PINK

Safety Assessment of Amino Acid Alkyl Amides as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	August 16, 2013
Panel Meeting Date:	September 9-10, 2013

The 2013 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, DPA. This report was prepared by Christina Burnett, Scientific Analyst/Writer, and Bart Heldreth, Ph.D., Chemist CIR.

Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett
Scientific Writer/Analyst
Date: August 16, 2013
Subject: Draft Tentative Report on Amino Acid Alkyl Amides

At the June 2013 CIR Expert Panel Meeting, the Panel issued an insufficient data announcement on the safety assessment of amino acid alkyl amides ingredients. The data needs included:

(1) dermal irritation and sensitization data for lauroyl lysine at the highest use concentration reported (45%); and
(2) dermal irritation and sensitization data for sodium lauroyl glutamate at the highest use concentration reported (40%).

Since the announcement, we have received HRIPT data on sodium lauryl glutamate in products at concentrations of 22% and 30% (tested at 1% and 10% dilutions, respectively). The data have been incorporated in the report in Table 9. The comments that were received from Council prior to the June meeting have been considered. Both the data and comments are available for your review in this report's package.

Please carefully review the draft abstract, discussion, and conclusion.

If the information now available is sufficient, the Panel should issue a Tentative Report with an appropriate discussion/conclusion. If the information is still insufficient, then a tentative conclusion of insufficient data should be issued.

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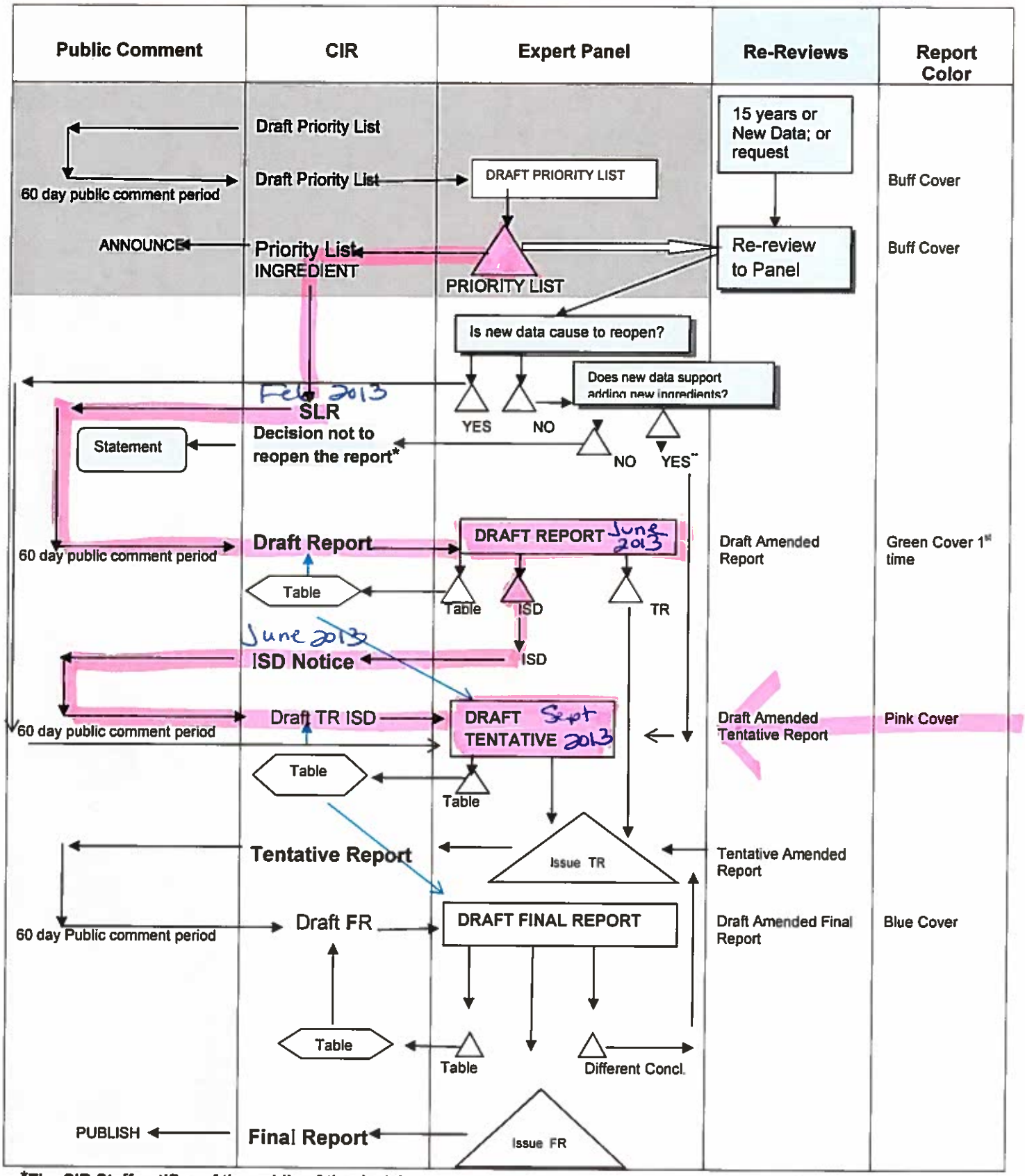
SAFETY ASSESSMENT FLOW CHART

Sept 2013



*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.

△ Expert Panel Decision

Amino Acids Alkyl Amides History

February 2013 – Scientific Literature Review announced.

June 2013 - The Panel issued an insufficient data announcement on the safety assessment of amino acid alkyl amides ingredients. The data needs included: (1) dermal irritation and sensitization data for lauroyl lysine at the highest use concentration reported (45%); and (2) dermal irritation and sensitization data for sodium lauroyl glutamate at the highest use concentration reported (40%).

Amino Acid Alkyl Amides Data Profile* – September 2013 – Writer, Christina Burnett							
	Reported Use	Chemical Properties	Irritation/ Sensitization - Animal	Irritation/ Sensitization - Clinical	Ocular/ Mucousal	Phototoxicity/ Photosensitization	Genotoxicity
Acetyl Arginine		X					
Acetyl Cysteine	X	X					
Acetyl Glutamic Acid		X					X
Acetyl Glutamine	X	X					
Acetyl Methionine	X	X					
Acetyl Proline			X	X	X		X
Acetyl Tyrosine	X	X		X	X	X	X
Capryloyl Glycine	X	X					
Cocoyl Glutamic Acid	X						
Dipalmitoyl Cystine		X					
Disodium Capryloyl Glutamate	X	X	X	X	X		X
Disodium Cocoyl Glutamate	X						
Disodium Hydrogenated Tallow Glutamate	X						
Disodium Lauroyl Glutamate	X						
Disodium Malyl Tyrosinate	X						
Disodium Stearoyl Glutamate	X						
Lauroyl Arginine	X	X			X		
Lauroyl Collagen Amino Acids	X						
Lauroyl Glutamic Acid		X					
Lauroyl Lysine	X						
Lauroyl Proline	X	X					
Lauroyl Silk Amino Acids	X						
Magnesium Palmitoyl Glutamate	X						
Oleoyl Tyrosine	X						
Palmitoyl Alanine		X					
Palmitoyl Arginine		X					
Palmitoyl Collagen Amino Acids	X						
Palmitoyl Glutamic Acid		X					
Palmitoyl Glycine	X	X					
Palmitoyl Isoleucine		X					
Palmitoyl Keratin Amino Acids	X						
Palmitoyl Proline	X	X					
Palmitoyl Silk Amino Acids	X						
Potassium Cocoyl Glutamate	X						
Potassium Cocoyl Glycinate	X						
Potassium Lauroyl Wheat Amino Acids	X						
Potassium Myristoyl Glutamate	X						
Sodium Cocoyl Alaninate	X						
Sodium Cocoyl Amino Acids	X						
Sodium Cocoyl Apple Amino Acids	X						
Sodium Cocoyl Collagen Amino Acids	X						
Sodium Cocoyl Glutamate	X			X	X	X	X
Sodium Cocoyl Glycinate	X						
Sodium Hydrogenated Tallowoyl Glutamate	X						
Sodium Lauroyl Aspartate	X						
Sodium Lauroyl Glutamate	X	X		X	X	X	X
Sodium Lauroyl Oat Amino Acids	X						
Sodium Lauroyl Silk Amino Acids			X	X			

Amino Acid Alkyl Amides Data Profile* – September 2013 – Writer, Christina Burnett							
	Reported Use	Chemical Properties	Irritation/ Sensitization - Animal	Irritation/ Sensitization - Clinical	Ocular/ Mucousal	Phototoxicity/ Photosensitization	Genotoxicity
Sodium Lauroyl Wheat Amino Acids	X						
Sodium Myristoyl Glutamate	X						
Sodium Palmitoyl Proline	X						
Sodium Palmoyl Glutamate	X						
Sodium Stearoyl Glutamate	X						
Stearoyl Glutamic Acid		X					
Stearoyl Leucine		X					
TEA-Cocoyl Alaninate	X						
TEA-Cocoyl Glutamate	X						
TEA-Lauroyl Collagen Amino Acids	X						
TEA-Lauroyl Glutamate	X						
Undecylenoyl Collagen Amino Acids	X						
Undecylenoyl Glycine	X						
Undecylenoyl Phenylalanine	X	X					
NO USES OR DATA WERE AVAILABLE FOR THE REMAINING AMINO ACID ALKYL AMIDES IN TABLE 1.							

*"X" indicates that data were available in a category for the ingredient

Search Strategy for Amino Acid Alkyl Amides

September 2012-November 2012: SCIFINDER search for Amino Acid Alkyl Amides:

- Using CAS #, 49 chemicals identified.
- Using name, 143 chemicals identified.
- Using properties, 50 chemicals identified.

Combined answer sets and deleted duplicates, limited to adverse reactions = 3095.
Limiting this list to document type and specific exposure types = 35.

November 2012 Merck search of CAS #/name yielded 5 hits

Searches also performed using TOXLINE and PUBMED using CAS # and names.

Searches difficult to perform due to nomenclature (amino acid name base).
Limits were not productive.
Little relevant data were discovered.

Searches excluded acute and repeated dose oral exposures, except for carcinogenicity studies.

Total references ordered: 34

Search updated July 18, 2013.

Minutes from Team and Full Panel Meetings on Amino Acid Alkyl Amides

June 10, 2013

Dr. Belsito's Team

DR. BELSITO: So we're now going to amino acid alkyl amides and there was a Wave 2 on this as well. This is the first time we're looking at this report of 115 ingredients, and there are amidases in the skin that can reduce these ingredients to the amine and fatty acids. But the data would suggest that these ingredients really don't make it into the skin. We've looked at the amino acids, and we've looked at many of the fatty acids that this whole family encompasses and found them safe for use in cosmetics. We have no data on reprotoxicity or carcinogenicity, but the question is do we need them or did we get it in Wave 2?

DR. BERGFELD: No, not in Wave 2.

DR. BELSITO: So the question is where we're going with these alkyl amides that we're looking at here. I guess the first question is for Dan and colleagues whether we're still happy with the family.

DR. LIEBLER: Yes.

DR. BELSITO: Okay, and then I guess the question I had here on page 5 of the report was as soon as I enlarge this lauroyl proline was the most used of these?

MS. BURNETT: The lauroyl lysine?

DR. BELSITO: Lysine rather? Okay, my sticker is in the wrong place. And so for a chemical that is the most used in this group to have only impurities data seems bizarre to me, and I'm just surprised we couldn't get more data on what would appear to me to be the lead ingredient here based upon use.

And then with that in mind, I thought that the low absorption sort of would bolster a need for not requesting reproductive or genotoxicity data, but I thought that it was insufficient for sensitization of lauroyl lysine at 45 percent and possibly for sodium lauroyl glutamate at 40 percent. We have none of that data. And I had a question for Dan as to how similar sodium lauryl glutamate and lauroyl lysine might be in terms of what they might break down to in the skin.

DR. LIEBLER: Yes, I think that's actually a fair point, Don. The compounds for which there are the most data are the glutamate derivatives, which are derivatives of acidic amino acids. Glutamate is one of the acidic side chain amino acids, whereas lysine is one of the basic side chain amino acids and could conceivably have different properties in terms of sensitization or irritation.

So I think it's reasonable to ask for sensitization data for lauroyl lysine because we don't have anything that's reasonably chemically analogous. It looks like there's a lot of data on acetyl proline and acetyl tyrosine, but proline is not really a basic amino acid nor is tyrosine. So they don't really suffice. And, of course, they're acetyls. They're actually probably fairly well absorbed. The lauroyl lysine is distinctive enough that there's nothing else on this list that's like it for which we have data.

DR. BELSITO: Okay.

DR. LIEBLER: I'm not expecting trouble, but we have nothing.

DR. BELSITO: Right. And I guess I just have to ask, did you put this in just to make sure we're reading it? Capryloyl gold of pleasure amino acids? Is that really an ingredient?

DR. LIEBLER: I already preordered mine for the collagens.

MS. BURNETT: It's really in the dictionary.

DR. BELSITO: Okay. And what is camelina sativa? I've never heard of that botanical. Does anyone I mean what's the is there a common name for it?

DR. LIEBLER: Gold of pleasure.

MS. BURNETT: Where do you see that?

DR. BELSITO: It's under the ingredients we're about to add. It's page 15 of 380.

DR. LIEBLER: It's in the middle of that table. It's the middle of Table 1.

MS. BURNETT: I know we looked it up, but I couldn't tell you what it is now.

DR. BELSITO: Okay. I mean I'm really I guess it doesn't matter going forward. So I guess from my issue we're opening it up. Dan says the family looks good, so we're adding everything you put and from a derm standpoint, insufficient. I would like to see sensitization of lauroyl lysine on 45 percent and sodium lauryl glutamate at 40 percent. And then ask my colleagues whether they're okay with the fact that we have no repro and very little genotox data because of absorption issues or if they have requests for those.

DR. LIEBLER: I'm fine without the repro and genotox on both of those. There's nothing remotely related to a structure alert for genotox, and I think absorption would be minimal to negligible.

DR. BELSITO: Carol, you were about to say something?

DR. EISENMANN: Well, I was a little concerned when I was looking at the search strategy when it says "all search is limited to dermal exposures" and also saying "there's no data on repro and genotox in cancer because frequently those endpoints you don't do by dermal exposure." So I'm not sure if those endpoints were really just dermal exposure, it might be worth looking at it again.

MS. BURNETT: I didn't I guess I should've I limited my phraseology in the search strategy too much. I don't exclude carcinogenicity in the searches. When I said that, I was meaning I was leaving out oral and the endpoints that we aren't concerned about, the oral, so that I wouldn't be searching through data constantly.

DR. EISENMANN: But for reproductive, developmental, and genotoxicity, you have to include all routes of exposure.

MS. BURNETT: Right, but you can still put in carcinogenicity to get you can search for carcinogenicity for a chemical.

DR. EISENMANN: Right.

DR. BRESLAWEC: What you're saying is you did not exclude the oral data for repro.

MS. BURNETT: Right, right. For your general acute studies, I exclude oral toxicity.

DR. EISENMANN: I was wondering because the search strategy does say "all search is limited to dermal," so I was concerned about that.

DR. KLAASSEN: Say that again. What are you eliminating?

MS. BURNETT: Your acute oral toxicity studies, acute and chronic, but I'm not excluding carcinogenicity or repro or genotox when I

DR. KLAASSEN: I guess

MS. BURNETT: It's just because these are amino acids. If I don't exclude

DR. KLAASSEN: Oh, just for this compound?

MS. BURNETT: Yes.

DR. KLAASSEN: Oh, okay. I thought you said in general.

MS. BURNETT: For this group. If I put in if I didn't limit it, I'd get hits forever because they're amino acids. I have to put some kind of limit.

DR. KLAASSEN: As long as you're talking about any amino acids. I thought you were talking about in general.

MS. BURNETT: No, not in general. No, just for this group because they're amino acids. In order to narrow the scope, I have to do some kind of exclusions.

DR. KLAASSEN: No problem.

DR. SNYDER: I have a question for Dan. On page 12, under toxicological studies, the first sentence says that these amino acids "will dissociate any amino acids and fatty acids in the presence of water." And then on page 13 we say that under the summary statement we say "by and large amino acids alkyl amides will not rapidly dissociate in the presence of water." So are those contradictory statements?

DR. LIEBLER: Yes, they are, and I made a change under toxicological studies, I rephrased

DR. BELSITO: Page?

DR. LIEBLER: Page 12 under toxicological studies, I changed the language to say "the amino acids alkyl amides in this assessment most likely undergo metabolic hydrolysis to amino acids and fatty acids in tissues."

DR. BELSITO: "Most likely undergo

DR. LIEBLER: "Metabolic hydrolysis into amino acids and fatty acids in tissues." And then that's consistent with the language on the next page, so they don't dissociate like acids and bases would or salts would, for example.

DR. SNYDER: Okay.

DR. BELSITO: Anything else? So we're going to open this family of 115 ingredients, and we're going to go insufficient for sensitization for the lauroyl lysine and the glutamate at this point. Is that correct? No other data needs?

DR. SNYDER: What irritation and sensitization data did we get in Wave 2? I don't have I wrote down that we got it, but I didn't write down specifically which

DR. BELSITO: I have it. I have the Wave 2.

DR. BERGFELD: This is not a re review, is it?

DR. BELSITO: No, we got sodium lauryl silk amino acids, the final product 20 percent in water; and sodium lauryl silk amino acids, the impurities. We got irritation and sensitization. We got ocular. We got a dermal 20 percent, but all on sodium lauryl.

DR. EISENMANN: And as I understand it, silk is mostly alanine, glycine, and serine.

DR. LIEBLER: So I don't think this sets aside the need for the data on the lauroyl lysine because this would actually fall under, probably under the concern about the well, I guess it was the LLNA we were talking about earlier with mixtures of ingredients. So you said that these are glycine, alanine, and serine primarily from silk? The main amino acids?

DR. EISENMANN: Yes.

DR. LIEBLER: Okay.

DR. SNYDER: Alanine, serine, and lysine? Is that what you said?

DR. LIEBLER: Glycine.

DR. SNYDER: Oh, glycine. Glycine, serine, and alanine. Thank you.

Dr. Marks' Team

DR. MARKS: Okay. Next is the draft report on amino acid, alkyl amides. And, Christina, you're still up here.

MS. BURNETT: Yes, I am.

DR. MARKS: And this is the first time we've seen this report and looked at these ingredients. There are 115 ingredients, and they're listed in a couple of different places in the report. And so, Ron and Toms, I guess the first thing Rons and Tom the first thing is, are the4se ingredients okay? Are there any that raise a flag and we should delete? And then the second, what are the needs? Do we need the repro and development the carcinogenecity? And then, I'll talk about the skin in a minute, unless you guys want to do that.

So the ingredients I was going to Table 1 and 3, but is there a better place in this report to look at those and say, yeah, these are all okay? You should have them right in the front, don't you, Christina, listed?

MS. BURNETT: No, Table 1.

DR. MARKS: Yeah, you do.

DR. HILL: Page 5 of the PDF has a listing.

MS. BURNETT: Yeah.

DR. MARKS: We'll see where I can cross these out. So this is a good way to go down and look at them alphabetically?

DR. HILL: For me it was simply because I would like to see all the acetyl amino acids removed. But that's just my personal opinion.

DR. SHANK: Why?

DR. SLAGA: Why? Yeah.

DR. HILL: Because all the rest of them are lipophyllic amides formed from amino acids, and I would predict their toxicology in general to be a lot different.

DR. SLAGA: But we already approved all of the alpha amino acids regardless.

DR. HILL: But acetyl amino acids are not the same as the amino acids.

DR. MARKS: So actually it isn't page 5 isn't good. They're the only ones in which you have data on. What page are those tables?

MS. BURNETT: Hold on a second.

DR. HILL: You mean the structures?

DR. MARKS: I don't care whether it's the structures or it's the

MR. ANSELL: Page 15 of the PDF.

MS. BURNETT: Thank you. My computer just crashed on me.

DR. MARKS: So that's Table 1. We could either go Table 1 where they're just where they're listed with definition and function, or is it the next table where it's the chemical structure picture?

DR. HILL: Yeah. So while we're all finding it, here's my rationale.

MR. ANSELL: That would be 23.

DR. MARKS: Yeah.

DR. HILL: We've got an amino acid with the carboxyl group free, so we've got a negatively charged group on one end. Actually if we have an ionizable side chain, then we have an additional ionized group. So for lauroyl, for example, two negative charges. And then these ones that are amide dermatides. We have a greasy tail. So effectively what we have is a surfactant, at least simplistically to look at. We've got a hydrophobic tail and a polar group on one end. So those sorts of things are going to get in membranes, and that's the way they will behave.

The acetyl amino acids, they will do something totally different because in that case, acetyl is small. The whole molecule would be much more hydrophyllic because it has at least one charge. Actually it would be very hydrophyllic for all of these.

