Safety Assessment of *Citrus* Plant- and Seed-Derived Ingredients as Used in Cosmetics

Status: Draft Tentative Report for Panel Review
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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina Burnett, Senior Scientific Writer/Analyst
Date: May 13, 2016
Subject: Draft Tentative Report of the Safety Assessment of *Citrus* Plant- and Seed-Derived Ingredients

Enclosed is the draft tentative report of the Safety Assessment of *Citrus* Plant- and Seed-Derived Ingredients as Used in Cosmetics. (It is identified as *cplant062016rep* in the pdf document.)

At the December 2015 meeting, the Panel issued an Insufficient Data Announcement for the 33 *Citrus* plant- and seed-derived ingredients described in the safety assessment. Data needs included:

- Method of manufacturing
- Chemical composition and impurities
- Irritation and sensitization, especially human repeated insult patch tests (HRIPT) on Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil and Citrus Grandis (Grapefruit) Seed Extract at maximum use concentrations or greater
- If the composition for these *Citrus* plant- and seed-derived ingredients are significantly different from that of the *Citrus* peel-, flower-, and leaf-derived ingredients, then data on systemic endpoints such as a 28-day dermal toxicity, reproductive and developmental toxicity, and genotoxicity, as well as UV absorption spectra are needed

Since the December meeting, unpublished data on the method of manufacturing and composition of Citrus Paradisi (Grapefruit) Seed Extract and Citrus Junos Seed Extract have been received as well as composition data on Citrus Glauca Seed Oil and Citrus Australasica Seed Oil. Composition data was found in the published literature on *Citrus junos* Sieb. seed extract and *Citrus sinensis* leaves, branches, and seed flour. These data have been incorporated into the report and highlighted with |brackets|. No other requested data have been received or identified by CIR staff. Comments received from the Council have been considered. The comments and the unpublished data can be found in this report's package (*cplant062016pcpc and cplant062016data1-5, respectively).*

Both the VCRP and the concentration of use data have been updated for these ingredients. Currently, Citrus Aurantium (Bitter Orange) Oil has the most reported uses of the ingredients in this report in cosmetic products, with a total of 295; more than half are in leave-on skin care preparations. This ingredient is not currently listed in the *International Cosmetic Ingredient Dictionary and Handbook* but has been included in this report due to the number of uses and presumed similarities to the other ingredients in this report. The ingredients with the next highest frequency of use are Citrus Aurantifolia (Lime) Oil (169 total uses) and Citrus Grandis (Grapefruit) Seed Extract (144 total uses); a majority of the uses for these ingredients are in leave-on skin care preparations. The results of the concentration of use survey indicate Citrus Aurantium Dulcis (Orange) Oil has the highest reported maximum concentration of use; it is used at up to 1% in a body and hand formulation. Citrus Aurantifolia (Lime) Oil had the second highest reported maximum concentration of use; it is used at up to 0.36% in a lipstick. Please note that the data requested at the December 2015 was based on the highest uses/concentrations reported at the time and that the ingredients with the highest uses/concentrations may have changed since then. (Citrus Grandis (Grapefruit) Seed Extract was previously reported to be used at up to 2% in a face and neck formulation and Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil was previously reported to be used at up to 1.5% in a body and hand formulation).

These ingredients function mainly as skin conditioning agents-miscellaneous; however, two ingredients (Citrus Sunki Seed Extract and Citrus Sunki Seed Oil) also are reported to function as skin bleaching agents, which are drug uses and not cosmetic uses. When considering these ingredients, the Panel should discuss these potential uses.

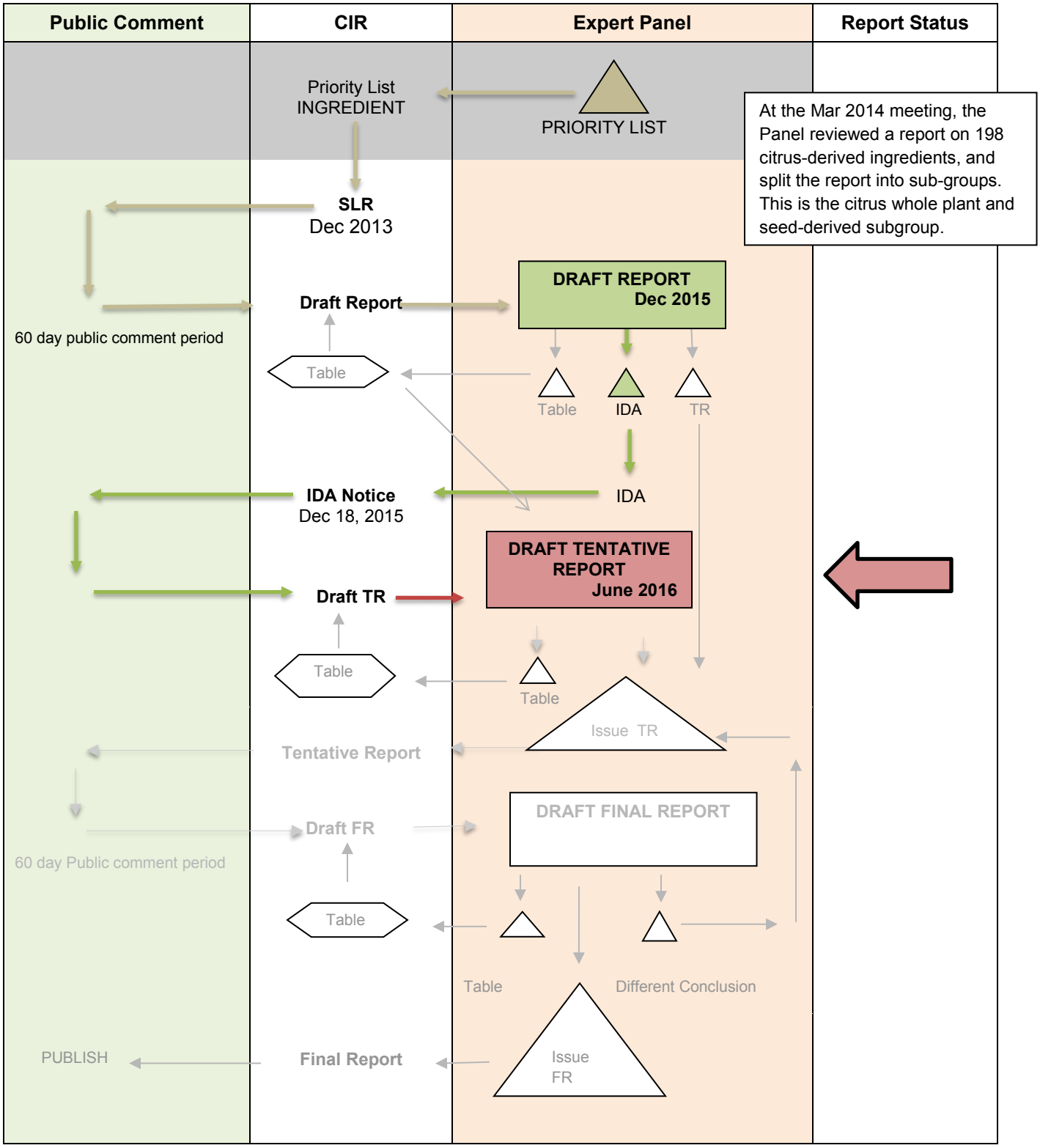
This report includes the ingredient Citrus Tangerina (Tangerine) Extract. Upon closer review of the definition, this ingredient should have been included in the Citrus fruit-derived ingredients report. Would the Panel like to remove this ingredient from this report and administratively add it to the Citrus fruit-derived ingredient report?

The Panel should carefully consider and discuss the data presented in this report and issue a Tentative Report.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Citrus Whole Plant & Seed-Derived Ingredients

MEETING June 2016



Citrus Plant- and Seed-Derived Ingredients History

December 2013 – Scientific Literature Review announced.

March 2014 - The Panel tabled further discussion of 198 citrus-derived ingredients to allow CIR staff to reorganize the report and to obtain clarification from RIFM on the functions of some of the ingredients. These ingredients were presented in a single safety assessment report addressing ingredients from all of the citrus plant species currently reported to be used in cosmetics in the International Cosmetic Ingredient Dictionary and Handbook. The Panel felt revising this report into smaller subgroups would be a manageable and meaningful alternative approach to assessing the safety of these ingredients. Based on the Panel's recommendation of grouping the ingredients by plant parts according to greatest number of uses, the first assessment reviewed by the Panel was citrus-derived peel oils, followed by citrus fruit-derived ingredients.

September 2015 – The Panel reviewed the report strategy for the remaining citrus ingredients. The Panel agreed that the remaining ingredients could be divided into 3 reports: citrus flower- and leaf-derived ingredients, citrus peel-derived ingredients, and citrus plant- and seed-derived ingredients. These reports can be reviewed concurrently.

December 2015 - The Panel requested additional data to support the safety of the 33 *Citrus* plant- and seed-derived ingredients. The additional data needed are:

- Method of manufacturing
- Chemical composition and impurities
- Irritation and sensitization, especially human repeated insult patch tests (HRIPT) on citrus aurantium amara (bitter orange) leaf/twig oil and citrus grandis (grapefruit) seed extract at maximum use concentrations or greater
- If the composition for these *Citrus* plant- and seed-derived ingredients are significantly different from that of the *Citrus* peel-, flower-, and leaf-derived ingredients, then data on systemic endpoints such as a 28-day dermal toxicity, reproductive and developmental toxicity, and genotoxicity, as well as UV absorption spectra are needed

Citrus Plant- and Seed-Derived Ingredients Data Profile – June 2016 – Writer, Christina Burnett										
	In-Use	**Physical/Chemical Properties**	**Method of Manufacturing**	**Composition/Impurities**	**Carcinogenicity**	**Irritation/Sensitization - Nonhuman**	**Irritation/Sensitization - Clinical**	**Ocular/Mucosal**	**Phototoxicity**	**Case Studies**
Citrus Aurantifolia (Lime) Oil	X									
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	X									
Citrus Aurantium Dulcis (Orange) Oil	X									
Citrus Aurantium Dulcis (Orange) Seed Extract	X									
Citrus Aurantium Sinensis Powder	X									
Citrus Australasica Seed Oil		X		X						
Citrus Glauca Seed Oil		X		X						
Citrus Grandis (Grapefruit) Extract	X									
Citrus Grandis (Grapefruit) Seed Extract	X									
Citrus Junos Extract	X									
Citrus Junos Seed Extract	X		X	X						
Citrus Junos Seed Oil	X									
Citrus Limon (Lemon) Flower/Leaf/Stem Extract	X									
Citrus Nobilis (Mandarin Orange)	X									
Citrus Nobilis (Mandarin Orange) Oil	X									
Citrus Paradisi (Grapefruit) Seed Extract	X		X	X						
Citrus Reticulata (Tangerine) Extract	X									
Citrus Tangerine (Tangerine) Extract	X									
Citrus Aurantium (Bitter Orange) Oil (not INCI ingredient)	X									
Citrus sinensis leaves and branches				X						
Citrus sinensis seed flour				X						
NO USES OR DATA WERE AVAILABLE FOR THE REMAINING CITRUS INGREDIENTS LISTED IN TABLE 1.										

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

Search Strategy for Citrus Plant- and Seed-Derived Ingredients

- August 2014 – miscellaneous searches for additional data on constituents
- Scifinder – February 26, 2013
  - Search for INCI citrus ingredients w/ CAS No. – 99 hits, 10 ordered
- PubMed – March 5,2013
  - Search for "citrus cosmetics" – 65 hits, 1 ordered
  - Search for "citrus sensitization" – 36 hits, 8 ordered
  - Search for "citrus dermal" – 12 hits, 0 ordered
  - Search for "citrus phototoxicity" – 24 hits, 10 ordered
- SciFinder – Aug 19 2013
  - toxicity of citrus ingredients – 11 hits; 1 ordered
  - carcinogenicity of citrus – 466 hits; 8 ordered
- SciFinder – Aug 20, 2013
  - Phototoxicity of citrus – 47 hits; 21 ordered
  - Dermal effects of citrus – 51 hits; 1 new ref found
  - Dermal absorption of citrus – 1 hit; not useful
  - Constituents of citrus – 116 hits;
  - Citrus – Belsito, Marks, Bergfeld, Api, RIFM– 2 found

Ordered a few others; printed some directly

Updated searches in November, 2013 – ordered an additional 4 references
Updated searches July 2015 with the term "citrus" – 1 new relevant reference found.
Updated searches October 2015 with the term "citrus AND toxicity" or "citrus AND irritation"– 0 new relevant references found.
Updated searches February –May 2016 with the term "citrus seed composition" (29 hits) and "citrus plant composition" (555 hits) and "citrus branch composition" (5 hits) and "citrus stem composition" (7 hits) – 4 relevant references found.

Online Info

- FDA
  - GRAS definitions
- Dr. Duke's Phytochemical and Ethnobotanical Databases
  - Due to volume of data, limited search to Citrus limon (Lemon), Citrus aurantifolia (Lime), Citrus paradisi (Grapefruit), Citrus sinensis (Sweet Orange), and Citrus aurantium (Bitter Orange)
- National Toxicology Program (NTP)
  - Bitter Orange Extract (mixture)
- SCCS/SCCP
  - Opinion on fragrance allergens in cosmetic products
  - Opinion on Furocoumarins in cosmetic products
- Sigma Aldrich
  - Citrus aurantiifolia (lime)
  - Citrus aurantium (bitter orange)
  - Citrus paradisi (grapefruit)
  - Citrus reticulata (tangerine)
- IFRA
  - 7-methoxycoumarin
  - Standard for citrus oils and other furocoumarins containing essential oils. Ingredients include:

Citrus Plant- and Seed-Derived Ingredients
December 14-15, 2015

Dr. Marks' Team

DR. MARKS: Okay. Can we move on to the next ingredient? Okay.

DR. SLAGA: Ditto.

MS. BURNETT: Yes. This one because it is the rest of the plant, I did not include the GRAS certification because I'm assuming we're not eating the bark so.

DR. HILL: I thought the same for the leaves and flowers.

