
Safety Assessment of Ceramides as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: May 16, 2014
Panel Meeting Date: June 9-10, 2014

The 2014 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This safety assessment was prepared by Ivan J. Boyer, Ph.D., Senior Toxicologist, Christina L. Burnett, Senior Scientific Analyst/Writer, and Bart Heldreth, Ph.D., Chemist.

Memorandum

To: CIR Expert Panel Members and Liaisons
From: Ivan Boyer, Senior Toxicologist
Date: May 16, 2014
Subject: Draft Safety Assessment on Ceramides

In March 2014, CIR issued a Scientific Literature Review (SLR) Notice to Proceed (SLR Notice) for Ceramides. These ingredients function primarily as hair conditioning agents and skin conditioning agents-miscellaneous. There are a total of 14 ingredients in this safety assessment.

An intensive search of information in the published scientific literature, online databases, and other sources on these ingredients provided insufficient information to justify preparation of a formal SLR. These searches identified efficacy studies on some of the named cosmetic ingredients, efficacy studies of other cosmetic ingredients or pharmaceuticals in which naturally-occurring ceramide levels in the skin were evaluated, or data on a pseudo-ceramides (such as that found in an approved medical device to serve a skin “barrier repair” function) that are not cosmetic ingredients. These studies were deemed not relevant for the assessment of safety for the use of ceramide ingredients in cosmetics. Thus, CIR issued the SLR Notice to alert interested parties that a safety assessment is being prepared and to request information in multiple areas, including:

- Impurities data
- Toxicokinetics data, especially dermal absorption
- If these ingredients exhibit appreciable dermal absorption, then oral animal toxicity data, including:
 - Reproductive/developmental toxicity (DART) data
 - Carcinogenicity data
 - Genotoxicity data
- If these ingredients have no appreciable dermal penetration, DART, genotoxicity, and carcinogenicity data may not be crucial, but would strengthen the safety assessment
- Oral, inhalation, and dermal toxicity data
- Dermal, ocular, and/or other mucous membrane irritation and sensitization data
- Other relevant safety information that may be available

Concentration of use data that were provided by the Personal Care Products Council (Council) have been received and incorporated into the report. No unpublished data or comments were received.

According to the FDA’s VCRP database, ceramide 3 has the most reported uses in cosmetic and personal care products, with a total of 359; the majority of the uses is in leave-on skin care preparations. Ceramide 2 has the second greatest

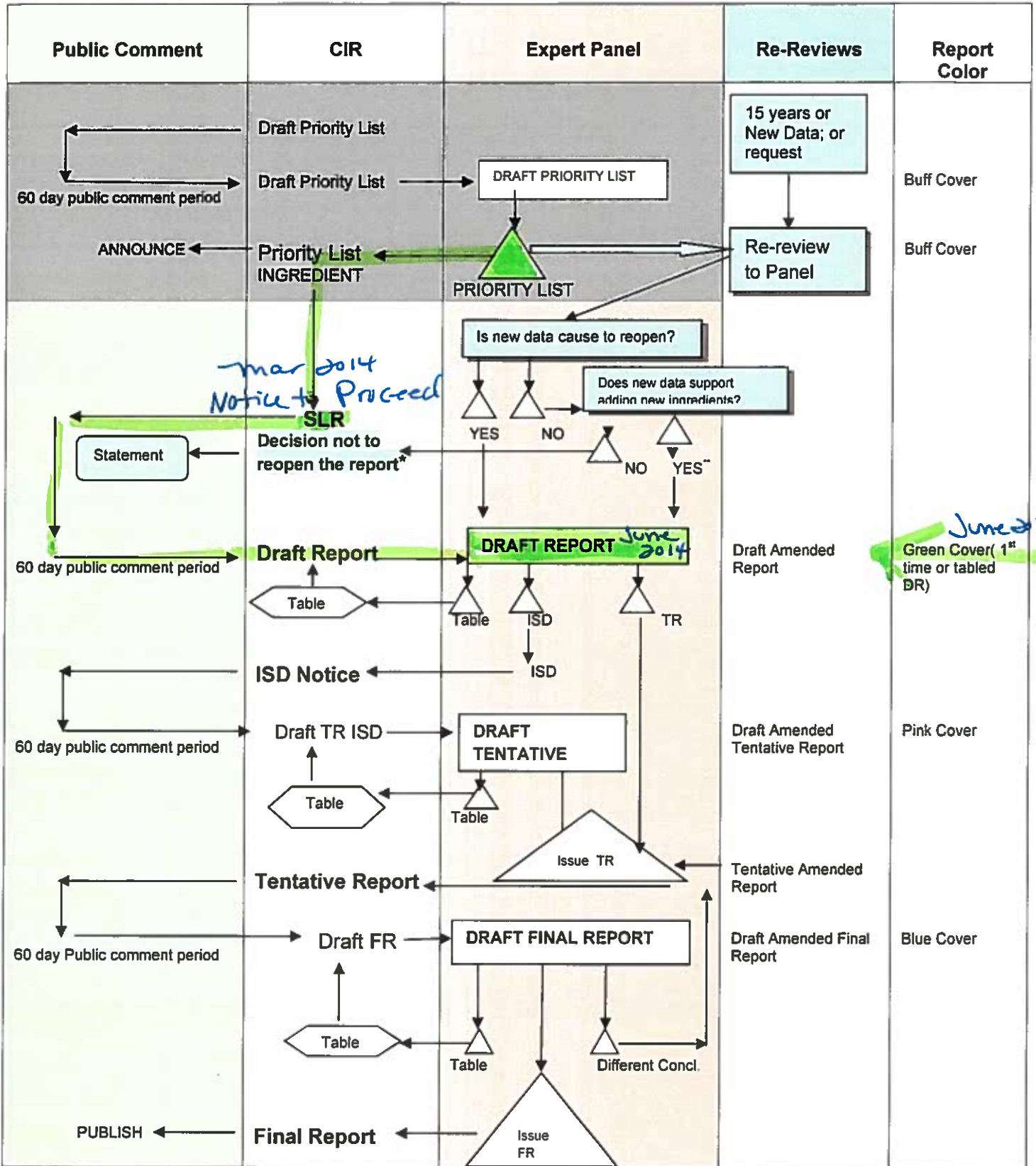
number of overall uses reported, with a total of 110; the majority of those uses is also in leave-on skin care preparations. In the Council's survey of use concentrations, ceramide 3 had a highest maximum use concentration range of $1.0 \times 10^{-8}\%$ to 0.2% with 0.2 % reported in lipstick and face and neck skin care preparations. Ceramide 2 had a highest maximum use concentration range of $5 \times 10^{-6}\%$ to 0.2%, with 0.2% reported in eye lotion and face and neck skin care preparations. Most of the other use concentrations that were reported had similar ranges. Ceramide 1A was not reported in the VCRP, but the industry survey indicated use in leave-on formulations at up to 0.01%. It should be presumed that ceramide 1A is used in at least one cosmetic formulation.