And so, in terms of bio handling, I know Dan doesn't like that word, but everybody knows exactly what that word means. In terms of bio handling, the acetyl compounds, one of which is used as a drug, by the way, an acetyl cysteine. So the acetyl compounds will behave very differently biologically than all of these lipophyllic amides.

And at the start of the discussion, they're suggesting that amidases in the skin would cleave these. That's probably not true because there are amidases in the skin, but they do very specific things. And in humans, the only other place where we have a rich presence of amidases is in the liver. So unless they reach a systemic circulation of traffic to the liver, then those amides are probably going to stay as amides, and then probably what's going to happen is these lipophyllic amino acid amides are going to and by the way, the whole ingredient class is named wrong, so I'll come back to that.

But these lipophyllic amides are probably going to set in lipids membranes and other lipid structures in the skin if it's dermal application. I'm not sure exactly where they'll end up if it's inhaled for example.

So I don't like lumping the acetyl because biologically I think they should behave extremely differently. And again, if you get the idea that the amidases that are present in the skin are doing very specific things, mostly related to the endocannabinoid system. Other than that, those amides are going to be quite stable, probably not hydrolyzed. So then we have basically surfactant, and then biologically where they distribute will be very different than the acetyl compound.

DR. SHANK: The acetyl methanine is a food additive, so

DR. HILL: Uh huh. And that's fine, but when you give some orally, you got all the enzymes in the gut. So that's a totally different situation than if you put dermally and you inhale it.

DR. SHANK: I agree, but we have skin toxicity data.

DR. HILL: On these? Not much. Not much on any of these. And I'm not worried about it. I think, you know, I think the bulk of these, the ones with the lipid tails will hang in the stratum corneum, and the anacetyl compounds, probably none of them represent anything of toxicological concern. I just have a philosophical problem with lumping them because biologically we expect them to be so different. Their toxicology should be, if they have any, should be very different.

DR. MARKS: So first, let me make a comment. Since we're in this electronic age, I may be focused more on the screen than my team members across from me. If somebody wants to make a comment and I don't recognize you, just don't hesitate to speak up.

So, Bart, I know you've been quietly raising your hand, but if I hadn't if Christina hadn't pointed out, don't hesitate or anybody else to say I'd like to make a comment.

MR. HELDRETH: Yeah. One comment I have is I certainly view read across as a fantastic reason for grouping chemicals together, but it's not generally the option. If there's any reason that it would save you time or make this process easier and more efficient to have chemicals in the same report, even though we may distinguish their properties or toxicology separately within that report, if it saves you time or effort, you can still keep them grouped together.

DR. HILL: I couldn't come up with any way where that would be true in this case.

MR. HELDRETH: Where what would be true?

DR. HILL: That would save any time or effort in the review process, because, again, bio handling of those anacetyl compounds compared to all of these lipophyllic amides is expected to be completely different. In entirety, they're just extremely different molecules. And anacetyl groups do get cleaved biologically, not easily in all cases, but with much more facility than these lipophyllic amides if they don't happen to be substraits.

MR. HELDRETH: Okay. So what I'm trying to get at is let's say we chop those off and put them in a separate report and brought them back to you next time, and you had

DR. HILL: I would vastly prefer that because I mean, you guys in CIR staff might not, but I would vastly prefer it because then I have compounds that are toxicologically similar and chemically similar in terms of biology. I mean (inaudible) chemistry in terms of structures as they relate to biology, and for anything else, who cares, other than volatility or whatever we're talking about sprays.

DR. MARKS: So let's go back, Ron and Tom. Do you have the same concerns about the metabolism of these on the skin? We know they're okay from

DR. SHANK: We have irritation data, normal irritation data, for acetyl proline in humans. We have sensitization data for acetyl proline, acetyl tyrosinomide hydroxyproline.

DR. HILL: That's fine, but my point

DR. SHANK: The acetyl methionine is a food additive, so I don't see a need for any more any problem with the acetyl aminoanoids.

DR. HILL: I don't either, but my point is it doesn't help me with read across whatsoever for all of these lipophyllic amides. I mean, to me, that is meaningless in terms of assessing their potential for toxicology and safety. It doesn't help me having those acetyls in there, and that's my point is put molecules together that are relevant to each other. And in this case, I think there's no cross relevance at all. Knowing that data on the anacetyl doesn't help me with any of these lipophyllic amides which are basically surfactants.

DR. SHANK: But we have data on some of the fatty acid akyl

DR. HILL: For that we can read across one to another, I think, quite a bit. But I'm just we'll see what Dan thinks, I guess.

DR. SHANK: Okay. Chemically I can see why you're why you split them, since we have data on both.

DR. HILL: Biologically they should be split, that's my point. They don't relate in terms of biology because we don't expect those lipophyllic amides to be hydrolyzed, I think, appreciably. We don't have data that says they are, and I don't believe they will be.

DR. SHANK: Okay, but

MS. GILL: So having the data on both

DR. HILL: Doesn't help with read across.

MS. GILL: doesn't help you at all.

DR. HILL: Me, uhn uhn. And that's my point. So then lumping them together really obfuscates the issue because recross is suggested where it shouldn't be.

DR. SHANK: So if you split the lipophyllic and non lipophyllic into two reports

DR. SLAGA: We'd have to do that on all of them.

DR. SHANK: Would you come up with the same conclusion that both are safe, both groups are safe?

DR. HILL: Probably, but for different reasons.

DR. SHANK: Okay.

DR. HILL: And that's the point.

DR. MARKS: So I get this dynamic tension of separating, keeping it all together. We can again let Dan weigh into that. Do you want to make a comment tomorrow, Ron, to that effect, where obviously on the beginning part of this? Tomorrow under discussion, if you would bring that up, Ron, that would be good.

I want to bring up to my team members, I actually thought maybe an insufficient data notice because of the lauroyl lysine has a great number of uses. It's

DR. SHANK: Which one?

DR. HILL: Lauroyl.

DR. MARKS: Yeah, lauroyl lysine. It has a lot of uses, 649 uses. Leave on is up to 45 percent concentration, yet there's no skin toxicology on that particular ingredient, and I thought if we're going to have a lead, we do have a lot of information on sodium cocylglutimate, but I'm not sure I could use read across on that. I wanted Ron, Tom, Ron, get your input.

I felt I'd like at least this one ingredient that has lots of uses, has a high leave on concentration, but I have no irritation or sensitization data on that that I would like to go forward with an "insufficient data" and see what would come forward with that specific ingredient. I'm not sure I can read across from the sodium cocylglutimate, which is leave on is one percent. So much lower concentration, and actually that's a five percent ocular irritant.

So what was your I mean, the other is we could move forward and just say "formulate to be non irritating," but I can't imagine there isn't some irritation or sensitization data on

DR. SHANK: I'm trying to find the concentrations for the sensitization.

MR. ANSELL: Which ingredient specifically?

DR. MARKS: The

DR. SHANK: Sodium lauroyl lysine.

DR. MARKS: Lauroyl lysine.

DR. SHANK: We have lauroyl glutimate data, if I can find it.

DR. HILL: Yeah. One of the things that was done in some of these reports with a lot more ingredients, and I realize it's a lot more work on the staff members who are way overloaded already, to prepare that read across table in multiple ways. So, for example, if it was prepared amino acid in addition to the way that it's in there, that would be really helpful because you could look and say, all right, we don't have lauroyl lysine, but we have capryloyl lysine, for example. And then what you have to do beyond that in reviewing is look at concentration of use and say, well, we do have that, but that's only one percent, and this one is 40 percent, so we probably yeah. Those are the kinds of things one has to do in the read across.

Sorry, I guess that should be left up to us, but yet there's a lot of leaps that have to be made to do the read across at all. I think it was Monice that did vegetable oil, I'm not sure. But basically the tables were put together in multiple ways so you could see these are lysine, these are glutimate, these are all it would help facilitate the review in this kind of question. Lillian's is in here, so she heard me at least.

DR. MARKS: So that was my concern is I didn't with an ingredient which was used so frequently and with a high concentration, I was concerned that there was really no direct skin toxicology. And I didn't really feel quite comfortable at this point saying, okay, it's not an irritant, it's not a sensitizer at 45 percent on a leave on. So that was my suggestion, insufficient data notice, because this is the first time we've seen it. We don't go out with a tentative report with "insufficient." But, Ron, Tom?

DR. SHANK: The sensitization data, Table 9, which is PDF page 46

DR. MARKS: Forty six, okay.

DR. SHANK: Gives sodium lauroyl glutimate well

DR. MARKS: Dermal sensitization.

DR. SHANK: No, this is but that was at five percent.

DR. MARKS: Yeah.

DR. SHANK: And you're saying it's

DR. MARKS: Forty five percent is leave on.

DR. SHANK: 45 percent.

DR. MARKS: Am I correct on that, Christina, when I looked in the use?

DR. SHANK: Well, that one is the one that's in Table 9, the glutimate.

DR. MARKS: Right.

DR. HILL: Right, and the other

DR. SHANK: And he's up to 40 percent.

DR. HILL: Right. And the other issue there is that the polar end, which is if there's going to be any sensitization would almost certainly come from that end, and particularly with lysine because it has an amino group on it. I'm not sure reading across from glutimate to the lysine was a great idea.

DR. MARKS: So am I correct in the 45 percent.

MS. BURNETT: Forty five percent for the lauroyl.

DR. MARKS: Yeah. So does that sound let me see. Who's presenting? I will be the one presenting tomorrow. That was my concern.

DR. HILL: What I was looking for are there any of these mixed amino acids that come from that have a high lysine

DR. SLAGA: It's early in the game. We can

DR. MARKS: Yeah, exactly. That's why now, but are there any other needs, Tom and Ron?

DR. SLAGA: I don't have any other

DR. MARKS: repro development, carcinogenicity, all those. You didn't have any concerns with these ingredients. So what I would do tomorrow is say an insufficient data notice. I'll move that, and I'd like to have the irritation and sensitization on that particular ingredient. Does that sound reasonable, Ron, Tom?

DR. SLAGA: Uh huh.

DR. HILL: Nobody else wanted to see tumor promotion effects? They wanted to use a very high concentration in the leave on.

DR. MARKS: That's what I that's why I asked

DR. HILL: Because I'm thinking in terms of membrane perturbations where you're modifying membranes in such a way

DR. SLAGA: Yeah, but if you don't find any irritation, then there might be a chance it's a promotion.

DR. HILL: If we don't have something giving irritation, do we expect that it couldn't still enhance the rates of growth of nascent tumors?

DR. SLAGA: Well, based on a large number of compounds that have been studied over the years, chronic inflammation is a hallmark of all those.

DR. HILL: Well, you know, the question in my mind is, causing a tumor to start, I don't expect any of these would likely do that versus facilitating the growth rate of one that's already there. I know we're in a place where we don't go very often, but when I see something that's clearly likely to be membrane modifying used in a leave on in very high concentrations, those are the questions that enter my mind in terms of safety.

DR. MARKS: Okay. So tomorrow I'll move that an insufficient data notice be issued, and that the how do you say that, lauroyl?

DR. SHANK: Lauroyl.

DR. MARKS: Lauroyl.

DR. HILL: Lauroyl.

DR. SHANK: That's right.

DR. MARKS: Whenever. I'm sure tomorrow I'll have a different pronunciation. At any rate, we'll know

(Laughter.)

DR. MARKS: Lysine, most importantly, Christina, you know what we're talking about, and I'll give the rationale for it, and we'll see where it goes. And we'll see what the Belsito team has to say.

MS. GILL: Jim, would you review one more time what data needs

DR. MARKS: Irritation and sensitization data, there's none, and my rationale for that is I couldn't use any read across. It has a lot of uses, 649. And its concentration is 45 percent in leave on. So undoubtedly there's data out there and an HRIPT on this in a leave on, close to that concentration.

DR. HILL: Well, alternatively I started to say, and I interrupt, is if one of these mixed amino acids is known to have a high lysine content, and is also used, and we also have data, then that would be, for me, equivalent. I'd be comfortable. But, gee, that one is used at an awfully high volume.

DR. MARKS: Yeah. The other is obviously, at least for me, the irritation that maybe is not going to be as pertinent because eventually we're going to arrive at a safe conclusion, and it'll probably be, since these are surfactants, they're formulated to be non irritating. So that probably takes that off of it. But I still would like to see some sensitization data.

DR. SHANK: Apparently last time this was discussed, there was an issue about malic acid. At least I have this in my notes

DR. MARKS: Last time it's discussed?

DR. HILL: I read it

DR. MARKS: This is the first time we saw this.

DR. SHANK: I don't think

DR. MARKS: Yeah, this is the first review.

MS. BURNETT: Yes, this is a draft.

DR. SHANK: Well, where did I come up with this

MS. BURNETT: Malic in the introduction

DR. SLAGA: That was related to amino

MS. BURNETT: Yeah, in the introduction of the constituents, the fatty acid stituents that had been reviewed. I'd point out that malic acid has a different conclusion saying it was insufficient for any other function other than use as a gates buster. That's where you might

DR. SHANK: That's where, thank you. Okay. I don't think that's an issue.

DR. MARKS: Okay.

DR. SHANK: But if it is, I think it can be handled in the discussion. And if it can't, then take that out. There's one ingredient called sodium malyl tyrosinate that's been added. And if malic acid is going to be insufficient, then take that out.

DR. MARKS: You want to bring that up tomorrow, Ron, when we get into the discussion point?

DR. SHANK: No.

(Laughter)

DR. SHANK: I think I have that one, though.

DR. MARKS: Okay. Any other comments?

(No response)

DR. MARKS: So I'm going to move oh, yes.

MR. RE: Malic acid in this report.

MS. BECKER: Can you come forward and introduce yourself, please?

DR. MARKS: Either yell or come to the table, Tom.

MR. RE: I'm Tom Re from L'Oreal. If malic acid is in this report, we could probably provide data to move beyond insufficiency.

DR. SHANK: Okay. I don't think it's a problem.

DR. MARKS: Thanks, Tom. Any other comments? Again, don't hesitate to speak up if I don't see you. The configuration of the room, my concentration on using Adobe Professional, and putting notes in here, all may compromise me being able to notice hands.

DR. HILL: I read the malic, and I remember writing it off immediately, the only ingredient that was even theoretically relevant to

DR. MARKS: Well, actually, Ron Shank had mentioned that what's within there's a malic.

DR. HILL: I remember when I read it, I was trying to figure out why that was even in the report. It was a theoretical possibility of being hydrolyzed, something in here. But to me, I doubted the likelihood of that, whatever it was.

DR. SHANK: That probably came from the other team.

DR. MARKS: Okay.

MS. BURNETT: It was

DR. MARKS: The other team has not had a chance to see this until today, or I should say

MS. BURNETT: It was one of the malic acids, and it was the one that kind of wasn't quite when I was doing the read across with the constituent like the others.

DR. HILL: Which ingredient?

MS. BURNETT: I'm trying to find it. I'm sorry.

DR. SHANK: Sodium malyl tyrosinate.

MS. BURNETT: Thank you. Disodium. Disodium.

DR. SHANK: Disodium, sorry.

MS. BURNETT: Disodium.

DR. MARKS: Okay.

MS. BURNETT: Malyl tyrosinate.

DR. HILL: Oh, yeah, because it's yeah. I thought that this one didn't belong in the report at all. That was my conclusion on that one. In addition to the anacetyl, I thought one should've been kicked out because it's not a no brainer.

DR. MARKS: Well, it doesn't have to be a no brainer. This is a first review.

DR. HILL: Yes.

DR. MARKS: So we can put anything in the report we want that requires lots of brains since it's not a re review. Now, is it chemically related in this and can you read across? I think that's another issue.

DR. HILL: So then the question was, I mean, that's a small enough molecule where I would be interested in the toxicology of that one specifically. And I would not want to read across for that from any of the others in the whole report.

DR. MARKS: So let's bring that up tomorrow in the discussion. And, Tom, if you want to comment tomorrow about that, you may. Okay.

MR. ANSELL: Well, that would bring us to another comment that didn't seem to be relevant before, but to the extent that you've thrown this on the table excuse me, to the extent that you've now thrown this on the table, let me point out that the staff was very clear that they searched only for topical data. To the extent you decided to extend the insufficiency beyond topical data, we would suggest then that the report needs to be tabled to go back and disagree with the staff's decision that they not look for anything other than topical data.

MS. BURNETT: I guess I shouldn't have worded. I still roam every procarcinogenic genotox. It was more of the oral toxicity that I did not

MR. ANSELL: Well, we don't necessarily disagree with that decision exactly

MS. BURNETT: Okay.

MR. ANSELL: The discussion at all with topical. But if by tomorrow we find ourselves going into areas other than topical, we may raise that as an issue.

DR. MARKS: Okay. At least with three quarters of us, we didn't have a sense like a big thing other than the topical toxic effects of the lead, in my mind, the lead ingredient in terms of use. Okay.

DR. HILL: And I'm sorry about that malyl. It was a big lag between when I first looked at this report and when I came back and made notes, and I totally missed that one.

DR. MARKS: Well, I think Ron after the discussion decided it wasn't as much of an issue for him. And then Tom seems to indicate there would be data there. So I guess tomorrow, how do you want to handle that, Ron? You're going to bring up when it comes to the discussion, you're going to bring up this acetyl.

DR. HILL: If we discuss the grouping, I will bring up the acetyl, and I will also say the malyl.

DR. MARKS: Well, no, I'm going to depend on you to bring it up because I'm always

DR. HILL: Okay.

DR. MARKS: for discussion.

DR. HILL: So I will bring up the acetyls and also that one.

DR. MARKS: Yep. And then we'll see how the teams resolve that tomorrow.

DR. SHANK: And you're going "insufficient."

DR. MARKS: "Insufficient" because of the

DR. SHANK: Sensitization.

DR. MARKS: Right. That is the motion I'll make. And the rest of this can be in a discussion. Okay. Any other comments? (No response.)

June 11, 2013

Full Panel

DR. MARKS: So, this is a draft report on the amino acid alkyl amides. This is the first time we saw these ingredients. There are 115 of them.

We've thought largely the needs were met, with the exception of irritation and sensitization picking lauroyl lysine. It has a lot of uses, 649. It's a leave on at 45 percent concentration, yet we have no safety data on its irritation or sensitization.

So, we would move our team would move that we issue an insufficient data notice to meet the need.

DR. BERGFELD: Is there a second?

DR. BELSITO: Well, I think it's insufficient. We can just go through what the insufficiencies are, but we had additional amines.

DR. BERGFELD: Okay. So, do you want to list your insufficiencies?

DR. MARKS: I already mentioned the insufficiency. Our team we didn't think that there were other significant deficiencies or insufficiencies. But obviously, we're curious for the Belsito team's.

DR. BELSITO: Okay, so the only other you know, we thought it was insufficient for sensitization and irritation. We agreed with lauroyl lysine because it's the most frequently used, and up to 45 percent, but we felt that that could not substitute for sensitization and irritation for sodium lauroyl glutamate, and thought that had a slightly different molecular structure, and that's used up to 40 percent. So, we're asking for data for both of those ingredients for sensitization and irritation.

I'm assuming that, given the low absorption, you're not concerned about the lack of reproductive toxicity and the amount of genotoxicity we have, we were not. But, just pointing that out.

DR. BERGFELD: Anything else?

DR. LIEBLER: Yeah, so we're just getting basically this gives us coverage that the lauroyl lysine would be the basic derivative and the glutamate would be the acidic derivative. So, if we have coverage on both of those, that would be preferential.

DR. BERGFELD: So, we haven't had a second on your motion. Will you re state your motion to see if there's a second?

DR. BELSITO: We had a second for insufficient, the question is

DR. BERGFELD: Oh, did you say

DR. BELSITO: Yeah.

DR. BERGFELD: I didn't see you say insufficient. Okay, all right.

DR. MARKS: Yeah, it just was what were the needs and Don has expounded upon those. So, that's fine.

DR. BERGFELD: So we have a motion for insufficient. Ron Hill, did you have another comment?

DR. HILL: We had a lengthy discussion because I was very unhappy that we were grouping the N acetyl amino acids with these lipophilic amino acid amides. I mean, I could elaborate on that, but it will be captured in the transcript, since it's moving on.

And also, if we are keeping the malyl tyrosine. We don't have much direct toxicology information on that, and we don't have information that that would be cleaved to malate and tyrosine in the skin. So, then as far as I'm concerned, since that's a small molecule potentially absorbable, at least into the layers of the skin where it could get into the that we I was hoping that ingredient would be ditched because it's not a no brainer. But if we're not going to ditch it at this stage, then I would like to see some toxicology data on that compound because it's dissimilar to all the rest.