DR. MARKS: So citrus plant and seed.

MS. BURNETT: But I couldn't feel confident in making the extrapolation there.

DR. HILL: Yes. Yes.

DR. SLAGA: Here comes that young man.

DR. MARKS: Okay, yes, ditto is right. So still Ron's and Tom, is the first review so I'm going to do it formally rather than just getting a ditto. Are there 33 ingredients? Okay.

DR. HILL: I think so.

DR. MARKS: Yes?

DR. HILL: Yes.

DR. MARKS: Okay. Very little data and needs are, well, it'll be an insufficient data announcement. Method of manufacture, composition and the HRIPTs, I'd like to see is the bitter orange leaf twig oil, that one point five percent, grapeseed extract at two percent. Now --

MS. BURNETT: Whoa, what was the first one? Bitter orange leaf twig oil?

DR. MARKS: Yes, at one point five percent.

MS. BURNETT: Okay.

DR. MARKS: And --

MS. BURNETT: And the grapefruit -- seed extract?

DR. MARKS: No, the grapefruit seed extract two percent.

MS. BURNETT: Okay. So we did have on this one and I pointed out in the memo that and in the two previous ones, there's inconsistencies in the VCRP and the INCI data. This one won't -- for us was the biggest glaring difference because the one that had the most uses is not in the INCI dictionary. And we actually feel that it might be a misnaming in the VCRP. We think it could be actually a peel oil or a fruit oil but due to the way it's named and how the other INCI definitions are, it sounds like it's a whole plant fruit oil or a whole plant oil.

So hopefully, maybe we can get some clarification from FDA or someone that will tell us what the actually is but for now, it's going to stay in the plant report until we know.

DR. MARKS: Which one are you talking about there because I have 276 uses for the bitter orange oil.

MS. BURNETT: Yes.

DR. MARKS: But that's not INCI ingredient, is that what you're talking about?

MS. BURNETT: It is not an INCI ingredient yes.

DR. MARKS: One of the concerns I had, now I won't put the preference here, is the citrus -- so an INCI seed extract and oil are not used but there's a reference to skin lightening, is that correct?

MS. BURNETT: There --

DR. MARKS: I'll show the --

MS. BURNETT: In the dictionary they have listed functions as.

DR. MARKS: It's not used but, you know, where is that? I'm sure I highlighted it somewhere.

MS. BURNETT: I know I put it in the memo, I think. It's in the memo for sure.

DR. MARKS: Yes. It's in the last -- second to the last paragraph, also reported functional skin bleaching agents which are drug use. It's not cosmetic. How do we want to -- I know this is insufficient data announcement but how -- we need to think about how we're going to address its function as a skin bleaching agent.

DR. HILL: Same as we did kojic acid. I'm not really being totally facetious. We looked for levels that didn't have that action.

DR. MARKS: Yes, so that's what I put here. Question mark, no for skin lightening which we aren't going to find, yes, Jay. How would you address this since it says this is a use as a skin bleaching agent and these doing --

DR. ANSELL: To the extent that a manufacturer put it in there, it would be an illegal, unapproved new drug. So I don't think that really is your concern.

DR. MARKS: So we should -- we put that in the discussion? This is a drug use?

MS. BURNETT: Yes.

DR. ANSELL: Yes. It's just not an application of the whole -- the purview of the expert panel.

DR. GILL: Well, we usually say that close to the introduction, if not in the introduction. That it's just not a cosmetics function. It's a drug function.

DR. ANSELL: Okay. So your conclusion, to the extent it says safe as used or unsafe as used, would exclude its use in that application.

DR. HILL: Well, I remember we did with kojic acid and this has been a while back, is that we looked for a level that didn't have that activity.

DR. MARKS: Yes.

DR. HILL: And limited up to that percent or something. I don't know that -- that was a clean compound though and this is -- it's a mixture.

MS. BURNETT: And with kojic acid they also saw -- it wasn't a permanent effect. The cells reversed or whatever eventually. It wasn't a permanent thing like it is with hydroquinone.

DR. HILL: But what about the seed extract? Do we even know? Yes, me neither.

DR. MARKS: We have to address it because if these two ingredients were put in a cosmetic ingredient, a possible effect could be skin lightening. So either we can say if it has that effect it's a drug use and shouldn't, unless, as you suggested, Ron, you know, there actually is a no -- narrow effect level for this in skin lightening which probably, I don't know if it exists or not. We can look for it. You could search. I assume it doesn't exist, Christina, or you would have found that.

MS. BURNETT: Yes. I don't even know exactly what species this is. It's not a typical species.

DR. MARKS: It's not being used so as a cosmetic --

DR. ANSELL: I think the focus would be the use concentrations in cosmetics. Does it have a, you know, an adverse effect that needs to be assessed.

DR. MARKS: Right.

DR. HILL: And we didn't have concentration information really on any of these at this juncture.

MS. BURNETT: Not those two. And Carol is performing new surveys on all three of these citrus drafts.

DR. HILL: That's what I thought I understood.

DR. ANSELL: Yes, we think for these -- the new citrus drafts, we think that there is a lot of data out there on composition. We think that we have not gone out to the manufacturers because it hasn't started (inaudible) -- haven't gone out for the manufacturers for this meeting and that we will come back with, you know, with that type of information.

DR. MARKS: Right.

DR. ANSELL: So I think at this point our position is, you know, to go through, ask your questions and --

DR. MARKS: Exactly.

DR. ANSELL: Yes, we'll have an opportunity to come back and respond to them.

DR. MARKS: Okay.

DR. GILL: I do want to clarify something, though, because we've talked about this in previous panel meetings where if it had this skin lightening function, we would say that's not the purview of the panel. Are we now saying because it's used but it also has the skin bleaching function, that we are looking at levels which when used as a cosmetic ingredient, it does not have that affect? Because now we're getting into this for all of the functions --

DR. HILL: That's what we did with kojic acid. That's exactly what we did with kojic acid.

DR. GILL: Well, that's not exactly the way we've been handling --

DR. HILL: I know.

DR. GILL: -- (inaudible) in the past couple of meetings.

DR. HILL: But that's what we did with kojic acid for exactly that reason.

DR. GILL: So now we seem to be looking for a level that says it does not have that sort of effect.

DR. MARKS: Well, no, I think there's seve -- that's going to be resolved as we delve into it in the next rendition of this but I doubt we'll find a level which will take us to below where skin lightening occurs. But that doesn't mean one couldn't look for it. And then, I have a feeling we're going to deal with this issue in the discussion that the CIR conclusion excludes use for drug action of skin lightening. Yes?

MR. STEINBERG: Does CIR review arbutin? Because that's the same type of issue.

DR. MARKS: Pardon?

MR. STEINBERG: Arbutin, you know, for data? Arbutin? I don't remember whether we reviewed it or not.

DR. MARKS: Yes, I don't remember that.

MR. STEINBERG: Because that would be like a (inaudible).

DR. HILL: The difficulty here is that since we don't have a pure substance, but rather, an extract, I don't know even how you would -- you'd have to have a constituent or constituents of interest that had that effect in order to --

DR. MARKS: Right, yes.

DR. HILL: And a way of standardizing and I bet there's no such --

DR. ANSELL: On the other hand, there's no evidence this is actually -- does lighten skin.

MS. BURNETT: That's just what it was reported.

DR. MARKS: So I can say clinically I have not run across this that's for sure. But -- and you didn't find any case reports? It's just --

DR. GILL: I think I just want to be cautious about going down that path because I think we're always going to be asking that question. Try and find a (inaudible) that's the skin lightening.

MS. DEWAN: Just to answer the question of frequency of use, we do have frequency of use data for bitter orange (inaudible) oil and it's quite -- used in quite high level.

MS. BURNETT: I'm sorry, I couldn't -- I have air conditioner hum. Let me come closer to you.

MS. DEWAN: The frequency of use data was for bitter orange. You asked for that. It's quite high.

MS. BURNETT: Yes, but we -- but it's not in the INCI dictionary, that ingredient.

MS. DEWAN: Right, I see that. Yes, I see that, right.

MS. BURNETT: So we know it's really high but there's a question as if --

MS. DEWAN: Where it's coming from.

MS. BURNETT: -- is that actually a whole plant oil or is that a --

MS. DEWAN: Yes, I think the monograph of INCI --

MS. BURNETT: -- peel or something else. We don't --

MS. DEWAN: The monograph of INCI can provide you that information. We don't have that. Yes.

MS. BURNETT: Okay. Okay.

DR. MARKS: Okay. So I think we've discussed this enough. Have we?

DR. SHANK: No.

DR. MARKS: No? Oh, sorry.

DR. SHANK: These are not GRAS ingredients.

DR. MARKS: Oh.

DR. SHANK: So I think we need 28-day dermal toxicity on these ingredients because we can't do penetration. They're mixtures so we'll have to do the dermal toxicity studies and then the immunogenicity data, bacterial and mammalian.

DR. ANSELL: If the composition is equivalent to the flowers and leaves then that --

DR. SHANK: That's the first needed composition, yes. So if they're very similar then it's okay. But if they're not and this is the whole plant, right?

DR. HILL: And then seeds. Seeds are not plants.

DR. SHANK: So I think there's a potential for the composition to be different. Then depending on the results of the dermal study we may need reproductive and developmental toxicity and UV absorption data in addition to your irritation and sensitization request.

DR. MARKS: Thank you, Ron.

DR. SHANK: You're welcome.

DR. MARKS: So I'm going to summarize this then. Our AI -- IDA announcement has more expanded needs, method of manufacture, composition, if the composition is not similar to the other citrus ingredients then we need 28-day dermal tox immunogenicity, repro, development, UV absorption and the HRIPTs which we mentioned before. So a pretty long list now. Thank you.

And that's all based on that these are not GRAS?

DR. SHANK: Correct.

DR. MARKS: Okay.

DR. HILL: And the identities and levels, you know, and that ought to be on the ingredients not here's the whole plant and by the way, they have seeds and these things are in there.

DR. MARKS: Okay. Any other comments? If not, let's move on to the next.

Dr. Belsito's Team

DR. BELSITO: Okay, so now we're going on to the citrus plant in seed-derived ingredients as used as cosmetics, and I guess the first comment I had is why the Citrus junos seed oil was not included in the other seed oils.

MS. BURNETT: We missed it, so we could back at it, or we could put it in --

DR. EISENMANN: Or it could have been added to the dictionary after that report was completed.

MS. BURNETT: I think that might have been what it was. We just didn't see it the first time around. So, it might have been -- yeah.

DR. BELSITO: Okay, and then again the same issue with mixing oils, waters, waxes, extracts, powders.

MS. BURNETT: I did take the GRAS wording out of this one, because it was pretty obvious that there's nothing edible here.

DR. BELSITO: So, I guess at the end of the day do we make these "insufficient for manufacturing impurities composition"? Or do we try to read across from all of the other documents we have, because there's not a whole lot here?

DR. LIEBLER: I don't think we can read across from anything having to do with fruit and seed, although, you know, some of these are so poorly defined. For example, does the whole plant include fruit components? And we just -- I know you don't know, because you wouldn't put it in if you did.

DR. EISENMANN: We're going to have to look into these "whole plant," because I don't believe them.

DR. LIEBLER: Yeah.

DR. EISENMANN: As I'm doing the concentration view survey, I'm asking people who report the "whole plant": Is this really a whole plant? These are likely fruit, to be honest, because at the very beginning, when greens were named they were named, you know, like lime oil, and then they got changed, and I think that the name didn't get changed unless somebody changed the definition to say it was the whole plant. But I just can't imagine. I think of a chipper and mulch rather than a cosmetic ingredient.
(Laughter)

DR. LIEBLER: It's the first thing I thought of too -- the wood chipper. (Laughter)

MS. BURNETT: I could see, like, during harvest, like the ones that have the combo leaf stem, like, you might get part of a branch thrown in the --

DR. EISENMANN: Those are probably real. It's the ones that are defined as a whole plant. There's a tangerine that says it's an extract -- it's an extract of a tangerine. It doesn't -- I mean it hadn't -- it didn't get changed to "whole plant." So that -- my guess is that whole fruit -- I mean, it's a fruit preparation.

MS. BURNETT: Right, and this is where we had the big problem with the discrepancy in the VCRP data where you have citrus aurantium -- bitter orange oil -- which, per definition -- well, in this -- the oils without any definition say it's a whole plant. This one is not in the INCI dictionary, but it has 276 uses.

DR. EISENMANN: It's probably the peel oil, because that's the main --

MS. BURNETT: That's what we suspected, too, but we need clarification. So, for now, it has to be in this report.

DR. EISENMANN: Mm-hmm, so, we need to do some work on these -- that is what I am saying -- where we haven't developed an official policy on what we're going to be doing yet. So, it's unlikely that they're whole plant extracts, unless it's making a sprout, and then that would be the whole plant. But --

DR. KLAASSEN: You don't think that it's --

DR. EISENMANN: I don't think so.

DR. KLAASSEN: You don't think it's enclosed the tree? (Laughter)

DR. EISENMANN: No. I think it's highly unlikely that they're doing a whole tree.

DR. KLAASSEN: Well, it says "plant."

DR. EISENMANN: I know.

DR. LIEBLER: Well, then, they can return the wood chipper. Is there a rental place?

DR. BELSITO: So, we have twigs, too, here.

DR. LIEBLER: Yes, and stems.

DR. EISENMANN: Well, actually, I did find some published papers that look at the composition of leaves versus twigs versus flowers, and so there are some data out there, published information on composition of various parts. But the whole plant ones are the ones that I think are spurious.

DR. BELSITO: But are we going to be able to clarify that?

DR. EISENMANN: I'm going to try, but I'm not going to promise anything because, like I've said, whenever somebody says they reporting news says during that process I'm going back and say is this real, and one response was: The name is correct. They wouldn't tell me, you know, they're not getting information on what it is. But I'm pretty sure it's a lime oil. It's made from the lime, not the plant.

DR. LIEBLER: Mm-hmm. I think we're just not really even at a starting point with these.

DR. EISENMANN: Hmm-mm.

DR. LIEBLER: No, no.

