow glutamate is the disodium salt of the hydrogenated tallow acid amide of glutamic acid. It conforms generally to the formula.	Hair conditioning agents; skin—conditioning agents—misc; surfactants—cleansing agents
Disodium *N*-lauroyl aspartate	Disodium *N*-lauroyl aspartate is the organic compound that conforms to the formula. *Disodium N-lauroyl aspartate is the disodium salt of the amide formed from the reaction of lauroyl chloride and aspartic acid.*	Surfactants—cleansing agents
Disodium lauroyl glutamate	Disodium lauroyl glutamate is the organic compound that conforms to the formula. *Disodium lauroyl glutamate is the disodium salt of the amide formed from the reaction of lauroyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Disodium malyl tyrosinate 126139-79-5	Disodium malyl tyrosinate is the organic compound that conforms to the formula. *Disodium malyl tyrosinate is the disodium salt of the amide formed from the reaction of malyl chloride and tyrosine.*	Skin conditioning agents—misc
Disodium stearoyl glutamate 38079-62-8	Disodium stearoyl glutamate is the organic compound that conforms to the formula. *Disodium stearoyl glutamate is the disodium salt of the amide formed from the reaction of stearoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Disodium undecylenoyl glutamate	Disodium undecylenoyl glutamate is the substituted amino acid that conforms to the formula. *Disodium undecenoyl glutamate is the disodium salt of the amide formed from the reaction of undecenoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Lauroyl arginine 42492-22-8	Lauroyl arginine is the substituted amino acid that conforms to the formula. *Lauroyl arginine is the amide formed from the reaction of lauroyl chloride and arginine.*	Hair conditioning agents; skin conditioning agents—emollient
Lauroyl collagen amino acids 68920-59-2	Lauroyl collagen amino acid is the product obtained by the condensation of lauric acid chloride with collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents
Lauroyl glutamic acid 3397-65-7	Lauroyl glutamic acid is the substituted amino acid that conforms to the formula. *Lauroyl glutamic acid is the amide formed from the reaction of lauroyl chloride and glutamic acid.*	Skin conditioning agents—misc
Lauroyl lysine 52315-75-0	Lauroyl lysine is the lauroyl derivative of lysine that conforms to the formula. *Lauroyl lysine is the ε-amide formed from the reaction of lauroyl chloride and lysine.*	Hair conditioning agents; skin conditioning agents—misc
Lauroyl proline 58725-39-6	Lauroyl proline is the organic compound that conforms to the formula. *Lauroyl proline is the amide formed from the reaction of lauroyl chloride and proline.*	Hair conditioning agents; skin conditioning agents—misc
Lauroyl silk amino acids	Lauroyl silk amino acid is the product obtained by the condensation of lauric acid chloride and silk amino acids.	Hair conditioning agents; surfactants—cleansing agents
Magnesium palmitoyl glutamate 57539-47-6	Magnesium palmitoyl glutamate is the substituted amino acid that conforms to the formula. *Magnesium palmitoyl glutamate is the magnesium salt of the amide formed from the reaction of palmitoyl chloride and glutamic acid.*	Skin-conditioning agents—misc
Myristoyl glutamic acid	Myristoyl glutamic acid is the substituted amino acid that conforms to the formula. *Myristoyl glutamic acid is the amide formed from the reaction of myristoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Oleoyl tyrosine	Oleoyl tyrosine is the organic compound that conforms to the formula. *Oleoyl tyrosine is the amide formed from the reaction of oleoyl chloride and tyrosine.*	Skin conditioning agents—misc

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition	Function
Palmitoyl alanine 56255-31-3	Palmitoyl alanine is the substituted amino acid that conforms to the formula. *Palmitoyl alanine is the amide formed from the reaction of palmitoyl chloride and alanine.*	Skin protectants
Palmitoyl arginine 58725-47-6	Palmitoyl arginine is the organic compound that conforms to the formula. *Palmitoyl arginine is the amide formed from the reaction of palmitoyl chloride and arginine.*	Hair conditioning agents; skin conditioning agents—emollient
Palmitoyl collagen amino acids	Palmitoyl collagen amino acid is the condensation product of palmitic acid chloride and collagen amino acids.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Palmitoyl glutamic acid 38079-66-2	Palmitoyl glutamic acid is the substituted amino acid that conforms to the formula. *Palmitoyl glutamic acid is the amide formed from the reaction of palmitoyl chloride and glutamic acid.*	Skin conditioning agents—misc
Palmitoyl glycine 2441-41-0	Palmitoyl glycine is the acylation product of glycine with palmitic acid chloride.	Hair conditioning agents; surfactants—cleansing agents
Palmitoyl gold of pleasure amino acids	Palmitoyl gold of pleasure amino acid is the condensation product of palmitic acid chloride and the amino acids obtained from the complete hydrolysis of the protein fraction derived from the seeds of gold of pleasure.	Hair conditioning agents; skin conditioning agents—emollient
Palmitoyl isoleucine 54617-29-7	Palmitoyl isoleucine is the substituted amino acid that conforms to the formula. *Palmitoyl isoleucine is the amide formed from the reaction of palmitoyl chloride and isoleucine.*	Skin protectants
Palmitoyl keratin amino acids	Palmitoyl keratin amino acid is the condensation product of palmitic acid chloride and keratin amino acids.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Palmitoyl millet amino acids	Palmitoyl millet amino acid is the condensation product of palmitic acid chloride and the amino acids obtained from the complete hydrolysis of the protein fraction of *Panicum miliaceum.*	Hair conditioning agents; skin conditioning agents—emollient
Palmitoyl oat amino acids	Palmitoyl oat amino acid is the condensation product of palmitic acid chloride and the amino acids obtained from the complete hydrolysis of the protein fraction of *Avena sativa* (oat).	Hair conditioning agents; skin conditioning agents—emollient
Palmitoyl pea amino acids	Palmitoyl pea amino acid is the condensation product of palmitic acid chloride and pea amino acids.	Hair conditioning agents; skin conditioning agents—misc
Palmitoyl proline 59441-32-6	Palmitoyl proline is the product obtained by the condensation of palmitic acid chloride with proline.	None reported
Palmitoyl quinoa amino acids	Palmitoyl quinoa amino acid is the condensation product of palmitic acid chloride and the amino acids obtained from the complete hydrolysis of the protein fraction derived from the seeds of *Chenopodium quinoa.*	Hair conditioning agents; skin conditioning agents—misc
Palmitoyl silk amino acids	Palmitoyl silk amino acid is the condensation product of palmitic acid chloride and silk amino acids.	Hair conditioning agents; surfactants—cleansing agents
Potassium caproyl tyrosine	Potassium caproyl tyrosine is the organic compound that conforms to the formula. *Potassium caproyl tyrosine is the potassium salt of the amide formed from the reaction of caproyl chloride and tyrosine.*	Skin conditioning agents—misc
Potassium capryloyl glutamate	Potassium capryloyl glutamate is the substituted amino acid that conforms to the formula. *Potassium capryloyl glutamate is the potassium salt of the amide formed from the reaction of capryloyl chloride and glutamic acid.*	Deodorant agents; surfactants—cleansing agents
Potassium cocoyl glutamate	Potassium cocoyl glutamate is the mixed potassium salts of the coconut acid amide of glutamic acid. It conforms generally to the formula.	Hair conditioning agents; surfactants—cleansing agents
Potassium cocoyl glycinate 301341-58-2	Potassium cocoyl glycinate is the organic compound that conforms to the formula. *Potassium cocoyl glycinate is the potassium salt of the amide formed from the reaction of coconut acid chloride and glycine.*	Hair conditioning agents; surfactants—cleansing agents
Potassium cocoyl rice amino acids	Potassium cocoyl rice amino acid is the potassium salt of the product obtained by the reaction of coconut acid chloride with rice amino acids.	Skin conditioning agents—emollient; skin conditioning agents—misc; surfactants—emulsifying agents; surfactants—foam boosters

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition	Function
Potassium lauroyl collagen amino acids	Potassium lauroyl collagen amino acid is the potassium salt of the condensation product of lauric acid chloride and collagen amino acids.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Potassium lauroyl glutamate 89187-78-0 (L-)	Potassium lauroyl glutamate is the substituted amino acid that conforms to the formula. *Potassium lauroyl glutamate is the potassium salt of the amide formed from the reaction of lauroyl chloride and glutamic acid.*	Hair conditioning agents; surfactants—cleansing agents
Potassium lauroyl oat amino acids	Potassium lauroyl oat amino acid is the potassium salt of the product obtained by the reaction of lauroyl chloride and oat amino acids.	Hair conditioning agents
Potassium lauroyl pea amino acids	Potassium lauroyl pea amino acid is the potassium salt of the reaction product of lauric acid chloride with the amino acids derived from the seeds of *Pisum sativum.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Potassium lauroyl silk amino acids	Potassium lauroyl silk amino acid is the potassium salt of the condensation product of lauric acid chloride and silk amino acids.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Potassium lauroyl wheat amino acids	Potassium lauroyl wheat amino acid is the potassium salt of the condensation product of lauric acid chloride and wheat amino acids.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Potassium myristoyl glutamate	Potassium myristoyl glutamate is the potassium salt of the myristic acid amide of glutamic acid. It conforms to the formula.	Hair conditioning agents; surfactants—cleansing agents
Potassium olivoyl/lauroyl wheat amino acids	Potassium olivoyl/lauroyl wheat amino acid is the potassium salt of the condensation product of olivoyl chloride, lauroyl chloride, and wheat amino acids.	Surfactants—cleansing agents
Potassium stearoyl glutamate	Potassium stearoyl glutamate is the potassium salt of stearoyl glutamic acid. *Potassium stearoyl glutamate is the potassium salt of the amide formed from the reaction of stearoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc
Potassium undecylenoyl glutamate	Potassium undecylenoyl glutamate is the substituted amino acid that conforms to the formula. *Potassium undecylenoyl glutamate is the potassium salt of the amide formed from the reaction of undecylenoyl chloride and glutamic acid.*	Abrasives; hair conditioning agents
Propionyl collagen amino acids	Propionyl collagen amino acid is the condensation product of propionic acid chloride with collagen amino acids.	Skin conditioning agents—occlusive
Sodium caproyl prolinate 1364318-34-2	Sodium caproyl prolinate is the organic compound that conforms to the formula. *Sodium caproyl prolinate is the sodium salt of the amide formed from the reaction of caproyl chloride and proline.*	Hair conditioning agents; skin conditioning agents—humectant; surfactants—cleansing agents
Sodium capryloyl glutamate	Sodium capryloyl glutamate is the substituted amino acid that conforms to the formula. *Sodium capryloyl glutamate is the sodium salt of the amide formed from the reaction of capryloyl chloride and glutamic acid.*	Deodorant agents; surfactants—cleansing agents
Sodium cocoyl alaninate 90170-45-9	Sodium cocoyl alaninate is the organic compound that conforms to the formula. *Sodium cocoyl alaninate is the sodium salt of the amide formed from the reaction of coconut acid chloride and alanine.*	Hair conditioning agents; surfactants—cleansing agents
Sodium cocoyl amino acids	Sodium cocoyl amino acid is the sodium salt of a mixture of amino acids acylated by cocoyl chloride.	Surfactants—cleansing agents
Sodium cocoyl apple amino acids	Sodium cocoyl apple amino acid is the sodium salt of the condensation product of coconut acid chloride and the amino acids obtained by the complete hydrolysis of the protein fraction isolated from the seeds of *Pyrus malus.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium cocoyl barley amino acids	Sodium cocoyl barley amino acid is the sodium salt of the condensation product of coconut acid chloride and the amino acids derived from barley protein.	Emulsion stabilizers; skin conditioning agents—misc; surfactants—emulsifying agents
Sodium cocoyl collagen amino acids	Sodium cocoyl collagen amino acid is the sodium salt of the condensation product of coconut acid chloride and collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition	Function
Sodium cocoyl glutamate 68187-32-6	Sodium cocoyl glutamate is the sodium salt of cocoyl glutamic acid. It conforms generally to the formula. *Sodium cocoyl glutamate is the sodium salt of the amide formed from the reaction of coconut acid chloride and glutamic acid.*	Surfactants—cleansing agents
Sodium cocoyl glutaminate	Sodium cocoyl glutaminate is the organic compound that conforms to the formula. *Sodium cocoyl glutaminate is the sodium salt of the amide formed from the reaction of coconut acid chloride and glutamine.*	Surfactants—cleansing agents
Sodium cocoyl glycinate 90387-74-9	Sodium cocoyl glycinate is the organic compound that conforms generally to the formula. *Sodium cocoyl glycinate is the sodium salt of the amide formed from the reaction of coconut acid chloride and glycine.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium cocoyl/ hydrogenated tallow glutamate	Sodium cocoyl/hydrogenated tallow glutamate is the organic compound that conforms generally to the formula. *Sodium cocoyl/hydrogenated tallow glutamate is the sodium salt of the mixture of cocoyl acid amides and hydrogenated tallow acid amides of glutamic acid.*	Surfactants—cleansing agents
Sodium cocoyl oat amino acids	Sodium cocoyl oat amino acid is the sodium salt of the condensation product of coconut acid chloride and the amino acids derived from avena sativa (oat) protein.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium cocoyl/palmoyl/ sunfloweroyl glutamate	Sodium cocoyl/palmoyl/sunfloweroyl glutamate is the sodium salt of the product formed by the reaction of glutamic acid with a mixture of coconut acid, palm acid, and sunflower seed acid.	Surfactants—cleansing agents; surfactants—emulsifying agents
Sodium cocoyl proline	Sodium cocoyl proline is the substituted amino acid that conforms to the formula. *Sodium cocoyl proline is the sodium salt of the amide formed from the reaction of coconut acid chloride and proline.*	Surfactants—cleansing agents; surfactants—solubilizing agents
Sodium cocoyl threoninate	Sodium cocoyl threoninate is the organic compound that conforms to the formula. *Sodium cocoyl threoninate is the sodium salt of the amide formed from the reaction of coconut acid chloride and threonine.*	Surfactants—cleansing agents; surfactants—emulsifying agents
Sodium cocoyl wheat amino acids	Sodium cocoyl wheat amino acid is the sodium salt of the condensation product of coconut acid chloride and the amino acids derived from triticum vulgare (wheat) protein.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium hydrogenated tallowoyl glutamate	Sodium hydrogenated tallowoyl glutamate is the sodium salt of the hydrogenated tallow acid amide of glutamic acid. It conforms generally to the formula.	Surfactants—cleansing agents
Sodium lauroyl aspartate 41489-18-3	Sodium lauroyl aspartate is the organic compound that conforms to the formula. *Sodium Lauroyl aspartate is the sodium salt of the amide formed from the reaction of lauroyl chloride and aspartic acid.*	Hair conditioning agents; surfactants—cleansing agents
Sodium lauroyl collagen amino acids	Sodium lauroyl collagen amino acid is the sodium salt of the condensation product of lauric acid chloride and collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents
Sodium lauroyl glutamate 29923-31-7 (L-) 29923-34-0 (DL-) 42926-22-7 (L-) 98984-78-2	Sodium lauroyl glutamate is the sodium salt of the lauric acid amide of glutamic acid. It conforms generally to the formula.	Hair conditioning agents
Sodium lauroyl millet amino acids	Sodium lauroyl millet amino acid is the sodium salt of the condensation product of lauric acid chloride and the amino acids obtained by the complete hydrolysis of the protein fraction of *Panicum miliaceum*.	Surfactants—cleansing agents
Sodium lauroyl/myristoyl aspartate	Sodium lauroyl/myristoyl aspartate is the sodium salt of the substituted amino acid that conforms generally to the formula. *Sodium lauroyl/myristoyl aspartate is the sodium salt of the amide formed from the reaction of a mixture of lauroyl chloride and myristoyl chloride with aspartic acid.*	Hair conditioning agents; surfactants—cleansing agents