And as far as the N acetyl, I guess it's a philosophical thing. It gets more ingredients through the review process, but I just objected completely to lumping them because and I know Dan doesn't like the word "bio handling", but we know exactly what that means. That we wouldn't expect the N acetyl amino acids to be handled the same way as all these lipophilic ones. That basically with these lipophilic amides, we don't have any information to suggest that they be cleaved in the skin. So then really, what we've got is a surfactant with a polar head group and a lipid on the end, and I expect that those would hang in the stratum corneum. Unlike the N acetyl I don't have any toxicological concerns about the N acetyl amino acids, just I don't like having them lumped together because I think biologically they would behave quite differently.

But the malyl in particular, malonyl in particular I would like to see some data directly on it if it's going to stay in.

DR. BERGFELD: Jim? Agreeable?

DR. MARKS: No, I would like to ask Dan's opinion on the chemistry of this, and obviously on subsequent tox.

DR. HILL: We're going insufficient, other than that malonyl. I mean, I don't

DR. MARKS: Yeah, it's an insufficient data, but since Ron, you brought it up

DR. HILL: I was just raising a philosophical question more than anything else.

DR. MARKS: Right.

DR. LIEBLER: Yeah, so I acknowledge Ron's basic point, that the variety of site chain substitutions or derivations, excuse me will impart differences in absorption behavior and so forth. I acknowledge that and I agree that it certainly differentiates these compounds. But, it doesn't rise to the level of making me feel that they can't be considered together as a group.

So, because I think there's not a toxicological consequence of that that would influence our decision so for that reason, I think it's practical to consider these all together.

DR. BERGFELD: However, the minutes will reflect Ron Hill's request. All right.

All those in favor, then, if there are no other discussant points of going insufficient on this ingredient, please indicate by raising your hands? Thank you.

(Motion approved by show of hands)

DR. MARKS: Now this is let me clarify this. There's an insufficient data notice. Yeah, we aren't going insufficient because it's just a notice at this point. So, we're not issuing a report, just a notice.

DR. ANDERSEN: This is the heads up to interested parties that additional data are needed, and were those data to not be provided, the next step would be a tentative safety assessment with an insufficient data conclusion. So, the opportunity to provide the data now exists.

DR. BRESLAWEC: Dr. Bergfeld, I'm being dense. What ingredient are you referring to, Dr. Hill?

DR. HILL: It's unfortunately

DR. BRESLAWEC: Thank you.

DR. HILL: because it's disodium we can't find

DR. BRESLAWEC: Yes, I couldn't find now I can find it.

DR. HILL: Disodium malyl tyrosine is the way it's listed in the dictionary, apparently.

DR. BRESLAWEC: Thank you.

Safety Assessment of Amino Acid Alkyl Amides as Used in Cosmetics

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The 2013 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, DPA. This report was prepared by Christina Burnett, Scientific Analyst/Writer, and Bart Heldreth, Ph.D., Chemist CIR.

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DRAFT ABSTRACT

The Cosmetic Ingredient Review Expert Panel reviewed the safety of amino acid alkyl amides, which function as skin and hair conditioning agents and as surfactants-cleansing agents in personal care products. After reviewing the relevant animal and human data presented, the Panel concluded the data are insufficient to support the safety of these cosmetic ingredients. The Panel determined that the following additional data are needed: (1) dermal irritation and sensitization data for lauroyl lysine at the highest use concentration reported (45%); and (2) dermal irritation and sensitization data for sodium lauroyl glutamate at the highest use concentration reported (40%).

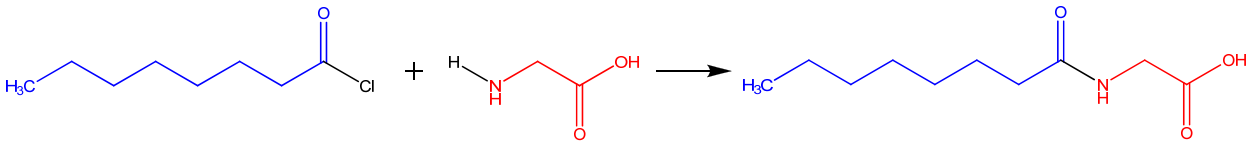
INTRODUCTION

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 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 in 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. For example, capryloyl glycine is the *N*-acylation product of glycine with caprylic acid chloride.



Caprylic Acid Chloride (a.k.a. Capryloyl Chloride) | Glycine | Capryloyl Glycine

Figure 1. Synthesis of the amino acid alkyl amide, Capryloyl Glycine.

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.

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] The 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%-41% disodium capryloyl glutamate, 32.6%-38% sodium cocoyl glutamate, and 36%-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%-6% propylene glycol, 3% caprylic acid (max.), 5% disodium glutamate (max.), and 6%-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%-6% propylene glycol, 5% (max.) sodium glutamate, 3% coconut acid, and 4%-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%-6% propylene glycol, 5% (max.) glutamic acid, 3% (max.) lauric acid, and 3%-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 ppm and $\leq$ 2 ppm, respectively.[17]

USE

Cosmetic

Table 5a presents the current product-formulation data for amino acid alkyl amides. These ingredients function primarily as skin and hair conditioning agents and surfactants.[18] According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP), 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.[19] 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 Personal Care Products 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.[20-22] 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 concentration 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 one 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 pump sprays.[23,24] 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., able to enter the lungs) to any appreciable amount.[25,26]

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 $\leq$ 5%secondary amine content and $\leq$ 50 μg/kg nitrosamine, and must be kept in nitrite-free containers.[27] The use of the remaining ingredients is not restricted under the rules governing cosmetic products in the European Union.

Non-Cosmetic

Amino acid alkyl amides are used in household detergents.[28]

Acetyl cysteine has been approved by the FDA to treat acetaminophen overdose and for mucolytic therapy.[29] Acetyl methionine is an approved direct food additive (21 CFR §172.372).

TOXICOKINETICS

Absorption, Distribution, Metabolism, 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.[30] 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-h dose period. At 6, 12, 32, and 48 h after 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 (HPLC) method.

In the formulation with water, the test material was found in the following mean distribution: 0.48% in receptor solution, 0.04% in dermis, 1.25% in epidermis, 4.64% in stratum corneum, and 83.15% in surface wash (total recovery was 89.55%). For the gel formulation, the test material was found in the following mean distribution: 1.03% in receptor solution, 0.07% in dermis, 1.15% in epidermis, 0. 70% in stratum corneum, and 88.59% in 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. [30]

TOXICOLOGICAL STUDIES

By and large, 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, oral toxicity is not expected. Systemic toxicity following dermal exposure is not expected to differ from that of oral exposure. Irritation and sensitization are of concern, and the focus in this report. Data from the previous safety assessments on α-amino acids and fatty acids support that these ingredients would not likely be irritants or sensitizers.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No published reproductive and developmental toxicity studies on amino acid alkyl amides were discovered and no unpublished data were submitted.

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 glutamic acid was negative in an in vivo mouse study.

CARCINOGENICITY

No published carcinogenicity studies on amino acid alkyl amides were discovered and no unpublished data were submitted.

IRRITATION AND SENSITIZATION

[From the CIR Safety Assessment of α-amino acids][2]: Cysteine HCl and methionine were used as negative controls in in vitro assays to predict potential skin irritants. In separate efficacy studies, arginine, cysteine, and glycine did not produce any adverse effects in rats, guinea pigs, or mouse skin models. Glutamic acid was used as a negative control in an in vitro study to identify skin sensitizers. Products containing amino acid ingredients at concentrations up to 2.784% were not dermal irritants or sensitizers in HRIPT studies. 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.

Irritation

In vitro and human dermal irritation studies are presented in Table 7. No irritation was observed in in vitro studies with disodium capryloyl glutamate. Acetyl proline was a mild irritant in another in vitro study. In human studies, acetyl proline, acetyl tyrosine, disodium capryloyl glutamate, sodium cocoyl glutamate, and sodium lauroyl glutamate were not dermal irritants.

Ocular

Non-human 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, disodium capryloyl glutamate, and sodium lauroyl glutamate. 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. No adverse effects were observed during in-use studies of products containing acetyl hydroxyproline and acetyl tyrosine in human subjects.

Sensitization

Non-human and human dermal sensitization studies are presented in Table 9. Sodium lauroyl silk amino acids when tested neat in a 20% solution was not sensitizing in a LLNA test. No sensitization was observed in human studies with 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%).

Phototoxicity

Non-human and human phototoxicity studies are presented in Table 10. In non-human and human studies, acetyl tyrosine was not phototoxic at concentrations up to 1 mg/ml and 10 mg/ml, respectively. Sodium cocoyl glutamate (up to 5%) and sodium lauroyl glutamate (up to 5%) were not phototoxic in human studies.

SUMMARY

The 115 amino acid alkyl amides 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. 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%, with the greatest concentration reported 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 then 50 μg/kg, and must be kept in nitrite-free containers. The use of 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.

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 glutamic acid was negative in an in vivo genotoxicity study.

No dermal irritation was observed in in vitro studies with disodium capryloyl glutamate. Acetyl proline was a mild irritant in another in vitro study. In human studies, acetyl proline, acetyl tyrosine, disodium capryloyl glutamate, sodium cocoyl glutamate, and sodium lauroyl glutamate were not dermal irritants.

No ocular irritation was observed in in vitro studies of acetyl tyrosine, disodium capryloyl glutamate, and sodium lauroyl glutamate. Severe irritation was observed in 1 study of sodium cocoyl glutamate at 5%. No adverse effects were observed during in-use studies of acetyl hydroxyproline and acetyl tyrosine in human subjects.

Sodium lauroyl silk amino acids when tested neat in a 20% solution was not sensitizing in a LLNA test. No sensitization was observed in human studies with 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%).

In non-human and human studies, acetyl tyrosine was not phototoxic at concentrations up to 1 mg/ml and 10 mg/ml 1000 μg/ml and 1%, respectively. Sodium cocoyl glutamate (up to 5%) and sodium lauroyl glutamate (up to 5%) were not phototoxic in human studies.

No published reproductive and development toxicity, or carcinogenicity on amino acid alkyl amides were discovered and no unpublished data were submitted.

DRAFT DISCUSSION

The Panel acknowledged that the safety of α-amino acids as direct food additives has been well supported based on extensive research of acute and chronic dietary exposures. The Panel determined that this body of research, coupled with the available irritation and sensitization data and the observation that use concentrations are much lower than the concentrations in foods consumed daily in the diet, provide a sufficient basis for determining the safety of amino acids in cosmetic products.

The Panel recognized that there are issues, i.e. MSG symptom complex and phenylketonuria associated with sodium glutamate and phenylalanine, respectively, in the diet for certain individuals. However, the Panel concluded that the concentrations of these amino acids in cosmetic products are low, and would not be conducive to significant absorption through dermal application or incidental ingestion, and thus, would not cause systemic reactions in individuals.

While the *International Cosmetic Dictionary and Handbook* does not distinguish among the α-amino acids used in cosmetics that are L-stereoisomers from those that are D-stereoisomers (or are mixtures of L- and D-stereoisomers), the Panel noted that the L-amino acids are Generally Recognized As Safe (GRAS) direct food additives by the FDA (except Methionine which is GRAS as a racemic mixture, and Glycine which is GRAS and has no stereocenter). Amino acids with a mixture of the 2 stereoisomers (DL-) have approved uses as food additives according to the USP Food Chemicals Codex. This safety assessment report addresses D- and L- stereoisomers of the amino acids acylated with acids or acid chlorides to form amides. The Panel does not anticipate that there are significant toxicological differences in cosmetic applications among the stereoisomers.

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 available. These ingredients reportedly are used at concentrations up to 0.65% in cosmetic products that may be aerosolized. The Panel noted that 95% – 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 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 the dangers inherent in using animal-derived ingredients, namely the transmission of infectious agents. They stressed that these ingredients must be free of detectible pathogenic viruses or infectious agents (e.g., bovine spongiform encephalopathy (BSE)). 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 noted the uncertainty regarding method of manufacturing. The Panel considered that vigorous acid hydrolysis would yield amino acids with little or no residual peptides, because such acid hydrolysis attacks all of the peptide bonds in a protein in a non-preferential manner. The Panel was concerned that enzymatic hydrolysis may fail to completely hydrolyze the source proteins and, thus, may produce di-, tri- or other peptides, as well as amino acids. Such residual peptide impurities may have the potential to cause allergic reactions in sensitive individuals. Further input on the usual methods used to produce amino acids from animal and plant proteins would be useful. If the methodology involves rigorous acid hydrolysis, there is less concern that residual small peptides will be present. In the absence of further clarification, the Panel stated that industry should manufacture amino acid alkyl amides in a way that ensures that no residual peptides remain.

The CIR Expert Panel requested additional data to support the safety of the 115 amino acid alkyl amides described in this safety assessment. The additional data needed are:

(1) dermal irritation and sensitization data for lauroyl lysine at the highest use concentration reported (45%); and

(2) dermal irritation and sensitization data for sodium lauroyl glutamate at the highest use concentration reported (40%).

These data, if made available, will span the chemical space for this group. It was also noted that any available data on disodium malyl tyrosinate would be useful.

DRAFT CONCLUSION

The CIR Expert Panel concluded that the available data or information are insufficient to make a determination that the amino acid alkyl amides listed are safe under the intended conditions of use. The 115 ingredients included in this safety assessment are:

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 cystine
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 prolineate
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

TABLES AND FIGURES

Table 1. Definitions and functions of the Amino Acid Alkyl Amides in this safety assessment.[18] (Any italicized text below represents additions made by CIR staff.)

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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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
Disodium Capryloyl Glutamate	Disodium Capryloyl Glutamate is the organic compound that conforms to the formula. *Disodum Capryloyl Glutamate is the disodium salt of the amide formed from the reaction of capryloyl chloride and glutamic acid.*	deodorant agents; surfactants-cleansing agents

Table 1. Definitions and functions of the Amino Acid Alkyl Amides in this safety assessment.[18] (Any italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
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 Acids 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 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 Acids 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.
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 Acids is the condensation product of palmitic acid chloride and Collagen Amino Acids.	hair conditioning agents; skin-conditioning agents-misc.; surfactants-cleansing agents

Table 1. Definitions and functions of the Amino Acid Alkyl Amides in this safety assessment.[18] (Any italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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
Potassium Lauroyl Collagen Amino Acids	Potassium Lauroyl Collagen Amino Acids 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 Acids 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 Acids 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

Table 1. Definitions and functions of the Amino Acid Alkyl Amides in this safety assessment.[18] (Any italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
Potassium Lauroyl Silk Amino Acids	Potassium Lauroyl Silk Amino Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids 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 Acids is the sodium salt of the condensation product of coconut acid chloride and Collagen Amino Acids.	hair conditioning agents; surfactants-cleansing agents
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 Acids 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

Table 1. Definitions and functions of the Amino Acid Alkyl Amides in this safety assessment.[18] (Any italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
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 Acids 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 Acids 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 Acids 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
Sodium Lauroyl Oat Amino Acids	Sodium Lauroyl Oat Amino Acids 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 Acids 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 Acids 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

Table 1. Definitions and functions of the Amino Acid Alkyl Amides in this safety assessment.[18] (Any italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
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 Acids 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 Acids 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 Acids 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
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 Acids 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 Acids 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 Acids 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 Acids 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

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% aq. 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 neither is a sensitizer or 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 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 one study, pyrolyzates 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-min 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.	10

Table 2. Constituent acids with CIR conclusions

Constituent	Conclusion (year issued; maximum use concentration reported)	Summary of Findings	Reference
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 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%.	[4]

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

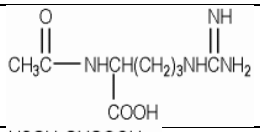
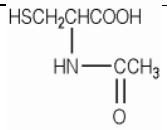
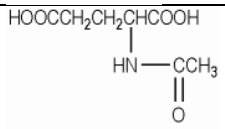
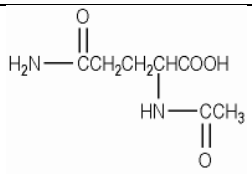
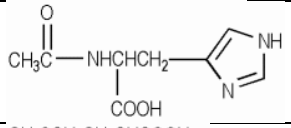
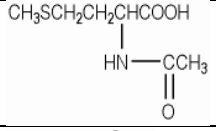
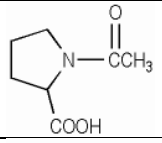
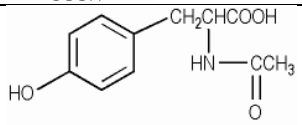
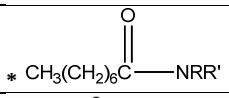
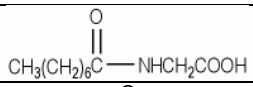
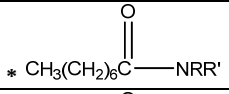
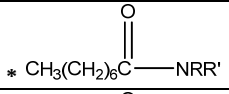
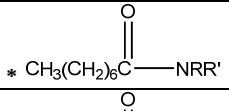
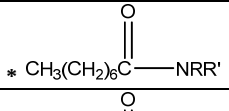
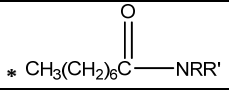
Acetyl Arginine	
Acetyl Cysteine	
Acetyl Glutamic Acid	
Acetyl Glutamine	
Acetyl Histidine	
Acetyl Methionine	
Acetyl Proline	
Acetyl Tyrosine	
Capryloyl Collagen Amino Acids	 where NRR' represents the amino acid residues from collagen
Capryloyl Glycine	
Capryloyl Gold of Pleasure Amino Acids	 where NRR' represents the amino acid residues from gold of pleasure
Capryloyl Keratin Amino Acids	 where NRR' represents the amino acid residues from keratin
Capryloyl Pea Amino Acids	 where NRR' represents the amino acid residues from pea
Capryloyl Quinoa Amino Acids	 where NRR' represents the amino acid residues from quinoa
Capryloyl Silk Amino Acids	 where NRR' represents the amino acid residues from silk

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

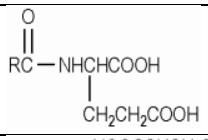
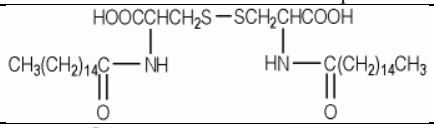
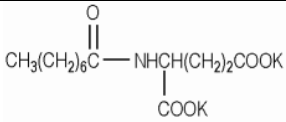
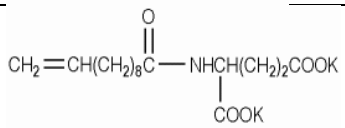
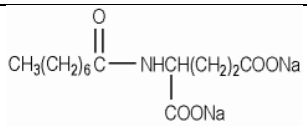
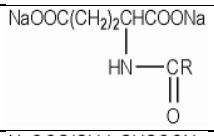
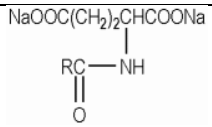
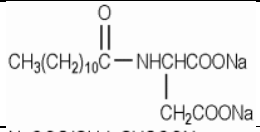
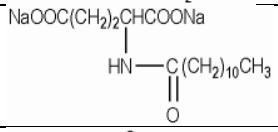
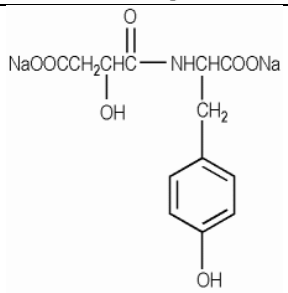
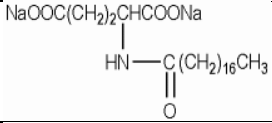
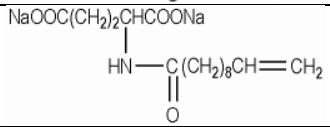
Cocoyl Glutamic Acid	 where RCO- represents the fatty acids derived from coconut oil.
Dipalmitoyl Cystine	
Dipotassium Capryloyl Glutamate	
Dipotassium Undecylenoyl Glutamate	
Disodium Capryloyl Glutamate	
Disodium Cocoyl Glutamate	 where RCO- represents the fatty acids derived from coconut oil.
Disodium 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	