DR. BERGFELD: It's repeat, repeat on the last ones.

DR. LIEBLER: Yeah, it is.

DR. BELSITO: Okay, so basically what we need are method of manufacture, impurities, chemical composition -- and, depending upon that, I guess sensitization, irritation. Since we're talking about skin and depending upon that, other end points may be necessary?

DR. LIEBLER: Yeah, and in fact it might be that some of these go into another report once they are defined. And it might leave us just with seeds. Seeds is the only thing that's not included in any of the other reports, unless we were to dump seeds in with fruit, because seeds are in the fruit.

DR. KLAASSEN: But very different compositions.

DR. EISENMANN: The composition's been --

DR. LIEBLER: But compositionally they're certainly different, that's right.
Okay, so --

DR. SNYDER: Question on the -- and it lists here, so about middle way down the left-hand column there you have citrus aurantium sinensis powder. We don't know the powder of what. It just says "powder."

MS. BURNETT: And the definition that leads to it being powder of the whole plant. It says "the powder obtained from the dried ground plant."

DR. SNYDER: Okay, thank you.

MS. BURNETT: So.

DR. BELSITO: Any other? Okay, so what I have is that we know that there are ingredients here that aren't in the INCI dictionary but we're going ahead and including them and that we're not sure that the grouping is correct, and once we have information on composition we may move some in or out to other reports. But as it stands now, we're going "insufficient" for all of these for manufacturing, impurities, chemical composition, sensitization, irritation, and concentration of use. And depending upon composition impurities, other toxicologic end points may be necessary.

DR. LIEBLER: Right.

DR. BELSITO: Okay?

MS. BURNETT: Mm-hmm.

DR. BELSITO: Okay, are we done Citrus?

MS. BURNETT: Yes. (Laughter)

Full Panel Meeting

DR. BERGFELD: One more? Oh, plant and seed, okay.

DR. MARKS: Yeah, that's what I tried to do.

DR. BERGFELD: I did it, too. Belsito, I'm sorry. Thank you.

DR. BELSITO: So this is, again, the first time we're looking at this report --

DR. BERGFELD: Too many citrus in a row.

DR. BELSITO: -- since it's been split. There are ingredients. And, again, questioning whether we made the right grouping here, putting the various derivatives of the plant and seed together. Also, we're now dealing with issues where we have data on material that is actually not in the INCI dictionary and how do we deal with that. Do we just use it as a reference? Do we say that those are safe as used since we're told by VCRP that they are being used? It's again a question that I think at some point we need to address.

And for this group, again, insufficient, exactly what we're asking for the others: Manufacturing impurities, composition, sensitization and irritation.

DR. BERGFELD: Is there a second?

DR. MARKS: Yeah, we would second that. The only other point that Ron Shank made is these are not GRAS ingredients, so we would want -- if the composition were not similar to the other citrus ingredients, then we would need the 28 dermal tox: Mutagenicity, reproductive, development, et cetera, (inaudible) absorption. Did I characterize that right, Ron?

So that's the only caveat, which is a little different in these citrus ingredients compared to the other ones.

DR. BERGFELD: Any comment on that?

DR. BELSITO: No, no comment on that. The only other comment is apparently we have overlooked Citrus junos seed oil with the plant seed oil reports or it was added to the dictionary after that report went out. So I guess the question is, in the interest of keeping related things together, is there some way of moving that to the plant see oil report, issuing an addendum, or do we keep it in this citrus seed report?

MS. BURNETT: There's also three other seed oils besides that in this report.

DR. BELSITO: Yes.

DR. BERGFELD: Is there a comment? Lillian? Bart?

DR. HELDRETH: I mean, it's at the Panel's discretion. We can keep them here and we can use data from the plant oils report if the Panel finds that that's useful or if the Panel would prefer to move these to the plant oils report, that would mean some of these are not identical to anything that's already in the plant oils report. That would require reopening that report, so it's a matter of is that something the Panel wants to do the work of. I mean, it'd be significantly more work. It just depends on if the Panel feels it's important.

DR. BELSITO: If it's going to be significantly more work, I would say no, but maybe somehow we could asterisk these and say for consideration of moving into the plant seed oil report when we reopen the report 15 years from now?

DR. HELDRETH: Absolutely. Absolutely. And I think in relation to this and the discussion we've been having today about the groupings, I think it's very important to look at the botanicals framework that the industry provided with us in a meeting within the last few years. And the first point on that was understanding what the composition of these materials are. So I think, as it's been mentioned, getting that

composition data will give us a better idea of whether these are grouped properly or not and how we could possibly subgroup them within the document. Because, of course, with these botanicals, we don't know what they are, things like read across, things like inference don't even make any sense. But having constituents that are alike and sources that are alike could actually make your job more efficient by reviewing these ingredients together.

DR. BERGFELD: Thank you. I'm going to call the question for insufficient. We've had two additions to that listing.

DR. MARKS: I'd like to bring up one other discussant point. In Christina's memo, the second to the last paragraph she talks about two ingredients, the Citrus sunki seed extract and the seed oil, have been reported the functions of being skin bleaching agents, which is a drug use and not a cosmetic use. These agents are actually not being used at this point in the discussion. How did your team handle that, Don? Do you just reiterate in the discussion that this is excluded because of a drug use of skin lightening?

DR. BELSITO: Yeah.

DR. MARKS: Or do we need something like a NOEL for skin lightening, which we aren't going to get?

DR. BELSITO: No. No, just that it would not be considered a cosmetic product if it had an effect on pigmentation.

DR. MARKS: Okay, good, I think.

DR. BERGFELD: Okay. All questions answered? Ron Hill?

DR. HILL: Yeah, I wanted to follow up on we talked about composition, that we need identities and levels in a particular ingredient, but because if we have an ingredient like extract, that could vary quite a bit depending on whose extract it was, what particular manufacturer was producing it. Some sense of really, based on what's available, how much those can vary because that's what's really needed to review a particular ingredient is when you say "extract," this kind of extract, in terms of available ingredient on the market being sold for use in cosmetics, what are those ranges? I think down the line if we have a meeting focused on this, we have to talk about that because the exact way that that extract is being prepared, is it supercritical fluid extraction? Is it sitting in ethanol at room temperature for a month? Is it boiling in methanol? Those can make a big difference in terms of extract and we haven't always been getting that to date on botanicals. And it goes to the ability to read across, to use that ugly term again, informing the toxicology in one ingredient versus another. And again, if it's used at .0005 percent maybe we care less than if it's a 5 percent.

DR. BERGFELD: I think that we'll take that under consideration when we look at these ingredient. I'm going to call for the vote then to go insufficient. All those in favor to go insufficient with the list that was prepared? Thank you.

Safety Assessment of *Citrus* Plant- and Seed-Derived Ingredients as Used in Cosmetics

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The 2016 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Christina Burnett, Senior Scientific Analyst/Writer.

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DRAFT ABSTRACT

The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) assessed the safety of 33 *Citrus* plant- and seed-derived ingredients, which are most frequently reported to function in cosmetics as fragrances and/or skin conditioning agents. The Panel reviewed the available data to determine the safety of these ingredients. Because final product formulations may contain multiple botanicals, each containing similar constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. Industry should use good manufacturing practices to limit impurities that could be present in botanical ingredients. The Panel concluded…(to be determined).

INTRODUCTION

This report assesses the safety of the 33 *Citrus* plant- and seed-derived ingredients listed below, which are reported to mainly function as skin conditioning agents-miscellaneous in cosmetic ingredients (Table 1).[1] Citrus Aurantium (Bitter Orange) Oil is not currently listed in the *International Cosmetic Ingredient Dictionary and Handbook* (Dictionary) but has been included in this report due to its high reported number of uses and presumed similarities to the other ingredients in this report. Two ingredients (Citrus Sunki Seed Extract and Citrus Sunki Seed Oil) are reported to function as skin bleaching agents, which are drug uses and not cosmetic uses and do not fall under CIR's purview.

Citrus Aurantifolia (Lime) Oil
Citrus Aurantium (Bitter Orange) Oil
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Extract
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil
Citrus Aurantium Dulcis (Orange) Flower/Leaf/Stem Powder
Citrus Aurantium Dulcis (Orange) Oil
Citrus Aurantium Dulcis (Orange) Seed Extract
Citrus Aurantium Sinensis Powder
Citrus Australasica Seed Oil
Citrus Depressa Seed Oil
Citrus Glauca Seed Oil
Citrus Grandis (Grapefruit)
Citrus Grandis (Grapefruit) Extract
Citrus Grandis Peel/Seed Extract
Citrus Grandis (Grapefruit) Seed Extract
Citrus Iyo Oil
Citrus Jabara Pericarp Extract
Citrus Junos Extract
Citrus Junos Seed Extract
Citrus Junos Seed Oil
Citrus Limon (Lemon) Flower/Leaf/Stem Extract
Citrus Limon (Lemon) Flower/Leaf/Stem Oil
Citrus Limon (Lemon) Leaf/Peel/Stem Oil
Citrus Nobilis (Mandarin Orange)
Citrus Nobilis (Mandarin Orange) Oil
Citrus Nobilis (Mandarin Orange) Water
Citrus Paradisi (Grapefruit) Seed Extract
Citrus Sunki Seed Extract
Citrus Sunki Seed Oil
Citrus Reticulata (Tangerine) Extract
Citrus Tangerina (Tangerine) Extract
Citrus Unshiu Extract
Citrus Unshiu Pericarp Extract

The Panel has previously reviewed the safety of *Citrus*-derived peel oils and *Citrus* fruit-derived ingredients in separate assessments and concluded that 14 *Citrus*-derived peel oil ingredients and the 80 *Citrus* fruit-derived ingredients are safe for use in both rinse-off and leave-on cosmetic products when formulated to be non-sensitizing and non-irritating, provided that leave-on products do not contain more than 0.0015% (15 ppm) 5-methoxypsoralen (5-MOP).[2,3] The Panel has also reviewed the safety of Citrus Aurantifolia (Lime) Seed Oil, Citrus Aurantifolia (Lime) Seed Oil unsaponifiables, Citrus Aurantium Dulcis (Orange) Seed Oil, Citrus Aurantium Dulcis (Orange) Seed Oil unsaponifiables, Citrus Grandis (Grapefruit) Seed Oil, Citrus Grandis (Grapefruit) Seed Oil Unsaponifiables, Citrus Limon (Lemon) Seed Oil, and Citrus Paradisi (Grapefruit) Seed Oil, and concluded that these ingredients were safe in the present practices of use and concentration as described in the safety assessment of plant-derived fatty acid oils.[3] The Panel is concurrently reviewing the safety of *Citrus* flower- and leaf-derived ingredients and *Citrus* peel-derived ingredients in separate reports.

CIR does not review ingredients that are known to function only as fragrance ingredients because, as fragrances, the safety of these ingredients is evaluated by the Research Institute for Fragrance Materials (RIFM). According to the *Dictionary*, four of the *Citrus* flower- and leaf-derived ingredients in this report are reported to function only as fragrance ingredients (see Table 2).[1] However, personal communications with RIFM in March 2015 did not identify these ingredients as fragrances included on their list of ingredients to be reviewed, thus CIR is reviewing the safety of these ingredients.

Botanical ingredients such as those derived from *Citrus* are comprised of numerous constituents, some of which have the potential to cause toxic effects; for example, bergapten (aka 5-methoxysporalen or 5-MOP) is a naturally-occurring phototoxic furanocoumarin (psoralen) in some *Citrus* ingredients. In this assessment, CIR is reviewing the potential toxicity of each *Citrus* plant- or seed-derived ingredient as a whole, complex substance. Except for specific constituents of concern that the Panel has identified, CIR is not reviewing the potential toxicity of the individual constituents of the *Citrus* plants and seeds from which the ingredients in this report are derived.

Note: In many of the published studies included in this assessment, the information provided is not sufficient to determine how well the substance being tested represents the cosmetic ingredient. In this safety assessment, if a substance tested in a study is not clearly a cosmetic ingredient, because of lack of information on the genus and species from which the

substance was derived and/or the method of extraction used, the test substance will be referred to by a common name (e.g. lemon extract). If the substance is clearly a cosmetic ingredient, the International Nomenclature of Cosmetic Ingredients (INCI) name will be used (e.g. "Citrus Limon (Lemon) Extract"). Additionally, some inconsistencies were noted in both taxonomic and INCI naming conventions. For example, this report includes the sweet orange ingredient described as Citrus Aurantium Dulcis (Orange) in the *International Cosmetic Ingredient Dictionary and Handbook.*[1] In contrast, most of the published literature and the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) refer to this ingredient as Citrus Sinensis (sweet Orange). Another example of a naming inconsistency is Citrus Grandis (Grapefruit); *Citrus grandis* is generally considered a name for a pomelo, which may also be referred to as *Citrus maxima*. *Citrus paradisi* appears to be the more widely accepted nomenclature for grapefruit. The INCI Committee of the Personal Care Products Council (Council) is working to correct some of these inconsistencies. The genus and species names associated with the ingredient names designated by the INCI Committee are listed in Table 3.[5]

CHEMISTRY

Definition and General Characterization

The definitions and functions of the *Citrus* plant- and seed-derived ingredients included in this report are provided in Table 1. The definition indicates what part(s) of the plant from which an ingredient is obtained. In some cases, the definition provides insight on the method(s) of manufacture. Essential oils are the hydrophobic, liquid, volatile aromatic compounds in the insoluble condensate fraction, and typically are small molecules, but their chemical structures can vary rather widely. Fixed oils, on the other hand are hydrophobic, nonvolatile, fatty compounds from plants (including *Citrus* seeds), animals or algae. These are primarily composed of glycerides, and to some extent, free fatty acids. Constituents of these *Citrus*-derived ingredients may include both oil types. The volatile nature of essential oils makes them more likely to be useful as fragrances, but that does not necessitate that fragrance is their only function.