The Panel should consider the lack of information available on which to base a safety assessment of these ingredients, and specify the data needed to complete the assessment.

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SAFETY ASSESSMENT FLOW CHART

Ceramides

June 2014



*The CIR Staff notifies of the public of the decision not to re-open the report and prepares a draft statement for review by the Panel. After Panel review, the statement is issued to the Public.

**If Draft Amended Report (DAR) is available, the Panel may choose to review; if not, CIR staff prepares DAR for Panel Review.



Ceramides History

March 2014 – Scientific Literature Review Notice announced.

Ceramides Data Profile – June 2014 – Writers, Ivan Boyer, Christina Burnett and Bart Heldreth

	In-Use	Physical/Chemical Properties	Method of Manufacturing	Composition	Toxicokinetics	Acute Toxicity	Repeated Dose Toxicity	Repro. /Develop. Toxicity	Genotoxicity	Carcinogenicity	Irritation/Sensitization - Animal	Irritation/Sensitization - Clinical	Ocular/Mucosal	Phototoxicity	Case Studies
Ceramide 1	X														
Ceramide 1A	X														
Ceramide 2	X														
Ceramide 3	X														
Ceramide 4															
Ceramide 5															
Ceramide 6 II	X														
Ceramide AP	X														
Ceramide AS															
Ceramide EOP	X														
Ceramide EOS	X														
Ceramide NP	X														
Ceramide NS	X														
Ceramide NS Dilaurate															

“X” indicates that data were available in the category for that ingredient.
 Shaded cells indicate ingredients that have been previously reviewed by CIR.

Search Strategy for Ceramide Ingredients

- PubMed – February 18, 2014
 - Search for “ceramide dermal sensitization” – 1 hit, 1 ordered
 - Search for “ceramide dermal irritation” – 0 hits
- SciFinder – February 19, 2014
 - Search for “ceramides toxicity review. – 106 hits, 31 ordered
- SciFinder – February 21, 2014
 - Search ceramides by name/CAS#, limited search by document type, adverse effects – 184 hits, 24 ordered
- From reading review papers ordered – March 11, 2014
 - Search for potentially relevant citations – 24 selected, 24 ordered
- SciFinder – March 12, 2014
 - Search for “ceramides safety” – 29 hits, 1 obtained

Online Info

- COSMOS Database – March 12, 2014
 - Search for “ceramide” or “ceramides” studies/data – 0 hits
- European Chemicals Agency (ECHA) Database – March 12, 2014
 - Search for INCI names and available CASNs, and “ceramide” – 0 hits
- Internet (Google Search Engine) – March 12, 2014
 - Search for “ceramides medical devices” – 1 potentially relevant hit, downloaded
- eChemPortal (OECD) – March 12, 2014
 - Search for studies/data on “ceramides” – 0 hits
- INCI Dictionary/Cosmetics InfoBase – March 12, 2014
 - Search for studies/data on “ceramide” or “ceramides” – 0 hits
- U.S. EPA HPV List and ToxRef DB – March 12, 2014
 - Search for studies/data on “ceramide” or “ceramides” – 0 hits
- eCFR – March 12, 2014
 - Search for Code of Federal Regulations (CFR) notices – 1 hit, downloaded
- National Toxicology Program (NTP) Database – April 24, 2014
 - Search for studies on “ceramide”(all or part of chemical name) – 0 hits
- SCCS/SCCP – April 24, 2014
 - Search for “ceramide” – 0 hits
- Sigma Aldrich – April 24, 2014
 - Search for “ceramide” MSDSs – 0 hits
- National Library of Medicine (NLM) ToxNet Hazardous Substance Data Bank – April 24, 2014
 - Search for “ceramide” – 0 relevant hits
- Internet (Google Search Engine) – April 24, 2014
 - Search for “ceramide 4,” “ceramide 5,” “ceramide AS,” and “ceramide NS” – 0 relevant hits

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INTRODUCTION

Ceramide ingredients function primarily as hair conditioning agents and skin conditioning agents-miscellaneous in cosmetics.¹ The full list of ingredients reviewed in this safety assessment is described in Table 1.