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition	Function
Sodium lauroyl oat amino acids	Sodium lauroyl oat amino acid is the sodium salt of the condensation product of lauric acid chloride with the amino acids derived from avena sativa (Oat) kernel protein.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium lauroyl silk amino acids	Sodium lauroyl silk amino acid is the sodium salt of the condensation product of lauric acid chloride and silk amino acids.	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium lauroyl wheat amino acids	Sodium lauroyl wheat amino acid is the sodium salt of the condensation product of lauric acid chloride and wheat amino acids.	Hair conditioning agents; skin—conditioning agents—misc; surfactants—cleansing agents
Sodium myristoyl glutamate 38517-37-2 38754-83-5 (DL-) 71368-20-2	Sodium myristoyl glutamate is the sodium salt of the myristic acid amide of glutamic acid. It conforms generally to the formula.	Surfactants—cleansing agents
Sodium olivoyl glutamate	Sodium olivoyl glutamate is the sodium salt of olivoyl glutamic acid. It conforms generally to the formula. *Sodium olivoyl glutamate is the sodium salt of the amide formed from the reaction of olivoyl chloride and glutamic acid.*	Surfactants—cleansing agents
Sodium palmitoyl proline 58725-33-0	Sodium palmitoyl proline is the substituted amino acid that conforms to the formula. *Sodium palmitoyl proline is the sodium salt of the amide formed from the reaction of palmitoyl chloride and proline.*	Skin conditioning agents—misc
Sodium palmoyl glutamate	Sodium palmoyl glutamate is the sodium salt of palmoyl glutamic acid. It conforms generally to the formula. *Sodium palmoyl glutamate is the sodium salt of the amide formed from the reaction of palm acid chloride and glutamic acid.*	Surfactants—cleansing agents
Sodium stearoyl glutamate 38517-23-6 79811-24-8 (L-)	Sodium stearoyl glutamate is the organic compound that conforms to the formula. *Sodium stearoyl glutamate is the sodium salt of the amide formed from the reaction of stearoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Sodium/TEA-lauroyl collagen amino acids	Sodium/TEA-lauroyl collagen amino acid is a mixture of sodium and triethanolamine salts of the condensation product of lauric acid chloride and collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents
Sodium/TEA-lauroyl keratin amino acids	Sodium/TEA-lauroyl keratin amino acid is a mixture of sodium and triethanolamine salts of the condensation product of lauric acid chloride and keratin amino acids.	Hair conditioning agents; surfactants—cleansing agents
Sodium/TEA-undecylenoyl collagen amino acids	Sodium/TEA-undecylenoyl collagen amino acid is a mixture of sodium and triethanolamine salts of the condensation product of undecylenic acid chloride and collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents
Sodium undecylenoyl glutamate	Sodium undecylenoyl glutamate is the substituted amino acid that conforms generally to the formula. *Sodium undecenoyl glutamate is the sodium salt of the amide formed from the reaction of undecenoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Stearoyl glutamic acid 3397-16-8	Stearoyl glutamic acid is the substituted amino acid that conforms to the formula. *Stearoyl glutamic acid is the amide formed from the reaction of stearoyl chloride and glutamic acid.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—cleansing agents
Stearoyl leucine 14379-43-2	Stearoyl leucine is the stearoyl derivative of leucine that conforms to the formula. *Stearoyl leucine is the amide formed from the reaction of stearoyl chloride and leucine.*	Hair conditioning agents; skin conditioning agents—misc; surfactants—emulsifying agents
TEA-cocoyl alaninate	TEA-cocoyl alaninate is the triethanolamine salt of the coconut acid amide of alanine. It conforms generally to the formula.	Hair conditioning agents; surfactants—cleansing agents
TEA-cocoyl glutamate 68187-29-1	TEA-cocoyl glutamate is the triethanolamine salt of the coconut acid amide of glutamic acid. It conforms generally to the formula.	Hair conditioning agents; surfactants—cleansing agents

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition	Function
TEA-cocoyl glutaminate	TEA-cocoyl glutaminate is the organic compound that conforms to the formula. *TEA-cocoyl glutaminate is the triethanolamine salt of the coconut acid amide of glutamine.*	Surfactants—cleansing agents
TEA-hydrogenated tallowoyl glutamate	TEA-hydrogenated tallowoyl glutamate is the triethanolamine salt of the hydrogenated tallow acid amide of glutamic acid. It conforms generally to the formula.	Hair conditioning agents; surfactants—cleansing agents
TEA-lauroyl collagen amino acids	TEA-lauroyl collagen amino acid is the triethanolamine salt of the condensation product of lauric acid chloride and collagen amino acids.	Hair conditioning agents; surfactants—cleansing agents
TEA-lauroyl glutamate 31955-67-6 53576-49-1	TEA-lauroyl glutamate is the triethanolamine salt of the lauric acid amide of glutamic acid. It conforms generally to the formula.	Hair conditioning agents; surfactants—cleansing agents
TEA-lauroyl keratin amino acids	TEA-lauroyl keratin amino acid is the triethanolamine salt of the condensation product of lauric acid chloride and keratin amino acids.	Hair conditioning agents; surfactants—cleansing agents
TEA-lauroyl/myristoyl aspartate	TEA-lauroyl/myristoyl aspartate is the triethanolamine salt of the substituted amino acid that conforms generally to the formula	Hair conditioning agents; surfactants—cleansing agents
Undecylenoyl collagen amino acids	Undecylenoyl collagen amino acid is the condensation product of undecylenoyl acid chloride and collagen amino acids.	Surfactants—cleansing agents
Undecylenoyl glycine	Undecylenoyl glycine is the acylation product of glycine with undecylenic acid chloride. It conforms to the formula.	Hair conditioning agents; surfactants—cleansing agents
Undecylenoyl phenylalanine 175357-18-3	Undecylenoyl phenylalanine is the substituted amino acid that conforms to the formula. *Undecylenoyl phenylalanine is the amide formed from the reaction of undecylenoyl chloride and phenylalanine.*	Skin protectants; skin conditioning agents—misc
Undecylenoyl wheat amino acids	Undecylenoyl wheat amino acid is the condensation product of undecylenic acid chloride and wheat amino acids.	Hair conditioning agents; surfactants—cleansing agents
Zinc lauroyl aspartate 899426-42-7	Zinc lauroyl aspartate is the organic compound that conforms to the formula. *Zinc lauroyl aspartate is the zinc salt of the amide formed from the reaction of lauroyl chloride and aspartic acid.*	Binders; surface modifiers

Abbreviations: CIR, Cosmetic Ingredient Review; misc, miscellaneous; TEA, triethanolamine.
[a]The italicized text represents additions made by CIR staff.

Physical and Chemical Properties

The ingredients in this report are typically water-soluble, waxy solids. Available chemical properties can be found in Table 4.

Method of Manufacturing

As shown in Figure 1, the ingredients in this report are most commonly manufactured by the acylation of a free amine of an amino acid with an acyl chloride, a reaction known as the Schotten-Baumann reaction.[11-13] A major side product for this reaction is hydrochloric acid, which can be easily removed.

Disodium capryloyl glutamate, sodium cocoyl glutamate, and sodium lauroyl glutamate. According to a supplier, disodium capryloyl glutamate, sodium cocoyl glutamate, and sodium lauroyl glutamate are produced via the Schotten-Baumann reaction.[14-16] The supplier also described the origin of starting materials: glutamic acid is obtained through formation of glucose/molasses or from wheat and capryloyl chloride, cocoyl chloride, and lauroyl chloride are obtained from caprylic acid, coconut acid, and lauric acid that come from cleavage and distillation of coconut oil. The respective resultant materials are aqueous solutions comprised of 37% to 41% disodium capryloyl glutamate, 32.6% to 38% sodium cocoyl glutamate, and 36% to 40% sodium lauroyl glutamate.

Sodium lauroyl silk amino acids. A supplier of sodium lauroyl silk amino acids reports that the material is prepared by acylation of a free amine of silk amino acid obtained by silk protein hydrolysis. The final product is a 20% water solution of sodium lauroyl silk amino acids.[17]

Impurities

Disodium capryloyl glutamate. A supplier has reported that disodium capryloyl glutamate may contain 4% to 6% propylene

Table 2. Constituent Acids With CIR Conclusions.

Constituent	Conclusion (year issued; maximum use concentration reported)	Summary of findings	Reference
Acetic acid	Safe as used (2012; 0.0004% in leave-ons; 0.3% in rinse-offs)	Central nervous system depression has been documented in animals exposed to acetic acid. Acetic acid has been labeled as a minor skin irritant, at low concentrations, in animal and human studies and a severe ocular irritant in a rabbit ocular irritation test. The sodium salt of acetic acid has a more than 2-fold higher toleration level than the pure free acid, and acetic acid is not mutagenic when buffered to physiological pH.	8
Coconut acid, olive acid, palm acid, sunflower seed acid	Safe as used (2011; coconut acid: no reported uses in leave-ons, 14% in rinse-offs; olive acid: no reported uses; palm acid: no reported uses in leave-ons, 17% in rinse-offs; sunflower seed acid: no reported uses)	The safety focus of use of the plant-derived fatty acid oils was on the potential for irritation and sensitization since the cosmetic ingredients reviewed were also found in the foods that are consumed daily. 5% aqueous solutions of a bar soap containing 13% sodium cocoate had irritation scores of 1.6-4.0/8 in animal studies. However, the remaining animal and clinical irritation and/or sensitization studies conducted on a large number of the oils included in this report, primarily in formulation, did not report any significant irritation or sensitization reactions, indicating that refined oils derived from plants are not dermal irritants or sensitizers.	5,6,9
Lauric acid, oleic acid, stearic acid	Safe as used (1987; reaffirmed in 2006; lauric acid 10%, oleic acid 25% and stearic acid >50% in leave-ons; lauric acid 25% and oleic and stearic acid 50% in rinse-offs)	Oleic, lauric, palmitic, and stearic acids are fatty acids with hydrocarbon chains ranging in length from 12 to 18 carbons with a terminal carboxyl group. These fatty acids are absorbed, digested, and transported in animals and humans. Little acute toxicity was observed when oleic, lauric, palmitic, or stearic acid or cosmetic formulations containing these fatty acids were given to rats orally at doses of 15-19 g/kg body weight. Feeding of 15% dietary oleic acid to rats in a chronic study resulted in normal growth and health, but reproductive capacity of female rats was impaired. Results from topical application of oleic, palmitic, and stearic acid to the skin of mice, rabbits, and guinea pigs produced little or no apparent toxicity. Studies using product formulations containing oleic and stearic acids indicate that it is neither a sensitizer nor photosensitizing agent. Animal studies also indicate that these fatty acids are not eye irritants. Lauric, stearic, and oleic acids were noncarcinogenic in separate animal tests. In primary and cumulative irritation clinical studies, oleic and stearic acids at high concentrations were nonirritating. Cosmetic product formulations containing oleic, lauric, palmitic, and stearic acids at concentrations ranging up to 13% were not primary or cumulative irritants nor sensitizers.	3,7
Malic acid	Safe for use as a pH adjuster, insufficient data for any other functions (2001; 1% in leave-ons and rinse-offs)	Malic acid is a direct food additive. In oral and IP tests with radioactive malic acid, most of the radioactivity was excreted as carbon dioxide. Oral LD_{50} values for mice, rats, and rabbits ranged from 2.66 to > 3.2, 1.60 to 3.5, and 3 to 5 g/kg, respectively. The intravenous LD_{50} value in rabbits was 2.4 g/kg and the intraperitoneal LD_{50} values in	10

(continued)

Table 2. (continued)