Physical and Chemical Properties

Citrus Australasica Seed Oil

Citrus Australasica Seed Oil is reported to be a straw/yellow colored liquid with a refractive index of 1.476 (specification range 1.450-1.490 at 20º C) and a specific gravity of 0.917 (specification range 0.900-0.940 at 20º C).[7]

Citrus Glauca Seed Oil

According to a supplier, Citrus Glauca Seed Oil is a light brown to dark brown liquid.[6] At 20º C, the refractive index is 1.472 (specification range 1.450-1.490) and the specific gravity is 0.921 (specification range 0.900-0.940).

Method of Manufacturing

Citrus Junos Seed Extract

A supplier has reported that Citrus Junos Seed Extract is produced by extracting dried seeds with 90% ethanolic solution, which is then filtered.[8] The material then undergoes sedimentation, filtration, and adjustment before packaging.

Citrus Paradisi (Grapefruit) Seed Extract

A supplier reported that Citrus Paradisi (Grapefruit) Seed Extract is manufactured by first grinding grapefruit seeds and then extracting in a mix of water and glycerin.[9] The mixture is then clarified and decontaminated by heat.

Constituents/Composition

The *Citrus* ingredients are complex botanicals made up of numerous constituents. Table 4 lists *Citrus* constituents that are established contact allergens, according the European Commission's Scientific Committee on Consumer Safety (SCCS).[10]

Citrus Australasica Seed Oil and Citrus Glauca Seed Oil

The fatty acid profiles for Citrus Australasica Seed Oil and Citrus Glauca Seed Oil are listed in Table 5.

Citrus Junos Seed Extract

A supplier reports that Citrus Junos Seed Extract is composed of saponin and sugar.[8] Impurities of heavy metals are not more than 20 ppm and arsenic is not more than 2 ppm.

The fatty acid profile for *Citrus junos* Sieb. ex Tanaka is also listed in Table 5.

Citrus Paradisi (Grapefruit) Seed Extract

A supplier reported that a trade name material contains 67.0% to 73.0% glycerin, 26.0% to 32.8% water, and 0.2% to 1.0% Citrus Paradisi (Grapefruit) Seed Extract.[9]

Citrus Sinensis

In gas chromatography and gas chromatography-mass spectroscopy analysis of the essential oils from the leaves and green branches of Egyptian navel orange trees (*Citrus sinensis* (L.) Osbeck var. Malesy), 33 and 24 compounds were identified, respectively, for the leaves and branches.[11] These compounds made up 96.0% and 97.9%, respectively of the total detected constituents. The major constituents were sabinene (36.5% leaves, 33.0% branches), terpinen-4-ol (8.2% leaves,

6.2% branches), δ-3-carene (7.0% leaves, 9.4% branches), limonene (6.8% leaves, 18.7% branches), trans-ocimene (6.7% leaves, 6.1% branches), and β-myrcene (4.5% leaves, 9.4% branches).

The composition of samples of dehulled sweet orange (Citrus *sinensis*) seed flour (dry weight) was reported to be 54.2% fat, 28.5% carbohydrate, 5.5% crude fiber, 3.1% crude protein, and 2.5% ash.[12] Mineral analysis showed high levels of calcium and potassium.

USE

Cosmetic

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

According to 2016 VCRP data, Citrus Aurantium (Bitter Orange) Oil has the most reported uses of the ingredients in this report in cosmetic products, with a total of 295; more than half are in leave-on skin care preparations (Table 6).[13] This ingredient is not currently in the *Dictionary* but has been included in this report due to the number of uses and presumed similarities to the other ingredients in this report. The ingredients with the next highest frequency of use are Citrus Aurantifolia (Lime) Oil (169 total uses) and Citrus Grandis (Grapefruit) Seed Extract (144 total uses); a majority of the uses for these ingredients are in leave-on skin care preparations. The results of the concentration of use survey indicate Citrus Aurantium Dulcis (Orange) Oil has the highest reported maximum concentration of use; it is used at up to 1% in a body and hand formulation.[14] Citrus Aurantifolia (Lime) Oil had the second highest reported maximum concentration of use; it is used at up to 0.36% in a lipstick.

In some cases, reports of uses were received from the VCRP, but no concentration of use data were provided. For example, Citrus Limon (Lemon) Flower/Leaf/Stem Extract is reported to be used in 8 formulations, but no use concentration data were available. In other cases, no reported uses were reported to the VCRP, but a maximum use concentration was provided in the industry survey. For example, Citrus Junos Seed Oil was not reported in the VCRP database to be in use, but the industry survey indicated that it is used in face and neck and body and hand formulations at up to 0.1%. It should be presumed that Citrus Junos Seed Oil is used in at least one cosmetic formulation.

Table 7 lists all *Citrus* plant- and seed-derived ingredients not indicated to be in use based on the VCRP data or the results of the Council concentration of use survey.

Some of these ingredients may be used in products that can come into contact with the eye or mucous membranes. For example, Citrus Aurantifolia (Lime) Oil is used in a lipstick at up to 0.36%. Additionally, some of these ingredients were reported to be used in hair sprays, fragrance preparations, face powder and body powders, spray deodorants, and spray skin care preparations and could possibly be inhaled. For example, Citrus Aurantifolia (Lime) Oil was reported to be used in body and hand sprays at a maximum concentration of 0.12% and Citrus Junos Seed Oil was reported to be used in face powders at up to 0.1%. 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 below 10 µm compared with pump sprays.[15-18] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[16,17] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[17] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[19-21]

The *Citrus* ingredients described in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU); however, furocoumarins are prohibited from use in cosmetics except for normal content in natural essences and in sun protection and bronzing products where the content shall be below 1 mg/kg.[21]

The International Fragrance Association (IFRA) has issued standards for *Citrus* oils and other furocoumarin-containing essential oils.[23] Finished products that are applied to the skin, excluding rinse-off products like bath preparations and soaps, must not contain more than 0.0015% or 15 ppm 5-MOP. This equates to 0.0075% or 75 ppm in a fragrance compound used at 20% in a consumer product that is applied to the skin. If the level of 5-MOP has not been determined, limits specified for individual oils should be observed, and when such oils are used in combination with other phototoxic ingredients, the potential for an additive effect should be considered and use levels should be reduced accordingly. Restrictions for furocoumarin-containing essential oils have been recommended for bergamot oil expressed, bitter orange oil expressed, grapefruit oil expressed, lemon oil cold pressed, and lime oil expressed.

An IFRA standard prohibits the use of 7-methoxycoumarin in fragrance compounds.[24] In commercially available natural sources (like essential oils, extracts, and absolutes), the level of naturally occurring 7-methoxycoumarin in the finished product must not exceed 100 ppm. Based on this standard, the maximum concentration of 7-methoxycoumarin in lime cold pressed oil is 0.1%, for example.

The IFRA has also set limits on the amounts of some *Citrus*-derived oils in finished products. For leave-on products applied to skin areas exposed to direct sunlight, these limits include: 1.25% bitter orange peel expressed;[25] 0.4% bergamot oil expressed;[26] 4% grapefruit oil expressed;[27] 2% lemon oil cold-pressed;[28] 0.7% lime oil expressed.[29] There are no restrictions for any of these oils in rinse-off products and products that are not applied to the skin. IFRA specified that if combinations of phototoxic fragrance ingredients are used, the use levels must be reduced accordingly, so that the sum of the concentrations of all phototoxic fragrance ingredients, expressed as a percentage of their respective recommended maximum levels, shall not exceed 100% in the consumer product. Additionally, the general standard described above for '*Citrus* oils and other furocoumarins-containing essential oils' must be considered.

Non-Cosmetic

Essential (or volatile) oils of limes, lemons, grapefruits, bitter oranges, oranges, and tangerines are described as flavoring agents in the *Food Chemicals Codex*, a compendium of internationally recognized standards published by the United States Pharmacopeia (USP) for the purity and identity of food ingredients.[30]

TOXICOKINETICS

No relevant published toxicokinetics studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted: these types of data are not expected since these botanical ingredients are mixtures of hundreds of constituents.

TOXICOLOGICAL STUDIES

Acute Toxicity

No relevant published acute toxicity studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

Repeated Dose Toxicity

No relevant published repeated dose toxicity studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No relevant published reproductive and developmental studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

GENOTOXICITY

No relevant published genotoxicity studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

CARCINOGENICITY

No relevant published carcinogenicity studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

IRRITATION AND SENSITIZATION

No relevant published irritation and sensitization studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

CLINICAL STUDIES

No relevant published clinical studies on *Citrus* plant- and seed-derived ingredients were identified in a literature search for these ingredients and no unpublished data were submitted.

SUMMARY

The 33 *Citrus* plant- and seed-derived ingredients described in this report function primarily as skin conditioning agents-miscellaneous. Botanical ingredients such as those derived from *Citrus* are composed of hundreds of constituents, some of which have the potential to cause toxic effects; for example, bergapten (aka 5-methoxypsoralen or 5-MOP) is a naturally-occurring, phototoxic furanocoumarin (psoralen) in *Citrus*. Presently, CIR reviewed the information available on the potential toxicity of each *Citrus* plant- and seed-derived ingredient as a whole, complex substance; CIR did not review the potential toxicity information on the individual constituents of which the *Citrus* plant- and seed-derived ingredients are comprised.

Citrus Aurantium (Bitter Orange) Oil has the most reported uses of the ingredients in this report in cosmetic products, with a total of 295; more than half of the uses are in leave-on skin care preparations. This ingredient is not currently in the *Dictionary* but has been included in this report due to its high reported number of uses and presumed similarities to the other ingredients in this report. The ingredients with the next highest frequency of use are Citrus Aurantifolia (Lime) Oil (169 total uses) and Citrus Grandis (Grapefruit) Seed Extract (144 total uses); a majority of the uses for these ingredients are in leave-on skin care preparations. The results of the concentration of use survey indicate Citrus Aurantium Dulcis (Orange) Oil has the highest reported maximum concentration of use; it is used at up to 1% in a body and hand formulation. Citrus Aurantifolia (Lime) Oil had the second highest reported maximum concentration of use; it is used at up to 0.36% in a lipstick.

The *Citrus* ingredients described in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU); however, furocoumarins are prohibited from use in cosmetics except for normal content in natural essences and in sun protection and bronzing products where the content shall be below 1 mg/kg.

IFRA also has issued standards for *Citrus* oils and other furocoumarin-containing essential oils. Finished products that are applied to the skin, excluding rinse-off products like bath preparations and soaps, must not contain more than 0.0015% or 15 ppm 5-MOP. If the level of 5-MOP has not been determined, limits specified for individual oils should be observed, and when such oils are used in combination with other phototoxic ingredients, the potential additive effect should be taken into consideration and use levels should be reduced accordingly.

No relevant published studies on the toxicokinetics, acute or repeated dose toxicity, reproductive and development toxicity, carcinogenicity, genotoxicity, irritation or sensitization, or clinical assessments of *Citrus* plant- and seed-derived ingredients were discovered and no unpublished data were submitted to address these topics.

TABLES

Table 1. Definitions and functions of *Citrus* plant- and seed-derived ingredients.[1]

Ingredient	Definition	Function
Citrus Aurantifolia (Lime) Oil CAS No. 8008-26-2	Citrus Aurantifolia (Lime) Oil is the volatile oil obtained from the whole plant, *Citrus aurantifolia.*	Fragrance Ingredients; Skin-Conditioning Agents - Miscellaneous
Citrus Aurantium (Bitter Orange) Oil	Not reported.	Not reported.
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Extract CAS No. 72968-50-4; 8016-38-4	Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Extract is the extract of the leaves and twigs of *Citrus aurantium amara.*	Skin-Conditioning Agents - Miscellaneous
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil is the volatile oil obtained from the leaves and twigs of *Citrus aurantium amara.*	Flavoring Agents; Fragrance Ingredients
Citrus Aurantium Dulcis (Orange) Flower/Leaf/Stem Powder	Citrus Aurantium Dulcis (Orange) Flower/Leaf/Stem Powder is the powder obtained from the dried, ground flowers, leaves and stems of *Citrus aurantium dulcis.*	Exfoliants
Citrus Aurantium Dulcis (Orange) Oil	Citrus Aurantium Dulcis (Orange) Oil is the volatile oil obtained from the whole plant, *Citrus aurantium dulcis*.	Fragrance Ingredients
Citrus Aurantium Dulcis (Orange) Seed Extract	Citrus Aurantium Dulcis (Orange) Seed Extract is the extract of the seeds of *Citrus aurantium dulcis.*	Skin-Conditioning Agents - Miscellaneous
Citrus Aurantium Sinensis Powder	Citrus Aurantium Sinensis Powder is the powder obtained the dried ground plant, *Citrus aurantium sinensis.*	Exfoliants
Citrus Australasica Seed Oil CAS No. 1174331-57-7 (generic)	Citrus Australasica Seed Oil is the fixed oil expressed from the seeds of *Citrus australasica.*	Antioxidants; Hair Conditioning Agents; Humectants; Skin-Conditioning Agents - Miscellaneous
Citrus Depressa Seed Oil	Citrus Depressa Seed Oil is the oil expressed from the seeds of *Citrus depressa.* The accepted scientific name for *Citrus depressa* is *Citrus reticulata.*	Skin-Conditioning Agents - Emollient
Citrus Glauca Seed Oil	Citrus Glauca Seed Oil is the oil expressed from the seeds of *Citrus glauca.*	Antioxidants; Humectants; Skin Protectants; Skin-Conditioning Agents - Emollient; Skin-Conditioning Agents - Humectant
Citrus Grandis (Grapefruit)	Citrus Grandis (Grapefruit) is a plant material derived from the whole plant, *Citrus grandis.*	Not reported
Citrus Grandis (Grapefruit) Extract	Citrus Grandis (Grapefruit) Extract is the extract of the whole plant, *Citrus grandis.*	Skin-Conditioning Agents - Miscellaneous
Citrus Grandis Peel/Seed Extract	Citrus Grandis Peel/Seed Extract is the extract of the peel and seeds of *Citrus grandis.*	Antifungal Agents; Antimicrobial Agents; Preservatives
Citrus Grandis (Grapefruit) Seed Extract	Citrus Grandis (Grapefruit) Seed Extract is the extract of the seeds of Citrus grandis.	Preservatives; Skin-Conditioning Agents - Miscellaneous
Citrus Iyo Oil	Citrus Iyo Oil is the oil expressed from the whole plant, *Citrus iyo*.	Skin-Conditioning Agents - Emollient
Citrus Jabara Pericarp Extract	Citrus Jabara Pericarp Extract is the extract of the pericarp of *Citrus jabara.*	Humectants; Skin-Conditioning Agents - Miscellaneous
Citrus Junos Extract	Citrus Junos Extract is the extract of the whole plant, *Citrus junos.*	Antioxidants
Citrus Junos Seed Extract	Citrus Junos Seed Extract is the extract of the seeds of *Citrus junos.*	Antioxidants
Citrus Junos Seed Oil	Citrus Junos Seed Oil is the oil expressed from the seeds of *Citrus junos.*	Skin-Conditioning Agents - Emollient
Citrus Limon (Lemon) Flower/Leaf/Stem Extract CAS No. 84929-31-7; 85085-28-5	Citrus Limon (Lemon) Flower/Leaf/Stem Extract is the extract of the flowers, leaves and stems of *Citrus limon.*	Fragrance Ingredients; Skin-Conditioning Agents - Miscellaneous
Citrus Limon (Lemon) Flower/Leaf/Stem Oil CAS No. 84929-31-7; 85085-28-5	Citrus Limon (Lemon) Flower/Leaf/Stem Oil is the volatile oil obtained from the flowers, leaves and stems of *Citrus limon.*	Fragrance Ingredients
Citrus Limon (Lemon) Leaf/Peel/Stem Oil CAS No. 84929-31-7; 85085-28-5	Citrus Limon (Lemon) Leaf/Peel/Stem Oil is the volatile oil obtained from the leaves, peels, and stems of *Citrus limon.*	Skin-Conditioning Agents - Miscellaneous
Citrus Nobilis (Mandarin Orange)	Citrus Nobilis (Mandarin Orange) is a plant material derived from the whole plant, *Citrus nobilis.*	Not reported
Citrus Nobilis (Mandarin Orange) Oil	Citrus Nobilis (Mandarin Orange) Oil is the volatile oil obtained from the whole plant, *Citrus nobilis.*	Fragrance Ingredients
Citrus Nobilis (Mandarin Orange) Water	Citrus Nobilis (Mandarin Orange) Water is an aqueous solution of the steam distillate obtained from *Citrus nobilis.*	Skin-Conditioning Agents - Miscellaneous
Citrus Paradisi (Grapefruit) Seed Extract CAS No. 90045-43-5 (generic)	Citrus Paradisi (Grapefruit) Seed Extract is the extract of the seeds of *Citrus paradisi.*	Skin-Conditioning Agents - Miscellaneous
Citrus Reticulata (Tangerine) Extract	Citrus Reticulata (Tangerine) Extract is the extract of the whole plant, *Citrus reticulata.*	Skin-Conditioning Agents - Miscellaneous
Citrus Sunki Seed Extract	Citrus Sunki Seed Extract is the extract of the seeds of *Citrus sunki.* The accepted scientific name for *Citrus sunki* is *Citrus reticulata.*	Antioxidants; Skin Bleaching Agents; Skin-Conditioning Agents - Miscellaneous