Many of the reports found in the published literature presented efficacy studies on the named cosmetic ingredients, efficacy studies of other cosmetic ingredients or pharmaceuticals in which naturally-occurring ceramide levels in the skin were evaluated, and data on pseudo-ceramides (such as that found in an approved medical device), which are not a cosmetic ingredients. These studies were not relevant to the assessment of safety of the use of the ceramide ingredients in cosmetics.

An intensive search of the scientific literature, databases, and other information sources on these ingredients provided insufficient relevant information to justify the preparation of a formal Scientific Literature Review (SLR). The Cosmetic Ingredient Review (CIR), therefore, issued a SLR Notice to Proceed in March 2014 to alert interested parties that a safety assessment was being prepared. CIR sought information in a wide range of areas, including:

- Impurities data;
- Toxicokinetics data, specifically dermal absorption; if these ingredients were to have appreciable dermal absorption, oral animal toxicity data, including reproductive/developmental toxicity and carcinogenicity data, are needed, as are genotoxicity data; these data may not be crucial if these ingredients have no appreciable dermal penetration, however, if they were available, they would improve the resulting safety assessment;
- Oral, inhalation, and/or dermal toxicity data;
- Dermal, ocular, and/or other mucous membrane irritation and sensitization data; and
- Any other relevant safety information that may be available.

CHEMISTRY

Generally, a ceramide is the amidation reaction product of a sphingoid base and a fatty acid.

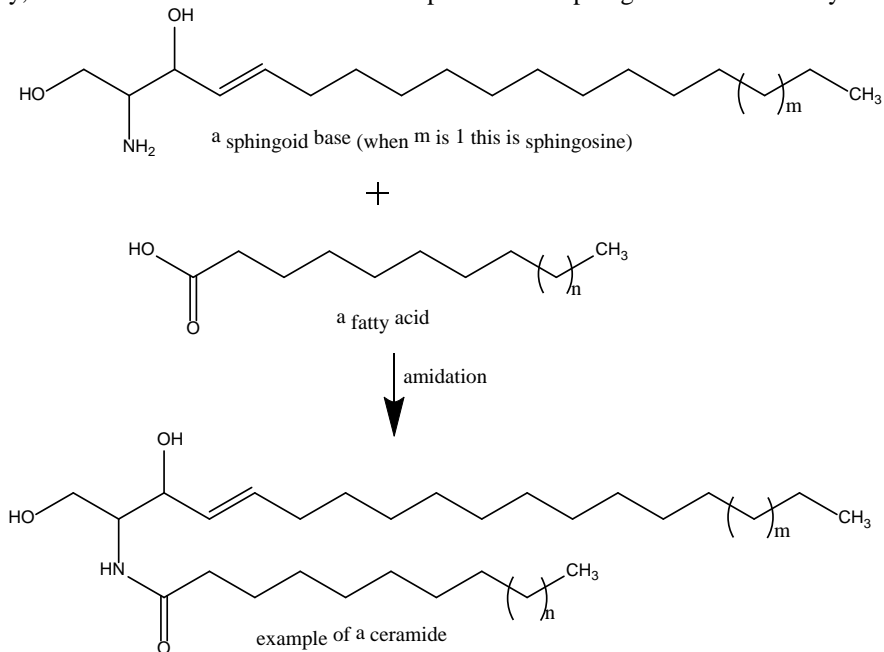


Figure 1. Example of a ceramide structure

The ingredients described herein vary principally in the chain lengths of both the sphingoid and fatty acid residues, and in the degree of unsaturation in those chains. Additionally, each of these ingredients is a mixture of ceramides, described in more detail in Table 1.

In biological systems, ceramides are synthesized by de novo synthesis, sphingomyelin hydrolysis, or through a salvage pathway.² Ceramide manufacture could be accomplished by a variety of synthetic methods, but most methods involve amidation of a fatty acid with a sphingoid base.³ This can be accomplished by reaction of the

sphingoid base with an acyl chloride, but the results are not selective and esterification and amidation occur concurrently. However, mild alkaline hydrolysis can selectively remove the esters. Alternatively, activating the fatty acid with a carbodiimide enables ceramide synthesis without esterification.

USE **Cosmetic**

Table 2 presents the current product-formulation use data for ceramide ingredients. These ingredients function primarily as hair conditioning agents and skin conditioning agents-miscellaneous.¹

According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP), ceramide 3 has the most reported uses in cosmetic and personal care products, with a total of 359; the majority of the uses are in leave-on skin care preparations.⁴ Ceramide 2 has the second greatest number of overall uses reported, with a total of 110; the majority of those uses are also in leave-on skin care preparations.

In the Personal Care Products Council's use concentration survey, ceramide 3 had a maximum-use concentration range of $1.0 \times 10^{-8}\%$ to 0.2%, with 0.2% reported in lipstick and face and neck skin care preparations.⁵ Ceramide 2 had a maximum-use concentration range of $5 \times 10^{-6}\%$ to 0.2%, with 0.2% reported in eye lotion and face and neck skin care preparations. Most of the other use concentrations that were reported had similar ranges.

In some cases, no reported uses were received from the VCRP, but a maximum-use concentration was provided in the industry survey. For example, ceramide 1A 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 up to 0.01%. It should be presumed that ceramide 1A is used in at least one cosmetic formulation.

Ceramide 4, ceramide 5, ceramide AS, and ceramide NS dilaurate were indicated not to be in use based on the VCRP data and the results of the Council concentration of use survey.