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

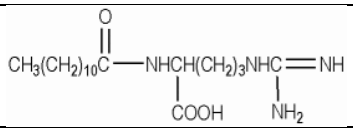
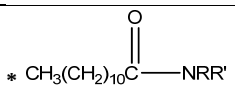
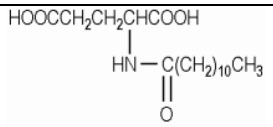
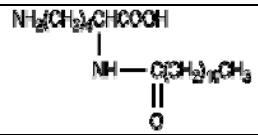
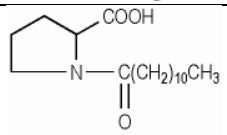
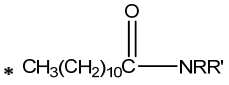
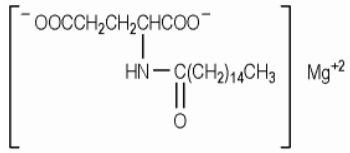
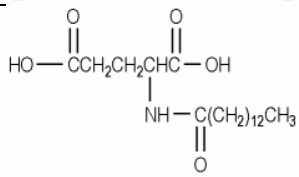
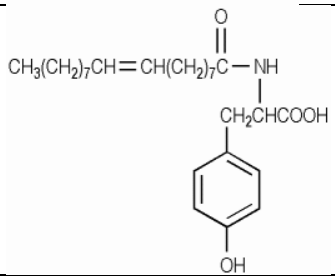
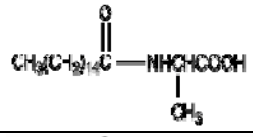
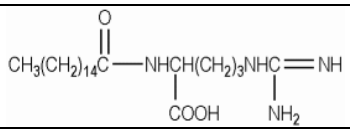
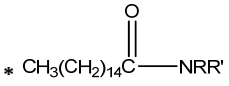
Lauroyl Arginine	
Lauroyl Collagen Amino Acids	 where NRR' represents the amino acid residues from collagen
Lauroyl Glutamic Acid	
Lauroyl Lysine	
Lauroyl Proline	
Lauroyl Silk Amino Acids	 where NRR' represents the amino acid residues from silk
Magnesium Palmitoyl Glutamate	
Myristoyl Glutamic Acid	
Oleoyl Tyrosine	
Palmitoyl Alanine	
Palmitoyl Arginine	
Palmitoyl Collagen Amino Acids	 where NRR' represents the amino acid residues from collagen

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

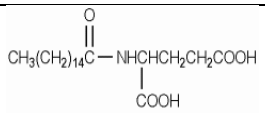
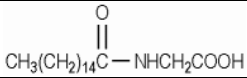
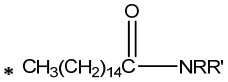
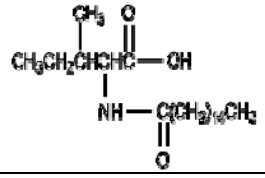
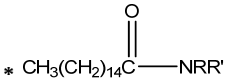
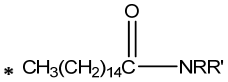
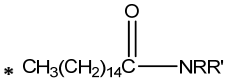
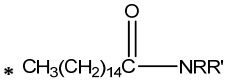
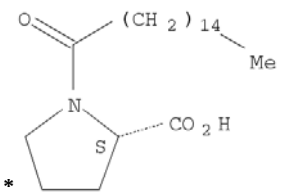
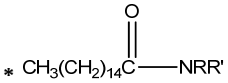
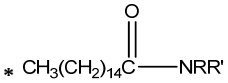
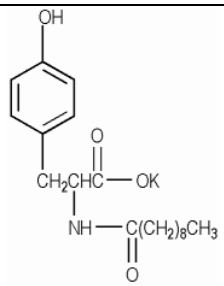
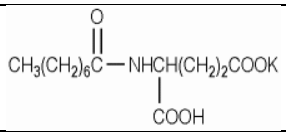
Palmitoyl Glutamic Acid	
Palmitoyl Glycine	
Palmitoyl Gold of Pleasure Amino Acids	*  where NRR' represents the amino acid residues from gold of pleasure
Palmitoyl Isoleucine	
Palmitoyl Keratin Amino Acids	*  where NRR' represents the amino acid residues from keratin
Palmitoyl Millet Amino Acids	*  where 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	

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

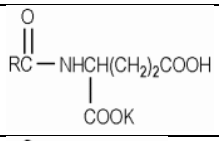
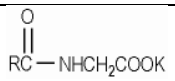
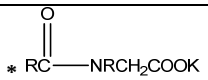
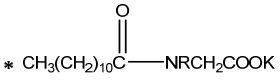
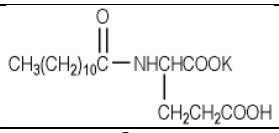
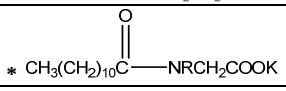
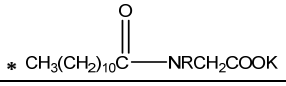
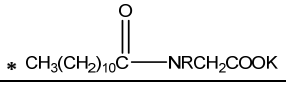
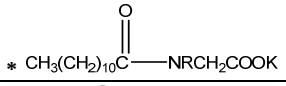
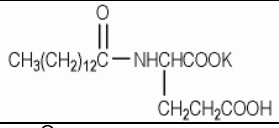
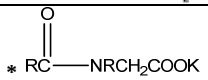
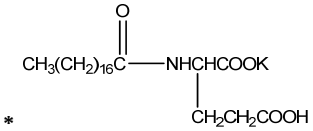
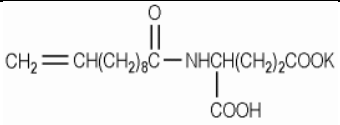
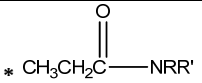
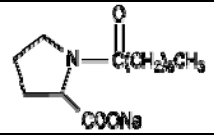
Potassium Cocoyl Glutamate	 where RCO- represents the fatty acids derived from coconut oil.
Potassium Cocoyl Glycinate	 where RCO- represents the cocoyl moiety.
Potassium Cocoyl Rice Amino Acids	*  where RCO- represents the cocoyl moiety and $NRCH_2COOK$ represents the salt of the rice amino acid residues
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	

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

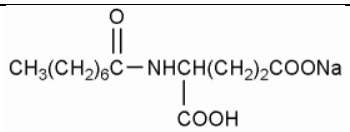
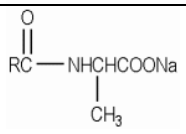
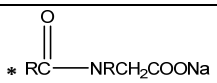
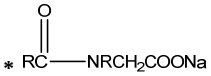
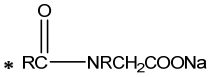
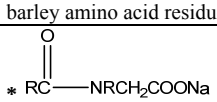
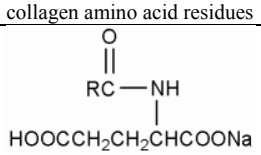
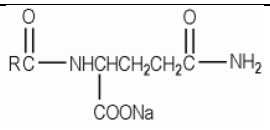
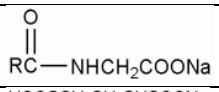
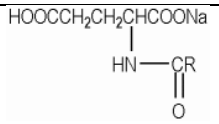
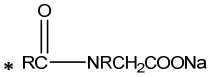
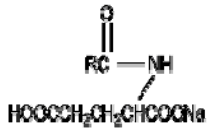
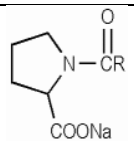
Sodium Capryloyl Glutamate	
Sodium Cocoyl Alaninate	 where RCO- represents the fatty acids derived from coconut oil.
Sodium Cocoyl Amino Acids	 where RCO- represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of amino acid residues
Sodium Cocoyl Apple Amino Acids	 where RCO- represents the 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.

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

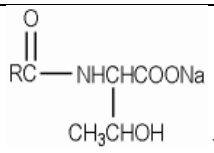
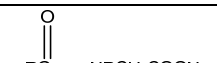
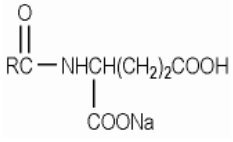
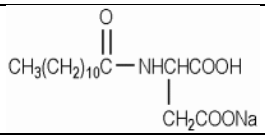
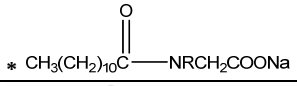
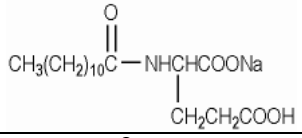
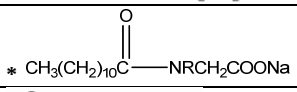
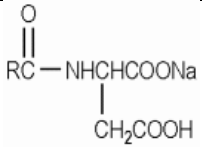
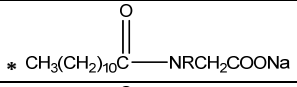
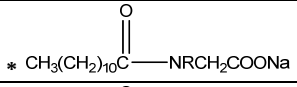
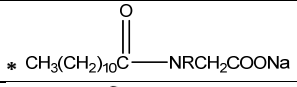
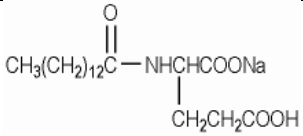
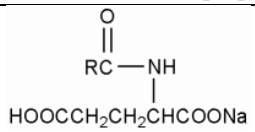
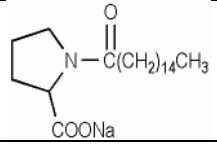
Sodium Cocoyl Threoninate		where RCO- represents the fatty acids derived from Cocos Nucifera (Coconut) Oil
Sodium Cocoyl Wheat Amino Acids		where RCO- represents the cocoyl moiety and $NRCH_2COONa$ represents the salt of wheat amino acid residues
Sodium Hydrogenated Tallowoyl Glutamate		where RCO- represents 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		

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

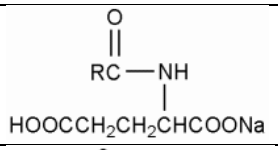
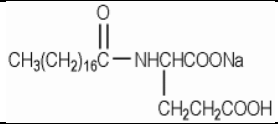
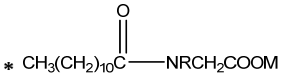
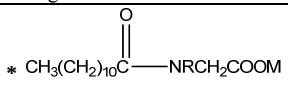
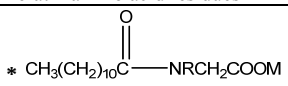
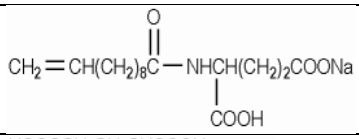
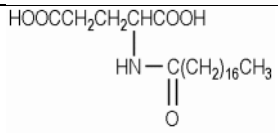
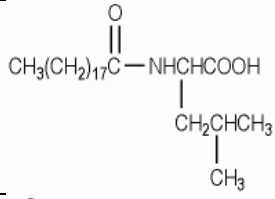
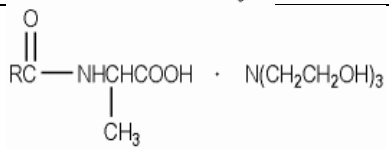
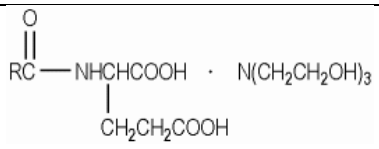
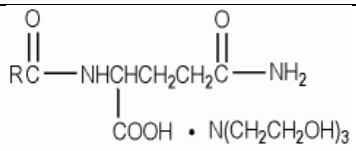
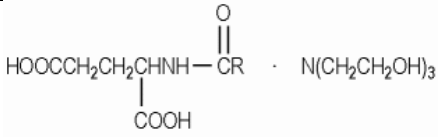
Sodium Palmoyl Glutamate		where RCO- represents the palmoyl radical.
Sodium Stearoyl Glutamate		
Sodium/TEA-Lauroyl Collagen Amino Acids		where $NRCH_2COOM$ represents the mixture of sodium and TEA salts of the collagen amino acid residues
Sodium/TEA-Lauroyl Keratin Amino Acids		where $NRCH_2COOM$ represents 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.

Table 3. Idealized structures of the ingredients in this safety assessment.[18] (The asterisk marked structures below represent additions made by CIR staff.)

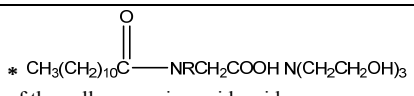
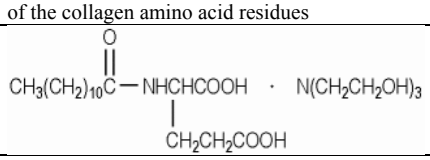
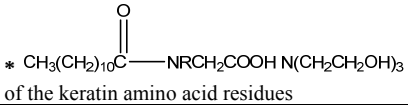
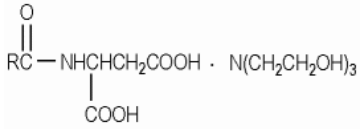
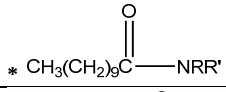
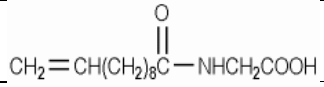
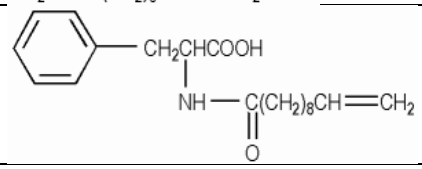
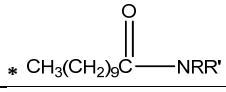
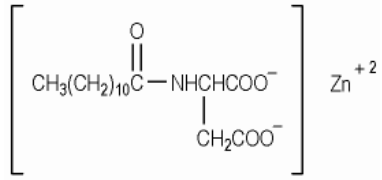
TEA-Lauroyl Collagen Amino Acids	 where $NRCH_2COOH\ N(CH_2CH_2OH)_3$ represents the TEA salt of the collagen amino acid residues
TEA-Lauroyl Glutamate	
TEA-Lauroyl Keratin Amino Acids	 where $NRCH_2COOH\ N(CH_2CH_2OH)_3$ represents the TEA salt of the keratin amino acid residues
TEA-Lauroyl/Myristoyl 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	

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	[31]
Molecular Volume cm^3/mol @ 20 ºC	126.0	[31]
Density/Specific Gravity @ 20 ºC	1.294	[31]
Vapor pressure mmHg@ 25 ºC	8.68×10^{-8}	[31]
Melting Point ºC	109-110	Merck
Boiling Point ºC	407.7	[31]
Solubility	Freely sol in water, alcohol. Practically insol in chloroform, ether	Merck
logP @ 25 ºC	-0.696	[31]
Disassociation constants (pKa, pKb) @ 25 ºC	3.25 most acidic; -0.91 most basic	[31]
Acetyl Glutamic Acid		
Molecular Weight g/mol	189.17	[31]
Molecular Volume cm^3/mol @ 20 ºC	139.6	[31]
Density/Specific Gravity @ 20 ºC	1.354	[31]
Vapor pressure mmHg@ 25 ºC	3.48×10^{-11}	[31]
Boiling Point ºC	495.9	[31]
logP @ 25 ºC	-2.131	[31]
Disassociation constants (pKa) @ 25ºC	3.45 most acidic; -0.86 most basic	[31]
Acetyl Glutamine		
Physical Form	Crystals from ethanol	Merck
Molecular Weight g/mol	188.18	[31]
Molecular Volume cm^3/mol @ 20 ºC	145.8	[31]
Density/Specific Gravity @ 20 ºC	1.290	[31]
Vapor pressure mmHg@ ºC	1.28×10^{-8}	[31]
Melting Point ºC	197	Merck
Boiling Point ºC	430.5	[31]
logP @ 25 ºC	-2.215	[31]
Disassociation constants (pKa) @ 25ºC	2.19 most acidic; 9.19 most basic	[31]

Table 4. Chemical properties of amino acids alkyl amides

Acetyl Methionine		
Physical Form	Crystals; large prisms from water (DL-); plates from water or ethyl acetate (D-)	Merck
Molecular Weight g/mol	191.25	[31]
Molecular Volume cm^3/mol @ 20 °C	158.9	[31]
Density/Specific Gravity @ 20 °C	1.202	[31]
Vapor pressure mmHg@ °C	1.72×10^{-9}	[31]
Melting Point °C	102-104; 114-115 (DL-); 104-105 (D-)	Merck
Boiling Point °C	453.6	[31]
Water Solubility g/100 ml @ 25 °C	9.12 (DL-); 30.7 (D-)	Merck
Other Solubility g/100 ml @ 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 @ 25 °C	-0.885	[31]
Disassociation constants (pKa) @ 25°C	3.50 most acidic; -0.84 most basic	[31]
Acetyl Tyrosine		
Molecular Weight g/mol	223.23	[31]
Molecular Volume cm^3/mol @ 20 °C	171.1	[31]
Density/Specific Gravity @ 20 °C	1.304	[31]
Vapor pressure mmHg@ °C	4.07×10^{-12}	[31]
Boiling Point °C	531.3	[31]
logP @ 25 °C	-1.676	[31]
Disassociation constants (pKa) @ 25°C	3.15 most acidic; -0.83 most basic	[31]
Capryloyl Glycine		
Molecular Weight g/mol	201.26	[31]
Molecular Volume cm^3/mol @ 20 °C	194.1	[31]
Density/Specific Gravity @ 20 °C	1.036	[31]
Vapor pressure mmHg@ °C	1.19×10^{-7}	[31]
Boiling Point °C	403.9	[31]
logP @ 25 °C	1.065	[31]
Disassociation constants (pKa) @ 25°C	3.62 most acidic; -0.98 most basic	[31]
Dipalmitoyl Cystine		
Molecular Weight g/mol	717.12	[31]
Molecular Volume cm^3/mol @ 20 °C	685.6	[31]
Density/Specific Gravity @ 20 °C	1.045	[31]
Vapor pressure mmHg@ 25 °C	3.93×10^{-32}	[31]
Boiling Point °C	852.2	[31]
logP @ 25 °C	12.988	[31]
Disassociation constants (pKa) @ 25°C	2.93 most acidic; -0.63 most basic	[31]

Table 4. Chemical properties of amino acids alkyl amides

Disodium Capryloyl Glutamate		
Physical Form @ 20 °C	Clear to light turbid liquid	[32]
Color	Colorless to light yellow	[32]
pH @ 20 °C	9.0-10.5	[32]
Lauroyl Arginine		
Molecular Weight g/mol	356.50	[31]
Molecular Volume cm^3/mol @ 20 °C	316.2	[31]
Density/Specific Gravity @ 20 °C	1.12	[31]
logP @ 25 °C	2.547	[31]
Disassociation constants (pKa) @ 25°C	3.60 most acidic; 13.84 most basic	[31]
Lauroyl Glutamic Acid		
Molecular Weight g/mol	329.43	[31]
Molecular Volume cm^3/mol @ 20 °C	304.7	[31]
Density/Specific Gravity @ 20 °C	1.081	[31]
Vapor pressure mmHg@ °C	2.95×10^{-13}	[31]
Melting Point °C	95-96	[11]
Boiling Point °C	543.6	[31]
logP @ 25 °C	2.964	[31]
Disassociation constants (pKa) @ 25°C	3.46 most acidic; -0.88 most basic	[31]
Lauroyl Proline		
Molecular Weight g/mol	297.43	[31]
Molecular Volume cm^3/mol @ 20 °C	288.3	[31]
Density/Specific Gravity @ 20 °C	1.031	[31]
Vapor pressure mmHg@ °C	6.01×10^{-10}	[31]
Boiling Point °C	465.3	[31]
logP @ 25 °C	5.356	[31]
Disassociation constants (pKa) @ 25°C	3.70 most acidic; -2.37 most basic	[31]
Palmitoyl Alanine		
Molecular Weight g/mol	327.50	[31]
Molecular Volume cm^3/mol @ 20 °C	343.1	[31]
Density/Specific Gravity @ 20 °C	0.954	[31]
Vapor pressure mmHg@ °C	2.73×10^{-11}	[31]
Boiling Point °C	498.4	[31]
logP @ 25 °C	5.495	[31]
Disassociation constants (pKa) @ 25°C	3.69 most acidic; -0.81 most basic	[31]

Table 4. Chemical properties of amino acids alkyl amides

Palmitoyl Arginine		
Molecular Weight g/mol	412.61	[31]
Molecular Volume cm^3/mol @ 20 °C	380.5	[31]
Density/Specific Gravity @ 20 °C	1.08	[31]
logP @ 25 °C	4.585	[31]
Disassociation constants (pKa) @ 25°C	3.60 most acidic; 13.84 most basic	[31]
Palmitoyl Glutamic Acid		
Molecular Weight g/mol	385.54	[31]
Molecular Volume cm^3/mol @ 20 °C	370.7	[31]
Density/Specific Gravity @ 20 °C	1.039	[31]
Vapor pressure mmHg@ °C	5.17×10^{-15}	[31]
Boiling Point °C	581.1	[31]
logP @ 25 °C	5.002	[31]
Disassociation constants (pKa) @ 25°C	3.46 most acidic; -0.88 most basic	[31]
Palmitoyl Glycine		
Molecular Weight g/mol	313.48	[31]
Molecular Volume cm^3/mol @ 20 °C	326.2	[31]
Density/Specific Gravity @ 20 °C	0.960	[31]
Vapor pressure mmHg@ °C	5.13×10^{-11}	[31]
Melting Point °C	122-125	[11]
Boiling Point °C	491.8	[31]
logP @ 25 °C	5.141	[31]
Disassociation constants (pKa) @ 25°C	3.59 most acidic; -1.01 most basic	[31]
Palmitoyl Isoleucine		
Molecular Weight g/mol	369.58	[31]
Molecular Volume cm^3/mol @ 20 °C	392.9	[31]
Density/Specific Gravity @ 20 °C	0.940	[31]
Vapor pressure mmHg@ °C	1.44×10^{-12}	[31]
Boiling Point °C	528.2	[31]
logP @ 25 °C	6.867	[31]
Disassociation constants (pKa) @ 25°C	3.67 most acidic; -0.81 most basic	[31]
Palmitoyl Proline		
Molecular Weight g/mol	353.54	[31]
Molecular Volume cm^3/mol @ 20 °C	354.3	[31]
Density/Specific Gravity @ 20 °C	0.997	[31]
Vapor pressure mmHg@ °C	7.58×10^{-12}	[31]