Table 1. Definitions and functions of *Citrus* plant- and seed-derived ingredients.[1]

Ingredient	Definition	Function
Citrus Sunki Seed Oil	Citrus Sunki Seed Oil is the oil expressed from the seeds of *Citrus sunki.* The accepted scientific name for *Citrus sunki* is *Citrus reticulata.*	Antioxidants; Skin Bleaching Agents; Skin-Conditioning Agents - Miscellaneous
Citrus Tangerina (Tangerine) Extract	Citrus Tangerina (Tangerine) Extract is the extract of the tangerine, *Citrus tangerina*.	Skin-Conditioning Agents - Miscellaneous
Citrus Unshiu Extract CAS No. 98106-71-9	Citrus Unshiu Extract is the extract of the whole plant, *Citrus unshiu.*	Skin-Conditioning Agents - Miscellaneous
Citrus Unshiu Pericarp Extract	Citrus Unshiu Pericarp Extract is the extract of the pericarp of *Citrus unshiu.*	Skin-Conditioning Agents - Miscellaneous

Table 2. *Citrus plant*- and seed-derived ingredients that potentially function solely as fragrance ingredients.

Citrus Aurantium Dulcis (Orange) Oil
Citrus Limon (Lemon) Flower/Leaf/Stem Oil
Citrus Nobilis (Mandarin Orange) Oil

.

Table 3.Review of *Citrus* genus species names[5]

Genus Species Name Used in INCI Names (common name)	Accepted Genus Species Name
Citrus aurantifolia (lime)	*Citrus x aurantifolia*
Citrus aurantium amara (bitter orange)	*Citrus x aurantium*
Citrus aurantium bergamia (bergamot)	*Citrus x limon*
Citrus aurantium dulcis (orange)	*Citrus x aurantium*
Citrus clementina (clementine)	*Citrus x aurantium*
Citrus depressa	*Citrus reticulata*
Citrus glauca	*Citrus glauca*
Citrus grandis (grapefruit or pomelo)	*Citrus maxima* or *Citrus x aurantium*
Citrus hassaku	*Citrus medica x Citrus x aurantium*
Citrus iyo	*Citrus x aurantium*
Citrus jabara	Not known
Citrus japonica (kumquat)	*Citrus japonica*
Citrus junos	*Citrus x junos*
Citrus limon (lemon)	*Citrus x limon*
Citrus madurensis	*Citrus x microcarpa*
Citrus medica vulgaris	*Citrus reticulata*
Citrus natsudaidai	*Citrus x aurantium*
Citrus nobilis (mandarin orange)	*Citrus reticulata*
Citrus paradisi (grapefruit)	*Citrus x aurantium*
Citrus reticulata (tangerine)	*Citrus reticulata*
Citrus shunkokan	Cultivated hybrid
Citrus sinensis (orange)	*Citrus x aurantium*
Citrus sphaerocarpa	Cultivated hybrid
Citrus sudachi	*Citrus reticulata*
Citrus tachibana	Not listed
Citrus tamurana	Cultivated hybrid
Citrus tangelo (tangelo)	*Citrus x aurantium*
Citrus tangerine (tangerine)	*Citrus reticulata*
Citrus tankan	*Citrus reticulata*
Citrus unshiu	*Citrus reticulata*

Table 4. Constituents that are established contact allergens in humans, according to the SCCS

Constituent	categorized according to number of patients reacting positively and to the number of patients tested (>1000 patients tested, unless indicated as r.t., i.e., rarely tested) [10]
β-caryophyllene	≤10 (oxidized and non-oxidized)
carvone	≤10 (r.t.)
citral	101 to 1000
citronellol	11-100
coumarin	101 to 1000
farnesol	101 to 1000
geraniol	101 to 1000
linalyl acetate	≤10
α- and β-pinene	11-100
(DL)-limonene	11-100 (non-oxidized); 101 to 1000 (oxidized)
tepineol (mixture of isomers)/α-terpineol	≤10
terpinolene	11-100

Table 5. Fatty acid profiles (area %) by gas chromatography.[6,7,31]

Fatty acid	Citrus Australisca Seed Oil	Citrus Glauca Seed Oil	*Citrus junos* Sieb. ex Takana seed oil*
undecanoic acid	NR	NR	3.27
myristic acid	0.07	NR	NR
palmitic acid	10.50	8.07	19.16
palmitoleic acid	0.24	0.17	0.62
margaric acid	0.08	0.05	NR
heptadecanconic acid	0.07	NR	NR
stearic acid	3.36	2.52	3.76
elaidic acid	0.11	NR	NR
oleic acid	36.55	47.39	32.01
cis-vaccenic acid	1.67	2.00	NR
linolelaidic acid	0.05	NR	NR
linoleic acid	41.01	36.28	33.99
α-linolenic acid	4.70	1.28	2.05
arachadic acid	0.40	0.31	0.26
11-eicosenoic acid	0.28	0.42	NR
behenic acid	0.42	0.61	NR
lignoceric acid	0.15	0.32	NR
unknown	NR	NR	4.48

*Reported as acid methyl esters.

Table 6. Frequency and concentration of use according to duration and type of exposure for *Citrus* plant- and seed-derived ingredients.[13,14]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Citrus Aurantifolia (Lime) Oil		**Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil[d]**		**Citrus Aurantium (Bitter Orange) Oil[e]**		**Citrus Aurantium Dulcis (Orange) Oil[f]**	
Totals[†]	**169**	**0.00000051-0.36**	**43**	**0.0000000026-0.0032**	**295**	**NR**	**4**	**0.0000032-1**
Duration of Use								
Leave-On	90	0.00049-0.36	25	0.00000014-0.0032	178	NR	3	0.000094-1
Rinse Off	69	0.00015-0.17	14	0.00000015-0.000013	96	NR	NR	0.000026-0.81
Diluted for (Bath) Use	10	0.00000051	4	0.0000000026	21	NR	1	0.0000032-0.94
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	0.00078-0.034
Incidental Ingestion	NR	0.0015-0.36	NR	NR	2	NR	NR	0.034-0.95
Incidental Inhalation-Spray	9; 34[a]; 29[b]	0.00049-0.12; 0.0015-0.1[a]; 0.00067[b]	11[a]; 11[b]	0.00000014-0.00000043; 0.0000025[a]	31; 37[a]; 49[b]	NR	1; 2[a]	0.0022-0.12; 0.0053-0.26[a]; 0.000094[b]
Incidental Inhalation-Powder	1[c]; 29[b]	0.022; 0.0075-0.023[c];0.00067	11[b]	0.000011[c]	1; 3[c]; 49[b]	NR	NR	0.0012-0.0014; 0.14-1[c]; 0.000094[b]
Dermal Contact	147	0.00000051-0.17	40	0.0000000026-0.0032	250	NR	3	0.0000032-1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	0.039[a]; 0.038-0.06[g]
Hair - Non-Coloring	22	0.00049-0.02	3	0.00000014-0.0000025	32	NR	1	0.0022-0.81
Hair-Coloring	NR	0.00015	NR	NR	11	NR	NR	0.000026-0.042
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	35	0.00000051-0.36	11	0.0000000026-0.000013	53	NR	1	0.0000032-0.95
Baby Products	3	NR	NR	NR	9	NR	NR	NR

	Citrus Aurantium Dulcis (Orange) Seed Extract[h]		**Citrus Aurantium Sinensis Powder[i]**		**Citrus Grandis (Grapefruit) Extract**		**Citrus Grandis (Grapefruit) Seed Extract**	
Totals[†]	**2**	**NR**	**1**	**NR**	**NR**	**0.0017-0.0059**	**144**	**0.0004-0.15**
Duration of Use								
Leave-On	2	NR	1	NR	NR	0.0017-0.003	85	0.076-0.15
Rinse Off	NR	NR	NR	NR	NR	0.0022-0.0059	51	0.0004-0.12
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	8	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	5	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	12	0.076
Incidental Inhalation-Spray	2[b]	NR	1[b]	NR	NR	0.0017-0.003	2; 28[a]; 17[b]	NR
Incidental Inhalation-Powder	2[b]	**NR**	1[b]	NR	NR	NR	17[b]; 2[c]	0.1[c]
Dermal Contact	2	NR	1	NR	NR	0.0022-0.0059	106	0.02-0.15
Deodorant (underarm)	NR	NR	NR	NR	NR	0.0024[g]	14[a]	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	0.0017-0.005	23	0.0004
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	0.0022-0.0059	26	0.076
Baby Products	NR	NR	NR	NR	NR	NR	7	NR

Table 6. Frequency and concentration of use according to duration and type of exposure for *Citrus* plant- and seed-derived ingredients.[13,14]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Citrus Junos Extract		**Citrus Junos Seed Extract[j]**		**Citrus Junos Seed Oil**		**Citrus Limon (Lemon) Flower/Leaf/Stem Extract**	
Totals[†]	**NR**	**0.0001**	**7**	**0.001-0.0045**	**NR**	**0.001-0.1**	**8**	**NR**
Duration of Use								
Leave-On	NR	NR	7	0.001-0.0045	NR	0.01-0.1	8	NR
Rinse Off	NR	0.0001	NR	0.001	NR	0.001	NR	NR
Diluted for (Bath) Use	NR	NR	NR	0.001	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	1	0.001	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	4[a]; 2[b]	NR	NR	NR	6[a]; 1[b]	NR
Incidental Inhalation-Powder	NR	NR	2[b]	0.0045[c]	NR	0.1; 0.1[c]	1[b]	NR
Dermal Contact	NR	NR	7	0.001-0.0045	NR	0.001-0.1	8	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	0.01	NR	NR
Hair-Coloring	NR	0.0001	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	0.001	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Citrus Nobilis (Mandarin Orange)		**Citrus Nobilis (Mandarin Orange) Oil**		**Citrus Paradisi (Grapefruit) Seed Extract**		**Citrus Reticulata (Tangerine) Extract**	
Totals[†]	**NR**	**0.0005**	**36**	**0.0009-0.035**	**52**	**NR**	**NR**	**0.0001-0.0051**
Duration of Use								
Leave-On	NR	NR	28	NR	39	NR	NR	0.0002-0.0051
Rinse Off	NR	NR	4	0.0009-0.035	13	NR	NR	0.0001-0.005
Diluted for (Bath) Use	NR	NR	4	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	1	0.035	1	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	8; 2[a]; 4[b]	NR	16[a]; 17[b]	NR	NR	0.0051[a]
Incidental Inhalation-Powder	NR	NR	4[b]; 1[c]	NR	17[b]; 1[c]	NR	NR	0.0002[c]
Dermal Contact	NR	0.0005	35	0.0009-0.0017	50	NR	NR	0.0002
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	0.0005	NR	NR	1	NR	NR	0.0001-0.0051
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	0.0005	7	0.0009-0.035	8	NR	NR	NR
Baby Products	NR	NR	2	NR	2	NR	NR	NR

Table 6. Frequency and concentration of use according to duration and type of exposure for *Citrus* plant- and seed-derived ingredients.[13,14]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Citrus Tangerina (Tangerine) Extract							
Totals[†]	**17**	**0.0000025-0.0045**						
Duration of Use								
Leave-On	5	0.0000025-0.0045						
Rinse Off	12	0.00001-0.00035						
Diluted for (Bath) Use	NR	0.0005						
Exposure Type								
Eye Area	NR	NR						
Incidental Ingestion	NR	NR						
Incidental Inhalation-Spray	1; 1[a]; 2[b]	0.0005; 0.00001[a]						
Incidental Inhalation-Powder	2[b]	0.0001-0.0045[c]						
Dermal Contact	6	0.0001-0.0045						
Deodorant (underarm)	NR	NR						
Hair - Non-Coloring	11	0.0000025-0.00035						
Hair-Coloring	NR	NR						
Nail	NR	NR						
Mucous Membrane	2	0.0001-0.0005						
Baby Products	NR	NR						

NR = Not reported.