Constituent	Conclusion (year issued; maximum use concentration reported)	Summary of findings	Reference
		mice and rats were 50 to 100 and 100 to 200 mg/kg, respectively. In repeated dose oral studies, rats fed malic acid had some changes in body weight gains and feed consumption, but no compound-related lesions were observed. No significant changes or lesions were observed in dogs fed malic acid repeatedly. Malic acid did not cause reproductive toxicity in mice, rats, or rabbits. Malic acid was moderately irritating to rabbit skin and was a strong irritant in guinea pigs. It also caused severe ocular irritation in rabbit eyes. Malic acid was not mutagenic in plate test, an Ames test, a suspension test, or a chromosomal aberration assay. In 1 study, pyrolysates of malic acid were not mutagenic, but in another study they were. Products formed from treatment of malic acid with aqueous solutions of chorine were mutagenic. In a test determining the subjective skin irritation potential, the average irritation scores over a 15-minute period were 39.4, 37.1, and 23.1 for malic acid at pH 3, 5, and 7, respectively. In predictive testing using patients with atopic dermatitis, 18 of 34 patients reacted to a diet high in malic and citric acids and 6 reacted to a diet high in malic acid. In assessing the effect of malic acid on cell renewal, an 18%, 10%, and 5% increase was observed at pH 3, 5, and 7, respectively. Malic acid was not toxic in a clinical efficacy and safety test.	
Myristic acid	Safe as used (2010; 15% in leave-ons; 50% in rinse-offs)	Myristic acid is approved as a food reagent and additive. Myristic acid enhanced the dermal penetration of several drugs. The acute oral LD_{50} and acute dermal LD_{50} of salts of myristic acid were >8 g/kg and >16 mL/kg, respectively, in rats. Acute dermal application of butyl myristate (2 g/kg) was nontoxic and nonirritating to rabbits. When 10 rabbits were treated with a single dermal dose of ethyl myristate (5 g/kg) resulted in the death of 2 over 7 days. The intraperitoneal and subcutaneous LD_{50} for isopropyl myristate exceeded 79.5 mL/kg in rats, and the intraperitoneal LD_{50} was >50.2 mL/kg in mice. No death occurred, and no evidence of systemic toxicity was found at necropsy when the rats were exposed to aerosolized isopropyl myristate. Myristic acid, isopropyl myristate, and myristyl myristate were minimally irritating to the eyes of rabbits. Butyl myristate was nonirritating to the rabbit eye. Myristic acid was nonirritating in a single insult occlusive patch test and slightly irritating in a repeat open patch test on rabbits. Butyl myristate was a moderate skin irritant in rabbits and guinea pigs. Isopropyl myristate and myristyl myristate were minimally irritating in several formulations in rabbits and mice. Isopropyl myristate was nonirritating when injected parenterally in albino rabbits. Butyl myristate and myristyl myristate were nonsensitizing to guinea pigs. Isopropyl myristate and myristyl myristate	[4]

(continued)

Table 2. (continued)

Constituent	Conclusion (year issued; maximum use concentration reported)	Summary of findings	Reference
		were comedogenic to rabbit ears. Isopropyl myristate tested negative in the Salmonella/ microsome test, with and without activation. In clinical primary and cumulative irritation studies, myristic acid was nonirritating. Isopropyl myristate can produce slight irritation but is not a human sensitizer at up to 50%.	

Abbreviations: CIR, Cosmetic Ingredient Review.

glycol, 3% caprylic acid (maximum), 5% disodium glutamate (maximum), and 6% to 8% sodium chloride.[14] Disodium capryloyl glutamate contains <2 ppm arsenic, <5 ppm antimony, <1 ppm lead, <2 ppm cadmium, <2 ppm mercury, <1 ppm nickel, <2 ppm chromium, and <10 ppm total heavy metals (as iron).

Sodium cocoyl glutamate. The same supplier has reported that sodium cocoyl glutamate may contain 4% to 6% propylene glycol, 5% (max) sodium glutamate, 3% coconut acid, and 4% to 5.5% sodium chloride.[16] Sodium cocoyl glutamate contains <2 ppm arsenic, <5 ppm antimony, <1 ppm lead, <2 ppm cadmium, <2 ppm mercury, <1 ppm nickel, <2 ppm chromium, and <10 ppm total heavy metals (as iron).

Sodium lauroyl glutamate. A supplier has reported that sodium lauroyl glutamate may contain 4% to 6% propylene glycol, 5% (maximum) glutamic acid, 3% (maximum) lauric acid, and 3% to 4.5% sodium chloride.[15] Sodium lauroyl glutamate contains <2 ppm arsenic, <5 ppm antimony, <1 ppm lead, <2 ppm cadmium, <2 ppm mercury, <1 ppm nickel, <2 ppm chromium, and <10 ppm total heavy metals (as iron).

Sodium lauroyl silk amino acids. A supplier of sodium lauroyl silk amino acids reports that the material has heavy metals and arsenic $\leq$20 and $\leq$2 ppm, respectively.[17]

Triethanolamine-containing ingredients. The issue of levels of free diethanolamine (DEA) that could be present as an impurity in the ingredients containing triethanolamine (TEA), and the potential of TEA to act as a precursor in nitrosamine formation by undergoing nitrosative cleavage, has been previously reviewed by the Panel.[18,19]

Use

Cosmetic

Table 5A contains the current product formulation data for amino acid alkyl amides. These ingredients function primarily as skin and hair conditioning agents and surfactants.[20] The safety of amino acid alkyl amides included in this safety assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetic 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 FDA's Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the industry in response to surveys conducted by the Personal Care Products Council (Council) of maximum reported use concentrations by product category.

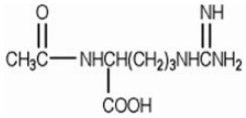
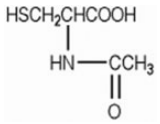
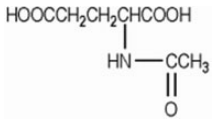
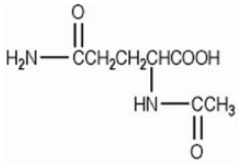
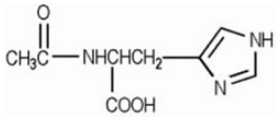
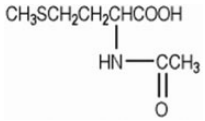
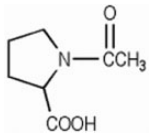
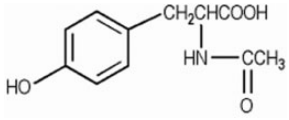
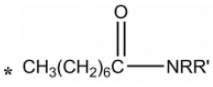
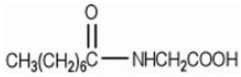
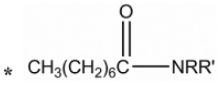
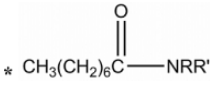
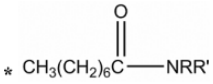
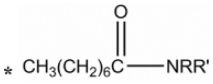
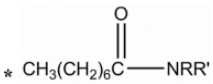
According to VCRP data, lauroyl lysine has the most reported uses in cosmetic and personal care products, with a total of 649; most uses are in leave-on eye and facial makeup.[21] Sodium cocoyl glutamate has the second greatest number of overall uses reported, with a total of 178; more than half of those uses are in rinse-off products.

In the Council's use concentration survey, lauroyl lysine had a wide maximum use concentration range of 0.001% to 45%, with the 45% reported in lipsticks.[22-24] Sodium lauroyl glutamate also had a wide maximum use concentration range of 0.003% to 40%, with the 40% reported in skin cleansing agents. All other use concentrations that were reported had similar ranges.

In some cases, reports of uses were received from the VCRP, but no concentrations of use data were available. For example, palmitoyl keratin amino acids are reported to be used in 5 formulations, but no use concentration data were available. In other cases, no reported uses were received from the VCRP, but a use concentration was provided in the industry survey. For example, cocoyl glutamic acid was not reported in the VCRP database to be in use, but the industry survey indicated that it is used in leave-on formulations at a maximum concentration of 24%. Cocoyl glutamic acid is used presumably in at least 1 cosmetic formulation. Ingredients with no reported uses or use concentrations are listed in Table 5B.

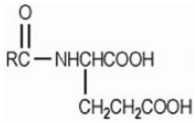
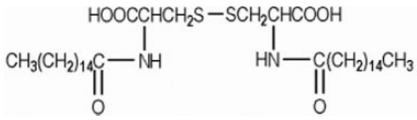
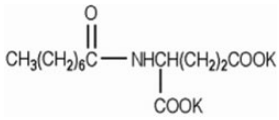
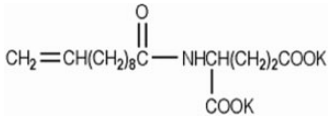
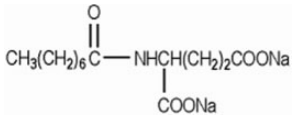
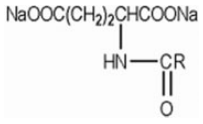
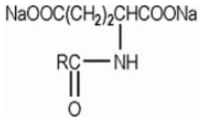
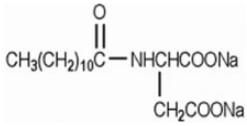
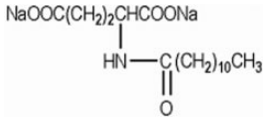
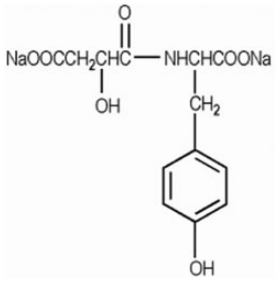
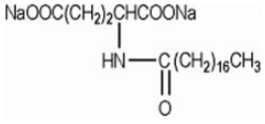
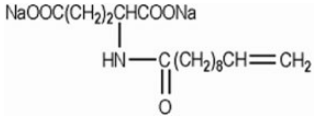
Several of the amino acid alkyl amides described in this report are used in cosmetic sprays, including pump hair, face, and body spray products, foundation spray products, and indoor tanning spray products, and could possibly be inhaled. The maximum concentration of amino acid alkyl amide reported to be used in a spray product is 0.65% palmitoyl proline in a pump hair spray. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater fraction of droplets/particles <10 μm compared with

Table 3. Idealized Structures of the Ingredients in This Safety Assessment.[20,69,a]

Acetyl arginine	
Acetyl cysteine	
Acetyl glutamic acid	
Acetyl glutamine	
Acetyl histidine	
Acetyl methionine	
Acetyl proline	
Acetyl tyrosine	
Capryloyl collagen amino acids	 * $CH_3(CH_2)_6C(=O)NRR'$ where NRR′ represents the amino acid residues from collagen
Capryloyl glycine	
Capryloyl gold of pleasure amino acids	 * $CH_3(CH_2)_6C(=O)NRR'$ where NRR′ represents the amino acid residues from gold of pleasure
Capryloyl keratin amino acids	 * $CH_3(CH_2)_6C(=O)NRR'$ where NRR′ represents the amino acid residues from keratin
Capryloyl pea amino acids	 * $CH_3(CH_2)_6C(=O)NRR'$ where NRR′ represents the amino acid residues from pea
Capryloyl quinoa amino acids	 * $CH_3(CH_2)_6C(=O)NRR'$ where NRR′ represents the amino acid residues from quinoa
Capryloyl silk amino acids	 * $CH_3(CH_2)_6C(=O)NRR'$ where NRR′ represents the amino acid residues from silk

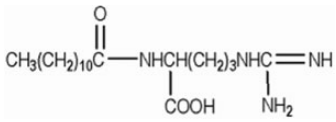
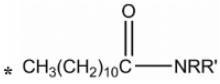
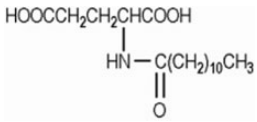
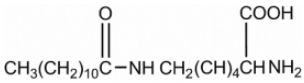
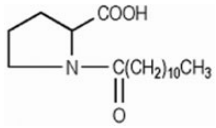
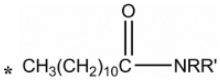
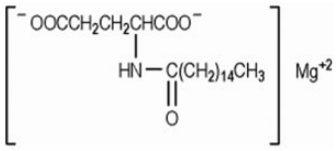
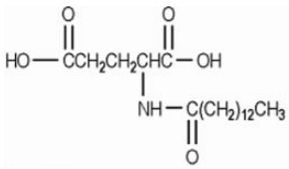
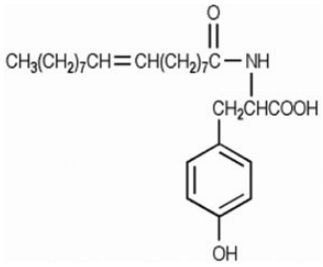
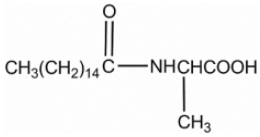
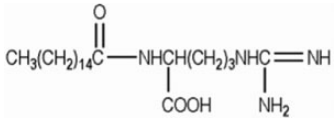
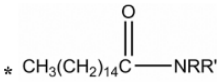
(continued)

Table 3. (continued)

Cocoyl glutamic acid	 where RCO− represents the fatty acids derived from coconut oil.
Dipalmitoyl cystine	
Dipotassium capryloyl glutamate	
Dipotassium undecylenoyl glutamate	
Disodium capryloyl glutamate	
Disodium cocoyl glutamate	 where RCO− represents the fatty acids derived from coconut oil
Disodium hydrogenated tallow glutamate	 where RCO− represents the fatty acids derived from hydrogenated tallow
Disodium *N*-lauroyl aspartate	
Disodium lauroyl glutamate	
Disodium malyl tyrosinate	
Disodium stearoyl glutamate	
Disodium undecylenoyl glutamate	

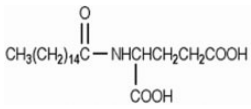
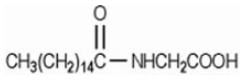
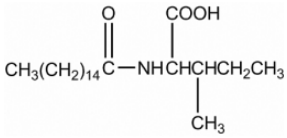
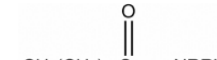
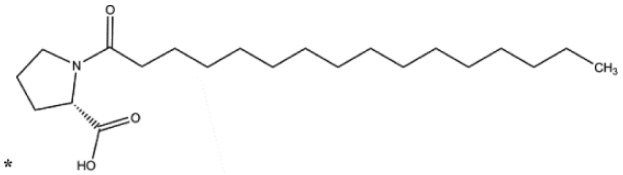
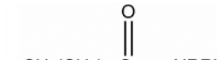
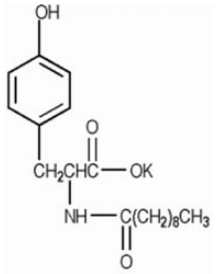
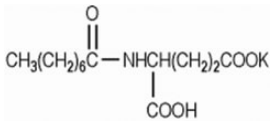
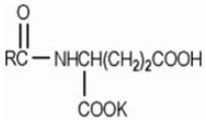
(continued)