Table 4. Chemical properties of amino acids alkyl amides

Boiling Point ºC	511.6	[31]
logP @ 25 ºC	7.394	[31]
Disassociation constants (pKa) @ 25ºC	3.69 most acidic; -2.37 most basic	[31]
Sodium Lauroyl Glutamate		
Physical Form @ 20 ºC	Clear to slightly turbid liquid	[28]
Color	Colorless to slightly yellow	[28]
Stearoyl Glutamic Acid		
Molecular Weight g/mol	413.594	[33]
Molecular Volume cm^3/mol @ 20 ºC	403.7	[31]
Density/Specific Gravity @ 20 ºC	1.024	[31]
Vapor pressure mmHg@ ºC	5.85×10^{-16}	[31]
Melting Point ºC	154.75	[33]
Boiling Point ºC	600.3	[31]
logP @ 25 ºC	6.021	[31]
Disassociation constants (pKa) @ 25ºC	3.46 most acidic; -0.88 most basic	[31]
Stearoyl Leucine		
Molecular Weight g/mol	397.63	[31]
Molecular Volume cm^3/mol @ 20 ºC	426.0	[31]
Density/Specific Gravity @ 20 ºC	0.933	[31]
Vapor pressure mmHg@ ºC	1.41×10^{-13}	[31]
Melting Point ºC	64-65	[13]
Boiling Point ºC	550.6	[31]
logP @ 25 ºC	7.886	[31]
Disassociation constants (pKa) @ 25ºC	3.67 most acidic; -0.81 most basic	[31]
Undecylenoyl Phenylalanine		
Molecular Weight g/mol	331.45	[31]
Molecular Volume cm^3/mol @ 20 ºC	316.3	[31]
Density/Specific Gravity @ 20 ºC	1.047	[31]
Vapor pressure mmHg@ ºC	1.70×10^{-12}	[31]
Boiling Point ºC	540.0	[31]
logP @ 25 ºC	3.155	[31]
Disassociation constants (pKa) @ 25ºC	3.63 most acidic; -0.82 most basic	[31]

Table 5a. Frequency and concentration of use (2012-2013) according to duration and type of exposure for Amino Acid Alkyl Amides.[19-22]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Acetyl Cysteine		**Acetyl Glutamine**		**Acetyl Methionine**	
Totals*	**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[a]	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 - Non-Coloring	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*	**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 - Non-Coloring	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*	**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[b]	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 - Non-Coloring	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	0.6-2[c]	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 5a. Frequency and concentration of use (2012-2013) according to duration and type of exposure for Amino Acid Alkyl Amides.[19-22]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc 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 - Non-Coloring	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*	**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 - Non-Coloring	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*	**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[d]
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 - Non-Coloring	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

Table 5a. Frequency and concentration of use (2012-2013) according to duration and type of exposure for Amino Acid Alkyl Amides.[19-22]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Oleoyl Tyrosine		**Palmitoyl Collagen Amino Acids**		**Palmitoyl Glycine**	
Totals*	**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 - Non-Coloring	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*	**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*	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	0.3**	NR	NR
Dermal Contact	4	NR	14	0.0017-0.46	2	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	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*	**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 - Non-Coloring	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

Table 5a. Frequency and concentration of use (2012-2013) according to duration and type of exposure for Amino Acid Alkyl Amides.[20]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Potassium Myristoyl Glutamate		**Sodium Cocoyl Alaninate**		**Sodium Cocoyl Amino Acids**	
Totals*	**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[e]
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 - Non-Coloring	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**	
Totals*	**21**	**0.3-3**	**13**	**0.02**	**178**	**0.004-10**
Duration of Use						
Leave-On	10	0.3	3	0.02	66	0.004-3
Rinse-Off	11	*0.5-3*	10	0.02	110	0.01-10
Diluted for (Bath) Use	NR	NR	NR	NR	2	NR
Exposure Type						
Eye Area	7	0.3	1	NR	8	0.004-0.6
Incidental Ingestion	NR	NR	NR	NR	7	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	0.03[f]
Incidental Inhalation-Powder	NR	NR	NR	NR	1	NR
Dermal Contact	18	0.3-3	2	NR	114	0.004-9
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	3	0.5	11	0.02	27	0.2-10
Hair-Coloring	NR	NR	NR	NR	30	3
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	4	NR	1	NR	31	0.2-3
Baby Products	NR	NR	NR	NR	NR	NR

	Sodium Cocoyl Glycinate		**Sodium Hydrogenated Tallowoyl Glutamate**		**Sodium Lauroyl Aspartate**	
Totals*	**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 - Non-Coloring	NR	NR	NR	NR	NR	2
Hair-Coloring	NR	NR	NR	NR	NR	NR
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

Table 5a. Frequency and concentration of use (2012-2013) according to duration and type of exposure for Amino Acid Alkyl Amides.[20]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Sodium Lauroyl Glutamate		**Sodium Lauroyl Oat Amino Acids**		**Sodium Lauroyl Wheat Amino Acids**	
Totals*	**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 - Non-Coloring	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*	**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 - Non-Coloring	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*	**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[g]	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 - Non-Coloring	6	0.03-0.2	NR	NR	2	2-10
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

Table 5a. Frequency and concentration of use (2012-2013) according to duration and type of exposure for Amino Acid Alkyl Amides.[20]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	TEA-Lauroyl Collagen Amino Acids		**TEA-Lauroyl Glutamate**		**Undecylenoyl Collagen Amino Acids**	
Totals*	**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 - Non-Coloring	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*	**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 - Non-Coloring	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

[a]1% in a face and neck spray.

[b]0.3% in a foundation spray.

[c]0.6% in hand soap categorized as "other personal cleanliness product".

[d]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.

[e]0.4% in pump hair spray.

[f]0.03% in a foundation spray.

[g]0.2% in an indoor tanning product, 0.3% in a body and hand spray

*0.46% in a body and hand spray, 0.65% in a pump hair spray.

**0.3% in a face powder

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

Table 6. Genotoxicity

Concentration/Dose	Method	Results	Reference
In Vitro			
ACETYL GLUTAMIC ACID			
333 to 5000 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, 1250, 2500, and 5000 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 2230 µg/mL under 3 h and 22 h 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	[32]
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	[38]
In Vivo			
ACETYL GLUTAMIC ACID			
500, 1000, or 2000 mg/kg	Bone marrow micronucleus assay in groups of 5 male and 5 female ICR mice.	No increased incidence of micronucleated polychromatic erythrocytes	[34]

Table 7. Dermal irritation studies.

Ingredient	Concentration	Method	Results	Reference
Non-Human				
Acetyl Proline	8% in a cream tested neat	MatTek EpiDerm assay	Very mild irritant	[39]
Disodium Capryloyl Glutamate	5% of a solution containing 37%-41% test material	MTT Viability assay	Not irritating	[32]
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.	[40]
Human				
Acetyl Proline	10% in a cream evaluated for treatment of eczema or active atopic dermatitis	Double-blind, randomized controlled usage study in 15 subjects where test material was applied to target lesion twice/day for 14 days	1subject had an acute chronic dermatitis reaction that was considered related to the test material	[41]
Acetyl Tyrosinamide	2% in a gel formulation	48-h patch test in 53 volunteers; semi-occluded	Not irritating	[42]
Acetyl Tyrosinamide	1.25%-2% in several gel and skin plumping cream formulations	48-h patch test in 51 volunteers; semi-occluded	1 subject had moderate erythema and edema post-application that became mild at the 72-h observation to the skin plumping cream containing 1.25% test material, another subject had mild erythema and edema 48-h to the same skin plumping cream formulation, which was barely perceptible at 72-h – this same subject had a barely perceptible erythema at 48-h to the skin plumping cream containing 2% of the test material, no reaction was observed at 72-h. The study concluded that the test material was not irritating in all formulations tested.	[43]
Disodium Capryloyl Glutamate	18% of a solution containing 37%-41% test material	Patch test with Finn Chambers in 20 volunteers; occluded	Not irritating	[32]
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	[38]
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 h. Application sites were measured for transepidermal water loss (TEWL) and graded for irritation reactions.	TEWL values of 1% SLG were significantly higher than those of the deionized water control.	[44]
Sodium Lauroyl Silk Amino Acids	6% active solution	HPT for irritancy in 20 volunteers, patches occluded	Minimally irritating. Cutaneous irritation index after 24h = 10.0, after 48 h = 2.5.	[45]

Table 8. Ocular irritation studies.

Ingredient	Concentration	Method	Results	Reference
Non-Human – In Vitro				
Acetyl Tyrosinamide	1.25% neat	EpiOcular irritation study	Not irritating	[46]
Disodium Caprylolyl Glutamate	2% as received	HET-CAM method	Not irritating	[32]
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	[47,48]
Sodium Lauroyl Glutamate	5% active matter	HET-CAM method	Not irritating	[38]
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%.	[49]
Sodium Lauroyl Silk Amino Acids	2.5% of a 20% solution	HET-CAM method	Slight irritation potential	[50]
Non-Human – In Vivo				
Lauroyl Arginine + mixture of collagen polypeptides with MW < 1000 Da	10%, pH adjusted to 7.0	Draize method in 6 male albino rabbits	Mean score was 7.5, not irritating	[51]
Human				
Acetyl Hydroxyproline	2% in a gel under eye treatment	4 week in-use study in 33 women; half contact lens wearers and half non-contact lens wearers	No adverse events during the study and no ophthalmic irritation potential	[52]
Acetyl Tyrosinamide	2% in a gel under eye treatment	4 week in-use study in 33 women; half contact lens wearers and half non-contact lens wearers	No adverse events during the study and no ophthalmic irritation potential	[53]

Table 9. Dermal sensitization studies.

Ingredient	Concentration	Method	Results	Reference
Non-Human				
Sodium Lauroyl Silk Amino Acids	25%, 50%, or 100% of a 20% solution in butanone	LLNA	Non-sensitizing. SI at 100% = 2.61	[54]
Human				
Acetyl Hydroxyproline	2% in a plumper gel	HRIPT in 109 volunteers; semi-occluded	Not irritating or sensitizing	[55]
Acetyl Proline	10% in a cream	HRIPT in 107 volunteers; semi-occluded	Not irritating or sensitizing	[56]
Acetyl Tyrosinamide	1% neat	HRIPT to a sodium lauryl sulfate pre-treated site with 26 volunteers; occluded	Non-sensitizing	[57]
Acetyl Tyrosinamide	2% in a plumper gel	HRIPT in 109 volunteers; semi-occluded	Not irritating or sensitizing	[58]
Disodium Capryloyl Glutamate	18% of a solution containing 37%-41% test material	Patch test with Finn Chambers in 20 volunteers; occluded	Non- sensitizing	[32]
Sodium Cocoyl Glutamate	5% active matter	Method not reported, but test was occluded	Non-sensitizing	[16]
Sodium Lauroyl Glutamate	5% active matter	Patch test with Finn Chambers in 20 volunteers; occluded	Non-sensitizing	[38]
Sodium Lauroyl Glutamate	10% dilution of a facial cream containing 30% test material	HRIPT in 103 volunteers; semi-occluded	Non-sensitizing	[59]
Sodium Lauroyl Glutamate	1% dilution of a skin cleansing product containing 22% test material	HRIPT in 55 volunteers	Four 1+ reactions during induction; non-sensitizing	[60]

Table 10. Phototoxicity and photosensitization

Ingredient	Concentration	Method	Results	Reference
Non-Human – In Vitro				
Acetyl Tyrosinamide	Eight doses up to 1000 µg/mL with and without UVA	Neutral red uptake assay in BALB/c 3T3 mouse fibroblasts	Not predicted to have phototoxic potential	[61]
Human				
Acetyl Tyrosinamide	1% neat	Human photocontact allergenicty assay with 25 volunteers; occluded	No photocontact-sensitizing potential	[62]
Sodium Cocoyl Glutamate	0.1%-5% aq. solutions	Not reported	No abnormality observed	[16]
Sodium Lauroyl Glutamate	0.1%-5% aq. solutions	Not reported	No abnormality observed	[15]

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2013 FDA VCRP RAW DATA

03B - Eyeliner	616911	ACETYL CYSTEINE	1
03G - Other Eye Makeup Preparations	616911	ACETYL CYSTEINE	3
05A - Hair Conditioner	616911	ACETYL CYSTEINE	3
05E - Rinses (non-coloring)	616911	ACETYL CYSTEINE	1
05F - Shampoos (non-coloring)	616911	ACETYL CYSTEINE	4
05G - Tonics, Dressings, and Other Hair Grooming Aids	616911	ACETYL CYSTEINE	1
05I - Other Hair Preparations	616911	ACETYL CYSTEINE	1
07C - Foundations	616911	ACETYL CYSTEINE	1
12F - Moisturizing	616911	ACETYL CYSTEINE	3
12G - Night	616911	ACETYL CYSTEINE	2
12H - Paste Masks (mud packs)	616911	ACETYL CYSTEINE	1
12I - Skin Fresheners	616911	ACETYL CYSTEINE	1
12J - Other Skin Care Preps	616911	ACETYL CYSTEINE	1
05A - Hair Conditioner	2490973	ACETYL GLUTAMINE	2
05F - Shampoos (non-coloring)	2490973	ACETYL GLUTAMINE	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	2490973	ACETYL GLUTAMINE	1
11G - Other Shaving Preparation Products	2490973	ACETYL GLUTAMINE	1
12F - Moisturizing	2490973	ACETYL GLUTAMINE	1
03B - Eyeliner	1115475	ACETYL METHIONINE	1
03G - Other Eye Makeup Preparations	1115475	ACETYL METHIONINE	3
05A - Hair Conditioner	1115475	ACETYL METHIONINE	1
05F - Shampoos (non-coloring)	1115475	ACETYL METHIONINE	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	1115475	ACETYL METHIONINE	1
05I - Other Hair Preparations	1115475	ACETYL METHIONINE	1
08A - Basecoats and Undercoats	1115475	ACETYL METHIONINE	1
03D - Eye Lotion	537553	ACETYL TYROSINE	1
03G - Other Eye Makeup Preparations	537553	ACETYL TYROSINE	1
05A - Hair Conditioner	537553	ACETYL TYROSINE	1
05E - Rinses (non-coloring)	537553	ACETYL TYROSINE	1
05F - Shampoos (non-coloring)	537553	ACETYL TYROSINE	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	537553	ACETYL TYROSINE	2
05I - Other Hair Preparations	537553	ACETYL TYROSINE	3
10E - Other Personal Cleanliness Products	537553	ACETYL TYROSINE	1
12A - Cleansing	537553	ACETYL TYROSINE	2
12C - Face and Neck (exc shave)	537553	ACETYL TYROSINE	2
12D - Body and Hand (exc shave)	537553	ACETYL TYROSINE	3
12F - Moisturizing	537553	ACETYL TYROSINE	4
12G - Night	537553	ACETYL TYROSINE	3
12I - Skin Fresheners	537553	ACETYL TYROSINE	1
13A - Suntan Gels, Creams, and Liquids	537553	ACETYL TYROSINE	1

13B - Indoor Tanning Preparations	537553	ACETYL TYROSINE	1
13C - Other Suntan Preparations	537553	ACETYL TYROSINE	1
02D - Other Bath Preparations	14246538	CAPRYLOYL GLYCINE	1
03C - Eye Shadow	14246538	CAPRYLOYL GLYCINE	1
03D - Eye Lotion	14246538	CAPRYLOYL GLYCINE	1
03G - Other Eye Makeup Preparations	14246538	CAPRYLOYL GLYCINE	1
04B - Perfumes	14246538	CAPRYLOYL GLYCINE	1
04E - Other Fragrance Preparation	14246538	CAPRYLOYL GLYCINE	1
05A - Hair Conditioner	14246538	CAPRYLOYL GLYCINE	1
05F - Shampoos (non-coloring)	14246538	CAPRYLOYL GLYCINE	8
05I - Other Hair Preparations	14246538	CAPRYLOYL GLYCINE	1
07A - Blushers (all types)	14246538	CAPRYLOYL GLYCINE	1
07C - Foundations	14246538	CAPRYLOYL GLYCINE	1
07I - Other Makeup Preparations	14246538	CAPRYLOYL GLYCINE	1
10A - Bath Soaps and Detergents	14246538	CAPRYLOYL GLYCINE	1
10B - Deodorants (underarm)	14246538	CAPRYLOYL GLYCINE	2
10C - Douches	14246538	CAPRYLOYL GLYCINE	3
10E - Other Personal Cleanliness Products	14246538	CAPRYLOYL GLYCINE	1
12A - Cleansing	14246538	CAPRYLOYL GLYCINE	12
12C - Face and Neck (exc shave)	14246538	CAPRYLOYL GLYCINE	9
12D - Body and Hand (exc shave)	14246538	CAPRYLOYL GLYCINE	6
12F - Moisturizing	14246538	CAPRYLOYL GLYCINE	14
12G - Night	14246538	CAPRYLOYL GLYCINE	1
12H - Paste Masks (mud packs)	14246538	CAPRYLOYL GLYCINE	2
12I - Skin Fresheners	14246538	CAPRYLOYL GLYCINE	1
12J - Other Skin Care Preps	14246538	CAPRYLOYL GLYCINE	4
07C - Foundations	999002859	DISODIUM CAPRYLOYL GLUTAMATE	1
12C - Face and Neck (exc shave)	999002859	DISODIUM CAPRYLOYL GLUTAMATE	1
03C - Eye Shadow	68187304	DISODIUM COCOYL GLUTAMATE	1
05F - Shampoos (non-coloring)	68187304	DISODIUM COCOYL GLUTAMATE	15
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	68187304	DISODIUM COCOYL GLUTAMATE	30
07A - Blushers (all types)	68187304	DISODIUM COCOYL GLUTAMATE	1
07B - Face Powders	68187304	DISODIUM COCOYL GLUTAMATE	2
07C - Foundations	68187304	DISODIUM COCOYL GLUTAMATE	4
10A - Bath Soaps and Detergents	68187304	DISODIUM COCOYL GLUTAMATE	5
10E - Other Personal Cleanliness Products	68187304	DISODIUM COCOYL GLUTAMATE	2
11E - Shaving Cream	68187304	DISODIUM COCOYL GLUTAMATE	1

12A - Cleansing	68187304	DISODIUM COCOYL GLUTAMATE	14
12D - Body and Hand (exc shave)	68187304	DISODIUM COCOYL GLUTAMATE	1
12A - Cleansing	999001859	DISODIUM LAUROYL GLUTAMATE	1
12C - Face and Neck (exc shave)	126139795	DISODIUM MALYL TYROSINATE	1
03C - Eye Shadow	20716307	DISODIUM STEAROYL GLUTAMATE	3
03F - Mascara	20716307	DISODIUM STEAROYL GLUTAMATE	2
03G - Other Eye Makeup Preparations	20716307	DISODIUM STEAROYL GLUTAMATE	10
07A - Blushers (all types)	20716307	DISODIUM STEAROYL GLUTAMATE	4
07B - Face Powders	20716307	DISODIUM STEAROYL GLUTAMATE	6
07C - Foundations	20716307	DISODIUM STEAROYL GLUTAMATE	56
07D - Leg and Body Paints	20716307	DISODIUM STEAROYL GLUTAMATE	1
07E - Lipstick	20716307	DISODIUM STEAROYL GLUTAMATE	3
07F - Makeup Bases	20716307	DISODIUM STEAROYL GLUTAMATE	4
07H - Makeup Fixatives	20716307	DISODIUM STEAROYL GLUTAMATE	2
07I - Other Makeup Preparations	20716307	DISODIUM STEAROYL GLUTAMATE	12
12C - Face and Neck (exc shave)	20716307	DISODIUM STEAROYL GLUTAMATE	9
12D - Body and Hand (exc shave)	20716307	DISODIUM STEAROYL GLUTAMATE	1
12F - Moisturizing	20716307	DISODIUM STEAROYL GLUTAMATE	15
12J - Other Skin Care Preps	20716307	DISODIUM STEAROYL GLUTAMATE	7
05F - Shampoos (non-coloring)	42492228	LAUROYL ARGININE	1
05A - Hair Conditioner	68920592	LAUROYL COLLAGEN AMINO ACIDS	1
03A - Eyebrow Pencil	52315750	LAUROYL LYSINE	8
03B - Eyeliner	52315750	LAUROYL LYSINE	10
03C - Eye Shadow	52315750	LAUROYL LYSINE	201
03D - Eye Lotion	52315750	LAUROYL LYSINE	4
03F - Mascara	52315750	LAUROYL LYSINE	37
03G - Other Eye Makeup Preparations	52315750	LAUROYL LYSINE	5