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

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

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

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

[d] Listed as Citrus Aurantium (Bitter Orange) Leaf/Twig Oil in the VCRP database.

[e] Only listed in the VCRP database, not in the INCI dictionary. Included because of assumed similarity.

[f] Listed as Citrus Sinensis (Sweet Orange) Plant Oil in the VCRP database.

[g]Not a spray deodorant.

[h] Listed as Citrus Sinensis (Sweet Orange) Seed Extract in the VCRP database.

[i] Listed as Citrus Sinensis (Orange) Powder in the VCRP database.

[j] Listed as Citrus Junos (Xiang Cheng) Seed Extract in the VCRP database.

Table 7. Ingredients that are not reported to be in use

Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Extract
Citrus Aurantium Dulcis (Orange) Flower/Leaf/Stem Powder
Citrus Australasica Seed Oil
Citrus Depressa Seed Oil
Citrus Glauca Seed Oil
Citrus Grandis (Grapefruit)
Citrus Grandis Peel/Seed Extract
Citrus Iyo Oil
Citrus Jabara Pericarp Extract
Citrus Limon (Lemon) Leaf/Peel/Stem Oil
Citrus Nobilis (Mandarin Orange) Water
Citrus Sunki Seed Extract
Citrus Sunki Seed Oil
Citrus Unshiu Extract
Citrus Unshiu Pericarp Extract

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2016 FDA VCRP RAW DATA – Citrus Plant and Seed

01A - Baby Shampoos	CITRUS AURANTIFOLIA (LIME) OIL	1
01B - Baby Lotions, Oils, Powders, and Creams	CITRUS AURANTIFOLIA (LIME) OIL	1
01C - Other Baby Products	CITRUS AURANTIFOLIA (LIME) OIL	1
02A - Bath Oils, Tablets, and Salts	CITRUS AURANTIFOLIA (LIME) OIL	6
02B - Bubble Baths	CITRUS AURANTIFOLIA (LIME) OIL	4
04B - Perfumes	CITRUS AURANTIFOLIA (LIME) OIL	1
04E - Other Fragrance Preparation	CITRUS AURANTIFOLIA (LIME) OIL	8
05A - Hair Conditioner	CITRUS AURANTIFOLIA (LIME) OIL	9
05F - Shampoos (non-coloring)	CITRUS AURANTIFOLIA (LIME) OIL	6
05G - Tonics, Dressings, and Other Hair Grooming Aids	CITRUS AURANTIFOLIA (LIME) OIL	5
05I - Other Hair Preparations	CITRUS AURANTIFOLIA (LIME) OIL	1
07F - Makeup Bases	CITRUS AURANTIFOLIA (LIME) OIL	1
07I - Other Makeup Preparations	CITRUS AURANTIFOLIA (LIME) OIL	3
10A - Bath Soaps and Detergents	CITRUS AURANTIFOLIA (LIME) OIL	17
10E - Other Personal Cleanliness Products	CITRUS AURANTIFOLIA (LIME) OIL	8
11B - Beard Softeners	CITRUS AURANTIFOLIA (LIME) OIL	6
11D - Preshave Lotions (all types)	CITRUS AURANTIFOLIA (LIME) OIL	1
11E - Shaving Cream	CITRUS AURANTIFOLIA (LIME) OIL	5
11F - Shaving Soap	CITRUS AURANTIFOLIA (LIME) OIL	1
11G - Other Shaving Preparation Products	CITRUS AURANTIFOLIA (LIME) OIL	2
12A - Cleansing	CITRUS AURANTIFOLIA (LIME) OIL	18
12C - Face and Neck (exc shave)	CITRUS AURANTIFOLIA (LIME) OIL	17
12D - Body and Hand (exc shave)	CITRUS AURANTIFOLIA (LIME) OIL	12
12F - Moisturizing	CITRUS AURANTIFOLIA (LIME) OIL	21
12G - Night	CITRUS AURANTIFOLIA (LIME) OIL	1
12H - Paste Masks (mud packs)	CITRUS AURANTIFOLIA (LIME) OIL	1
12I - Skin Fresheners	CITRUS AURANTIFOLIA (LIME) OIL	6
12J - Other Skin Care Preps	CITRUS AURANTIFOLIA (LIME) OIL	5
13A - Suntan Gels, Creams, and Liquids	CITRUS AURANTIFOLIA (LIME) OIL	1
02A - Bath Oils, Tablets, and Salts	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	3
02B - Bubble Baths	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	1
05A - Hair Conditioner	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	2
05F - Shampoos (non-coloring)	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	1

10A - Bath Soaps and Detergents	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	5
10E - Other Personal Cleanliness Products	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	2
12A - Cleansing	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	4
12C - Face and Neck (exc shave)	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	6
12D - Body and Hand (exc shave)	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	5
12F - Moisturizing	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	7
12G - Night	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	4
12J - Other Skin Care Preps	CITRUS AURANTIUM (BITTER ORANGE) LEAF/TWIG OIL	3
01A - Baby Shampoos	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
01B - Baby Lotions, Oils, Powders, and Creams	CITRUS AURANTIUM (BITTER ORANGE) OIL	3
01C - Other Baby Products	CITRUS AURANTIUM (BITTER ORANGE) OIL	5
02A - Bath Oils, Tablets, and Salts	CITRUS AURANTIUM (BITTER ORANGE) OIL	16
02B - Bubble Baths	CITRUS AURANTIUM (BITTER ORANGE) OIL	3
02C - Bath Capsules	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
02D - Other Bath Preparations	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
04A - Cologne and Toilet waters	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
04B - Perfumes	CITRUS AURANTIUM (BITTER ORANGE) OIL	14
04E - Other Fragrance Preparation	CITRUS AURANTIUM (BITTER ORANGE) OIL	15
05A - Hair Conditioner	CITRUS AURANTIUM (BITTER ORANGE) OIL	10
05B - Hair Spray (aerosol fixatives)	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
05C - Hair Straighteners	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
05E - Rinses (non-coloring)	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
05F - Shampoos (non-coloring)	CITRUS AURANTIUM (BITTER ORANGE) OIL	13
05G - Tonics, Dressings, and Other Hair Grooming Aids	CITRUS AURANTIUM (BITTER ORANGE) OIL	4
05I - Other Hair Preparations	CITRUS AURANTIUM (BITTER ORANGE) OIL	2
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	CITRUS AURANTIUM (BITTER ORANGE) OIL	4
06D - Hair Shampoos (coloring)	CITRUS AURANTIUM (BITTER ORANGE) OIL	7
07E - Lipstick	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
07F - Makeup Bases	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
07G - Rouges	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
07I - Other Makeup Preparations	CITRUS AURANTIUM (BITTER ORANGE) OIL	3
09C - Other Oral Hygiene Products	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
10A - Bath Soaps and	CITRUS AURANTIUM (BITTER ORANGE) OIL	20

Detergents		
10E - Other Personal Cleanliness Products	CITRUS AURANTIUM (BITTER ORANGE) OIL	10
11E - Shaving Cream	CITRUS AURANTIUM (BITTER ORANGE) OIL	2
12A - Cleansing	CITRUS AURANTIUM (BITTER ORANGE) OIL	23
12C - Face and Neck (exc shave)	CITRUS AURANTIUM (BITTER ORANGE) OIL	14
12D - Body and Hand (exc shave)	CITRUS AURANTIUM (BITTER ORANGE) OIL	35
12F - Moisturizing	CITRUS AURANTIUM (BITTER ORANGE) OIL	24
12G - Night	CITRUS AURANTIUM (BITTER ORANGE) OIL	2
12H - Paste Masks (mud packs)	CITRUS AURANTIUM (BITTER ORANGE) OIL	4
12I - Skin Fresheners	CITRUS AURANTIUM (BITTER ORANGE) OIL	6
12J - Other Skin Care Preps	CITRUS AURANTIUM (BITTER ORANGE) OIL	44
13B - Indoor Tanning Preparations	CITRUS AURANTIUM (BITTER ORANGE) OIL	1
01B - Baby Lotions, Oils, Powders, and Creams	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	2
01C - Other Baby Products	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	5
02A - Bath Oils, Tablets, and Salts	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	5
02B - Bubble Baths	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	3
03D - Eye Lotion	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	2
03F - Mascara	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	3
04E - Other Fragrance Preparation	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	1
05A - Hair Conditioner	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	8
05B - Hair Spray (aerosol fixatives)	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	1
05E - Rinses (non-coloring)	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	1
05F - Shampoos (non-coloring)	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	9
05G - Tonics, Dressings, and Other Hair Grooming Aids	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	4
07C - Foundations	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	10
07F - Makeup Bases	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	1
09A - Dentifrices	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	9
09B - Mouthwashes and Breath Fresheners	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	2
09C - Other Oral Hygiene Products	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	1
10A - Bath Soaps and Detergents	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	6
10B - Deodorants (underarm)	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	14
12A - Cleansing	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	13
12C - Face and Neck (exc shave)	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	6
12D - Body and Hand (exc	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	11

shave)		
12F - Moisturizing	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	10
12H - Paste Masks (mud packs)	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	2
12I - Skin Fresheners	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	12
12J - Other Skin Care Preps	CITRUS GRANDIS (GRAPEFRUIT) SEED EXTRACT	3
03G - Other Eye Makeup Preparations	CITRUS JUNOS (XIANG CHENG) SEED EXTRACT	1
12C - Face and Neck (exc shave)	CITRUS JUNOS (XIANG CHENG) SEED EXTRACT	1
12D - Body and Hand (exc shave)	CITRUS JUNOS (XIANG CHENG) SEED EXTRACT	1
12F - Moisturizing	CITRUS JUNOS (XIANG CHENG) SEED EXTRACT	4
12C - Face and Neck (exc shave)	CITRUS LIMON (LEMON) FLOWER/LEAF/STEM EXTRACT	1
12F - Moisturizing	CITRUS LIMON (LEMON) FLOWER/LEAF/STEM EXTRACT	6
12J - Other Skin Care Preps	CITRUS LIMON (LEMON) FLOWER/LEAF/STEM EXTRACT	1
01B - Baby Lotions, Oils, Powders, and Creams	CITRUS NOBILIS (MANDARIN ORANGE) OIL	1
01C - Other Baby Products	CITRUS NOBILIS (MANDARIN ORANGE) OIL	1
02A - Bath Oils, Tablets, and Salts	CITRUS NOBILIS (MANDARIN ORANGE) OIL	4
04B - Perfumes	CITRUS NOBILIS (MANDARIN ORANGE) OIL	4
04E - Other Fragrance Preparation	CITRUS NOBILIS (MANDARIN ORANGE) OIL	4
07I - Other Makeup Preparations	CITRUS NOBILIS (MANDARIN ORANGE) OIL	1
09A - Dentifrices	CITRUS NOBILIS (MANDARIN ORANGE) OIL	1
10A - Bath Soaps and Detergents	CITRUS NOBILIS (MANDARIN ORANGE) OIL	2
12A - Cleansing	CITRUS NOBILIS (MANDARIN ORANGE) OIL	1
12D - Body and Hand (exc shave)	CITRUS NOBILIS (MANDARIN ORANGE) OIL	4
12F - Moisturizing	CITRUS NOBILIS (MANDARIN ORANGE) OIL	2
12J - Other Skin Care Preps	CITRUS NOBILIS (MANDARIN ORANGE) OIL	11
01B - Baby Lotions, Oils, Powders, and Creams	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
01C - Other Baby Products	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
05A - Hair Conditioner	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
07I - Other Makeup Preparations	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
09A - Dentifrices	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
10A - Bath Soaps and Detergents	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	7
11B - Beard Softeners	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1

12A - Cleansing	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	4
12C - Face and Neck (exc shave)	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	4
12D - Body and Hand (exc shave)	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	13
12F - Moisturizing	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	14
12G - Night	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
12J - Other Skin Care Preps	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	2
13A - Suntan Gels, Creams, and Liquids	CITRUS PARADISI (GRAPEFRUIT) SEED EXTRACT	1
02A - Bath Oils, Tablets, and Salts	CITRUS SINENSIS (SWEET ORANGE) PLANT OIL	1
04B - Perfumes	CITRUS SINENSIS (SWEET ORANGE) PLANT OIL	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	CITRUS SINENSIS (SWEET ORANGE) PLANT OIL	1
12I - Skin Fresheners	CITRUS SINENSIS (SWEET ORANGE) PLANT OIL	1
12C - Face and Neck (exc shave)	CITRUS SINENSIS (SWEET ORANGE) POWDER	1
12D - Body and Hand (exc shave)	CITRUS SINENSIS (SWEET ORANGE) SEED EXTRACT	2
04E - Other Fragrance Preparation	CITRUS TANGERINA (TANGERINE) EXTRACT	1
05A - Hair Conditioner	CITRUS TANGERINA (TANGERINE) EXTRACT	4
05F - Shampoos (non-coloring)	CITRUS TANGERINA (TANGERINE) EXTRACT	6
05G - Tonics, Dressings, and Other Hair Grooming Aids	CITRUS TANGERINA (TANGERINE) EXTRACT	1
10A - Bath Soaps and Detergents	CITRUS TANGERINA (TANGERINE) EXTRACT	2
12C - Face and Neck (exc shave)	CITRUS TANGERINA (TANGERINE) EXTRACT	1
12D - Body and Hand (exc shave)	CITRUS TANGERINA (TANGERINE) EXTRACT	1
12J - Other Skin Care Preps	CITRUS TANGERINA (TANGERINE) EXTRACT	1

Memorandum

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

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: January 8, 2016

SUBJECT: Information on Citrus Paradisi (Grapefruit) Seed Extract

Greentech Biotechnologies. 2015. Manufacturing process Citrus Paradisi (Grapefruit) Seed Extract.