Some of these ingredients were reported to be used in hair sprays and body and hand or moisturizing sprays and could possibly be inhaled. For example, ceramide 3 was reported to be used in body and hand sprays at a maximum concentration of $1.0 \times 10^{-3}\%$. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters $>10 \mu\text{m}$, with propellant sprays yielding a greater fraction of droplets/particles below $10 \mu\text{m}$ compared with pump sprays.⁶⁻⁹ Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.^{7,8}

TOXICOKINETICS

Data on the absorption, distribution, metabolism, and excretion of ceramides were not found in the published literature, nor were unpublished data provided.

TOXICOLOGICAL STUDIES

Data on acute and repeated dose toxicity of ceramides were not found in the published literature, nor were unpublished data provided.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Data on reproductive and developmental toxicity of ceramides were not found in the published literature, nor were unpublished data provided.

GENOTOXICITY

Data on genotoxicity of ceramides were not found in the published literature, nor were unpublished data provided.

CARCINOGENICITY

Data on carcinogenicity of ceramides were not found in the published literature, nor were unpublished data provided.

IRRITATION AND SENSITIZATION

Data on irritation and sensitization of ceramides were not found in the published literature, nor were unpublished data provided.

SUMMARY

The ceramide ingredients function as hair conditioning agents and skin conditioning agents-miscellaneous in cosmetics. According to information supplied to FDA, ceramide 3 has the most reported uses in cosmetic and personal care products, with a total of 359; the majority of the uses are in leave-on skin care preparations. Ceramide 2 has the second greatest number of overall uses reported, with a total of 110; the majority of those uses are also in leave-on skin care preparations. In the Personal Care Products Council's use concentration survey, ceramide 3 had a maximum-use concentration range of $1.0 \times 10^{-8}\%$ to 0.2%, with 0.2% reported in lipstick and face and neck skin care preparations. Ceramide 2 had a maximum-use concentration range of $5 \times 10^{-6}\%$ to 0.2%, with 0.2% reported in eye lotion and face and neck skin care preparations. Most of the other use concentrations that were reported had similar ranges.

Data on the toxicokinetics, acute and repeated dose toxicity, genotoxicity, carcinogenicity, reproductive and developmental toxicity, or irritation and sensitization of ceramides were not found in the published literature.

TABLES AND FIGURES**Table 1.** Definitions and idealized structures of the ingredients in this safety assessment.¹

Ingredient CAS No.	Definition / Structure
Ceramide 1 100403-19-8	<p data-bbox="440 369 1427 396">Ceramide 1 is the N-acylated phytosphingosine having the erythro structure that conforms generally to the formula:</p> <div data-bbox="440 396 1097 661" style="text-align: center;"> $\begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}_2\text{CHCHCHCH}_2\text{OH} \\ \quad \\ \text{OH} \quad \text{HN}-\text{C}(\text{CH}_2)_{26}\text{O}-\text{C}(\text{CH}_2)_{16}\text{CH}_3 \\ \quad \quad \quad \quad \quad \quad \\ \quad \quad \quad \text{O} \quad \quad \quad \text{O} \end{array}$ </div> <p data-bbox="440 661 805 688">where n has a value ranging from 10 to 20.</p>
Ceramide 1A 100403-19-8	<p data-bbox="440 688 1427 737">Ceramide 1 A is the N-acylated phytosphingosine having the erythro structure that conforms generally to the formula:</p> <div data-bbox="440 737 1097 1039" style="text-align: center;"> $\begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}_2\text{CHCHCHCH}_2\text{OH} \\ \quad \\ \text{OH} \quad \text{HN}-\text{C}(\text{CH}_2)_{26}\text{O}-\text{C}(\text{CH}_2)_7\text{CH} \\ \quad \quad \quad \quad \quad \quad \\ \quad \quad \quad \text{O} \quad \quad \quad \text{O} \\ \quad \quad \quad \quad \quad \quad \quad \\ \quad \quad \quad \quad \quad \quad \quad \text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH} \\ \quad \quad \quad \quad \quad \quad \quad \\ \quad \quad \quad \quad \quad \quad \quad \text{O} \end{array}$ </div> <p data-bbox="440 1039 805 1066">where n has a value ranging from 10 to 20.</p>
Ceramide 2 100403-19-8	<p data-bbox="440 1073 1427 1100">Ceramide 2 is the N-acylated sphingolipid having the erythro structure that conforms generally to the formulas:</p> <div data-bbox="440 1100 881 1669" style="text-align: center;"> $\begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}_2\text{CH}_2\text{CHCHCH}_2\text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_m\text{C}-\text{NH} \\ \\ \text{O} \end{array}$ $\begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}=\text{CHCHCHCH}_2\text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_m\text{C}-\text{NH} \\ \\ \text{O} \end{array}$ </div> <p data-bbox="440 1669 1154 1696">where m has a value ranging from 14 to 28 and n has a value ranging from 10 to 16.</p>

Table 1. Definitions and idealized structures of the ingredients in this safety assessment.¹