04B - Perfumes	52315750	LAUROYL LYSINE	2
04C - Powders (dusting and talcum, excluding aftershave talc)	52315750	LAUROYL LYSINE	1
04E - Other Fragrance Preparation	52315750	LAUROYL LYSINE	2
05A - Hair Conditioner	52315750	LAUROYL LYSINE	3
05E - Rinses (non-coloring)	52315750	LAUROYL LYSINE	1
07A - Blushers (all types)	52315750	LAUROYL LYSINE	65
07B - Face Powders	52315750	LAUROYL LYSINE	172
07C - Foundations	52315750	LAUROYL LYSINE	55
07D - Leg and Body Paints	52315750	LAUROYL LYSINE	1
07E - Lipstick	52315750	LAUROYL LYSINE	24
07F - Makeup Bases	52315750	LAUROYL LYSINE	3
07G - Rouges	52315750	LAUROYL LYSINE	9
07H - Makeup Fixatives	52315750	LAUROYL LYSINE	4
07I - Other Makeup Preparations	52315750	LAUROYL LYSINE	10
08E - Nail Polish and Enamel	52315750	LAUROYL LYSINE	1
12C - Face and Neck (exc shave)	52315750	LAUROYL LYSINE	8
12D - Body and Hand (exc shave)	52315750	LAUROYL LYSINE	1
12F - Moisturizing	52315750	LAUROYL LYSINE	14
12H - Paste Masks (mud packs)	52315750	LAUROYL LYSINE	2
12J - Other Skin Care Preps	52315750	LAUROYL LYSINE	3
13B - Indoor Tanning Preparations	52315750	LAUROYL LYSINE	2
13C - Other Suntan Preparations	52315750	LAUROYL LYSINE	1
12J - Other Skin Care Preps	58725396	LAUROYL PROLINE	1
05F - Shampoos (non-coloring)	999002635	LAUROYL SILK AMINO ACIDS	1
12F - Moisturizing	999002635	LAUROYL SILK AMINO ACIDS	1
07C - Foundations	999001497	MAGNESIUM PALMITOYL GLUTAMATE	1
08G - Other Manicuring Preparations	999001497	MAGNESIUM PALMITOYL GLUTAMATE	1
12C - Face and Neck (exc shave)	999001497	MAGNESIUM PALMITOYL GLUTAMATE	4
12F - Moisturizing	999001497	MAGNESIUM PALMITOYL GLUTAMATE	5
12G - Night	999001497	MAGNESIUM PALMITOYL GLUTAMATE	2
12I - Skin Fresheners	999001497	MAGNESIUM PALMITOYL GLUTAMATE	1
12J - Other Skin Care Preps	999001497	MAGNESIUM PALMITOYL GLUTAMATE	1
13B - Indoor Tanning Preparations	999002305	OLEOYL TYROSINE	1
13C - Other Suntan Preparations	999002305	OLEOYL TYROSINE	2
12E - Foot Powders and Sprays	977098820	PALMITOYL COLLAGEN AMINO ACIDS	1

03D - Eye Lotion	2441410	PALMITOYL GLYCINE	1
03G - Other Eye Makeup Preparations	2441410	PALMITOYL GLYCINE	2
12G - Night	2441410	PALMITOYL GLYCINE	2
05A - Hair Conditioner	977158374	PALMITOYL KERATIN AMINO ACIDS	1
12D - Body and Hand (exc shave)	977158374	PALMITOYL KERATIN AMINO ACIDS	2
12F - Moisturizing	977158374	PALMITOYL KERATIN AMINO ACIDS	2
07C - Foundations	59441326	PALMITOYL PROLINE	1
08G - Other Manicuring Preparations	59441326	PALMITOYL PROLINE	1
12C - Face and Neck (exc shave)	59441326	PALMITOYL PROLINE	4
12F - Moisturizing	59441326	PALMITOYL PROLINE	5
12G - Night	59441326	PALMITOYL PROLINE	2
12I - Skin Fresheners	59441326	PALMITOYL PROLINE	1
12J - Other Skin Care Preps	59441326	PALMITOYL PROLINE	1
07C - Foundations	977169871	PALMITOYL SILK AMINO ACIDS	2
12A - Cleansing	977100085	POTASSIUM COCOYL GLUTAMATE	6
02D - Other Bath Preparations	999001480	POTASSIUM COCOYL GLYCINATE	1
10A - Bath Soaps and Detergents	999001480	POTASSIUM COCOYL GLYCINATE	2
10E - Other Personal Cleanliness Products	999001480	POTASSIUM COCOYL GLYCINATE	1
12A - Cleansing	999001480	POTASSIUM COCOYL GLYCINATE	12
10E - Other Personal Cleanliness Products	977166930	POTASSIUM LAUROYL WHEAT AMINO ACIDS	1
12A - Cleansing	977166930	POTASSIUM LAUROYL WHEAT AMINO ACIDS	3
12A - Cleansing	977185559	POTASSIUM MYRISTOYL GLUTAMATE	5
01C - Other Baby Products	90170459	SODIUM COCOYL ALANINATE	2
03G - Other Eye Makeup Preparations	90170459	SODIUM COCOYL ALANINATE	2
05F - Shampoos (non-coloring)	90170459	SODIUM COCOYL ALANINATE	2
12A - Cleansing	90170459	SODIUM COCOYL ALANINATE	2
05A - Hair Conditioner	999001175	SODIUM COCOYL AMINO ACIDS	2
05F - Shampoos (non-coloring)	999001175	SODIUM COCOYL AMINO ACIDS	4
05G - Tonics, Dressings, and Other Hair Grooming Aids	999001175	SODIUM COCOYL AMINO ACIDS	5

05H - Wave Sets	999001175	SODIUM COCOYL AMINO ACIDS	1
06D - Hair Shampoos (coloring)	999001175	SODIUM COCOYL AMINO ACIDS	1
07C - Foundations	999001175	SODIUM COCOYL AMINO ACIDS	1
10A - Bath Soaps and Detergents	999001175	SODIUM COCOYL AMINO ACIDS	1
11A - Aftershave Lotion	999001175	SODIUM COCOYL AMINO ACIDS	1
12A - Cleansing	999001175	SODIUM COCOYL AMINO ACIDS	2
12D - Body and Hand (exc shave)	999001175	SODIUM COCOYL AMINO ACIDS	1
12F - Moisturizing	999001175	SODIUM COCOYL AMINO ACIDS	1
12J - Other Skin Care Preps	999001175	SODIUM COCOYL AMINO ACIDS	1
03B - Eyeliner	999002683	SODIUM COCOYL APPLE AMINO ACIDS	7
05F - Shampoos (non-coloring)	999002683	SODIUM COCOYL APPLE AMINO ACIDS	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	999002683	SODIUM COCOYL APPLE AMINO ACIDS	2
10E - Other Personal Cleanliness Products	999002683	SODIUM COCOYL APPLE AMINO ACIDS	4
12A - Cleansing	999002683	SODIUM COCOYL APPLE AMINO ACIDS	4
12H - Paste Masks (mud packs)	999002683	SODIUM COCOYL APPLE AMINO ACIDS	2
12J - Other Skin Care Preps	999002683	SODIUM COCOYL APPLE AMINO ACIDS	1
03B - Eyeliner	977166054	SODIUM COCOYL COLLAGEN AMINO ACID	1
05A - Hair Conditioner	977166054	SODIUM COCOYL COLLAGEN AMINO ACID	9
05G - Tonics, Dressings, and Other Hair Grooming Aids	977166054	SODIUM COCOYL COLLAGEN AMINO ACID	1
05I - Other Hair Preparations	977166054	SODIUM COCOYL COLLAGEN AMINO ACID	1
10E - Other Personal Cleanliness Products	977166054	SODIUM COCOYL COLLAGEN AMINO ACID	1
02B - Bubble Baths	68187326	SODIUM COCOYL GLUTAMATE	1
02D - Other Bath Preparations	68187326	SODIUM COCOYL GLUTAMATE	1
03B - Eyeliner	68187326	SODIUM COCOYL GLUTAMATE	2
03C - Eye Shadow	68187326	SODIUM COCOYL GLUTAMATE	1
03D - Eye Lotion	68187326	SODIUM COCOYL GLUTAMATE	2
03G - Other Eye Makeup Preparations	68187326	SODIUM COCOYL GLUTAMATE	3
05A - Hair Conditioner	68187326	SODIUM COCOYL GLUTAMATE	1
05F - Shampoos (non-coloring)	68187326	SODIUM COCOYL GLUTAMATE	22

05G - Tonics, Dressings, and Other Hair Grooming Aids	68187326	SODIUM COCOYL GLUTAMATE	1
05I - Other Hair Preparations	68187326	SODIUM COCOYL GLUTAMATE	3
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	68187326	SODIUM COCOYL GLUTAMATE	30
07A - Blushers (all types)	68187326	SODIUM COCOYL GLUTAMATE	1
07B - Face Powders	68187326	SODIUM COCOYL GLUTAMATE	1
07C - Foundations	68187326	SODIUM COCOYL GLUTAMATE	9
09A - Dentifrices	68187326	SODIUM COCOYL GLUTAMATE	6
09C - Other Oral Hygiene Products	68187326	SODIUM COCOYL GLUTAMATE	1
10A - Bath Soaps and Detergents	68187326	SODIUM COCOYL GLUTAMATE	12
10E - Other Personal Cleanliness Products	68187326	SODIUM COCOYL GLUTAMATE	10
11E - Shaving Cream	68187326	SODIUM COCOYL GLUTAMATE	1
12A - Cleansing	68187326	SODIUM COCOYL GLUTAMATE	26
12C - Face and Neck (exc shave)	68187326	SODIUM COCOYL GLUTAMATE	9
12D - Body and Hand (exc shave)	68187326	SODIUM COCOYL GLUTAMATE	7
12F - Moisturizing	68187326	SODIUM COCOYL GLUTAMATE	11
12G - Night	68187326	SODIUM COCOYL GLUTAMATE	4
12H - Paste Masks (mud packs)	68187326	SODIUM COCOYL GLUTAMATE	1
12I - Skin Fresheners	68187326	SODIUM COCOYL GLUTAMATE	4
12J - Other Skin Care Preps	68187326	SODIUM COCOYL GLUTAMATE	8
07C - Foundations	90387749	SODIUM COCOYL GLYCINATE	1
10E - Other Personal Cleanliness Products	90387749	SODIUM COCOYL GLYCINATE	10
12A - Cleansing	90387749	SODIUM COCOYL GLYCINATE	21
12A - Cleansing	977067450	SODIUM HYDROGENATED TALLOW GLUTAMATE	1
12C - Face and Neck (exc shave)	977067450	SODIUM HYDROGENATED TALLOW GLUTAMATE	1
03B - Eyeliner	41489183	SODIUM LAUROYL ASPARTATE	1
03C - Eye Shadow	41489183	SODIUM LAUROYL ASPARTATE	1
07G - Rouges	41489183	SODIUM LAUROYL ASPARTATE	2
01A - Baby Shampoos	29923317	SODIUM LAUROYL GLUTAMATE	2
02B - Bubble Baths	29923317	SODIUM LAUROYL GLUTAMATE	5
03E - Eye Makeup Remover	29923317	SODIUM LAUROYL GLUTAMATE	1
04C - Powders (dusting and talcum, excluding aftershave talc)	29923317	SODIUM LAUROYL GLUTAMATE	1
05F - Shampoos (non-coloring)	29923317	SODIUM LAUROYL GLUTAMATE	19
10A - Bath Soaps and Detergents	29923317	SODIUM LAUROYL GLUTAMATE	12
10E - Other Personal Cleanliness Products	29923317	SODIUM LAUROYL GLUTAMATE	3

11G - Other Shaving Preparation Products	29923317	SODIUM LAUROYL GLUTAMATE	1
12A - Cleansing	29923317	SODIUM LAUROYL GLUTAMATE	24
12D - Body and Hand (exc shave)	29923317	SODIUM LAUROYL GLUTAMATE	1
12F - Moisturizing	29923317	SODIUM LAUROYL GLUTAMATE	2
12H - Paste Masks (mud packs)	29923317	SODIUM LAUROYL GLUTAMATE	1
12J - Other Skin Care Preps	29923317	SODIUM LAUROYL GLUTAMATE	3
01A - Baby Shampoos	167074675	SODIUM LAUROYL OAT AMINO ACIDS	1
02B - Bubble Baths	167074675	SODIUM LAUROYL OAT AMINO ACIDS	4
02D - Other Bath Preparations	167074675	SODIUM LAUROYL OAT AMINO ACIDS	1
05F - Shampoos (non-coloring)	167074675	SODIUM LAUROYL OAT AMINO ACIDS	23
05G - Tonics, Dressings, and Other Hair Grooming Aids	167074675	SODIUM LAUROYL OAT AMINO ACIDS	3
10A - Bath Soaps and Detergents	167074675	SODIUM LAUROYL OAT AMINO ACIDS	17
10E - Other Personal Cleanliness Products	167074675	SODIUM LAUROYL OAT AMINO ACIDS	16
12A - Cleansing	167074675	SODIUM LAUROYL OAT AMINO ACIDS	22
12C - Face and Neck (exc shave)	167074675	SODIUM LAUROYL OAT AMINO ACIDS	1
12D - Body and Hand (exc shave)	167074675	SODIUM LAUROYL OAT AMINO ACIDS	3
12F - Moisturizing	167074675	SODIUM LAUROYL OAT AMINO ACIDS	3
12J - Other Skin Care Preps	167074675	SODIUM LAUROYL OAT AMINO ACIDS	4
12A - Cleansing	999002314	SODIUM LAUROYL WHEAT AMINO ACIDS	1
03B - Eyeliner	38517372	SODIUM MYRISTOYL GLUTAMATE	1
03C - Eye Shadow	38517372	SODIUM MYRISTOYL GLUTAMATE	1
03G - Other Eye Makeup Preparations	38517372	SODIUM MYRISTOYL GLUTAMATE	8
07C - Foundations	38517372	SODIUM MYRISTOYL GLUTAMATE	26
07F - Makeup Bases	38517372	SODIUM MYRISTOYL GLUTAMATE	2
07G - Rouges	38517372	SODIUM MYRISTOYL GLUTAMATE	2
07I - Other Makeup Preparations	38517372	SODIUM MYRISTOYL	2

		GLUTAMATE	
08B - Cuticle Softeners	38517372	SODIUM MYRISTOYL GLUTAMATE	1
12A - Cleansing	38517372	SODIUM MYRISTOYL GLUTAMATE	7
12C - Face and Neck (exc shave)	38517372	SODIUM MYRISTOYL GLUTAMATE	1
12F - Moisturizing	38517372	SODIUM MYRISTOYL GLUTAMATE	1
10B - Deodorants (underarm)	999002008	SODIUM PALMITOYL PROLINE	1
12A - Cleansing	999002008	SODIUM PALMITOYL PROLINE	1
12F - Moisturizing	999002008	SODIUM PALMITOYL PROLINE	1
12G - Night	999002008	SODIUM PALMITOYL PROLINE	1
12J - Other Skin Care Preps	999002008	SODIUM PALMITOYL PROLINE	3
03D - Eye Lotion	38517236	SODIUM STEAROYL GLUTAMATE	4
03G - Other Eye Makeup Preparations	38517236	SODIUM STEAROYL GLUTAMATE	1
05A - Hair Conditioner	38517236	SODIUM STEAROYL GLUTAMATE	4
05I - Other Hair Preparations	38517236	SODIUM STEAROYL GLUTAMATE	2
07C - Foundations	38517236	SODIUM STEAROYL GLUTAMATE	3
07I - Other Makeup Preparations	38517236	SODIUM STEAROYL GLUTAMATE	1
10B - Deodorants (underarm)	38517236	SODIUM STEAROYL GLUTAMATE	3
10E - Other Personal Cleanliness Products	38517236	SODIUM STEAROYL GLUTAMATE	3
11E - Shaving Cream	38517236	SODIUM STEAROYL GLUTAMATE	1
12A - Cleansing	38517236	SODIUM STEAROYL GLUTAMATE	6
12C - Face and Neck (exc shave)	38517236	SODIUM STEAROYL GLUTAMATE	18
12D - Body and Hand (exc shave)	38517236	SODIUM STEAROYL GLUTAMATE	15
12F - Moisturizing	38517236	SODIUM STEAROYL GLUTAMATE	48
12G - Night	38517236	SODIUM STEAROYL GLUTAMATE	5
12J - Other Skin Care Preps	38517236	SODIUM STEAROYL GLUTAMATE	3
13B - Indoor Tanning Preparations	38517236	SODIUM STEAROYL GLUTAMATE	3
12A - Cleansing	999002261	TEA-COCOYL ALANINATE	2
01C - Other Baby Products	68187291	TEA-COCOYL GLUTAMATE	1
04E - Other Fragrance Preparation	68187291	TEA-COCOYL GLUTAMATE	1

05F - Shampoos (non-coloring)	68187291	TEA-COCOYL GLUTAMATE	2
07I - Other Makeup Preparations	68187291	TEA-COCOYL GLUTAMATE	2
10A - Bath Soaps and Detergents	68187291	TEA-COCOYL GLUTAMATE	13
10E - Other Personal Cleanliness Products	68187291	TEA-COCOYL GLUTAMATE	23
11E - Shaving Cream	68187291	TEA-COCOYL GLUTAMATE	1
12A - Cleansing	68187291	TEA-COCOYL GLUTAMATE	17
12C - Face and Neck (exc shave)	68187291	TEA-COCOYL GLUTAMATE	5
05G - Tonics, Dressings, and Other Hair Grooming Aids	977099301	TEA-LAUROYL COLLAGEN AMINO ACID	3
10E - Other Personal Cleanliness Products	60239727	TEA-LAUROYL GLUTAMATE	1
05F - Shampoos (non-coloring)	977169882	UNDECYLENOYL COLLAGEN AMINO ACIDS	2
03D - Eye Lotion	999001119	UNDECYLENOYL GLYCINE	1
04E - Other Fragrance Preparation	999001119	UNDECYLENOYL GLYCINE	1
05F - Shampoos (non-coloring)	999001119	UNDECYLENOYL GLYCINE	4
08G - Other Manicuring Preparations	999001119	UNDECYLENOYL GLYCINE	2
12E - Foot Powders and Sprays	999001119	UNDECYLENOYL GLYCINE	2
07C - Foundations	999001661	UNDECYLENOYL PHENYLALANINE	1
12A - Cleansing	999001661	UNDECYLENOYL PHENYLALANINE	1
12C - Face and Neck (exc shave)	999001661	UNDECYLENOYL PHENYLALANINE	1
12D - Body and Hand (exc shave)	999001661	UNDECYLENOYL PHENYLALANINE	1
12F - Moisturizing	999001661	UNDECYLENOYL PHENYLALANINE	8
12G - Night	999001661	UNDECYLENOYL PHENYLALANINE	1
12J - Other Skin Care Preps	999001661	UNDECYLENOYL PHENYLALANINE	5

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 8, 2013

SUBJECT: HRIPTs of Products containing Sodium Lauryl Glutamate

TKL Research, Inc. 2004. Repeated insult patch study of a facial cleansing cream containing 30% Sodium Lauroyl Glutamate (10% dilution tested).

International Research Services Inc. 2006. A study to assess the skin sensitization potential of one product when applied to the skin of 50 healthy human subjects in a shared panel assay (skin cleansing product containing 22% Sodium Lauroyl Glutamate tested at a 1% dilution).

1101 17th Street, N.W., Suite 300 | Washington, D.C. 20036-4702 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

REPEATED INSULT PATCH STUDY

TKL STUDY NO. [redacted]

[redacted]

CONDUCTED FOR:

[redacted]

DATE OF REPORT:

January 21, 2004

TKL Research, Inc., 4 Forest Avenue, Paramus, NJ 07652 Tel (201) 587-0500 Fax (201) 587-0878 Email: info@tklresearch.com

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APPENDICES

SIGNATURES

Kathleen Georgeian
Kathleen Georgeian, Clinical Research Coordinator and Manager, Dermatologic Safety Testing

1/21/04
Date

Jonathan S. Dosik, MD
Principal Investigator

1/20/04
Date

STATEMENT OF QUALITY ASSURANCE

This report has been reviewed by the TKL Research, Inc. (TKL) Corporate Quality Assurance Department and the report accurately reflects the raw data for this study.

Clinical research studies are performed by TKL in accordance with all applicable federal regulations and proposed guidelines for Good Clinical Practices, which include:

21 CFR Part 312,	Investigational New Drug Application
21 CFR Part 50,	Protection of Human Subjects
21 CFR Part 56,	Institutional Review Boards

Henry Bonner
Quality Assurance

1/21/04
Date

TITLE OF STUDY

Repeated Insult Patch Study

SPONSOR

[redacted]

STUDY MATERIAL

[redacted] Facial cleansing cream

Test material is a 10% dilution of a facial cream containing 30% sodium lauroyl glutamate (CAS 29923-31-7).