Greentech Biotechnoliges indicates that the trade name material they sell to the cosmetics industry contains:

Glycerin	67.0-73.0%
Water	26.0-32.8%
Citrus Paradisi (Grapefruit) Seed Extract	0.2-1.0%

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Version 2 (27/04/15)

PROCEDE D'OBTENTION / MANUFACTURING PROCESS

Nom Commercial /Trade Name : PAMPLEMOUSSE PEPIN EXTRAIT HYDROGLYCERINE 70 (400253) / GRAPEFRUIT SEED HYDROGLYCERINED EXTRAIT 70 (400253)

Broyage des pépins de pamplemousse / Grinding of grapefruit seeds

↓

Extraction dans un mélange eau / glycérine /
Extaction in a mix of water and glycerin

↓

Clarification / Clarification

↓

Décontamination à la chaleur / Heat decontamination

Jean-Yves BERTHON
PDG / CEO

Po / For and on behalf

Noémie MORETTON
Chargée réglementaire / Regulatory department

GREENTECH
Biopôle Clermont-Limagne - 63360 Saint-Beauzire - France
Tél : 04 73 33 99 00 - Fax : 04 73 33 91 32
E-mail : greentech@greentech.fr – web site : www.greentech.fr

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: January 12, 2016

SUBJECT: Citrus Glauca Seed Oil and Citrus Australasica Seed Oil

Native Extracts. 2014. Certificate of analysis NSO Desert Lime Seed Oil Organic (Citrus Glauca Seed Oil).

Native Extracts. 2015. Certificate of analysis NSO Finger Lime Seed Oil Organic (Citrus Australasica Seed Oil).

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Certificate of Analysis

NSO Desert Lime Seed Oil Organic

ANE0146

Citrus Glauca Seed Oil

Customer:	Batch No. 3414-04
Appearance @ 20°C:	Mobile liquid
Colour:	Light brown to dark brown

Analysis	Result	Specification	Comments
Refractive Index @ 20°C:	1.473	1.450 – 1.490	Pass
Specific Gravity @ 20°C:	0.921	0.900 – 0.940	Pass

Date of Manufacture:	04/14
Date Of Expiry	04/16

When stored within advised conditions, re-test after 12 months then at 3 monthly intervals up to a maximum life of 24 months.

Note: Certain materials will degrade more rapidly than others and ultimate life is dependant upon good package and storage conditions

We hereby certify that the above material meets the required specification and is released for free sale.

www.nativeextracts.com.au P:+61 2 6624 5191 F:+61 2 6624 2434

56 Lancaster Drive GOONELLABAH NSW 2480 AUSTRALIA

Southern Cross University

Southern Cross Plant Science
Analytical Research Laboratory

T +61 2 6622 3211 • W. scu.edu.au/scps • T Block Level 3 Military Road, Lismore NSW 2480 Australia • ABN 41995 651524 • TGA MI-0122004-LI 0002641

CERTIFICATE OF ANALYSIS

SAMPLE	Desert Lime Seed Oil Extract
CUSTOMER	Native Extracts
CERTIFICATION DATE	11 April 2014
CUSTOMER LOT/BATCH No.	3414-04
LABORATORY REFERENCE	ARL141421
JOB No.	A140496

TEST	RESULTS	TEST METHOD
	Area %	
palmitic acid*	8.07	ARL-TM149
palmitoleic acid*	0.17	
margaric acid*	0.05	
stearic acid*	2.52	
oleic acid*	47.39	
cis-vaccenic acid*	2.00	
linoleic acid*	36.28	
α-linolenic acid*	1.28	
arachidic acid*	0.31	
11-eicosenoic acid*	0.42	
behenic acid*	0.61	
lignoceric acid*	0.32	

* Assay by GC (FID detection –area percent report)

MS DALE SAVINS
ANALYTICAL OFFICER

MR ASHLEY DOWELL
MANAGER - ARL

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==================================================================
Injection Date  : 4/9/2014 12:27:46 AM          Seq. Line :  12
Sample Name     : 3414-04                        Location : Vial 11
Acq. Operator   : DAS                                Inj :   1
                                               Inj Volume : 1 µl
Acq. Method     : D:\METHODS\QAMETH~1\FAMES35.M
Last changed    : 4/8/2014 3:03:48 PM by DAS
Analysis Method : D:\METHODS\QAMETH~1\FAMES35.M
Last changed    : 4/10/2014 12:28:14 PM by DAS
                  (modified after loading)
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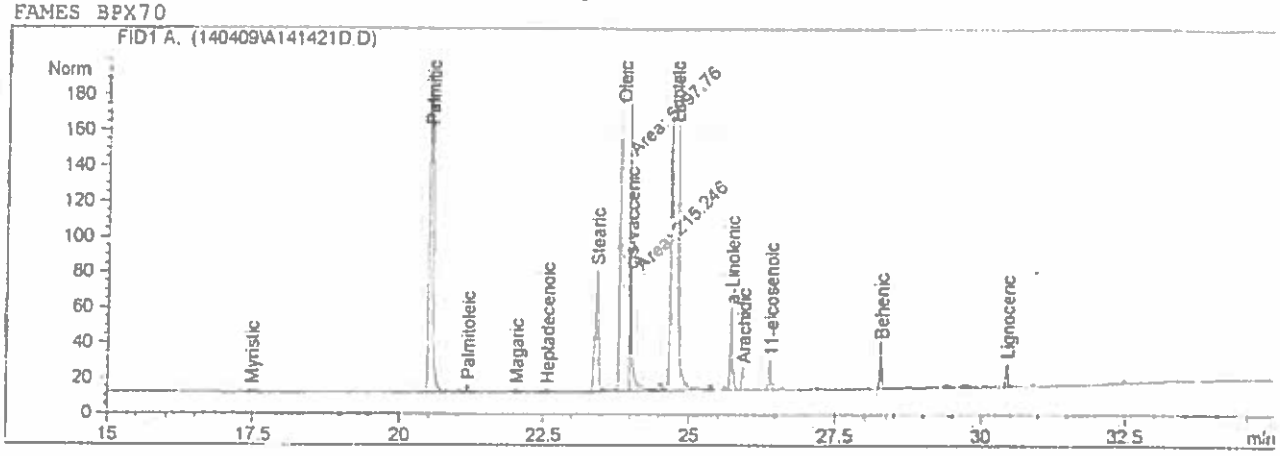
FAMES BPX70

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==================================================================
                        Area Percent Report
==================================================================