Ingredient CAS No.	Definition / Structure
Ceramide 3 100403-19-8 72968-43-5	<p data-bbox="422 296 1427 323">Ceramide 3 is the N-acylated phytosphingosine having the erythro structure that conforms generally to the formula:</p> $ \begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}_2\text{CH} \text{---} \text{CH} \text{---} \text{CH} \text{---} \text{CH}_2\text{OH} \\ \quad \\ \text{OH} \quad \text{HN} \text{---} \text{C}(\text{CH}_2)_m\text{CH}_3 \\ \quad \quad \quad \\ \quad \quad \quad \text{O} \end{array} $ <p data-bbox="422 590 1427 632">where m has a value ranging from 12 to 28 in which the acyl moiety may be saturated, mono-unsaturated, or di-unsaturated and n has a value ranging from 10 to 20.</p>
Ceramide 4 100403-19-8	<p data-bbox="422 638 1427 665">Ceramide 4 is the N-acylated sphingolipid having the erythro structure that conforms generally to the formula:</p> $ \begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}=\text{CH} \text{---} \text{CH} \text{---} \text{CH} \text{---} \text{CH}_2\text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_m\text{CH} \text{---} \text{C} \text{---} \text{NH} \\ \quad \quad \\ \text{OH} \quad \quad \text{O} \end{array} $ <p data-bbox="422 932 1427 1003">where m has a value ranging from 13 to 27 in which the acyl moiety may be saturated or mono-unsaturated and n has a value ranging from 10 to 16. Ceramide 4 is similar to Ceramide 5, however, the acylating hydroxy acids are generally shorter in Ceramide 4 than in Ceramide 5.</p>
Ceramide 5 100403-19-8	<p data-bbox="422 1010 1427 1037">Ceramide 5 is the N-acylated sphingolipid having the erythro structure that conforms generally to the formula:</p> $ \begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}=\text{CH} \text{---} \text{CH} \text{---} \text{CH} \text{---} \text{CH}_2\text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_m\text{CH} \text{---} \text{C} \text{---} \text{NH} \\ \quad \quad \\ \text{OH} \quad \quad \text{O} \end{array} $ <p data-bbox="422 1304 1427 1375">where m has a value ranging from 13 to 27 in which the acyl moiety may be saturated or mono-unsaturated and n has a value ranging from 10 to 16. Ceramide 5 is similar to Ceramide 4, however, the acylating hydroxy acids are generally longer in Ceramide 5 than in Ceramide 4.</p>
Ceramide 6 II 100403-19-8	<p data-bbox="422 1381 1427 1423">Ceramide 6 II is the N-acylated phytosphingosine having the erythro structure that conforms generally to the formula:</p> $ \begin{array}{c} \text{OH} \\ \\ \text{CH}_3(\text{CH}_2)_n\text{CH}_2\text{CH} \text{---} \text{CH} \text{---} \text{CH} \text{---} \text{CH}_2\text{OH} \\ \quad \\ \text{OH} \quad \text{HN} \text{---} \text{C} \text{---} \text{CH}(\text{CH}_2)_m\text{CH}_3 \\ \quad \quad \quad \quad \\ \quad \quad \quad \text{O} \quad \text{OH} \end{array} $ <p data-bbox="422 1690 1427 1717">where m has a value ranging from 13 to 27 and n has a value ranging from 12 to 20.</p>
Ceramide AP	Ceramide AP is the N-acylated sphingolipid consisting of Phytosphingosine having the D-erythro structure linked to an alpha-hydroxy saturated or unsaturated fatty acid.
Ceramide AS	Ceramide AS is the N-acylated sphingolipid consisting of sphingosine having the D-erythro structure linked to an alpha-hydroxy saturated or unsaturated fatty acid.
Ceramide EOP	Ceramide EOP is the N-acylated sphingolipid consisting of Phytosphingosine having the D-erythro structure linked to an esterified omega-hydroxy saturated or unsaturated fatty acid.

Table 1. Definitions and idealized structures of the ingredients in this safety assessment.¹

Ingredient CAS No.	Definition / Structure
Ceramide EOS	Ceramide EOS is the N-acylated sphingolipid consisting of sphingosine having the D-erythro structure linked to an esterified omega-hydroxy saturated or unsaturated fatty acid.
Ceramide NP	Ceramide NP is the N-acylated sphingolipid consisting of Phytosphingosine having the D-erythro structure linked to normal saturated or unsaturated fatty acid.
Ceramide NS	Ceramide NS is the N-acylated sphingolipid consisting of sphingosine having the D-erythro structure linked to a normal saturated or unsaturated fatty acid.
Ceramide NS Dilaurate	Ceramide NS Dilaurate is the diester of Ceramide NS and lauric acid.

Table 2. Frequency (2014) and concentration of use (2013) according to duration and type of exposure for ceramide ingredients.^{4,5}

	<i># of Uses</i>	<i>Max Conc of Use (%)</i>	<i># of Uses</i>	<i>Max Conc of Use (%)</i>	<i># of Uses</i>	<i>Max Conc of Use (%)</i>	<i># of Uses</i>	<i>Max Conc of Use (%)</i>
	Ceramide NP		Ceramide NS					
Totals¹	16	0.00005-0.2	14	0.001-0.006				
<i>Duration of Use</i>								
Leave-On	16	0.00005-0.2	14	0.001-0.006				
Rinse Off	NR	0.0005-0.01	NR	0.001				
Diluted for (Bath) Use	NR	0.001	NR	NR				
<i>Exposure Type</i>								
Eye Area	2	0.0025-0.005	1	NR				
Incidental Ingestion	NR	0.2	NR	NR				
Incidental Inhalation-Spray? ^{2,6}	13	NR	13	NR				
Reported Spray ³	NR	NR	NR	NR				
Incidental Inhalation-Powder? ^{4,6}	13	0.01	13	NR				
Reported Powder ⁵	NR	NR	NR	NR				
Dermal Contact	16	0.00005-0.1	14	0.001-0.006				
Deodorant (underarm)-Spray? ²	NR	NR	NR	NR				
Reported Spray ³	NR	NR	NR	NR				
Reported as Not Spray ³	NR	NR	NR	NR				
Hair - Non-Coloring	NR	NR	NR	NR				
Hair-Coloring	NR	NR	NR	NR				
Nail	NR	NR	NR	NR				
Mucous Membrane	NR	0.001-0.2	NR	NR				
Baby Products	1	NR	NR	NR				

NR = Not reported.

1. Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
2. It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.
3. Use in a spray product has been reported in response to a survey conducted by the Council.
4. It is possible these products may be powders, but it is not specified whether the reported uses are powders.
5. Use in a powder product has been reported in response to a survey conducted by the Council.
6. Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.
 - a. 0.00065% in an aerosol hair spray.
 - b. 0.1% in a rinse-off "other" skin care preparation.
 - c. 0.0001% in a spray tonic, dressing, or other hair grooming aid.
 - d. 0.0000001%-0.00065% in an aerosol hair spray; 0.000001% in a pump hair spray; 0.0001% in a spray tonic, dressing, or other hair grooming aid; 0.001% in a body and hand spray; 0.0005% in a moisturizing pump spray.
 - e. 0.01% in a face and neck spray.
 - f. 0.01% in a face and neck spray.
 - g. 0.00065% in an aerosol hair spray; 0.00003% in a pump spray.

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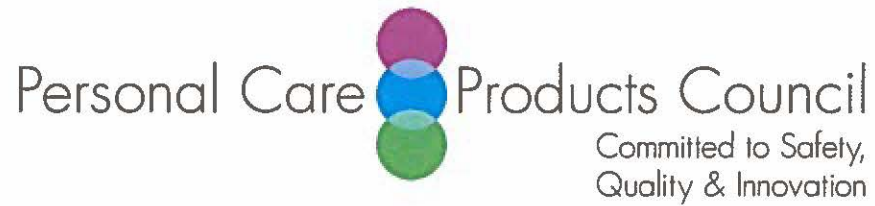
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2014 FDA VCRP Raw Data

03D - Eye Lotion	CERAMIDE 1	5
03F - Mascara	CERAMIDE 1	3
07C - Foundations	CERAMIDE 1	3
07E - Lipstick	CERAMIDE 1	4
07G - Rouges	CERAMIDE 1	1
07I - Other Makeup Preparations	CERAMIDE 1	2
11A - Aftershave Lotion	CERAMIDE 1	1
11G - Other Shaving Preparation Products	CERAMIDE 1	2
12A - Cleansing	CERAMIDE 1	2
12C - Face and Neck (exc shave)	CERAMIDE 1	7
12D - Body and Hand (exc shave)	CERAMIDE 1	5
12F - Moisturizing	CERAMIDE 1	6
12G - Night	CERAMIDE 1	7
12H - Paste Masks (mud packs)	CERAMIDE 1	2
12J - Other Skin Care Preps	CERAMIDE 1	4
03A - Eyebrow Pencil	CERAMIDE 2	1
03B - Eyeliner	CERAMIDE 2	1
03C - Eye Shadow	CERAMIDE 2	4
03D - Eye Lotion	CERAMIDE 2	11
03F - Mascara	CERAMIDE 2	5
03G - Other Eye Makeup Preparations	CERAMIDE 2	8
05A - Hair Conditioner	CERAMIDE 2	1
05F - Shampoos (non-coloring)	CERAMIDE 2	7
05G - Tonics, Dressings, and Other Hair Grooming Aids	CERAMIDE 2	2
07A - Blushers (all types)	CERAMIDE 2	1
07B - Face Powders	CERAMIDE 2	1
07C - Foundations	CERAMIDE 2	5
07E - Lipstick	CERAMIDE 2	9
07I - Other Makeup Preparations	CERAMIDE 2	9
12A - Cleansing	CERAMIDE 2	2
12C - Face and Neck (exc shave)	CERAMIDE 2	12
12F - Moisturizing	CERAMIDE 2	21
12G - Night	CERAMIDE 2	7
12H - Paste Masks (mud packs)	CERAMIDE 2	1
12J - Other Skin Care Preps	CERAMIDE 2	2
01B - Baby Lotions, Oils, Powders, and Creams	CERAMIDE 3	2
01C - Other Baby Products	CERAMIDE 3	1
03B - Eyeliner	CERAMIDE 3	1
03C - Eye Shadow	CERAMIDE 3	6
03D - Eye Lotion	CERAMIDE 3	8
03F - Mascara	CERAMIDE 3	4
03G - Other Eye Makeup Preparations	CERAMIDE 3	10
04E - Other Fragrance Preparation	CERAMIDE 3	1
05A - Hair Conditioner	CERAMIDE 3	15