Table 3. (continued)

Lauroyl arginine	
Lauroyl collagen amino acids	 * $CH_3(CH_2)_{10}C(=O)NRR'$ where NRR′ represents the amino acid residues from collagen
Lauroyl glutamic acid	
Lauroyl lysine	
Lauroyl proline	
Lauroyl silk amino acids	 * $CH_3(CH_2)_{10}C(=O)NRR'$ where NRR′ represents the amino acid residues from silk
Magnesium palmitoyl glutamate	
Myristoyl glutamic acid	
Oleoyl tyrosine	
Palmitoyl alanine	
Palmitoyl arginine	
Palmitoyl collagen amino acids	 * $CH_3(CH_2)_{14}C(=O)NRR'$ where NRR′ represents the amino acid residues from collagen

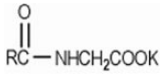
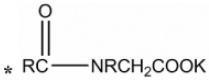
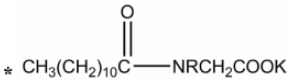
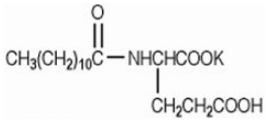
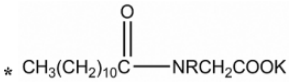
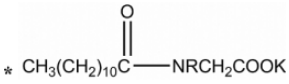
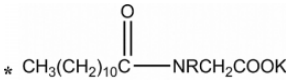
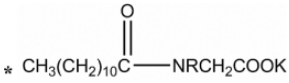
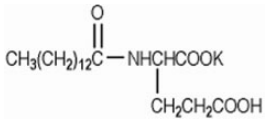
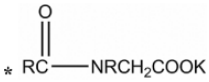
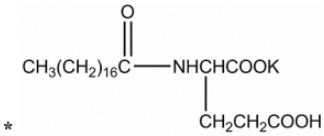
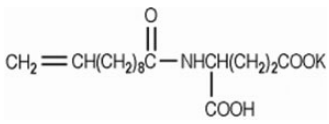
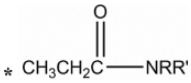
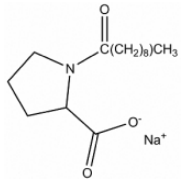
(continued)

Table 3. (continued)

Palmitoyl glutamic acid	
Palmitoyl glycine	
Palmitoyl gold of pleasure amino acids	*  where NRR′ represents the amino acid residues from gold of pleasure
Palmitoyl isoleucine	
Palmitoyl keratin amino acids	*  where NRR′ represents the amino acid residues from keratin
Palmitoyl millet amino acids	*  where NRR′ represents the amino acid residues from millet
Palmitoyl oat amino acids	*  where NRR′ represents the amino acid residues from oat
Palmitoyl pea amino acids	*  where NRR′ represents the amino acid residues from pea
Palmitoyl proline	* 
Palmitoyl quinoa amino acids	*  where NRR′ represents the amino acid residues from quinoa
Palmitoyl silk amino acids	*  where NRR′ represents the amino acid residues from silk
Potassium caproyl tyrosine	
Potassium capryloyl glutamate	
Potassium cocoyl glutamate	 where RCO− represents the fatty acids derived from coconut oil

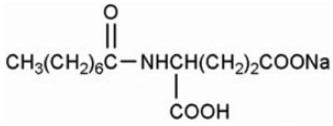
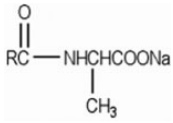
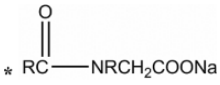
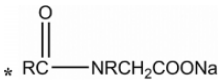
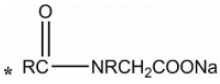
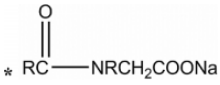
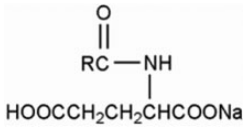
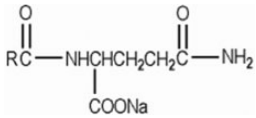
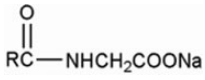
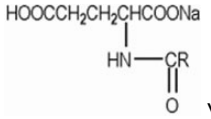
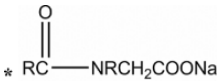
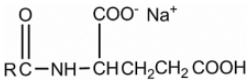
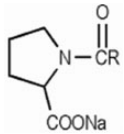
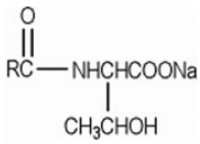
(continued)

Table 3. (continued)

Potassium cocoyl glycinate	 where RCO– represents the cocoyl moiety
Potassium cocoyl rice amino acids	*  where RCO– represents the cocoyl moiety and $NRCH_2COOK$ represents the salt of the rice amino acid residues
Potassium lauroyl collagen amino acids	*  where $NRCH_2COOK$ represents the salt of the collagen amino acid residues
Potassium lauroyl glutamate	
Potassium lauroyl oat amino acids	*  where $NRCH_2COOK$ represents the salt of the oat amino acid residues
Potassium lauroyl pea amino acids	*  where $NRCH_2COOK$ represents the salt of the pea amino acid residues
Potassium lauroyl silk amino acids	*  where $NRCH_2COOK$ represents the salt of the silk amino acid residues
Potassium lauroyl wheat amino acids	*  where $NRCH_2COOK$ represents the salt of the wheat amino acid residues
Potassium myristoyl glutamate	
Potassium olivoyl/lauroyl wheat amino acids	*  where RCO– represents the olivoyl/lauroyl moiety and $NRCH_2COOK$ represents the salt of the wheat amino acid residues
Potassium stearoyl glutamate	* 
Potassium undecylenoyl glutamate	
Propionyl collagen amino acids	*  where NRR' represents the amino acid residues from collagen
Sodium caproyl prolinate	

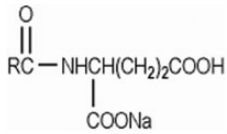
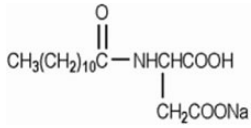
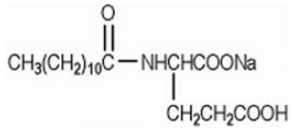
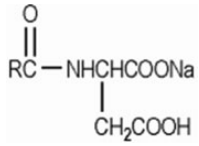
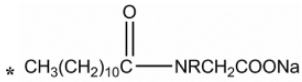
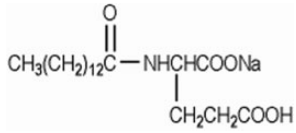
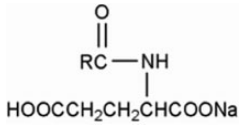
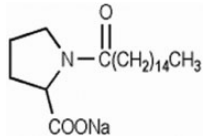
(continued)

Table 3. (continued)

Sodium capryloyl glutamate	
Sodium cocoyl alaninate	 where RCO– represents the fatty acids derived from coconut oil
Sodium cocoyl amino acids	 where RCO– represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of amino acid residues
Sodium cocoyl apple amino acids	 where RCO– represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of apple amino acid residues
Sodium cocoyl barley amino acids	 where RCO– represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of barley amino acid residues
Sodium cocoyl collagen amino acids	 where RCO– represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of collagen amino acid residues
Sodium cocoyl glutamate	 where RCO– represents the fatty acids derived from coconut oil
Sodium cocoyl glutaminate	 where RCO– represents the fatty acids derived from coconut oil
Sodium cocoyl glycinate	 where RCO– represents the cocoyl moiety
Sodium cocoyl/hydrogenated tallow glutamate	 where RCO– represents a mixture of fatty acids derived from coconut oil and hydrogenated tallow
Sodium cocoyl oat amino acids	 where RCO– represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of oat amino acid residues
Sodium cocoyl/palmoyl/ sunfloweroyl glutamate	 where RCO– represents the mixture of fatty acids
Sodium cocoyl proline	 where RCO– represents the fatty acids derived from coconut oil
Sodium cocoyl threoninate	 where RCO– represents the fatty acids derived from *Cocos nucifera* (coconut) oil

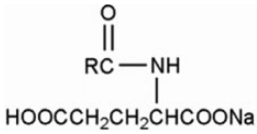
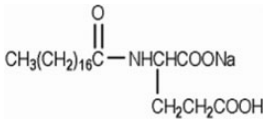
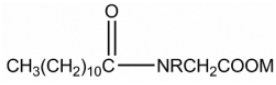
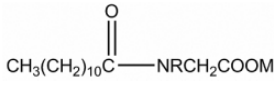
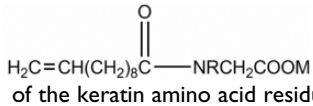
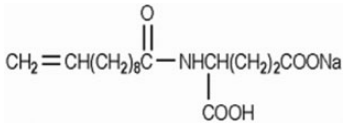
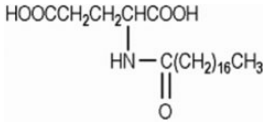
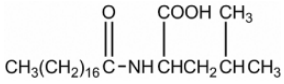
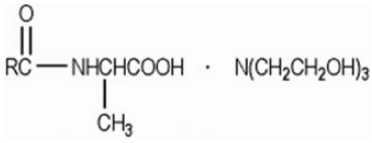
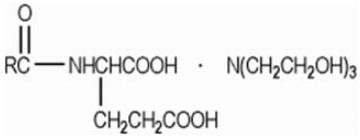
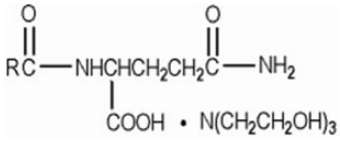
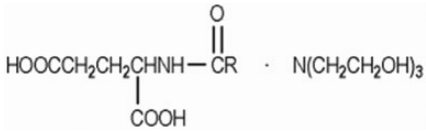
(continued)

Table 3. (continued)

Sodium cocoyl wheat amino acids	 where RCO– represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of wheat amino acid residues
Sodium hydrogenated tallowoyl glutamate	 where RCO– represents the fatty acids derived from hydrogenated tallow
Sodium lauroyl aspartate	
Sodium lauroyl collagen amino acids	 where $NRCH_2COONa$ represents the salt of the collagen amino acid residues
Sodium lauroyl glutamate	
Sodium lauroyl millet amino acids	 where $NRCH_2COONa$ represents the salt of the millet amino acid residues
Sodium lauroyl/myristoyl aspartate	 where RCO– represents the lauroyl/myristoyl grouping
Sodium lauroyl oat amino acids	 where $NRCH_2COONa$ represents the salt of the oat amino acid residues
Sodium lauroyl silk amino acids	 where $NRCH_2COONa$ represents the salt of the silk amino acid residues
Sodium lauroyl wheat amino acids	 where $NRCH_2COONa$ represents the salt of the wheat amino acid residues
Sodium myristoyl glutamate	
Sodium olivoyl glutamate	 where RCO– represents the fatty acids derived from olive oil
Sodium palmitoyl proline	

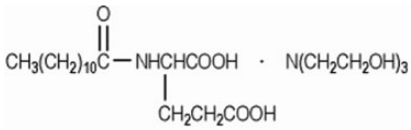
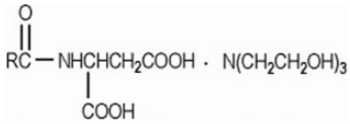
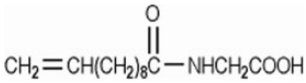
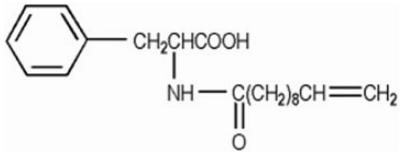
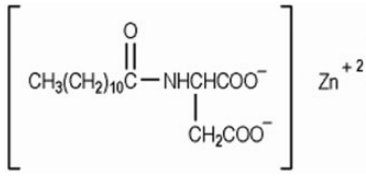
(continued)

Table 3. (continued)

Sodium palmoyl glutamate	 where RCO– represents the palmoyl radical
Sodium stearoyl glutamate	
Sodium/TEA-lauroyl collagen amino acids	*  where $NRCH_2COOM$ represents the mixture of sodium and TEA salts of the collagen amino acid residues
Sodium/TEA-lauroyl keratin amino acids	*  where $NRCH_2COOM$ represents the mixture of sodium and TEA salts of the keratin amino acid residues
Sodium/TEA-undecylenoyl collagen amino acids	*  where $NRCH_2COOM$ represents the mixture of sodium and TEA salts of the keratin amino acid residues
Sodium undecylenoyl glutamate	
Stearoyl glutamic acid	
Stearoyl leucine	
TEA-cocoyl alaninate	 where RCO– represents the fatty acids derived from coconut oil
TEA-cocoyl glutamate	 where RCO– represents the fatty acids derived from coconut oil
TEA-cocoyl glutaminate	 where RCO– represents the coconut acid moiety
TEA-hydrogenated tallowoyl glutamate	 where RCO– represents the fatty acids derived from hydrogenated tallow
TEA-lauroyl collagen amino acids	*  where $NRCH_2COOH\ N(CH_2CH_2OH)_3$ represents the TEA salt of the collagen amino acid residues

(continued)

Table 3. (continued)

TEA-lauroyl glutamate	
TEA-lauroyl keratin amino acids	*  where $NRCH_2COOH\ N(CH_2CH_2OH)_3$ represents the TEA salt of the keratin amino acid residues
TEA-lauroyl/myristoyl aspartate	 where RCO− represents the lauroyl/myristoyl grouping
Undecylenoyl collagen amino acids	*  where NRR′ represents the amino acid residues from collagen
Undecylenoyl glycine	
Undecylenoyl phenylalanine	
Undecylenoyl wheat amino acids	*  where NRR′ represents the amino acid residues from wheat
Zinc lauroyl aspartate	

Abbreviations: CIR, Cosmetic Ingredient Review; TEA, triethanolamine.
[a]The asterisk marked structures represent additions made by CIR staff.

pump sprays.[25,26] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (ie, able to enter the lungs) to any appreciable amount.[27,28]

In the European Union, trialkylamines, trialkanolamines, and their salts (ingredients containing TEA) may only be used up to 2.5%, must be at least 99% pure, are not to be used with nitrosating systems, must have ≤5% secondary amine content and ≤50 μg/kg nitrosamine, and must be kept in nitrite-free containers.[29] The use of the remaining ingredients is not restricted under the rules governing cosmetic products in the European Union.