DATE STUDY INITIATED

October 27, 2003

DATE STUDY COMPLETED

December 4, 2003

DATE OF REPORT

January 21, 2004

INVESTIGATIVE PERSONNEL

Jonathan S. Dosik, MD
Principal Investigator

Kathleen Georgeian
Clinical Research Coordinator
and Manager, Dermatologic Safety Testing

Tina Kelly
Assistant Manager, Dermatologic Safety Testing

CLINICAL SITE

TKL RESEARCH, INC
71 Franklin Turnpike
Waldwick, NJ 07463

SUMMARY

One study material, [redacted] was evaluated as a 10% w/v aqueous solution to determine its ability to sensitize the skin of normal volunteer subjects using a semi-occlusive repeated insult patch study. One hundred three subjects completed the study.

Under the conditions employed in this study, there was no evidence of sensitization to [redacted]

1.0 OBJECTIVE

The objective of this study was to determine the ability of the study material to cause sensitization by repeated applications to the skin of humans under controlled patch study conditions.

2.0 RATIONALE

Substances that come into contact with human skin need to be evaluated for their propensity to irritate and/or sensitize. Once an appropriate pre-clinical safety evaluation has been performed, a reproducible, standardized, quantitative patch evaluation procedure must be used to demonstrate that a particular material can be applied safely to human skin without significant risk of adverse reactions. The method herein employed is generally accepted for such a purpose.

Repeated insult patch evaluation is a modified predictive patch study that can detect weak sensitizers that require multiple applications to induce a cell-mediated (Type IV) immune response sufficient to cause an allergic reaction. Irritant reactions may also be detected using this evaluation method, although this is not the primary purpose of this procedure. Results are interpreted according to interpretive criteria based upon published works, as well as the clinical experience of TKL Research, Inc. These interpretive criteria are periodically reviewed and amended as new information becomes available.

3.0 STUDY DESIGN

3.1 STUDY POPULATION

A sufficient number of subjects were enrolled to provide 100 completed subjects.

3.1.1 Inclusion Criteria

Individuals eligible for inclusion in the study were those who:

1. were males or females, 18 years of age or older, in general good health;

2. were free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, would have interfered with the study results or increased the risk of adverse events;

3. were of any skin type or race, providing the skin pigmentation would allow discernment of erythema;

4. had completed a medical screening procedure; and

5. had read, understood, and signed an informed consent agreement.

3.1.2 Exclusion Criteria

Individuals excluded from participation in the study were those who:

1. had any visible skin disease at the study site which, in the opinion of the investigative personnel, would have interfered with the evaluation;

2. were receiving systemic or topical drugs or medication which, in the opinion of the investigative personnel, would have interfered with the study results;

3. had psoriasis and/or active atopic dermatitis/eczema;

4. were females who were pregnant, planning to become pregnant during the study, or breast-feeding; and/or

5. had a known sensitivity to cosmetics, skin care products, or topical drugs as related to the material being evaluated.

3.1.3 Informed Consent

A properly executed informed consent document in compliance with FDA regulations (21 CFR Part 50) was obtained from each subject prior to entering the study. The signed informed consent document is maintained in the study file. In addition, the subject was provided with a copy of the informed consent document (see Appendix IV).

3.2 DESCRIPTION OF STUDY

3.2.1 Outline of Study Procedures

Subjects participated in the study over a 6-week period involving 3 phases: (1) Induction, (2) Rest, and (3) Challenge. Prior to study entry, the subjects were screened to assure that they met the inclusion/exclusion criteria. Informed consent was obtained. Each subject was provided with a schedule of the study activities. All subjects were told to avoid wetting the patches and were asked not to engage in activities that caused excessive perspiration. They were instructed to notify the staff if they experienced any discomfort beyond mild itching or observed any adverse changes at the patch sites, while on the study or within 2 weeks of completing the study.

The Induction Phase consisted of 9 consecutive applications of the study material and subsequent evaluations of the patch sites. Prior to application of the patches, the sites were outlined with a skin marker, eg, gentian violet. The subjects were required to remove the patches approximately 24 hours after application. They returned to the facility at 48-hour intervals to have the sites evaluated and identical patches applied to the same sites. Patches applied on Friday were removed by subjects after 24 hours. The sites were evaluated on the following Monday, ie, 72 hours after patch application*.

* A Monday or Friday holiday could result in evaluation at 96 hours after patch application.

Following the ninth evaluation, the subjects were dismissed for a rest period of approximately 10-15 days.

Subjects who were absent once during the induction phase received a make-up (MU) patch at the last induction visit. The MU applications were graded 48 hours later at the MU visit, or were recorded as N9G (no ninth grading).

The Challenge Phase was initiated during the sixth week of the study. Identical patches were applied to sites previously unexposed to the study material. The patches were removed by subjects after 24 hours and the sites graded after additional 24-hour and 48-hour periods (ie, 48 and 72 hours after application). Rechallenge was performed whenever there was evidence of possible sensitization.

To be considered a completed case, a subject must have had 9 applications and no fewer than 8 subsequent readings during induction, and a single application and 2 readings during challenge. Only completed cases were used to assess sensitization.

3.2.2 Definitions Used for Grading Responses

The symbols found in the scoring scales below were used to express the response observed at the time of examination:

- = No reaction
? = Minimal or doubtful response, slightly different from surrounding normal skin
\+ = Definite erythema, no edema
++ = Definite erythema, definite edema
+++ = Definite erythema, definite edema and vesiculation

SPECIAL NOTATIONS

E = Marked/severe erythema
S = Spreading of reaction beyond patch site (ie, reaction where material did not contact skin)
p = Papular response > 50%
pv = Papulovesicular response > 50%
D = Damage to epidermis: oozing, crusting and/or superficial erosions
I = Itching
X = Subject absent
PD = Patch dislodged
NA = Not applied
NP = Not patched (due to reaction achieved)
N9G = No ninth grading

3.2.3 Evaluation of Responses

All responses were graded by a trained dermatologic evaluator meeting TKL's strict certification requirements to standardize the assignment of response grades.

4.0 NATURE OF STUDY MATERIAL

4.1 STUDY MATERIAL SPECIFICATIONS

Identification	:	[redacted] Facial cleansing cream
Amount Applied	:	0.2 mL
Special Instructions	:	Prepared fresh daily as a 10% w/v aqueous solution. Applied to patch no longer than 15 minutes prior to patch application.

4.2 STORAGE, HANDLING, AND DOCUMENTATION OF STUDY MATERIAL

Receipt of the material used in this study was documented in a general logbook, which serves as a permanent record of the receipt, storage, and disposition of all study material received by TKL. On the basis of information provided by the sponsor, the study material was considered reasonably safe for evaluation on human subjects. A sample of the study material was reserved and will be stored for a period of 6 months. At the conclusion of the clinical study, the remaining study material was discarded or returned to the sponsor and the disposition documented in the logbook. All information regarding the receipt, storage, and disposition of the study material was also recorded on a Clinical Material Record form (see Appendix III), which is incorporated in this study report. All study material is kept in a locked product storage room accessible to clinical staff members only.

4.3 APPLICATION OF STUDY MATERIAL

Study material was applied to the patch as instructed. The patch was applied to the infrascapular area of the back, either to the right or left of the midline, or to the upper arm.

4.4 DESCRIPTION OF PATCH CONDITIONS

Material evaluated under occlusive patch conditions was applied to a 2-cm x 2-cm Webril pad attached to a non-porous, plastic film adhesive bandage (3M medical tape). The patch was secured with hypoallergenic tape (Micropore), as needed.

Material evaluated under semi-occlusive patch conditions was applied to a 2-cm x 2-cm Webril pad. The pad was affixed to the skin with hypoallergenic tape (Micropore).

5.0 INTERPRETATION

Sensitization is characterized by an acute allergic contact dermatitis. Typical sensitization reactions begin with an immunologic response in the dermis resulting in erythema, edema formation, and secondary epidermal damage (vesiculation), sometimes extending beyond the patch site and often accompanied by itching. Sensitization reactions tend to be delayed. The reaction typically becomes evident between 24 and 48 hours, peaks at 48-72 hours and subsequently subsides. The reaction is often greater at 72 hours than at 48 hours. The severity of the reaction is generally greater during the challenge phase of a Repeated Insult Patch Test (RIPT) than that seen during induction.

Irritant reactions are characterized as a non-immunologic, localized, superficial, exudative, inflammatory response of the skin due to an externally applied material. The typical initial reaction does not develop much edema or vesiculation but results in scaling, drying, cracking, oozing, crusting, and erosions. The reaction is usually sharply delineated, not spreading beyond the patch site. Irritant reactions are typically evident by 24 hours and diminish over the next 48-72 hours. Removal of the offending agent results in gradual improvement of the epidermal damage. The reaction seen at 72 hours is, therefore, less severe than that seen at 48 hours. Finally, the severity of the reaction experienced in the challenge phase is generally similar to that seen during induction.

If the results of the study indicate the likelihood of sensitization, the recommended practice is to rechallenge the subjects who have demonstrated sensitization-like reactions to confirm that these reactions are, indeed, associated with the product. Our preferred rechallenge procedure involves the application of the product to naïve sites, under both occlusive and semi-occlusive patch conditions. Use of the semi-occlusive patch condition helps to differentiate irritant and sensitization reactions. Generally speaking, if a product is a sensitizer it will produce a similar reaction under both occlusion and semi-occlusion. Whereas, if the product has caused an irritant reaction, the reactions will be less pronounced under the semi-occlusive condition.

6.0 PROTOCOL

See Protocol - Appendix V.

7.0 DOCUMENTATION AND RETENTION OF DATA

The case report forms (CRFs) are designed to identify each subject by subject number and initials, and to record demographics, examination results, adverse events, and end of study status. Originals or copies of all CRFs, source documents, IRB documents (if required), correspondence, study reports, and all source data will be kept on hard-copy file for a minimum of 5 years from completion of the study. Storage is maintained either at a TKL facility in a secured room accessible only to TKL employees, or at an offsite location which provides a secure environment with burglar/fire alarm systems, camera detection and controlled temperature and humidity. Documentation will be available for the sponsor's review on the premises of TKL.

8.0 RESULTS AND DISCUSSION

One hundred eight subjects between the ages of 21 and 71 were enrolled and 103 completed the study (see Tables 1 and 2 in Appendix I and Data Listings 1 and 2 in Appendix II).

The following table summarizes subject enrollment and disposition.

Number enrolled:		108
Number discontinued:		5
Lost to follow-up:	1	
Voluntary withdrawal:	4	
Number completed:		103

Source: Table 1, Appendix 1

There were no adverse events.

A summary of response data is provided in Table 3, Appendix I. Individual dermatological response grades are provided in Data Listing 3, Appendix II.

9.0 CONCLUSION

Under the conditions employed in this study, there was no evidence of sensitization to [redacted]

10.0 REFERENCES

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Stotts, J. Planning, conduct and interpretation of human predictive sensitization patch tests. In: Drill VA, Lazar P, eds. Current Concepts In Cutaneous Toxicity. New York:Academic Press, 1980:41-53.

APPENDIX I

SUMMARY TABLES

TKL STUDY NO. [redacted]

TABLE 1: SUMMARY OF SUBJECT ENROLLMENT AND DISPOSITION

	N	(%)
SUBJECTS ENROLLED	108	
SUBJECTS COMPLETED ALL PHASES	103	(95.4)
TOTAL SUBJECTS DISCONTINUED	5	(4.6)
LOST TO FOLLOW-UP	1	(0.9)
VOLUNTARY WITHDRAWAL	4	(3.7)

NOTE: ALL PERCENTAGES ARE RELATIVE TO TOTAL SUBJECTS ENROLLED

SEE DATA LISTING 1 FOR FURTHER DETAIL

PROGRAM: DISPSMY.SAS/USES: FINAL/18DEC03:11:28:37

TKL STUDY NO. [redacted]
TABLE 2: SUMMARY OF SUBJECT DEMOGRAPHICS
ALL ENROLLED SUBJECTS

AGE	
N (%) 18 TO 44	45 (41.7)
N (%) 45 TO 64	43 (39.8)
N (%) 65 AND UP	20 (18.5)
MEAN (SD)	50.0 (12.3)
MEDIAN	48.5
RANGE	21.9 TO 71.9
GENDER	
N (%) MALE	14 (13.0)
N (%) FEMALE	94 (87.0)
RACE	
N (%) AMER INDIAN	1 (0.9)
N (%) CAUCASIAN	101 (93.5)
N (%) HISPANIC	5 (4.6)
N (%) OTHER	1 (0.9)

SEE DATA LISTING 2 FOR FURTHER DETAIL

PROGRAM: DEMOSMY.SAS/USES: DEMOGS/18DEC03:11:28:37

[redacted]
TKL STUDY NO. [redacted]
TABLE 3: SUMMARY OF DERMATOLOGIC RESPONSE GRADES
NUMBER OF SUBJECTS BY PRODUCT

PRODUCT= [redacted]

	INOUCTION READING									MAKE-	CHALLENGE PHASE		
RESPONSE	1	2	3	4	5	6	7	8	9	UP	48HR	72HR	96HR(*)
-	104	101	103	103	100	100	99	101	103	17	103	103	
TOTAL EVALUABLE	104	101	103	103	100	100	99	101	103	17	103	103	
NUMBER ABSENT	0	3	1	1	3	3	4	2	0		0	0	
NUMBER DISCONTINUED	4	4	4	4	5	5	5	5	5		5	5	

MAXIMUM ELICITED RESPONSE DURING INDUCTION
ALL SUBJECTS COMPLETING INOUCTION (N=103)

RESPONSE	N(%) SUBJECTS
-	103 (100.0%)

(*) WHEN REQUIRED

KEY TO SYMBOLS:
- = NO REACTION
? = MINIMAL OR DOUBTFUL RESPONSE, SLIGHTLY DIFFERENT FROM SURROUNDING NORMAL SKIN
+ = DEFINITE ERYTHEMA, NO EDEMA
++ = DEFINITE ERYTHEMA, DEFINITE EDEMA
+++ = DEFINITE ERYTHEMA, DEFINITE EDEMA AND VESICULATION
D = DAMAGE TO EPIDERMIS: OOZING, CRUSTING AND/OR SUPERFICIAL EROSIONS
P = PAPULAR RESPONSE >50%

PROGRAM: SUMMARY.SAS/USES: RESPONSE, PRODLIST, FINAL/18DEC03:11:28:41

APPENDIX II

DATA LISTINGS

TKL STUDY NO. [redacted]
DATA LISTING 1: SUBJECT ENROLLMENT AND DISPOSITION

SUBJECT NO.	STUDY DATES SCREENED	1ST APPLIC	CHALL APPLIC	ENDED	LAST READING #	COMPLETION STATUS	DAYS ON STUDY
1	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
2	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
3	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
4	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
5	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
6	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
7	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
8	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
9	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
10	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
11	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
12	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
13	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
14	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
15	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
16	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
17	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
18	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
19	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
20	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
21	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
22	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
23	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
24	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
25	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
26	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
27	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
28	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
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35	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
36	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
37	10/27/03	10/27/03		10/29/03	I0	S	3
38	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
39	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39

KEY: LAST READING # (I=INDUCTION PHASE, C=CHALLENGE PHASE)
COMPLETION STATUS (C=COMPLETED, L=LOST TO FOLLOW-UP, S=VOLUNTARY WITHDRAWAL
V=PROTOCOL VIOLATION, AE=ADVERSE EVENT, O=OTHER)

PROGRAM: DISPLIST.SAS/USES: DEMOGS, RESPONSE, FINAL/18DEC03:11:28:27

TKL STUDY NO. [redacted]
DATA LISTING 1: SUBJECT ENROLLMENT AND DISPOSITION

SUBJECT NO.	STUDY DATES SCREENED	1ST APPLIC	CHALL APPLIC	ENDED	LAST READING #	COMPLETION STATUS	DAYS ON STUDY
40	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
41	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
42	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
43	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
44	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
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48	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
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50	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
51	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
52	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
53	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
54	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
55	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
56	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
57	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
58	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
59	10/27/03	10/27/03		10/29/03	I0	S	3
60	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
61	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
62	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
63	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
64	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
65	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
66	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
67	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
68	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
69	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
70	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
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73	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
74	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
75	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
76	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
77	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
78	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39

KEY: LAST READING # (I=INDUCTION PHASE, C=CHALLENGE PHASE)
COMPLETION STATUS (C=COMPLETED, L=LOST TO FOLLOW-UP, S=VOLUNTARY WITHDRAWAL
V=PROTOCOL VIOLATION, AE=ADVERSE EVENT, O=OTHER)

PROGRAM: DISPLIST.SAS/USES: DEMOGS, RESPONSE, FINAL/18DEC03:11:28:27

TKL STUDY NO. [redacted]
DATA LISTING 1: SUBJECT ENROLLMENT AND DISPOSITION

SUBJECT NO.	STUDY DATES SCREENED	1ST APPLIC	CHALL APPLIC	ENDED	LAST READING #	COMPLETION STATUS	DAYS ON STUDY
79	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
80	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
81	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
82	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
83	10/27/03	10/27/03		10/29/03	I0	S	3
84	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
85	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
86	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
87	10/27/03	10/27/03		10/31/03	I0	L	5
88	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
89	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
90	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
91	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
92	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
93	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
94	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
95	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
96	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
97	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
98	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
99	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
100	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
101	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
102	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
103	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
104	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
105	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
106	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
107	10/27/03	10/27/03	12/01/03	12/04/03	C2	C	39
108	10/27/03	10/27/03		11/10/03	I4	S	15

KEY: LAST READING # (I=INDUCTION PHASE, C=CHALLENGE PHASE)
COMPLETION STATUS (C=COMPLETED, L=LOST TO FOLLOW-UP, S=VOLUNTARY WITHDRAWAL
V=PROTOCOL VIOLATION, AE=ADVERSE EVENT, O=OTHER)

PROGRAM: DISPLIST.SAS/USES: DEMOGS, RESPONSE, FINAL/18DEC03:11:28:27

TKL STUDY NO. [redacted]
DATA LISTING 2: SUBJECT DEMOGRAPHICS

SUBJECT NO.	AGE	GENDER	RACE
1	39.6	FEMALE	HISPANIC
2	65.5	FEMALE	CAUCASIAN
3	67.9	FEMALE	CAUCASIAN
4	52.3	FEMALE	CAUCASIAN
5	55.5	MALE	CAUCASIAN
6	68.5	FEMALE	CAUCASIAN
7	40.5	MALE	CAUCASIAN
8	66.1	FEMALE	CAUCASIAN
9	49.0	FEMALE	CAUCASIAN
10	67.9	FEMALE	CAUCASIAN
11	34.5	FEMALE	CAUCASIAN
12	70.3	MALE	CAUCASIAN
13	60.5	FEMALE	CAUCASIAN
14	54.1	FEMALE	CAUCASIAN
15	51.6	FEMALE	CAUCASIAN
16	43.7	FEMALE	CAUCASIAN
17	53.2	FEMALE	CAUCASIAN
18	56.0	FEMALE	CAUCASIAN
19	57.3	FEMALE	CAUCASIAN
20	42.3	FEMALE	CAUCASIAN
21	64.6	FEMALE	CAUCASIAN
22	41.5	FEMALE	CAUCASIAN
23	53.3	FEMALE	CAUCASIAN
24	40.1	FEMALE	CAUCASIAN
25	30.1	FEMALE	CAUCASIAN
26	60.2	FEMALE	CAUCASIAN
27	51.1	FEMALE	CAUCASIAN
28	43.1	FEMALE	CAUCASIAN
29	63.1	FEMALE	CAUCASIAN
30	35.7	FEMALE	CAUCASIAN
31	66.8	FEMALE	CAUCASIAN
32	71.9	MALE	CAUCASIAN
33	66.8	FEMALE	CAUCASIAN
34	71.4	MALE	CAUCASIAN
35	68.8	FEMALE	CAUCASIAN
36	46.3	FEMALE	CAUCASIAN
37	45.0	FEMALE	CAUCASIAN
38	45.5	FEMALE	CAUCASIAN
39	34.3	FEMALE	CAUCASIAN
40	38.9	FEMALE	CAUCASIAN