05B - Hair Spray (aerosol fixatives)	CERAMIDE 3	1
05E - Rinses (non-coloring)	CERAMIDE 3	2
05F - Shampoos (non-coloring)	CERAMIDE 3	15
05G - Tonics, Dressings, and Other Hair Grooming Aids	CERAMIDE 3	11
05I - Other Hair Preparations	CERAMIDE 3	4
07B - Face Powders	CERAMIDE 3	2
07C - Foundations	CERAMIDE 3	14
07E - Lipstick	CERAMIDE 3	48
07G - Rouges	CERAMIDE 3	1
07I - Other Makeup Preparations	CERAMIDE 3	8
10A - Bath Soaps and Detergents	CERAMIDE 3	3
10E - Other Personal Cleanliness Products	CERAMIDE 3	4
11A - Aftershave Lotion	CERAMIDE 3	1
11E - Shaving Cream	CERAMIDE 3	2
11G - Other Shaving Preparation Products	CERAMIDE 3	2
12A - Cleansing	CERAMIDE 3	12
12C - Face and Neck (exc shave)	CERAMIDE 3	50
12D - Body and Hand (exc shave)	CERAMIDE 3	13
12F - Moisturizing	CERAMIDE 3	69
12G - Night	CERAMIDE 3	22
12H - Paste Masks (mud packs)	CERAMIDE 3	6
12I - Skin Fresheners	CERAMIDE 3	3
12J - Other Skin Care Preps	CERAMIDE 3	14
13A - Suntan Gels, Creams, and Liquids	CERAMIDE 3	4
03D - Eye Lotion	CERAMIDE 6 II	6
03F - Mascara	CERAMIDE 6 II	2
07C - Foundations	CERAMIDE 6 II	3
07E - Lipstick	CERAMIDE 6 II	4
07G - Rouges	CERAMIDE 6 II	1
07I - Other Makeup Preparations	CERAMIDE 6 II	2
11A - Aftershave Lotion	CERAMIDE 6 II	1
11G - Other Shaving Preparation Products	CERAMIDE 6 II	2
12A - Cleansing	CERAMIDE 6 II	1
12C - Face and Neck (exc shave)	CERAMIDE 6 II	9
12D - Body and Hand (exc shave)	CERAMIDE 6 II	3
12F - Moisturizing	CERAMIDE 6 II	5
12G - Night	CERAMIDE 6 II	7
12H - Paste Masks (mud packs)	CERAMIDE 6 II	1
12J - Other Skin Care Preps	CERAMIDE 6 II	5
03D - Eye Lotion	CERAMIDE AP	1
12C - Face and Neck (exc shave)	CERAMIDE AP	11
12F - Moisturizing	CERAMIDE AP	1
12G - Night	CERAMIDE AP	1
03D - Eye Lotion	CERAMIDE EOP	1

12C - Face and Neck (exc shave)	CERAMIDE EOP	11
12F - Moisturizing	CERAMIDE EOP	1
12G - Night	CERAMIDE EOP	1
03D - Eye Lotion	CERAMIDE EOS	1
12C - Face and Neck (exc shave)	CERAMIDE EOS	11
12F - Moisturizing	CERAMIDE EOS	1
12G - Night	CERAMIDE EOS	1
01C - Other Baby Products	CERAMIDE NP	1
03D - Eye Lotion	CERAMIDE NP	2
12C - Face and Neck (exc shave)	CERAMIDE NP	11
12F - Moisturizing	CERAMIDE NP	1
12G - Night	CERAMIDE NP	1
03D - Eye Lotion	CERAMIDE NS	1
12C - Face and Neck (exc shave)	CERAMIDE NS	11
12F - Moisturizing	CERAMIDE NS	1
12G - Night	CERAMIDE NS	1



TO: Lillian Gill, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

A handwritten signature in black ink, appearing to read "HBreslawec", is written to the right of the "FROM:" field.

DATE: November 4, 2013

SUBJECT: Concentration of Use by FDA Product Category: Ceramides

Concentration of Use by FDA Product Category*

Ceramide 1
Ceramide 2
Ceramide 3
Ceramide 4
Ceramide 5

Ceramide 1 A
Ceramide AP
Ceramide AS
Ceramide EOP
Ceramide EOS

Ceramide 6 II
Ceramide NP
Ceramide NS
Ceramide NS Dilaurate

Ingredient	FDA Code†	Product Category	Maximum Concentration of Use
Ceramide 1	03D	Eye lotion	0.00002%
Ceramide 1	03F	Mascara	0.00005%
Ceramide 1	05A	Hair conditioners	0.000325%
Ceramide 1	05B	Hairsprays aerosol	0.00065%
Ceramide 1	05F	Shampoos (noncoloring)	0.00065%
Ceramide 1	07B	Face powders	0.0001%
Ceramide 1	07C	Foundations	0.0001%
Ceramide 1	07E	Lipstick	0.001%
Ceramide 1	08A	Basecoats and undercoats (manicuring preparations)	0.1%
Ceramide 1	12C	Face and neck products not spray	0.00002-0.045%
Ceramide 1	12D	Body and hand products not spray	0.00001%
Ceramide 1	12F	Moisturizing products not spray	0.0000005-0.0001%
Ceramide 1	12G	Night products not spray	0.0001%
Ceramide 1	12H	Paste masks and mud packs	0.00001%
Ceramide 1	12J	Other skin care preparations	0.000001-0.00001%
Ceramide 2	03A	Eyebrow pencil	0.1%
Ceramide 2	03B	Eye liner	0.01%
Ceramide 2	03C	Eye shadow	0.01-0.1%
Ceramide 2	03D	Eye lotion	0.000005-0.2%
Ceramide 2	03F	Mascara	0.0008-0.01%

Ceramide 2	03G	Other eye makeup preparations	0.01%
Ceramide 2	05A	Hair conditioners	0.0001-0.001%
Ceramide 2	05F	Shampoos (noncoloring)	0.01%
Ceramide 2	05G	Tonics, dressings and other hair grooming aids spray	0.01% 0.0001%
Ceramide 2	07B	Face powders	0.01%
Ceramide 2	07C	Foundations	0.001-0.1%
Ceramide 2	07E	Lipstick	0.018-0.064%
Ceramide 2	07H	Makeup fixatives	0.007%
Ceramide 2	07I	Other makeup preparations	0.01-0.05%
Ceramide 2	08B	Cuticle softeners	0.0004%
Ceramide 2	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0004-0.001%
Ceramide 2	12C	Face products not spray	0.0004-0.2%
Ceramide 2	12D	Body and hand products not spray	0.0004-0.05%
Ceramide 2	12F	Moisturizing products not spray	0.0004-0.07%
Ceramide 2	12G	Night products not spray	0.1%
Ceramide 2	12J	Other skin care preparations rinse-off	0.0035% 0.1%
Ceramide 3	03B	Eye liner	0.02%
Ceramide 3	03C	Eye shadow	0.005%
Ceramide 3	03D	Eye lotion	0.002-0.05%
Ceramide 3	03F	Mascara	0.0025%
Ceramide 3	03G	Other eye makeup preparations	0.005%
Ceramide 3	05A	Hair conditioners	0.000001-0.013%
Ceramide 3	05B	Hair sprays aerosol pump spray	0.00000001-0.00065% 0.000001%
Ceramide 3	05F	Shampoos (noncoloring)	0.000001-0.00065%
Ceramide 3	05G	Tonics, dressings and other hair grooming aids	