Noncosmetic

Amino acid alkyl amides are used in household detergents.[30] Acetyl cysteine has been approved by the FDA to treat acetaminophen overdose via intravenous injection and for mucolytic therapy.[31] Acetyl methionine is an approved direct food additive (21 CFR §172.372).

Toxicokinetics

Absorption, Distribution, Metabolism, and Excretion

Acetyl tyrosine. A percutaneous absorption study of 3 formulations containing 1.75% acetyl tyrosine was performed in vitro on human trunk skin using the finite dose technique and Franz diffusion cells.[32] The formulations were a gel, a cream, and a water solution in silicone. Each formulation was evaluated on 3 replicate sections from 2 different donors of ex vivo human trunk skin. At dosing, 10 mg formulation/cm^2/skin section equivalent volume was dispensed by pipette and a glass rod was used to evenly distribute the formulation into the skin. The percutaneous absorption of the test material was determined over a 48-hour dose period. At 6, 12, 32, and 48 hours after

Table 4. Chemical Properties of Amino Acids Alkyl Amides.

Property	Value	Reference
Acetyl arginine		
Molecular weight, g/mol	216.24	PubChem
Acetyl cysteine		
Physical form	Crystals in water	Merck
Odor	Slight acetic	Merck
Molecular weight, g/mol	163.19	[70]
Molecular volume, cm^3/mol at 20°C	126.0	[70]
Density/specific gravity at 20°C	1.294	[70]
Vapor pressure, mm Hg at 25°C	8.68×10^{-8}	[70]
Melting point, °C	109-110	Merck
Boiling point, °C	407.7	[70]
Solubility	Freely soluble in water, alcohol. Practically insoluble in chloroform, ether	Merck
logP at 25°C	−0.696	[70]
Dissociation constants (pKa, pKb) at 25°C	3.25 most acidic; −0.91 most basic	[70]
Acetyl glutamic acid		
Molecular weight, g/mol	189.17	[70]
Molecular volume, cm^3/mol at 20°C	139.6	[70]
Density/specific gravity at 20°C	1.354	[70]
Vapor pressure, mm Hg at 25°C	3.48×10^{-11}	[70]
Boiling point, °C	495.9	[70]
logP at 25°C	−2.131	[70]
Dissociation constants (pKa) at 25°C	3.45 most acidic; −0.86 most basic	[70]
Acetyl glutamine		
Physical form	Crystals from ethanol	Merck
Molecular weight, g/mol	188.18	[70]
Molecular volume, cm^3/mol at 20°C	145.8	[70]
Density/specific gravity at 20°C	1.290	[70]
Vapor pressure, mm Hg	1.28×10^{-8}	[70]
Melting point, °C	197	Merck
Boiling point, °C	430.5	[70]
logP at 25°C	−2.215	[70]
Dissociation constants (pKa) at 25°C	2.19 most acidic; 9.19 most basic	[70]
Acetyl methionine		
Physical form	Crystals; large prisms from water (DL-); plates from water or ethyl acetate (D-)	Merck
Molecular weight, g/mol	191.25	[70]
Molecular volume, cm^3/mol at 20°C	158.9	[70]
Density/specific gravity at 20°C	1.202	[70]
Vapor pressure, mm Hg	1.72×10^{-9}	[70]
Melting point, °C	102-104; 114-115 (DL-); 104-105 (D-)	Merck
Boiling point, °C	453.6	[70]
Water solubility, g/100 mL at 25°C	9.12 (DL-); 30.7 (D-)	Merck
Other solubility, g/100 mL at 25°C	Acetone 10.0 (DL-) and 29.6 (D-); ethyl acetate 2.29 (DL-) and 7.04 (D-); chloroform 1.33 (DL-) and 6.43 (D-)	Merck
logP at 25°C	−0.885	[70]
Dissociation constants (pKa) at 25°C	3.50 most acidic; −0.84 most basic	[70]
Acetyl tyrosine		
Molecular weight, g/mol	223.23	[70]
Molecular volume, cm^3/mol at 20°C	171.1	[70]
Density/specific gravity at 20°C	1.304	[70]
Vapor pressure, mm Hg	4.07×10^{-12}	[70]
Boiling point, °C	531.3	[70]
logP at 25°C	−1.676	[70]
Dissociation constants (pKa) at 25°C	3.15 most acidic; −0.83 most basic	[70]
Capryloyl glycine		
Molecular weight, g/mol	201.26	[70]
Molecular volume, cm^3/mol at 20°C	194.1	[70]
Density/specific gravity at 20°C	1.036	[70]

(continued)

Table 4. (continued)

Property	Value	Reference
Vapor pressure, mm Hg	1.19×10^{-7}	70
Boiling point, °C	403.9	70
logP at 25°C	1.065	70
Dissociation constants (pKa) at 25°C	3.62 most acidic; −0.98 most basic	70
Dipalmitoyl cystine		
Molecular weight, g/mol	717.12	70
Molecular volume, cm^3/mol at 20°C	685.6	70
Density/specific gravity at 20°C	1.045	70
Vapor pressure, mm Hg at 25°C	3.93×10^{-32}	70
Boiling point, °C	852.2	70
logP at 25°C	12.988	70
Dissociation constants (pKa) at 25°C	2.93 most acidic; −0.63 most basic	70
Disodium capryloyl glutamate		
Physical form at 20°C	Clear to light turbid liquid	38
Color	Colorless to light yellow	38
pH at 20°C	9.0-10.5	38
Lauroyl arginine		
Molecular weight, g/mol	356.50	70
Molecular volume, cm^3/mol at 20°C	316.2	70
Density/specific gravity at 20°C	1.12	70
logP at 25°C	2.547	70
Dissociation constants (pKa) at 25°C	3.60 most acidic; 13.84 most basic	70
Lauroyl glutamic acid		
Molecular weight, g/mol	329.43	70
Molecular volume, cm^3/mol at 20°C	304.7	70
Density/specific gravity at 20°C	1.081	70
Vapor pressure, mm Hg	2.95×10^{-13}	70
Melting point, °C	95-96	11
Boiling point, °C	543.6	70
logP at 25°C	2.964	70
Dissociation constants (pKa) at 25°C	3.46 most acidic; −0.88 most basic	70
Lauroyl proline		
Molecular weight, g/mol	297.43	70
Molecular volume, cm^3/mol at 20°C	288.3	70
Density/specific gravity at 20°C	1.031	70
Vapor pressure, mm Hg	6.01×10^{-10}	70
Boiling point, °C	465.3	70
logP at 25°C	5.356	70
Dissociation constants (pKa) at 25°C	3.70 most acidic; −2.37 most basic	70
Palmitoyl alanine		
Molecular weight, g/mol	327.50	70
Molecular volume, cm^3/mol at 20°C	343.1	70
Density/specific gravity at 20°C	0.954	70
Vapor pressure, mm Hg	2.73×10^{-11}	70
Boiling point, °C	498.4	70
logP at 25°C	5.495	70
Dissociation constants (pKa) at 25°C	3.69 most acidic; −0.81 most basic	70
Palmitoyl arginine		
Molecular weight, g/mol	412.61	70
Molecular volume, cm^3/mol at 20°C	380.5	70
Density/specific gravity at 20°C	1.08	70
logP at 25°C	4.585	70
Dissociation constants (pKa) at 25°C	3.60 most acidic; 13.84 most basic	70
Palmitoyl glutamic acid		
Molecular weight, g/mol	385.54	70
Molecular volume, cm^3/mol at 20°C	370.7	70
Density/specific gravity at 20°C	1.039	70
Vapor pressure, mm Hg	5.17×10^{-15}	70

(continued)

Table 4. (continued)

Property	Value	Reference
Boiling point, °C	581.1	70
logP at 25°C	5.002	70
Dissociation constants (pKa) at 25°C	3.46 most acidic; −0.88 most basic	70
Palmitoyl glycine		
Molecular weight, g/mol	313.48	70
Molecular volume, cm^3/mol at 20°C	326.2	70
Density/specific gravity at 20°C	0.960	70
Vapor pressure, mm Hg	5.13×10^{-11}	70
Melting point, °C	122-125	11
Boiling point, °C	491.8	70
logP at 25°C	5.141	70
Dissociation constants (pKa) at 25°C	3.59 most acidic; −1.01 most basic	70
Palmitoyl isoleucine		
Molecular weight, g/mol	369.58	70
Molecular volume, cm^3/mol at 20°C	392.9	70
Density/specific gravity at 20°C	0.940	70
Vapor pressure, mm Hg	1.44×10^{-12}	70
Boiling point, °C	528.2	70
logP at 25°C	6.867	70
Dissociation constants (pKa) at 25°C	3.67 most acidic; −0.81 most basic	70
Palmitoyl proline		
Molecular weight, g/mol	353.54	70
Molecular volume, cm^3/mol at 20°C	354.3	70
Density/specific gravity at 20°C	0.997	70
Vapor pressure, mm Hg	7.58×10^{-12}	70
Boiling point, °C	511.6	70
logP at 25°C	7.394	70
Dissociation constants (pKa) at 25°C	3.69 most acidic; −2.37 most basic	70
Sodium lauroyl glutamate		
Physical form at 20°C	Clear to slightly turbid liquid	30
Color	Colorless to slightly yellow	30
Stearoyl glutamic acid		
Molecular weight, g/mol	413.594	71
Molecular volume, cm^3/mol at 20°C	403.7	70
Density/specific gravity at 20°C	1.024	70
Vapor pressure, mm Hg	5.85×10^{-16}	70
Melting point, °C	154.75	71
Boiling point, °C	600.3	70
logP at 25°C	6.021	70
Dissociation constants (pKa) at 25°C	3.46 most acidic; −0.88 most basic	70
Stearoyl leucine		
Molecular weight, g/mol	397.63	70
Molecular volume, cm^3/mol at 20°C	426.0	70
Density/specific gravity at 20°C	0.933	70
Vapor pressure, mm Hg	1.41×10^{-13}	70
Melting point, °C	64-65	13
Boiling point, °C	550.6	70
logP at 25°C	7.886	70
Dissociation constants (pKa) at 25°C	3.67 most acidic; −0.81 most basic	70
Undecylenoyl phenylalanine		
Molecular weight, g/mol	331.45	70
Molecular volume, cm^3/mol at 20°C	316.3	70
Density/specific gravity at 20°C	1.047	70
Vapor pressure, mm Hg	1.70×10^{-12}	70
Boiling point, °C	540.0	70
logP at 25°C	3.155	70
Dissociation constants (pKa) at 25°C	3.63 most acidic; −0.82 most basic	70

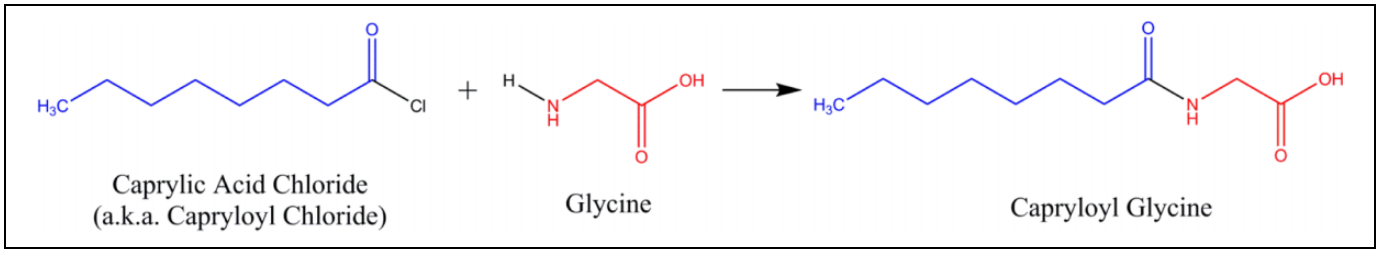


Figure 1. Synthesis of the amino acid alkyl amide, capryloyl glycine.

application, the dermal receptor solution was removed in its entirety, replaced with stock receptor solution, and 4 mL aliquot was saved for subsequent analysis. After the last receptor solution collection, the skin surface was washed twice with 50:50 methanol:water to collect unabsorbed formulation from the skin. The glass rod used for dosing, the surface wash, stratum corneum, epidermis, and dermis were recovered and evaluated for compound content. The samples were analyzed for test material content using high-performance liquid chromatography method.

In the formulation with water, the test material was found in the following mean distribution: 0.48% in the receptor solution, 0.04% in the dermis, 1.25% in the epidermis, 4.64% in the stratum corneum, and 83.15% in the surface wash (total recovery was 89.55%). For the gel formulation, the test material was found in the following mean distribution: 1.03% in the receptor solution, 0.07% in the dermis, 1.15% in the epidermis, 0. 70% in the stratum corneum, and 88.59% in the surface wash (total recovery was 91.53%). Finally, in the cream formulation, the test material was found in the following mean distribution: 2.70% in the receptor solution, 0.39% in the dermis, 15.96% in the epidermis, 11.91% in the stratum corneum, and 54.34% in the surface wash (total recovery was 85.30%). The authors of the study concluded that acetyl tyrosine in all 3 formulations evaluated does penetrate into and through ex vivo human skin using the in vitro finite dose.[32]

Toxicological Studies

The amino acid alkyl amides in this assessment will not rapidly dissociate (beyond zwitterion formation) in the presence of water, but action by amidases is the most likely first step of metabolism if dermal penetration occurs. Exposure to these ingredients, hence, would also involve exposures to amino acid and fatty acid metabolites of these ingredients. Because most of these amino acids and fatty acids are found in the foods we consume daily, systemic toxicity is not expected. Systemic toxicity following dermal exposure is not expected to differ from that of oral exposure. This report is focused on irritation and sensitization. Although most surfactants have the potential for some irritation, data from the previous safety assessments on α-amino acids and fatty acids support that these ingredients, as used in cosmetics, would not likely be irritants or sensitizers.