TKL STUDY NO. [redacted]
OATA LISTING 2: SUBJECT DEMOGRAPHICS

SUBJECT NO.	AGE	GENDER	RACE
41	49.5	MALE	CAUCASIAN
42	56.4	FEMALE	CAUCASIAN
43	49.6	FEMALE	CAUCASIAN
44	45.3	FEMALE	CAUCASIAN
45	37.5	FEMALE	HISPANIC
46	62.2	FEMALE	CAUCASIAN
47	56.6	FEMALE	CAUCASIAN
48	39.9	FEMALE	CAUCASIAN
49	40.2	FEMALE	CAUCASIAN
50	62.3	FEMALE	CAUCASIAN
51	68.2	FEMALE	CAUCASIAN
52	41.0	FEMALE	CAUCASIAN
53	30.6	FEMALE	HISPANIC
54	46.4	FEMALE	CAUCASIAN
55	49.1	FEMALE	HISPANIC
56	40.3	FEMALE	CAUCASIAN
57	44.0	MALE	CAUCASIAN
58	37.3	FEMALE	CAUCASIAN
59	38.0	FEMALE	CAUCASIAN
60	35.7	FEMALE	CAUCASIAN
61	51.6	MALE	CAUCASIAN
62	45.5	FEMALE	CAUCASIAN
63	68.4	FEMALE	CAUCASIAN
64	58.6	FEMALE	CAUCASIAN
65	33.5	FEMALE	CAUCASIAN
66	54.5	MALE	CAUCASIAN
67	48.7	FEMALE	CAUCASIAN
68	43.2	FEMALE	CAUCASIAN
69	45.2	FEMALE	CAUCASIAN
70	68.6	FEMALE	CAUCASIAN
71	36.4	FEMALE	CAUCASIAN
72	68.6	FEMALE	CAUCASIAN
73	39.7	FEMALE	CAUCASIAN
74	37.6	FEMALE	CAUCASIAN
75	68.8	FEMALE	CAUCASIAN
76	56.5	FEMALE	CAUCASIAN
77	63.1	MALE	CAUCASIAN
78	42.9	FEMALE	CAUCASIAN
79	40.9	FEMALE	CAUCASIAN
80	42.8	FEMALE	CAUCASIAN

TKL STUDY NO. [redacted]
DATA LISTING 2: SUBJECT DEMOGRAPHICS

SUBJECT NO.	AGE	GENDER	RACE
81	59.0	MALE	CAUCASIAN
82	36.0	FEMALE	CAUCASIAN
83	66.5	FEMALE	CAUCASIAN
84	69.9	FEMALE	CAUCASIAN
85	37.1	MALE	CAUCASIAN
86	40.6	FEMALE	CAUCASIAN
87	63.3	FEMALE	CAUCASIAN
88	41.2	FEMALE	AMER IND
89	51.3	FEMALE	CAUCASIAN
90	53.2	MALE	CAUCASIAN
91	42.1	FEMALE	BIRACIAL
92	70.2	MALE	CAUCASIAN
93	47.0	FEMALE	CAUCASIAN
94	33.5	FEMALE	CAUCASIAN
95	68.7	FEMALE	CAUCASIAN
96	38.9	FEMALE	CAUCASIAN
97	40.3	FEMALE	CAUCASIAN
98	40.1	FEMALE	CAUCASIAN
99	49.9	FEMALE	CAUCASIAN
100	34.4	FEMALE	CAUCASIAN
101	60.5	FEMALE	CAUCASIAN
102	42.4	FEMALE	CAUCASIAN
103	31.2	FEMALE	HISPANIC
104	31.4	FEMALE	CAUCASIAN
105	62.5	FEMALE	CAUCASIAN
106	39.0	FEMALE	CAUCASIAN
107	21.9	FEMALE	CAUCASIAN
108	48.2	FEMALE	CAUCASIAN

PROGRAM: DEMOLIST.SAS/USES: DEMOGS/18DEC03:11:28:27

[redacted]

TKL STUDY NO. [redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= [redacted]

SUBJECT NO.	INDUCTION READING 1	2	3	4	5	6	7	8	9	MU	CHALLENGE PHASE 48HR	72HR	96HR(*)
1	-	-	-	-	-	-	-	-	-		-	-	
2	-	-	-	-	X	-	-	-	-	-	-	-	
3	-	-	-	-	-	-	-	-	-		-	-	
4	-	-	-	-	-	-	-	-	-		-	-	
5	-	-	-	-	-	-	-	-	-		-	-	
6	-	-	-	-	-	-	-	-	-		-	-	
7	-	-	-	-	-	-	-	-	-		-	-	
8	-	-	-	-	-	-	-	-	-		-	-	
9	-	-	-	-	-	-	-	-	-		-	-	
10	-	-	-	-	-	-	-	-	-		-	-	
11	-	-	-	-	-	-	-	-	-		-	-	
12	-	-	-	-	-	-	-	-	-		-	-	
13	-	-	-	-	-	-	-	-	-		-	-	
14	-	-	-	-	-	-	-	-	-		-	-	
15	-	-	-	-	-	-	-	-	-		-	-	
16	-	-	-	-	-	-	-	-	-		-	-	
17	-	-	-	-	-	-	-	-	-		-	-	
18	-	-	-	-	-	-	-	-	-		-	-	
19	-	-	-	-	-	-	X	-	-	-	-	-	
20	-	X	-	-	-	-	-	-	-	-	-	-	

KEY TO SYMBOLS:

- = NO REACTION
? = MINIMAL OR DOUBTFUL RESPONSE, SLIGHTLY DIFFERENT FROM SURROUNDING NORMAL SKIN

+ = DEFINITE ERYTHEMA, NO EDEMA
++ = DEFINITE ERYTHEMA, DEFINITE EDEMA

+++ = DEFINITE ERYTHEMA, DEFINITE EDEMA AND VESICULATION

N9G = NO NINTH GRADING NA=NOT APPLIED NP=NOT PATCHED DUE TO REACTION ACHIEVED
X = READING NOT PERFORMED DUE TO MISSED VISIT OR SUBJECT DISCONTINUATION
D = DAMAGE TO EPIDERMIS: OOZING, CRUSTING AND/OR SUPERFICIAL EROSIONS
P = PAPULAR RESPONSE >50% NR=DATA NOT RECORDED
MU = MAKE-UP READING FOR MISSED INDUCTION VISIT

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/18DEC03:11:28:28

[redacted]
TKL STUDY NO. [redacted]
DATA LISTING 3: DERMATOLOGIC RESPONSE GRAOES
BY PRODUCT AND SUBJECT

PRODUCT= [redacted]

SUBJECT	INDUCTION READING										CHALLENGE PHASE		
NO.	1	2	3	4	5	6	7	8	9	MU	4BHR	72HR	96HR(*)
21	-	-	-	-	-	-	-	-	-		-	-	
22	-	-	-	-	-	-	-	-	-		-	-	
23	-	-	-	-	-	-	-	-	-		-	-	
24	-	-	-	-	-	-	X	-	-	-	-	-	
25	-	-	-	-	-	-	-	-	-		-	-	
26	-	-	-	-	-	-	-	-	-		-	-	
27	-	-	-	-	-	-	-	-	-		-	-	
28	-	-	-	-	-	-	-	-	-		-	-	
29	-	-	-	-	-	-	-	-	-		-	-	
30	-	-	-	-	X	-	-	-	-	-	-	-	
31	-	-	-	-	-	-	-	-	-		-	-	
32	-	-	-	-	-	-	-	-	-		-	-	
33	-	-	-	-	-	-	-	-	-		-	-	
34	-	-	-	-	-	-	-	-	-		-	-	
35	-	-	-	-	-	-	-	-	-		-	-	
36	-	-	-	-	-	-	-	-	-		-	-	
37	X	X	X	X	X	X	X	X	X		X	X	
38	-	-	-	X	-	-	-	-	-	-	-	-	
39	-	-	-	-	-	-	-	-	-		-	-	
40	-	-	-	-	-	X	-	-	-	-	-	-	
41	-	X	-	-	-	-	-	-	-	-	-	-	
42	-	-	-	-	-	-	-	-	-		-	-	
43	-	-	-	-	-	-	-	-	-		-	-	
44	-	-	-	-	-	-	-	-	-		-	-	
45	-	-	-	-	-	-	-	-	-		-	-	
46	-	-	-	-	-	-	-	-	-		-	-	
47	-	-	-	-	-	-	-	-	-		-	-	
48	-	-	-	-	-	-	-	-	-		-	-	
49	-	-	-	-	-	-	-	-	-		-	-	
50	-	-	-	-	-	-	-	-	-		-	-	
51	-	-	-	-	-	-	-	-	-		-	-	
52	-	-	-	-	-	-	-	-	-		-	-	

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/18DEC03:11:28:28

[redacted]
TKL STUDY NO. [redacted]
DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= [redacted]

SUBJECT	INDUCTION READING										CHALLENGE PHASE		
NO.	1	2	3	4	5	6	7	8	9	MU	48HR	72HR	96HR(*)
53	-	-	-	-	-	-	-	-	-		-	-	
54	-	-	-	-	-	-	-	-	-		-	-	
55	-	-	-	-	-	-	-	-	-		-	-	
56	-	-	-	-	-	-	-	-	-		-	-	
57	-	-	-	-	-	-	-	X	-	-	-	-	
58	-	-	-	-	-	-	-	-	-		-	-	
59	X	X	X	X	X	X	X	X	X		X	X	
60	-	-	-	-	-	-	-	-	-		-	-	
61	-	-	-	-	-	-	-	-	-		-	-	
62	-	-	-	-	-	-	-	-	-		-	-	
63	-	-	-	-	-	-	-	-	-		-	-	
64	-	-	-	-	-	-	-	-	-		-	-	
65	-	-	-	-	-	-	-	-	-		-	-	
66	-	-	-	-	-	-	-	-	-		-	-	
67	-	-	-	-	-	-	-	-	-		-	-	
68	-	-	-	-	-	X	-	-	-	-	-	-	
69	-	-	-	-	-	-	-	-	-		-	-	
70	-	-	-	-	-	-	-	-	-		-	-	
71	-	-	-	-	-	X	-	-	-	-	-	-	
72	-	-	-	-	-	-	X	-	-	-	-	-	
73	-	-	-	-	-	-	-	-	-		-	-	
74	-	-	-	-	-	-	-	-	-		-	-	
75	-	-	-	-	-	-	-	-	-		-	-	
76	-	-	-	-	-	-	-	X	-	-	-	-	
77	-	-	-	-	-	-	-	-	-		-	-	
78	-	-	-	-	-	-	-	-	-		-	-	
79	-	-	-	-	-	-	-	-	-		-	-	
80	-	-	-	-	-	-	-	-	-		-	-	
81	-	X	-	-	-	-	-	-	-	-	-	-	
82	-	-	-	-	X	-	-	-	-	-	-	-	
83	X	X	X	X	X	X	X	X	X		X	X	
84	-	-	-	-	-	-	-	-	-		-	-	

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/18DEC03:11:28:28

[redacted]
TKL STUDY NO. [redacted]
DATA LISTING 3: DERMATDLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= [redacted]

SUBJECT	INDUCTION READING										CHALLENGE PHASE		
NO.	1	2	3	4	5	6	7	8	9	MU	48HR	72HR	96HR(*)
85	-	-	-	-	-	-	-	-	-		-	-	
86	-	-	-	-	-	-	-	-	-		-	-	
87	X	X	X	X	X	X	X	X	X		X	X	
88	-	-	-	-	-	-	X	-	-	-	-	-	
89	-	-	-	-	-	-	-	-	-		-	-	
90	-	-	-	-	-	-	-	-	-		-	-	
91	-	-	-	-	-	-	-	-	-		-	-	
92	-	-	-	-	-	-	-	-	-		-	-	
93	-	-	-	-	-	-	-	-	-		-	-	
94	-	-	-	-	-	-	-	-	-		-	-	
95	-	-	-	-	-	-	-	-	-		-	-	
96	-	-	-	-	-	-	-	-	-		-	-	
97	-	-	-	-	-	-	-	-	-		-	-	
98	-	-	-	-	-	-	-	-	-		-	-	
99	-	-	-	-	-	-	-	-	-		-	-	
100	-	-	-	-	-	-	-	-	-		-	-	
101	-	-	X	-	-	-	-	-	-	-	-	-	
102	-	-	-	-	-	-	-	-	-		-	-	
103	-	-	-	-	-	-	-	-	-		-	-	
104	-	-	-	-	-	-	-	-	-		-	-	
105	-	-	-	-	-	-	-	-	-		-	-	
106	-	-	-	-	-	-	-	-	-		-	-	
107	-	-	-	-	-	-	-	-	-		-	-	
108	-	-	-	-	X	X	X	X	X		X	X	

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/18DEC03:11:28:28

INTERNATIONAL RESEARCH SERVICES INC.

A STUDY TO ASSESS THE SKIN SENSITIZATION POTENTIAL OF ONE (1) PRODUCT WHEN APPLIED TO THE SKIN OF 50 HEALTHY HUMAN SUBJECTS IN A SHARED PANEL ASSAY

FINAL REPORT

PROTOCOL NO. 31580206KN
Version 1.2

Skin cleansing product containing
22% Sodium Lauroyl Glutamate
tested at 1% dilution
(0.22% Sodium Lauroyl
Glutamate tested)

Submitted to:

[redacted]

September 5, 2006

STUDY SITE:
International Research Services, Inc.
385 Main Street, Suite 2
Rockland, ME 04841
(207) 594-7574

INVESTIGATOR:
Nancy Egan, M.D.

STUDY COORDINATOR:
Josette Stone, B.A.

222 Grace Church Street • Port Chester, NY 10573 • (914) 937-9483 • 1-800-548-0158 • Fax (914) 937-8067

September, 2006

[redacted]

Re: A Study To Assess The Skin Sensitization Potential Of One (1) Product When Applied To The Skin Of 50 Healthy Human Subjects In A Shared Panel Assay; IRSI 31580206KN

This report accurately reflects the data derived from the procedures and materials tested in this study. The conclusions are based on an interpretation of the data and have been reviewed by the Principal Investigator and by personnel from International Research Services, Inc. responsible for assuring its accuracy.

E.K. Boisits 4/7/06

Edward K. Boisits, Ph.D.
Vice President, Clinical Research

S. Schwartz 08.07.06

Stephen R. Schwartz, MS
President

TABLE OF CONTENTS

SUMMARY / RESULTS & DISCUSSION

The objective of the present study was to assess the skin sensitization potential of **SPP-12** when applied to the skin of human subjects in accordance with a modified Draize Assay. The study was initiated on April 17, 2006 and May 1, 2006. The study was completed on May 26, 2006 and June 9, 2006. Sixty-one (61) subjects were enrolled and fifty-five (55) subjects completed the study. Six (6) subjects were discontinued due to personal reasons. One (1) non-product-related adverse experience was reported.

Product **SPP-12** produced four (4) 1+ reactions during the induction phase of the study. Upon challenge with the test product, no reactions were observed at either the forty-eight (48) or ninety-six (96) hour evaluation intervals.

In conclusion, under the conditions employed in this study, no evidence of sensitization to **SPP-12** was observed.

Nancy Egan, M.D.

1.0 INVESTIGATOR/STUDY LOCATION/STATUS

The study was initiated on April 17, 2006 and May 1, 2006 and was conductcd in the facilities of International Research Services, Inc. in Rockland, Maine. Nancy Egan, M.D., was the Principal Investigator. The study was completcd on May 26, 2006 and June 9, 2006. Sixty-one (61) subjects were enrolled and fifty-five (55) subjects completed.

2.0 TEST PRODUCTS

The following products were supplied in sufficient quantity by [redacted]

#	PRODUCT NAME & DESCRIPTION	PRODUCT NUMBER	TEST AS
1	SPP-12		1% with Distilled Water

3.0 STUDY PROCEDURE

This study was conducted as per the protocol found in Appendix III.

4.0 STUDY DEMOGRAPHICS

4.1 DEMOGRAPHICS

Age Mean (years)	Sex	Race
45.83 ± 16.72	Male - 15 (27.3%) Female - 40 (72.7%)	Caucasian - 53 (96.4%) Hispanic - 1 (1.8%) Asian - 1 (1.8%)

4.2 STATUS

Enrolled	Discontinued	Completed
61	6 – Discontinued for personal reasons	55

4.0 STUDY DEMOGRAPHICS (Continued)

4.3 ADVERSE EXPERIENCES

There was one (1) adverse experience recorded during this study.

Subject #	Description & Severity	Date of Onset	Outcome/Status	Relationship to Product
4077	Sprained Left shoulder-Severe	04/20/06	Ongoing/completed	None

Subject number 4077 reported a left shoulder sprain, due to a fall on 4/20/06. The subject treated with Tylenol (500mg/2x/day) and chiropractic treatment. Symptoms were ongoing but improving at the end of the study.

5.0 PROTOCOL DEVIATIONS

None.

6.0 Q.A. STATEMENT

One hundred percent of the data generated by the statistician was checked against the source documentation by a member of the staff who has not participated in the study conduct. The report then went through internal Q.A. and validation.

7.0 DEFINITION OF DATA ANALYSIS TERMS

"Insult" = Induction (ten applications). Usually conducted after 48 hours or 72 hours on weekends/holidays.

"CHLG" = Challenge readings at 48 hours (patch removed). Challenge reading at 72 hours (no patch applied between 48 hour and 72 hour reading). Patches applied for challenge 10-14 days after last induction reading.

"Total" = Total (right column) induction results. Does not include challenge results. Total (left margin) number of subjects present at each induction or challenge visit.

"Not Applied" = Number of subjects to whom patches were not applied at a given time point.

"Absent" = Number of subjects not present at a given induction or challenge visit. Subjects who make up a visit with 24 hours are not listed as absent. All such instances are recorded on the examination CRF.

"Mean Induction Value" = $\frac{\text{Cumulative scores for a given time point}}{\text{Total number of subjects present at the same time point}}$

"Mean Reaction Value" = $\frac{\text{Cumulative scores for a given time point}}{\text{Total number of subjects with reactions at the same time point}}$

APPENDIX I

REACTION DATA

INTERNATIONAL RESEARCH SERVICES, INC.

RIPT STUDY #31560206KM 08/08/06.2

SPP-12

	INSULT										CHLG 48HR	CHLG 96HR	TOTAL
	-1-	-2-	-3-	-4-	-5-	-6-	-7-	-8-	-9-	-10-			
NEGATIVE	55	55	55	55	55	55	53	53	55	51	55	55	542
1.0							2	2					4
2.0													
3.0													
4.0													
NOT APPLIED										4			4
ABSENT													
TOTAL	55	55	55	55	55	55	55	55	55	55	55	55	550
MIV							0.03	0.03					
MRV							1.00	1.00					1.00

MIV = MEAN INDUCTION VALUE
MRV = MEAN REACTION VALUE

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

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

DATE: June 5, 2013

SUBJECT: Comments on the Draft Report on the Amino Acid Alkyl Amides Prepared for the June 10-11, 2013 CIR Expert Panel Meeting

Key Issues

Based on the search strategy for these ingredients that states "All searches limited to dermal exposures." It is not clear that all relevant data were identified. If all the search strategies were indeed limited to dermal exposure, it is not appropriate to state that no reproductive and developmental or carcinogenicity data were discovered. The dermal route of exposure is rarely used for the reproductive/developmental and carcinogenicity endpoints. Therefore, this report should be tabled so that a complete search can be conducted for these endpoints.

The 28-day oral study of Acetyl Glutamic Acid noted in the title of reference 26 should be added to this report.

Additional Comments

p.1 - As the hydrolyzed protein ingredients will be in a separate report, and because they are not relevant to this review, "and hydrolyzed protein ingredients" needs to be deleted from the Introduction.

p.2 - As only one use concentration (24%) was reported for Cocoyl Glutamic Acid, please change: "at maximum concentrations ranging from 24%" to "at a maximum concentration of 24%."

p.3 - The following sentence does not make sense: "In turn, dermal toxicity would not be expected to be different from oral exposures." Dermal effects are unlikely to occur following oral exposure. Perhaps the sentence should be: "Systemic toxicity following dermal exposure would not expected to be different from oral exposure." Because oral studies were not included in this report, it is not clear how it known what effects may occur following oral exposure.

p.3 - Please include the species studied in the *in vivo* genotoxicity study.

p.3 - Please provide some indication of the concentrations of amino acids tested in the irritation and sensitization studies previously reviewed.

p.3 - It should also be noted that the *in vitro* studies predicting ocular irritation are in Table 8.

p.3 - Please include the species used in the studies of Sodium Cocoyl Glutamate. In the description of the in-use studies, please add: "products containing...".

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p.4 - Please include some indication of the concentrations tested, e.g., the highest concentration tested, in the sensitization and phototoxicity studies.

p.4 - The phototoxicity studies should not be under the sensitization heading.

p.4, Clinical Use and Summary - It is misleading to state that there were no clinical use studies identified. What are the cosmetic use studies and reference 32 (described as a double-blind, randomized controlled usage study)? If it is more appropriate to present clinical studies in other sections, perhaps this section is not needed in this report.

p.4 - In the Summary, please indicate that the greatest amount of dermal penetration (amount in receptor fluid plus the amount in the skin; abut 30%) of Acetyl Tyrosinamide was from a cream formulation.

p.4 - In the Summary, please give some indication of the concentrations of the ingredients that were not sensitizing and not phototoxic.