		spray	0.0001%
Ceramide 3	07A	Blushers (all types)	0.002%
Ceramide 3	07B	Face powders	0.0001-0.01%
Ceramide 3	07C	Foundations	0.00025-0.1%
Ceramide 3	07E	Lipstick	0.01-0.2%
Ceramide 3	07G	Rouges	0.08%
Ceramide 3	07H	Makeup fixatives	0.1%
Ceramide 3	11E	Shaving cream (aerosol, brushless and lather)	0.0015%
Ceramide 3	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00055-0.01%
Ceramide 3	12C	Face and neck products not spray	0.001-0.2%
Ceramide 3	12D	Body and hand products not spray spray	0.0005-0.1% 0.001%
Ceramide 3	12F	Moisturizing products not spray pump spray	0.0003-0.1% 0.0005%
Ceramide 3	12G	Night products not spray	0.001-0.05%
Ceramide 3	12H	Pastes masks and mud packs	0.005%
Ceramide 3	12J	Other skin care preparations	0.00005-0.001%
Ceramide 3	13A	Suntan products not spray	0.0009%
Ceramide 1 A	03D	Eye lotion	0.01%
Ceramide AP	03D	Eye lotion	0.01%
Ceramide AP	03F	Mascara	0.0025%
Ceramide AP	07B	Face powders	0.01%
Ceramide AP	07C	Foundations	0.0025%
Ceramide AP	07E	Lipstick	0.01%
Ceramide AP	12C	Face and neck products not spray	0.1%
Ceramide AP	12D	Body and hand products not spray	0.01%

Ceramide AP	12F	Moisturizing products not spray	0.01%
Ceramide AP	12G	Night products not spray	0.002-0.2%
Ceramide AP	12H	Paste masks and mud packs	0.0005%
Ceramide AP	12J	Other skin care preparations	0.00005-0.001%
Ceramide EOP	03D	Eye lotion	0.01%
Ceramide EOP	03F	Mascara	0.00005%
Ceramide EOP	07B	Face powders	0.0001%
Ceramide EOP	07C	Foundations	0.0001%
Ceramide EOP	07E	Lipstick	0.001%
Ceramide EOP	12C	Face and neck products not spray spray	0.00005-0.01% 0.01%
Ceramide EOP	12D	Body and hand products not spray	0.00001%
Ceramide EOP	12F	Moisturizing products not spray	0.0001%
Ceramide EOP	12G	Night products not spray	0.0001-0.002%
Ceramide EOP	12H	Paste masks and mud packs	0.00001%
Ceramide EOP	12J	Other skin care preparations	0.000001-0.00001%
Ceramide EOS	12C	Face and neck products not spray spray	0.01% 0.01%
Ceramide 6 II	03D	Eye lotion	0.01%
Ceramide 6 II	03F	Mascara	0.0025%
Ceramide 6 II	05A	Hair conditioners	0.00033%
Ceramide 6 II	05B	Hair sprays aerosol	0.00065%
Ceramide 6 II	05F	Shampoos (noncoloring)	0.00065%
Ceramide 6 II	07B	Face powders	0.01%
Ceramide 6 II	07C	Foundations	0.0025%
Ceramide 6 II	07E	Lipstick	0.01%

Ceramide 6 II	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0001%
Ceramide 6 II	12C	Face and neck products not spray	0.01-0.1%
Ceramide 6 II	12D	Body and hand products not spray	0.01%
Ceramide 6 II	12F	Moisturizing products not spray pump spray	0.01% 0.00003%
Ceramide 6 II	12G	Night products not spray	0.2%
Ceramide 6 II	12H	Paste masks and mud packs	0.0005%
Ceramide 6 II	12J	Other skin care preparations	0.00005-0.001%
Ceramide NP	02D	Other bath preparations	0.001%
Ceramide NP	03D	Eye lotion	0.05%
Ceramide NP	03F	Mascara	0.0025%
Ceramide NP	07B	Face powders	0.01%
Ceramide NP	07C	Foundations	0.1%
Ceramide NP	07E	Lipstick	0.2%
Ceramide NP	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.01%
Ceramide NP	12C	Face and neck products not spray	0.0025%
Ceramide NP	12F	Moisturizing products not spray	0.03-0.1%
Ceramide NP	12G	Night products not spray	0.001-0.01%
Ceramide NP	12H	Paste masks and mud packs	0.0005%
Ceramide NP	12J	Other skin care preparations	0.00005-0.001%
Ceramide NS	07C	Foundations	0.001%
Ceramide NS	12A	Skin cleansing (cold creams, cleansing lotions liquids and pads)	0.001%
Ceramide NS	12G	Night creams, lotions and powders not spray	0.006%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

†Product category codes used by FDA

Information collected in 2013
Table prepared: November 4, 2013