Reproductive and Developmental Toxicity

Acetyl Cysteine

In teratology studies, no evidence of impaired fertility or toxicity to fetuses was observed in rats at oral doses up to 2,000 mg/kg/d acetyl cysteine and in rabbits at oral doses up to 1,000 mg/kg/d acetyl cysteine.[33] No further details were provided.

Male rats treated orally with 250 mg/kg/d acetyl cysteine for 15 weeks did not experience adverse effects to fertility or reproductive performance.[33] No further details were provided.

Genotoxicity

In vitro and in vivo genotoxicity studies are presented in Table 6. In in vitro studies, acetyl glutamic acid, acetyl proline, acetyl tyrosine, disodium capryloyl glutamate, sodium cocoyl glutamate, and sodium lauroyl glutamate were negative for genotoxicity. Acetyl cysteine was not genotoxic in an Ames test but had positive results in in vitro mouse lymphoma test. Acetyl cysteine and acetyl glutamic acid were negative in in vivo mouse studies.[16,33-39]

Carcinogenicity

No published carcinogenicity studies on amino acid alkyl amides were identified by a literature search for these ingredients and no unpublished data were submitted.

Irritation and Sensitization

Data from a previous CIR safety assessment of α-amino acids[2] indicate that cysteine HCl and methionine were used as negative controls in in vitro assays to predict potential skin irritants; arginine (up to 5%), aspartic acid (up to 0.2%), cysteine (up to 5%), glycine (up to 2%), magnesium aspartate (up to 0.1%), serine (up to 0.3%), and tyrosine (up to 1%) did not produce any adverse effects in rats, guinea pigs, or mouse skin models in separate dermal and ocular studies; and glutamic acid was used as a negative control in an in vitro study to identify skin sensitizers. The data also showed that products containing amino acid ingredients at concentrations up to 2.784% were not dermal irritants or sensitizers in HRIPT studies, and in several validation studies for in vitro phototoxicity assays, histidine was used as a negative control. Neither magnesium aspartate up to 0.5% nor 1% tyrosine was phototoxic in assays using yeast.

Table 5A. Frequency and Concentration of Use (2012-2013) According to Duration and Type of Exposure for Amino Acid Alkyl Amides.[21-24]

	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)
	Acetyl cysteine		Acetyl glutamine		Acetyl methionine	
Totals[a]	23	0.0005-0.1	8	0.01-1	9	0.00001
Duration of use						
Leave-on	14	0.0005-0.1	2	0.01-1	7	0.00001
Rinse-off	9	NR	6	0.1	2	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	4	NR	NR	NR	4	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	1[b]	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	13	0.0005-0.03	2	0.01-1	4	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	10	0.1	6	NR	4	0.00001
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	1	NR
Mucous membrane	NR	NR	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Acetyl tyrosine		Capryloyl glycine		Cocoyl glutamic acid	
Totals[a]	29	0.03-0.3	75	0.05-2	NR	24
Duration of use						
Leave-on	23	0.08-0.3	46	0.09-2	NR	NR
Rinse-off	6	0.03	28	0.05-2	NR	24
Diluted for (bath) use	NR	NR	1	NR	NR	NR
Exposure type						
Eye area	2	0.3	3	0.4-2	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	3	NR	4	0.1	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	21	0.03-0.3	62	0.05-2	NR	24
Deodorant (underarm)	NR	NR	2	0.1	NR	NR
Hair—noncoloring	8	0.3	10	0.4-2	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	1	NR	6	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Disodium capryloyl glutamate		Disodium cocoyl glutamate		Disodium hydrogenated tallow glutamate	
Totals[a]	2	0.4	76	0.02-3	NR	0.1-1
Duration of use						
Leave-on	2	NR	9	0.02-0.3	NR	0.1
Rinse-off	NR	0.4	67	0.6-3	NR	1
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	1	0.02-0.05	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	0.3[c]	NR	NR
Incidental inhalation—powder	NR	NR	2	0.1	NR	NR
Dermal contact	2	0.4	31	0.02-3	NR	0.1-1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	NR	15	NR	NR	NR
Hair—coloring	NR	NR	30	NR	NR	NR
Nail	NR	NR	NR	0.05	NR	NR
Mucous membrane	NR	NR	7	2[d]	NR	NR
Baby products	NR	NR	NR	NR	NR	NR

(continued)

Table 5A. (continued)

	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)
	Disodium lauroyl glutamate		Disodium malyl tyrosinate		Disodium stearoyl glutamate	
Totals	1	NR	1	NR	135	0.000006-6
Duration of use						
Leave-on	NR	NR	NR	NR	135	0.000006-6
Rinse-off	1	NR	NR	NR	NR	0.1-0.3
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	15	0.05-1
Incidental ingestion	NR	NR	NR	NR	3	0.000006-0.02
Incidental inhalation—spray	NR	NR	NR	NR	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	6	0.2-6
Dermal contact	1	NR	1	NR	130	0.03-6
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	NR	NR	NR	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	NR	NR	NR	3	0.000006-0.02
Baby products	NR	NR	NR	NR	NR	NR
	Lauroyl arginine		Lauroyl collagen amino acids		Lauroyl lysine	
Totals[a]	1	NR	1	NR	649	0.001-45
Duration of use						
Leave-on	NR	NR	NR	NR	643	0.001-45
Rinse-off	1	NR	1	NR	6	0.001-0.3
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	265	0.005-10.2
Incidental ingestion	NR	NR	NR	NR	24	0.2-45
Incidental inhalation—spray	NR	NR	NR	NR	7	NR
Incidental inhalation—powder	NR	NR	NR	NR	173	0.005-12
Dermal contact	NR	NR	NR	NR	583	0.005-14
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	1	NR	1	NR	4	0.001-0.3
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	1	0.001
Mucous membrane	NR	NR	NR	NR	24	0.2-45
Baby products	NR	NR	NR	NR	NR	NR
	Lauroyl proline		Lauroyl silk amino acids		Magnesium palmitoyl glutamate	
Totals[a]	1	NR	2	NR	15	0.0006-0.2
Duration of use						
Leave-on	1	NR	1	NR	15	0.0006-0.2
Rinse-off	NR	NR	1	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	NR	NR	0.2[e]
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	1	NR	1	NR	14	0.0006-0.2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	NR	1	NR	NR	0.2
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	1	0.001-0.002
Mucous membrane	NR	NR	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR

(continued)

Table 5A. (continued)

	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)
	Oleoyl tyrosine		Palmitoyl collagen amino acids		Palmitoyl glycine	
Totals[a]	3	NR	1	NR	5	1
Duration of use						
Leave-on	3	NR	1	NR	5	1
Rinse-off	NR	NR	NR	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	3	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	3	NR	1	NR	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	3	NR	1	NR	5	1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	NR	NR	NR	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	NR	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Palmitoyl keratin amino acids		Palmitoyl proline		Palmitoyl silk amino acids	
Totals[a]	5	NR	15	0.0017-0.65	2	NR
Duration of use						
Leave-on	4	NR	15	0.0017-0.65	2	NR
Rinse-off	1	NR	NR	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	0.46-0.65[a]	NR	NR
Incidental inhalation—powder	NR	NR	NR	0.3[f]	NR	NR
Dermal contact	4	NR	14	0.0017-0.46	2	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	1	NR	NR	0.42-0.65	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	1	0.0055	NR	NR
Mucous membrane	NR	NR	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Potassium cocoyl glutamate		Potassium cocoyl glycinate		Potassium lauroyl wheat amino acids	
Totals[a]	6	0.03-12	16	1-39	4	0.7
Duration of use						
Leave-on	NR	0.03	NR	2	NR	NR
Rinse-off	6	3-12	15	1-39	4	0.7
Diluted for (bath) use	NR	6	1	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	NR	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	6	0.03-12	16	1-39	4	0.7
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	8	NR	NR	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	3-6	4	1	1	NR
Baby products	NR	NR	NR	NR	NR	NR

(continued)

Table 5A. (continued)

	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)
	Potassium myristoyl glutamate		Sodium cocoyl alaninate		Sodium cocoyl amino acids	
Totals[a]	5	11-27	8	NR	21	0.4-2.8
Duration of use						
Leave-on	NR	NR	4	NR	10	0.4-1
Rinse-off	5	11-27	4	NR	11	0.4-2.8
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	2	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	NR	NR	0.4[g]
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	5	11-27	6	NR	8	2.8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	NR	2	NR	12	0.4-1
Hair—coloring	NR	NR	NR	NR	1	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	NR	NR	NR	1	2.8
Baby products	NR	NR	2	NR	NR	NR
	Sodium cocoyl apple amino acids		Sodium cocoyl collagen amino acids		Sodium cocoyl glutamate	
Duration of use	21	0.3-3	13	0.02	178	0.004-10
Leave-on						
Rinse-off	10	0.3	3	0.02	66	0.004-3
Diluted for (bath) use	11	0.5-3	10	0.02	110	0.01-10
Exposure type	NR	NR	NR	NR	2	NR
Eye area						
Incidental ingestion	7	0.3	1	NR	8	0.004-0.6
Incidental inhalation—spray	NR	NR	NR	NR	7	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	0.03[h]
Dermal contact	NR	NR	NR	NR	1	NR
Deodorant (underarm)	18	0.3-3	2	NR	114	0.004-9
Hair—noncoloring	NR	NR	NR	NR	NR	NR
Hair—coloring	3	0.5	11	0.02	27	0.2-10
Nail	NR	NR	NR	NR	30	3
Mucous membrane	NR	NR	NR	NR	NR	NR
Baby products	4	NR	1	NR	31	0.2-3
Duration of use	NR	NR	NR	NR	NR	NR
	Sodium cocoyl glycinate		Sodium hydrogenated tallowoyl glutamate		Sodium lauroyl aspartate	
Totals[a]	32	0.2-20	2	0.8	4	0.005-2
Duration of use						
Leave-on	1	NR	1	0.8	4	0.005-0.2
Rinse-off	31	0.2-20	1	NR	NR	2
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	2	0.1
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	NR	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	0.2
Dermal contact	32	0.2-20	2	0.8	4	0.005-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	NR	NR	NR	NR	NR	2
Hair—coloring	NR	NR	NR	NR	NR	NR

(continued)

Table 5A. (continued)

	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	10	0.2-3	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Sodium lauroyl glutamate		Sodium lauroyl oat amino acids		Sodium lauroyl wheat amino acids	
Totals[a]	75	0.003-40	98	0.04-5	1	NR
Duration of use						
Leave-on	7	0.03-4	14	0.4-0.8	NR	NR
Rinse-off	63	0.003-40	79	0.04-5	1	NR
Diluted for (bath) use	5	4	5	0.9	NR	NR
Exposure type						
Eye area	1	NR	NR	5	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	NR	NR	NR
Incidental inhalation—powder	1	NR	NR	NR	NR	NR
Dermal contact	54	0.003-40	71	0.09-5	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	21	3	27	0.04-0.4	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	20	4	38	0.09-5	NR	NR
Baby products	2	NR	1	NR	NR	NR
	Sodium myristoyl glutamate		Sodium palmitoyl proline		Sodium palmoyl glutamate	
Totals[a]	51	0.1-31	7	NR	NR	2-22
Duration of use						
Leave-on	44	0.1-5	6	NR	NR	NR
Rinse-off	7	0.1-31	1	NR	NR	2-22
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	10	0.1	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	1	NR	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	50	0.1-31	7	NR	NR	2-22
Deodorant (underarm)	NR	NR	1	NR	NR	NR
Hair—noncoloring	NR	NR	NR	NR	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	1	0.5	NR	NR	NR	NR
Mucous membrane	NR	31	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Sodium stearoyl glutamate		TEA-cocoyl alaninate		TEA-cocoyl glutamate	
Totals[a]	120	0.03-2	2	0.8	65	2-10.5
Duration of use						
Leave-on	106	0.2-2	NR	NR	9	2
Rinse-off	14	0.03 -1.1	2	0.8	56	2-10.5
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	5	1	NR	NR	NR	NR
Incidental ingestion	NR	1	NR	NR	NR	NR
Incidental inhalation—spray	6	0.2-0.3[i]	NR	NR	1	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	114	0.2-2	2	0.8	63	2.1-10.5
Deodorant (underarm)	3	NR	NR	NR	NR	NR
Hair—noncoloring	6	0.03-0.2	NR	NR	2	2-10

(continued)

Table 5A. (continued)

	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)	No. of uses	Maximum concentration of use (%)
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	3	1	NR	NR	36	2.1-3
Baby products	NR	NR	NR	NR	1	NR
	TEA-lauroyl collagen amino acids		TEA-lauroyl glutamate		Undecylenoyl collagen amino acids	
Totals[a]	3	0.4	1	NR	2	NR
Duration of use						
Leave-on	3	0.4	NR	NR	NR	NR
Rinse-off	NR	NR	1	NR	2	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Exposure type						
Eye area	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—spray	NR	NR	NR	NR	NR	NR
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR
Dermal contact	NR	NR	1	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	3	0.4	NR	NR	2	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	NR	1	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Undecylenoyl glycine		Undecylenoyl phenylalanine			
Totals[a]	10	0.3	18	0.5-2		
Duration of use						
Leave-on	6	0.3	17	0.5-2		
Rinse-off	4	NR	1	NR		
Diluted for (bath) use	NR	NR	NR	NR		
Exposure type						
Eye area	1	0.3	NR	NR		
Incidental ingestion	NR	NR	NR	NR		
Incidental inhalation—spray	3	NR	NR	NR		
Incidental inhalation—powder	NR	NR	NR	NR		
Dermal contact	4	0.3	18	0.5-2		
Deodorant (underarm)	NR	NR	NR	NR		
Hair—noncoloring	4	NR	NR	NR		
Hair—coloring	NR	NR	NR	NR		
Nail	2	NR	NR	NR		
Mucous membrane	NR	NR	NR	NR		
Baby products	NR	NR	NR	NR		

Abbreviations: NR, not reported; TEA, triethanolamine.
[a]0.46% in a body and hand spray; 0.65% in a pump hair spray.
[b]1% in a face and neck spray.
[c]0.3% in a foundation spray.
[d]0.6% in hand soap categorized as "other personal cleanliness product."
[e]0.2% in a pump hair spray; 0.2% in a spray tonic, dressing, and other hair grooming aids; and 0.2% in a body and hand spray.
[f]0.3% in a face powder.
[g]0.4% in pump hair spray.
[h]0.03% in a foundation spray.
[i]0.2% in an indoor tanning product; 0.3% in a body and hand spray.

Table 5B. Amino Acid Alkyl Amides Not Reported in Use

Acetyl arginine
Acetyl glutamic acid
Acetyl histidine
Acetyl proline
Capryloyl collagen amino acids
Capryloyl gold of pleasure amino acids
Capryloyl keratin amino acids
Capryloyl pea amino acids
Capryloyl quinoa amino acids
Capryloyl silk amino acids
Dipalmitoyl cystine
Dipotassium capryloyl glutamate
Dipotassium undecylenoyl glutamate
Disodium N-lauroyl aspartate
Disodium undecylenoyl glutamate
Lauroyl glutamic acid
Myristoyl glutamic acid
Palmitoyl alanine
Palmitoyl arginine
Palmitoyl glutamic acid
Palmitoyl gold of pleasure amino acids
Palmitoyl isoleucine
Palmitoyl millet amino acids
Palmitoyl oat amino acids
Palmitoyl pea amino acids
Palmitoyl quinoa amino acids
Potassium caproyl tyrosine
Potassium capryloyl glutamate
Potassium cocoyl rice amino acids
Potassium lauroyl collagen amino acids
Potassium lauroyl glutamate
Potassium lauroyl oat amino acids
Potassium lauroyl pea amino acids
Potassium lauroyl silk amino acids
Potassium olivoyl/lauroyl wheat amino acids
Potassium stearoyl glutamate
Potassium undecylenoyl glutamate
Propionyl collagen amino acids
Sodium capryloyl prolinate
Sodium capryloyl glutamate
Sodium cocoyl barley amino acids
Sodium cocoyl glutaminate
Sodium cocoyl/hydrogenated tallow glutamate
Sodium cocoyl oat amino acids
Sodium cocoyl/palmoyl/sunfloweroyl glutamate
Sodium cocoyl proline
Sodium cocoyl threoninate
Sodium cocoyl wheat amino acids
Sodium lauroyl collagen amino acids
Sodium lauroyl millet amino acids
Sodium lauroyl/myristoyl aspartate
Sodium lauroyl silk amino acids
Sodium lauroyl/myristoyl aspartate
Sodium lauroyl silk amino acids
Sodium olivoyl glutamate
Sodium/TEA-lauroyl collagen amino acids
Sodium/TEA-lauroyl keratin amino acids
Sodium/TEA-undecylenoyl collagen amino acids
Sodium undecylenoyl glutamate
Stearoyl glutamic acid
Stearoyl leucine
TEA cocoyl glutaminate
TEA-hydrogenated tallowyl glutamate
TEA-lauroyl keratin amino acids
TEA-lauroyl/myristoyl aspartate
Undecylenoyl wheat amino acids
Zinc lauroyl aspartate

(continued)

Abbreviation: TEA, triethanolamine.

Irritation

Dermal. In vitro and human dermal irritation studies are presented in Table 7. No irritation was observed in in vitro studies with disodium capryloyl glutamate when tested at concentrations of 1.85% to 2.05%. A cream containing 8% acetyl proline was a mild irritant in another in vitro study. In rabbits, lauroyl lysine was nonirritating when tested at a concentration of 20%, whereas sodium lauroyl glutamate was a mild irritant at a concentration of 5%. In human studies, acetyl proline (up to 10%), acetyl tyrosine (up to 2%), disodium capryloyl glutamate (up to 7.38%), sodium cocoyl glutamate (up to 10%), sodium lauroyl glutamate (up to 10%), and sodium lauroyl silk amino acids (up to 6%) were not dermal irritants.[16,38-47]

Ocular. Nonhuman in vitro and in vivo and human ocular irritation studies are presented in Table 8. No ocular irritation was observed in in vitro studies of acetyl tyrosine (up to 1.25%), disodium capryloyl glutamate (up to 2%), and sodium lauroyl glutamate (up to 5%). Severe irritation was observed with sodium cocoyl glutamate at 5% using the hen's egg test chorioallantoic membrane (HET-CAM) method, but it was not irritating in another study with an unknown concentration. Slight irritation was observed with sodium lauroyl silk amino acids at 0.5% using the HET-CAM method. Lauroyl arginine in a mixture at 10% was not irritating to rabbit eyes. No adverse effects were observed during in-use studies of eye-area products containing acetyl hydroxyproline (up to 2%) and acetyl tyrosine (up to 2%) in human participants.[15,16,38,39,48-55]

Sensitization

Nonhuman and human dermal sensitization studies are presented in Table 9. Sodium lauroyl silk amino acids when tested in a 20% solution were not sensitizing in an LLNA. In guinea pigs, lauroyl lysine and sodium lauroyl glutamate were not sensitizers at concentrations of 50% and 5%, respectively. No sensitization was observed in human studies with products containing acetyl hydroxyproline (up to 2%), acetyl proline (up to 10%), acetyl tyrosine (up to 2%), disodium capryloyl glutamate (up to 7.38%), lauroyl lysine (up to 12.5%), sodium cocoyl glutamate (up to 5%), and sodium lauroyl glutamate (up to 5%).[16,38,39,56-66]

Table 6. Genotoxicity.

Concentration/dose	Method	Results	Reference
In vitro			
Acetyl cysteine			
Concentrations not provided	Ames test, details not provided	Not genotoxic	33
Concentrations not provided	Mouse lymphoma cell (L5178Y/TK$^{+/-}$) forward mutation test, details not provided	Positive	33
Acetyl glutamic acid			
333 to 5,000 μg/plate with and without S9 metabolic activation	Bacterial reverse mutation assay in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and *Escherichia coli* strain WP2uvrA	Not mutagenic	34
Acetyl proline			
0.4%, 0.2%, 0.1%, 0.05%, 0.025%, and 0.0125% with S9 metabolic activation	Ames II assay in *S typhimurium* strains TA 98 and mixed strains	Not mutagenic	35
Acetyl tyrosinamide			
0, 313, 625, 1,250, 2,500, and 5,000 μg/plate with and without S9 metabolic activation	Bacterial reverse mutation assay in *S typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and *E coli* strain WP2uvrA	Negative	36
Up to 2,230 μg/mL under 3-hour and 22-hour treatment with and without metabolic activation	Chromosomal aberration assay in cultured peripheral blood lymphocytes	Negative	37
Disodium capryloyl glutamate			
Details not provided	Ames test (details not provided)	Not mutagenic	38
Sodium cocoyl glutamate			
Details not provided	Ames test (details not provided)	Not mutagenic	16
Sodium lauroyl glutamate			
Details not provided	Ames test (details not provided)	Not mutagenic	39
In vivo			
Acetyl cysteine			
Concentrations not provided	Mouse micronucleus test, details not provided	Not genotoxic	33
Acetyl glutamic acid			
500, 1,000, or 2,000 mg/kg	Bone marrow micronucleus assay in groups of 5 male and 5 female ICR mice	No increased incidence of micronucleated polychromatic erythrocytes	34

Phototoxicity

Nonhuman and human phototoxicity studies are presented in Table 10. In nonhuman and human studies, acetyl tyrosine was not phototoxic at concentrations up to 1 and 10 mg/mL, respectively. Sodium cocoyl glutamate (up to 5%) and sodium lauroyl glutamate (up to 5%) were not phototoxic in human studies.[15,16,67,68]

Summary

The 115 amino acid alkyl amides in this report mainly function as skin and hair conditioning agents and as surfactants—cleansing agents in personal care products. These ingredients are comprised of amino acids acylated with acids or acid chlorides at the amino acid nitrogen to form amides (except for lauroyl lysine, which is formed by acylation at the epsilon nitrogen). By and large, the ingredients in this report will not rapidly dissociate (beyond zwitterion formation) in the presence of water, but action by amidases is the most likely first step of metabolism if dermal penetration occurs. The relative exposure, hence, could include exposure to amino acid and fatty acid metabolites of these ingredients.

Lauroyl lysine has the most reported uses in cosmetic and personal care products, with a total of 649; most uses are in leave-on eye and facial makeup. Sodium cocoyl glutamate has the second greatest number of overall uses reported, with a total of 178; more than half of those uses are in rinse-off products. Lauroyl lysine is used at maximum concentrations up to 45% in lipsticks.

In the European Union, trialkylamines, trialkanolamines, and their salts (ingredients containing TEA) may be used only up to 2.5%, must be at least 99% pure, are not to be used with nitrosating systems, must have secondary amine content no greater than 0.5% and nitrosamine content no greater than 50 μg/kg, and must be kept in nitrite-free containers. The remaining ingredients are not restricted under the rules governing cosmetic products in the European Union.

Amino acid alkyl amides are used in household detergents. The FDA has approved acetyl cysteine in drug therapies. Acetyl methionine is an approved direct food additive.

In a study of 3 formulations containing 1.75% acetyl tyrosine, the test material was found to penetrate into and through ex vivo human skin, with the greatest penetration (approximately 30%) from a cream formulation.

Table 7. Dermal Irritation Studies.

Ingredient	Concentration	Method	Results	Reference
Nonhuman				
Acetyl proline	8% in a cream tested neat	MatTek EpiDerm assay	Very mild irritant	42
Disodium capryloyl glutamate	5% of a solution containing 37%-41% test material	MTT viability assay	Not irritating	38
Lauroyl lysine	5% and 20% in olive oil	Primary skin irritation test in 6 male New Zealand white rabbits	Nonirritating	44
Sodium lauroyl glutamate	5% in distilled water	Primary skin irritation test in 4 male New Zealand white rabbits	Mild irritant	45
Sodium lauroyl silk amino acids	20% solution, pH 7.2-7.3	4 hour, semi-occluded acute dermal irritation study in New Zealand white rabbits	Mild irritant to rabbit skin according to Draize (PII = 1.8). No corrosive effects noted	72
Human				
Acetyl proline	10% in a cream evaluated for treatment of eczema or active atopic dermatitis	Double-blind, randomized controlled usage study in 15 participants where test material was applied to target lesion twice/day for 14 days	1 participant had an acute chronic dermatitis reaction that was considered related to the test material	43
Acetyl tyrosinamide	2% in a gel formulation	48-hour patch test in 53 volunteers; 0.2 g applied by 1 sq in pad and semi-occluded	Not irritating	40
Acetyl tyrosinamide	1.25%-2% in several gel and skin plumping cream formulations	48-hour patch test in 51 volunteers; 0.2 g applied by 1 sq in pad and semi-occluded	1 participant had moderate erythema and edema postapplication that became mild at the 72-hour observation to the skin plumping cream containing 1.25% test material, another participant had mild erythema and edema 48 hours to the same skin plumping cream formulation, which was barely perceptible at 72 hours—this same participant had a barely perceptible erythema at 48 hours to the skin plumping cream containing 2% of the test material, no reaction was observed at 72 hours. The study concluded that the test material was not irritating in all formulations tested	41
Disodium capryloyl glutamate	18% of a solution containing 37%-41% test material	Patch test with Finn Chambers in 20 volunteers; occluded	Not irritating	38
Sodium cocoyl glutamate	10% active matter	Flex wash test	Not irritating	16
Sodium lauroyl glutamate	10% active matter	Flex wash test in 20 volunteers	Irritation index below 0.5, not irritating	39
Sodium lauroyl glutamate	A 1% solution and in mixtures with SLS at 0.75%, 0.50% and 0.25%	15 volunteers received test material on test sites with polypropylene chambers for 24 hours. Application sites were measured for transepidermal water loss (TEWL) and graded for irritation reactions	TEWL values of 1% sodium lauroyl glutamate were significantly higher than those of the deionized water control	46
Sodium lauroyl silk amino acids	6% active solution	HPT for irritancy in 20 volunteers for 48 hours, Finn Chambers, patches occluded	Minimally irritating. Cutaneous irritation index after 24 hours = 10.0, after 48 hours = 2.5	47

Table 8. Ocular Irritation Studies.

Ingredient	Concentration	Method	Results	Reference
Nonhuman—in vitro				
Acetyl tyrosinamide	1.25% neat	EpiOcular irritation study	Not irritating	49
Disodium capryloyl glutamate	2% as received	HET-CAM method	Not irritating	38
Sodium cocoyl glutamate	Not reported	Red blood cell test	Not irritating	16
Sodium cocoyl glutamate	5%	HET-CAM method	Score = 13, strong or severe irritation	50,51
Sodium lauroyl glutamate	5% active matter	HET-CAM method	Not irritating	39
Sodium lauroyl glutamate	Not reported	Red blood cell test	Not irritating	15
Sodium lauroyl glutaminate	Up to 1%	Rabbit corneal epithelium model by measurement of viability with MTT assay	Viability at concentration 0.5% was 32.7%. The 50% inhibitory concentration (IC50) was 0.934%	52
Sodium lauroyl silk amino acids	2.5% of a 20% solution	HET-CAM method	Slight irritation potential	53
Nonhuman—in vivo				
Lauroyl arginine + mixture of collagen polypeptides with MW < 1,000 Da	10%, pH adjusted to 7.0	Draize method in 6 male albino rabbits	Mean score was 7.5, not irritating	55
Human				
Acetyl hydroxyproline	2% in a gel under eye treatment	4-week in-use study in 33 women; half contact lens wearers and half noncontact lens wearers	No adverse events during the study and no ophthalmic irritation potential	54
Acetyl tyrosinamide	2% in a gel under eye treatment	4-week in-use study in 33 women; half contact lens wearers and half noncontact lens wearers	No adverse events during the study and no ophthalmic irritation potential	48

Abbreviation: HET-CAM, hen's egg test chorioallantoic membrane.

In teratology studies, no evidence of impaired fertility or toxicity to fetuses was observed in rats at oral doses up to 2,000 mg/kg/d acetyl cysteine and in rabbits at oral doses up to 1,000 mg/kg/d acetyl cysteine. Male rats treated orally with 250 mg/kg/d acetyl cysteine for 15 weeks did not experience adverse effects to fertility or reproductive performance.

In in vitro studies, acetyl glutamic acid, acetyl proline, acetyl tyrosine, disodium capryloyl glutamate, sodium cocoyl glutamate, and sodium lauroyl glutamate were negative for genotoxicity. Acetyl cysteine was not genotoxic in an Ames test but had positive results in in vitro mouse lymphoma test. Acetyl cysteine and acetyl glutamic acid were negative in in vivo mouse studies.

No irritation was observed in in vitro studies with disodium capryloyl glutamate when tested at concentrations of 1.85% to 2.05%. A cream containing 8% acetyl proline was a mild irritant in another in vitro study. In rabbits, lauroyl lysine was nonirritating when tested at a concentration of 20%, whereas sodium lauroyl glutamate was a mild irritant at a concentration of 5%. In human studies, acetyl proline (up to 10%), acetyl tyrosine (up to 2%), disodium capryloyl glutamate (up to 7.38%), sodium cocoyl glutamate (up to 10%), sodium lauroyl glutamate (up to 10%), and sodium lauroyl silk amino acids (up to 6%) were not dermal irritants.

No ocular irritation was observed in in vitro studies of acetyl tyrosine (up to 1.25%), disodium capryloyl glutamate (up to 2%), and sodium lauroyl glutamate (up to 5%). Severe irritation was observed with sodium cocoyl glutamate at 5% using the HET-CAM method, but it was not irritating in another study with an unknown concentration. Slight irritation was observed with sodium lauroyl silk amino acids at 0.5% using the HET-CAM method. Lauroyl arginine in a mixture at 10% was not irritating to rabbit eyes. No adverse effects were observed during in-use studies of eye-area products containing acetyl hydroxyproline (up to 2%) and acetyl tyrosine (up to 2%) in human participants.

Sodium lauroyl silk amino acids when tested in a 20% solution was not sensitizing in an LLNA. No sensitization was observed in human studies with products containing acetyl hydroxyproline (up to 2%), acetyl proline (up to 10%), acetyl tyrosine (up to 2%), disodium capryloyl glutamate (up to 7.38%), sodium cocoyl glutamate (up to 5%), and sodium lauroyl glutamate (up to 5%).

Acetyl tyrosine was not phototoxic in a nonhuman study at up to 1000 μg/mL, nor was it phototoxic in a human study at 1%.

No published carcinogenicity studies on amino acid alkyl amides were identified by a literature search for these ingredients and no unpublished data were submitted.

Discussion

The Panel acknowledged that the safety of α-amino acids, acetyl methionine, and acetyl cysteine has been well supported by extensive studies and evaluation of acute and chronic dietary exposures (α-amino acids, acetyl methionine), use as approved food additives (α-amino acids, acetyl methionine), or therapeutic use (acetyl cysteine). The Panel determined

Table 9. Dermal Sensitization Studies.

Ingredient	Concentration	Method	Results	Reference
Nonhuman				
Lauroyl lysine	50% in olive oil for both induction and challenge phases	Modified maximization test in 15 female Dunkin-Hartley albino guinea pigs	Not sensitizing	56
Sodium lauroyl glutamate	5% in water for induction, 2.5% in water for challenge	Modified maximization test in 10 female Dunkin-Hartley albino guinea pigs	Not sensitizing	59
Sodium lauroyl silk amino acids	25%, 50%, or 100% of a 20% solution in butanone	LLNA	Nonsensitizing. SI at 100% = 2.61	62
Human				
Acetyl hydroxyproline	2% in a plumper gel	HRIPT in 109 volunteers; 0.2 g applied by a 1 sq in pad and semi-occluded	Not irritating or sensitizing	63
Acetyl proline	10% in a cream	HRIPT in 107 volunteers; 0.2 g applied by a 1 sq in pad and semi-occluded	Not irritating or sensitizing	64
Acetyl tyrosinamide	1% neat	HRIPT to a sodium lauryl sulfate pretreated site with 26 volunteers; during challenge, 0.05 mL applied under a 15-mm disc and occluded	Nonsensitizing	65
Acetyl tyrosinamide	2% in a plumper gel	HRIPT in 109 volunteers; applied by 1 sq in pad and semi-occluded	Not irritating or sensitizing	66
Disodium capryloyl glutamate	18% of a solution containing 37%-41% test material	Patch test with Finn Chambers in 20 volunteers; occluded	Nonsensitizing	38
Lauroyl lysine	8.36% in a blush product	HRIPT in 102 volunteers, 0.2 g applied by a 1 sq in pad and occluded	Not irritating or sensitizing	57
Lauroyl lysine	12.5% in a facial powder	Predictive patch test study in 600 volunteers; unreported amount applied by a 1/2 sq in gauze pad and occluded	Not an irritant, a skin-fatiguing agent, or a sensitizer	58
Sodium cocoyl glutamate	5% active matter	Method not reported, but test was occluded	Nonsensitizing	16
Sodium lauroyl glutamate	5% active matter	Patch test with Finn Chambers in 20 volunteers; occluded	Nonsensitizing	39
Sodium lauroyl glutamate	10% dilution of a facial cream containing 30% test material	HRIPT in 103 volunteers; 0.2 mL applied by a 2 cm^2 pad and semi-occluded	Nonsensitizing	61
Sodium lauroyl glutamate	1% dilution of a skin cleansing product containing 22% test material	HRIPT in 55 volunteers	Four 1+ reactions during induction; nonsensitizing	60

Note: SI = stimulation index.

that this body of research, coupled with irritation and sensitization data and the expectation that exposure from cosmetics is lower than from food consumed daily in the diet and would not result in significant systemic exposure (as discussed in the current report on amino acids), provides sufficient basis for determining the safety of amino acid–derived ingredients in cosmetic products.

Safety test data on dermal irritation and sensitization for the ingredients with the highest use concentrations, lauroyl lysine and sodium lauroyl glutamate, adequately supported the safety of the use of these ingredients in cosmetics. These ingredients function primarily as skin and hair conditioning agents and surfactants. The Panel noted that most surfactants exhibit some irritancy, as was the case with sodium lauroyl glutamate at 5% in a guinea pig study. Products using these ingredients should be formulated to be nonirritating.

The Panel discussed the issue of incidental inhalation exposure from hair sprays, face and body sprays, foundation sprays, and indoor tanning sprays. No inhalation data were identified or provided. These ingredients reportedly are used at concentrations up to 0.65% in cosmetic products that may be aerosolized. The Panel noted that 95% to 99% of droplets/particles would not be respirable to any appreciable amount. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic toxic effects. The Panel considered other data available to characterize the potential amino acid alkyl amides to cause systemic toxicity, irritation, sensitization, or other effects. They noted that numerous studies and reviews have been published in the literature regarding the safety of dietary

Table 10. Phototoxicity and Photosensitization.

Ingredient	Concentration	Method	Results	Reference
Nonhuman—in vitro				
Acetyl tyrosinamide	Eight doses up to 1,000 μg/mL with and without UVA	Neutral red uptake assay in BALB/c3T3 mouse fibroblasts	Not predicted to have phototoxic potential	67
Human				
Acetyl tyrosinamide	1% neat	Human photocontact allergenicity assay with 25 volunteers; 40 mg applied to a 2 cm^2 site and occluded	No photocontact-sensitizing potential	68
Sodium cocoyl glutamate	0.1%-5% aqueous solutions	Not reported	No abnormality observed	16
Sodium lauroyl glutamate	0.1%-5% aqueous solutions	Not reported	No abnormality observed	15

exposure to amino acids, including studies on oral acute and chronic toxicity, carcinogenicity, and genotoxicity, which found no safety concerns for these substances in the amounts at which they are consumed in flavoring agents. Additionally, little or no irritation was observed in multiple tests of dermal and ocular exposure. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

The Panel expressed concern about animal-derived ingredients, namely the transmission of infectious agents. They stressed that these ingredients must be free of detectible pathogenic viruses or infectious agents (eg, bovine spongiform encephalopathy). These ingredients should be produced according to good manufacturing procedures and should conform to regulations for producing substances from animal-derived materials.

The Panel also expressed concern regarding pesticide residues and heavy metals that may be present in botanical ingredients. Because the plant proteins from which amino acids alkyl amides are produced are extensively processed, it is unlikely that these impurities would remain.

The Panel raised the issue of levels of free DEA that could be present as an impurity in the ingredients containing TEA and indicated that the levels of free DEA must not exceed those considered safe by the Panel, as stated in the current report on DEA, which is up to 0.64%. The Panel also discussed that tertiary alkyl amines such as TEA do not react with *N*-nitrosating agents directly to form *N*-nitroso compounds, but they can act as precursors in nitrosamine formation by undergoing nitrosative cleavage. The resulting secondary amine can then be *N*-nitrosated to products that may be carcinogenic.

The Panel noted the uncertainty regarding method of manufacturing. The Panel stated that industry should manufacture amino acid alkyl amides in a way that minimizes residual peptide content.

Conclusion

The Panel concluded that the 115 amino acid alkyl amides listed below are safe in the present practices of use and concentration in cosmetics, when formulated to be nonirritating.

acetyl arginine*
acetyl cysteine
acetyl glutamic acid*
acetyl glutamine
acetyl histidine*
acetyl methionine
acetyl proline*
acetyl tyrosine
capryloyl collagen amino acids*
capryloyl glycine
capryloyl gold of pleasure amino acids*
capryloyl keratin amino acids*
capryloyl pea amino acids*
capryloyl quinoa amino acids*
capryloyl silk amino acids*
cocoyl glutamic acid
dipalmitoyl cysteine*
dipotassium capryloyl glutamate
dipotassium undecylenoyl glutamate*
disodium capryloyl glutamate
disodium cocoyl glutamate
disodium hydrogenated tallow glutamate
disodium *N*-lauroyl aspartate*
disodium lauroyl glutamate
disodium malyl tyrosinate
disodium stearoyl glutamate
disodium undecylenoyl glutamate*
lauroyl arginine
lauroyl collagen amino acids
lauroyl glutamic acid*
lauroyl lysine
lauroyl proline
lauroyl silk amino acids
magnesium palmitoyl glutamate
myristoyl glutamic acid*
oleoyl tyrosine
palmitoyl alanine*
palmitoyl arginine*
palmitoyl collagen amino acids
palmitoyl glutamic acid*
palmitoyl glycine
palmitoyl gold of pleasure amino acids*
palmitoyl isoleucine*

palmitoyl keratin amino acids
palmitoyl millet amino acids*
palmitoyl oat amino acids*
palmitoyl pea amino acids*
palmitoyl proline
palmitoyl quinoa amino acids*
palmitoyl silk amino acids
potassium caproyl tyrosine*
potassium capryloyl glutamate*
potassium cocoyl glutamate
potassium cocoyl glycinate
potassium cocoyl rice amino acids*
potassium lauroyl collagen amino acids*
potassium lauroyl glutamate*
potassium lauroyl oat amino acids*
potassium lauroyl pea amino acids*
potassium lauroyl silk amino acids*
potassium lauroyl wheat amino acids
potassium myristoyl glutamate
potassium olivoyl/lauroyl wheat amino acids*
potassium stearoyl glutamate*
potassium undecylenoyl glutamate*
propionyl collagen amino acids*
sodium caproyl prolinate*
sodium capryloyl glutamate*
sodium cocoyl alaninate
sodium cocoyl amino acids
sodium cocoyl apple amino acids
sodium cocoyl barley amino acids*
sodium cocoyl collagen amino acids
sodium cocoyl glutamate
sodium cocoyl glutaminate*
sodium cocoyl glycinate
sodium cocoyl/hydrogenated tallow glutamate*
sodium cocoyl oat amino acids*
sodium cocoyl/palmoyl/sunfloweroyl glutamate*
sodium cocoyl proline*
sodium cocoyl threoninate*
sodium cocoyl wheat amino acids*
sodium hydrogenated tallowoyl glutamate
sodium lauroyl aspartate
sodium lauroyl collagen amino acids*
sodium lauroyl glutamate
sodium lauroyl millet amino acids*
sodium lauroyl/myristoyl aspartate*
sodium lauroyl oat amino acids
sodium lauroyl silk amino acids*
sodium lauroyl wheat amino acids
sodium myristoyl glutamate
sodium olivoyl glutamate*
sodium palmitoyl proline
sodium palmoyl glutamate
sodium stearoyl glutamate
sodium/TEA-lauroyl collagen amino acids*
sodium/TEA-lauroyl keratin amino acids*
sodium/TEA-undecylenoyl collagen amino acids*
sodium undecylenoyl glutamate*
stearoyl glutamic acid*
stearoyl leucine*
TEA-cocoyl alaninate
TEA-cocoyl glutamate
TEA-cocoyl glutaminate*
TEA-hydrogenated tallowoyl glutamate*
TEA-lauroyl collagen amino acids
TEA-lauroyl glutamate
TEA-lauroyl keratin amino acids*
TEA-lauroyl/myristoyl aspartate*
undecylenoyl collagen amino acids
undecylenoyl glycine
undecylenoyl phenylalanine
undecylenoyl wheat amino acids*
zinc lauroyl aspartate*

*Not in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, Suite 1200, 1620 L Street, NW, Washington, DC 20036, USA.

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Christina L. Burnett contributed to conception and design, contributed to acquisition, analysis, and interpretation, and drafted the manuscript. Bart Heldreth contributed to conception and design, contributed to acquisition, analysis, and interpretation, drafted the manuscript, and critically revised the manuscript. Lillian J. Gill, F. Alan Andersen, Wilma F. Bergfeld, Donald V. Belsito, Ronald A. Hill, Curtis D. Klaassen, Daniel C. Liebler, James G. Marks, Ronald C. Shank, Thomas J. Slaga, and Paul W. Snyder contributed to conception and design, contributed to analysis and interpretation, and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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