Sorted By              :      Signal
Calib. Data Modified   :      4/10/2014 12:28:33 PM
Multiplier             :      1.0000
Dilution               :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A,
```

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Area %	Name
1	4.004		0.0000	0.00000	0.00000	Butyric
2	4.245		0.0000	0.00000	0.00000	Caproic
3	6.444		0.0000	0.00000	0.00000	caprylic
4	9.965		0.0000	0.00000	0.00000	Capric
5	11.949		0.0000	0.00000	0.00000	Undecanoic
6	13.815		0.0000	0.00000	0.00000	Lauric
7	15.655		0.0000	0.00000	0.00000	Tridecanoic
8	17.476	PB	0.0849	6.32938	0.05884	Myristic
9	18.233		0.0000	0.00000	0.00000	Myristoleic
10	19.045		0.0000	0.00000	0.00000	Pentadecanoic
11	19.831		0.0000	0.00000	0.00000	Pentadecenoic
12	20.539	BB	0.0570	868.29419	8.07216	Palmitic
13	21.178	BB	0.0782	17.91258	0.16653	Palmitoleic
14	22.028	PP	0.0669	5.08891	0.04731	Margaric
15	22.564	PB	0.0671	4.37264	0.04065	Heptadecenoic
16	23.428	BB	0.0664	270.81921	2.51769	Stearic
17	23.712		0.0000	0.00000	0.00000	Elaidic
18	23.872	MF	0.0861	5097.75879	47.39166	Oleic
19	24.007	FM	0.0543	215.24644	2.00105	cis-vaccenic
20	24.234		0.0000	0.00000	0.00000	Linolelaidic
21	24.525	VV	0.0654	18.52619	0.17223	?

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Area %	Name
22	24.774	VB	0.0869	3902.58765	36.28067	Linoleic
23	25.255		0.0000	0.00000	0.00000	g-Linolenic
24	25.380	BP	0.0599	13.16887	0.12243	?
25	25.730	BV	0.0513	138.53137	1.28787	a-Linolenic
26	25.935	VP	0.0484	33.40139	0.31052	Arachidic
27	26.399	BP	0.0480	44.70197	0.41557	11-eicosenoic
28	27.153		0.0000	0.00000	0.00000	Heneicosanoic
29	27.234		0.0000	0.00000	0.00000	Eicosadienoic
30	27.739		0.0000	0.00000	0.00000	8,11,14-Eicosatrienoic
31	28.120		0.0000	0.00000	0.00000	11,14,17-Eicosatrienoic
32	28.194		0.0000	0.00000	0.00000	Arachidonic
33	28.281	PB	0.0469	65.88040	0.61246	Behenic
34	28.775		0.0000	0.00000	0.00000	Erucic
35	29.086		0.0000	0.00000	0.00000	Eicosapentaenoic
36	29.399	PB	0.0646	8.02631	0.07462	?
37	29.607		0.0000	0.00000	0.00000	Docosadienoic
38	29.761	PP	0.0891	11.96799	0.11126	?
39	30.460	PB	0.0505	34.04356	0.31649	Lignoceric
40	31.006		0.0000	0.00000	0.00000	Nervonic
41	31.695		0.0000	0.00000	0.00000	Docosahexaenoic

Totals : 1.07567e4

Results obtained with enhanced integrator!
2 Warnings or Errors :

Warning : Calibration warnings (see calibration table listing)
Warning : Calibrated compound(s) not found

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*** End of Report ***

Certificate of Analysis

NSO Finger Lime Seed Oil Organic

ANE0147

Citrus Australasica Seed Oil

Customer:	Batch No. 17915-01
Appearance @ 20°C:	Mobile liquid
Colour:	Straw/ yellow

Analysis	Result	Specification	Comments
Refractive Index @ 20°C:	1.476	1.450 – 1.490	Pass
Specific Gravity @ 20°C:	0.917	0.900 – 0.940	Pass

Date of Manufacture:	9/15
Date Of Expiry	9/17

When stored within advised conditions, re-test after 12 months then at 3 monthly intervals up to a maximum life of 24 months.

Note: Certain materials will degrade more rapidly than others and ultimate life is dependant upon good package and storage conditions

We hereby certify that the above material meets the required specification and is released for free sale.

www.nativeextracts.com.au P:+61 2 6624 5191 F:+61 2 6624 2434
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Southern Cross University

Southern Cross Plant Science
Analytical Research Laboratory

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CERTIFICATE OF ANALYSIS

SAMPLE	NSO Finger Lime Seed Oil Organic
CUSTOMER	Native Extracts
CERTIFICATION DATE	12 October 2015
CUSTOMER LOT/BATCH No.	17915-01
LABORATORY REFERENCE	ARL154418
JOB No.	A151539

TEST	RESULTS	TEST METHOD
	Area %	
myristic	0.07	ARL-TM149*
palmitic acid	10.50	
palmitoleic	0.24	
margaric	0.08	
heptadecanoic	0.07	
stearic	3.36	
elaidic	0.11	
oleic	36.55	
cis-vaccenic	1.67	
linolelaidic	0.05	
linoleic	41.01	
a-linolenic	4.70	
arachidic	0.40	
11-eicosenoic	0.28	
behenic	0.42	
lignoceric	0.15	

* Assay by GC (FID detection –area percent report)

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MR ASHLEY DOWELL
MANAGER - ARL

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==========================================================================
Injection Date  : 9/23/2015 2:46:39 PM          Seq. Line :   9
Sample Name     : SI# 17915-01                   Location : Vial 58
Acq. Operator   : das+jc                              Inj :   1
                                               Inj Volume : 1 µl

Acq. Method     : D:\METHODS\QAMETH~1\FAMES35.M
Last changed    : 8/25/2015 12:33:47 PM by das
Analysis Method : D:\METHODS\QAMETH~1\FAME35D.M
Last changed    : 10/12/2015 10:18:01 AM by das
                  (modified after loading)
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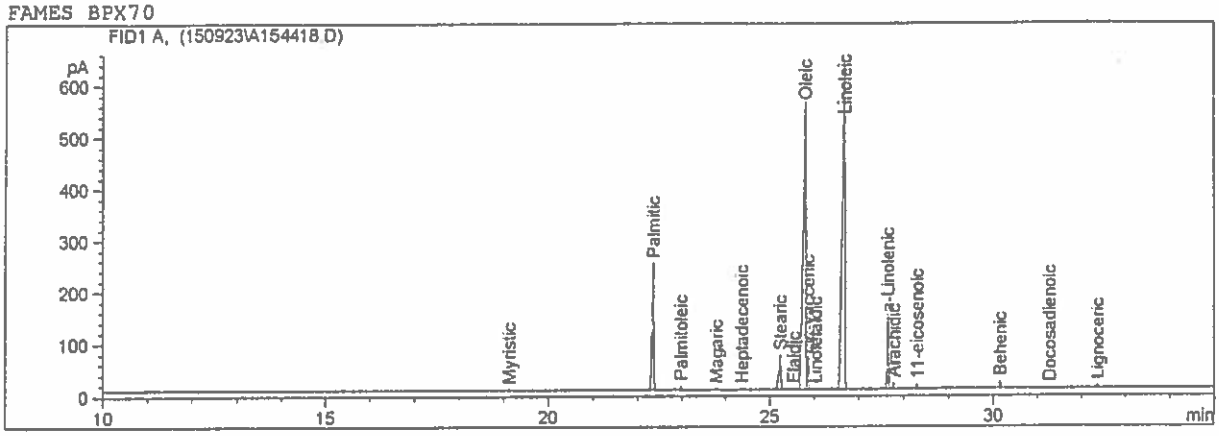
FAMES BPX70

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==========================================================================
                            Area Percent Report
==========================================================================

Sorted By              :      Signal
Calib. Data Modified   :      10/12/2015 10:17:36 AM
Multiplier             :      1.0000
Dilution               :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Area %	Name
1	3.897		0.0000	0.00000	0.00000	Butyric
2	5.054		0.0000	0.00000	0.00000	Caproic
3	7.676		0.0000	0.00000	0.00000	caprylic
4	11.545		0.0000	0.00000	0.00000	Capric
5	13.574		0.0000	0.00000	0.00000	Undecanoic
6	15.532		0.0000	0.00000	0.00000	Lauric
7	17.382		0.0000	0.00000	0.00000	Tridecanoic
8	19.131	BB	0.0365	4.49046	0.06701	Myristic
9	20.021		0.0000	0.00000	0.00000	Myristoleic
10	20.766		0.0000	0.00000	0.00000	Pentadecanoic
11	21.639		0.0000	0.00000	0.00000	cis-10-pentadecenoic
12	22.368	BB	0.0457	703.89459	10.50462	Palmitic
13	22.981	VB	0.0336	15.97333	0.23838	Palmitoleic
14	23.791	BB	0.0374	5.61823	0.08384	Magaric
15	24.372	BP	0.0351	4.61254	0.06884	Heptadecenoic
16	25.243	BV	0.0507	225.24422	3.36145	Stearic
17	25.548	VV	0.0960	7.32122	0.10926	Elaidic
18	25.810	VV	0.0600	2448.94702	36.54703	Oleic
19	25.873	VV	0.0297	111.65526	1.66629	cic-vaccenic
20	26.036	VB	0.0422	3.59759	0.05369	Linolelaidic
21	26.405	VV	0.0548	5.08734	0.07592	?

Data File D:\DATA\150923\A154418.D Sample Name: SI# 17915-01

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Area %	Name
22	26.699	VV	0.0638	2747.76733	41.00649	Linoleic
23	27.162		0.0000	0.00000	0.00000	g-Linolenic
24	27.259	VB	0.0339	5.50733	0.08219	?
25	27.531	PV	0.0407	4.36128	0.06509	?
26	27.661	VV	0.0347	315.23422	4.70442	a-Linolenic
27	27.788	VB	0.0348	26.85065	0.40071	Arachidic
28	28.298	VP	0.0359	19.07755	0.28471	11-eicosenoic
29	28.994		0.0000	0.00000	0.00000	Heneicosanoic
30	29.134		0.0000	0.00000	0.00000	Eicosadienoic
31	29.684		0.0000	0.00000	0.00000	8,11,14-Eicosatrienoic
32	30.055		0.0000	0.00000	0.00000	Arachidonic
33	30.116		0.0000	0.00000	0.00000	11,14,17-Eicosatrienoic
34	30.166	VP	0.0330	28.34632	0.42303	Behenic
35	30.667		0.0000	0.00000	0.00000	Erucic
36	31.051		0.0000	0.00000	0.00000	Eicosapentaenoic
37	31.281	VV	0.0361	3.54760	0.05294	Docosadienoic
38	31.475		0.0000	0.00000	0.00000	Tricosanoic
39	31.645	VV	0.0705	3.52128	0.05255	?
40	32.361	BBA	0.0330	10.15501	0.15155	Lignoceric
41	32.861		0.0000	0.00000	0.00000	Nervonic
42	33.723		0.0000	0.00000	0.00000	Docosahexaenoic

Totals : 6700.81036

Results obtained with enhanced integrator!
2 Warnings or Errors :

Warning : Calibration warnings (see calibration table listing)
Warning : Calibrated compound(s) not found

==========

*** End of Report ***

Memorandum

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

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: February 10, 2016

SUBJECT: Citrus Junos Seed Extract

Anonymous. 2016. **Summary** information: Junos Seed Extract.

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Citrus Junos Seed Extract

- Method of manufacture; especially clarification of the plant part(s) that is the source of the ingredients. Are the ingredients defined as derived from the "whole plant" really derived from the "whole plant" including roots? If the ingredient is derived from the fruit, does this include the peel
- Chemical composition and impurities
- Dermal irritation and sensitization data on products containing the highest concentrations of these ingredients, especially human repeated insult patch tests (HRIPT) on Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil and Citrus Grandis (Grapefruit) Seed Extract
- If the composition of these *Citrus* plant- and seed-derived ingredients are significantly different from that of the *Citrus* peel-, flower-, and leaf-derived ingredients, then data on systemic endpoints such as a 28-day dermal toxicity, reproductive and developmental toxicity, and genotoxicity, as well as UV absorption spectra are needed

Method of manufacture	Dried raw material (Seed only)⇒extract with 90vol% ethanolic solution ⇒filtrate⇒sedimentation⇒filtrate⇒adjustment⇒packaging
Chemical composition	sugar and saponin
Impurities	Heavy metals : Not more than 20ppm , Arsenic : Not more than 2ppm
Safety data	No data

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Memorandum

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

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: February 11, 2016

SUBJECT: Concentration of Use by FDA Product Category: Citrus Seed- and Plant-Derived Ingredients

Concentration of Use by FDA Product Category – Citrus Seed-and Plant Derived Ingredients*

Citrus Aurantium Dulcis (Orange) Seed Extract
Citrus Australasica Seed Oil
Citrus Depressa Seed Oil
Citrus Glauca Seed Oil
Citrus Grandis (Grapefruit) Seed Extract
Citrus Jabara Pericarp Extract
Citrus Junos Seed Extract
Citrus Junos Seed Oil
Citrus Paradisi (Grapefruit) Seed Extract
Citrus Sunki Seed Extract
Citrus Sunki Seed Oil
Citrus Unshiu Pericarp Extract
Citrus Aurantifolia (Lime) Oil
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Extract
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil
Citrus Aurantium (Bitter Orange) Oil
Citrus Aurantium Dulcis (Orange) Flower/Leaf/Stem Powder
Citrus Aurantium Dulcis (Orange) Oil
Citrus Aurantium Sinensis Powder
Citrus Grandis (Grapefruit) Extract
Citrus Grandis (Grapefruit)
Citrus Grandis Peel/Seed Extract
Citrus Iyo Oil
Citrus Junos Extract
Citrus Limon (Lemon) Flower/Leaf/Stem Extract
Citrus Limon (Lemon) Flower/Leaf/Stem Oil
Citrus Limon (Lemon) Leaf/Peel/Stem Oil
Citrus Nobilis (Mandarin Orange) Oil
Citrus Nobilis (Mandarin Orange) Water
Citrus Nobilis (Mandarin Orange)
Citrus Reticulata (Tangerine) Extract
Citrus Tangerina (Tangerine) Extract**
Citrus Unshiu Extract

Ingredient	Product Category	Maximum Concentration of Use
Citrus Grandis (Grapefruit) Seed Extract	Hair conditioners	0.0004%
Citrus Grandis (Grapefruit) Seed Extract	Lipstick	0.076%
Citrus Grandis (Grapefruit) Seed Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.02%
Citrus Grandis (Grapefruit) Seed Extract	Face and neck products Not spray	0.1%
Citrus Grandis (Grapefruit) Seed Extract	Night products Not spray	0.15%
Citrus Grandis (Grapefruit) Seed Extract	Paste masks and mud packs	0.1-0.12%
Citrus Junos Seed Extract	Bath oils, tablets and salts	0.001%
Citrus Junos Seed Extract	Eye lotions	0.001%
Citrus Junos Seed Extract	Foundations	0.001%
Citrus Junos Seed Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.001%
Citrus Junos Seed Extract	Face and neck products Not spray	0.0045%
Citrus Junos Seed Extract	Moisturizing products Not spray	0.001%
Citrus Junos Seed Oil	Tonics, dressings and other hair grooming aids Not spray	0.01%
Citrus Junos Seed Oil	Face powders	0.1%

Citrus Junos Seed Oil	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.001%
Citrus Junos Seed Oil	Face and neck products Not spray	 0.1%
Citrus Junos Seed Oil	Body and hand products Not spray	 0.1%
Citrus Aurantifolia (Lime) Oil	Bath oils, tablets and salts	0.00000051%
Citrus Aurantifolia (Lime) Oil	Powders (dusting and talcum)	0.022%
Citrus Aurantifolia (Lime) Oil	Hair conditioners	0.00057%
Citrus Aurantifolia (Lime) Oil	Hair sprays Pump spray	 0.00049%
Citrus Aurantifolia (Lime) Oil	Shampoos (noncoloring)	0.00057-0.02%
Citrus Aurantifolia (Lime) Oil	Tonics, dressings and other hair grooming aids Not spray	0.02% 0.0027%
Citrus Aurantifolia (Lime) Oil	Hair dyes and colors	0.00015%
Citrus Aurantifolia (Lime) Oil	Blushers	0.01%
Citrus Aurantifolia (Lime) Oil	Lipstick	0.36%
Citrus Aurantifolia (Lime) Oil	Mouth washes and breath fresheners	0.0015%
Citrus Aurantifolia (Lime) Oil	Bath soaps and detergents	0.0014-0.17%
Citrus Aurantifolia (Lime) Oil	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0035-0.083%
Citrus Aurantifolia (Lime) Oil	Face and neck products Not spray	 0.019%
Citrus Aurantifolia (Lime) Oil	Body and hand products Not spray Spray	 0.0075-0.023% 0.0075-0.12%
Citrus Aurantifolia (Lime) Oil	Foot powders and sprays	0.00067%
Citrus Aurantifolia (Lime) Oil	Skin fresheners	0.1%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Bath oils, tablets and salts	0.0000000026%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Hair conditioners	0.00000015%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Hair sprays Aerosol Pump spray	 0.00000014% 0.00000043%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Shampoos (noncoloring)	0.00000084%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Tonics, dressings and other hair grooming aids	0.0000025%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Bath soaps and detergents	0.000013%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Body and hand products Not spray	 0.000011%
Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Face and neck products Not spray or powder	 0.0032%

Citrus Aurantium Amara (Bitter Orange) Leaf/Twig Oil	Other skin care preparations	0.0032%
Citrus Aurantium Dulcis (Orange) Oil	Bath oils, tablets and salts	0.0000032-0.94%
Citrus Aurantium Dulcis (Orange) Oil	Eye shadows	0.004%
Citrus Aurantium Dulcis (Orange) Oil	Eye lotions	0.034%
Citrus Aurantium Dulcis (Orange) Oil	Eye makeup removers	0.00078%
Citrus Aurantium Dulcis (Orange) Oil	Perfumes	0.0034%
Citrus Aurantium Dulcis (Orange) Oil	Powders (dusting and talcum)	0.0012%
Citrus Aurantium Dulcis (Orange) Oil	Hair conditioners	0.016-0.13%
Citrus Aurantium Dulcis (Orange) Oil	Hair sprays Aerosol Pump spray	 0.063% 0.0022%
Citrus Aurantium Dulcis (Orange) Oil	Rinses (noncoloring)	0.034%
Citrus Aurantium Dulcis (Orange) Oil	Shampoos (noncoloring)	0.0025-0.81%
Citrus Aurantium Dulcis (Orange) Oil	Tonics, dressings and other hair grooming aids Not spray	0.0053-0.26% 0.0053%
Citrus Aurantium Dulcis (Orange) Oil	Hair dyes and colors	0.000026%
Citrus Aurantium Dulcis (Orange) Oil	Other hair coloring preparations	0.042%
Citrus Aurantium Dulcis (Orange) Oil	Blushers	0.047%
Citrus Aurantium Dulcis (Orange) Oil	Face powders	0.0014%
Citrus Aurantium Dulcis (Orange) Oil	Foundations	0.014-0.02%
Citrus Aurantium Dulcis (Orange) Oil	Lipstick	0.034-0.95%
Citrus Aurantium Dulcis (Orange) Oil	Makeup bases	0.05%
Citrus Aurantium Dulcis (Orange) Oil	Other makeup preparations	0.024%
Citrus Aurantium Dulcis (Orange) Oil	Dentifrices	0.06%
Citrus Aurantium Dulcis (Orange) Oil	Bath soaps and detergents	0.022-0.12%
Citrus Aurantium Dulcis (Orange) Oil	Deodorants Not spray Aerosol	 0.038-0.06% 0.039%
Citrus Aurantium Dulcis (Orange) Oil	Shaving cream	0.0015-0.03%
Citrus Aurantium Dulcis (Orange) Oil	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.05-0.2%
Citrus Aurantium Dulcis (Orange) Oil	Face and neck products Not spray Spray	 0.14-0.18% 0.011%
Citrus Aurantium Dulcis (Orange) Oil	Body and hand products Not spray Spray	 0.2-1% 0.12%
Citrus Aurantium Dulcis (Orange) Oil	Foot products	0.000094%
Citrus Aurantium Dulcis (Orange) Oil	Moisturizing products Not spray	 0.05%
Citrus Aurantium Dulcis (Orange) Oil	Night products Not spray	 0.05%
Citrus Aurantium Dulcis (Orange) Oil	Paste masks and mud packs	0.1%
Citrus Aurantium Dulcis (Orange) Oil	Suntan products	

	Not spray	0.02%
Citrus Grandis (Grapefruit) Extract	Hair conditioners	0.005%
Citrus Grandis (Grapefruit) Extract	Hair sprays Pump spray	 0.0017%
Citrus Grandis (Grapefruit) Extract	Shampoos (noncoloring)	0.003%
Citrus Grandis (Grapefruit) Extract	Tonics, dressings and other hair grooming aids Aerosol	 0.003%
Citrus Grandis (Grapefruit) Extract	Bath soaps and detergents	0.0022-0.0059%
Citrus Grandis (Grapefruit) Extract	Deodorant Not spray	 0.0024%
Citrus Junos Extract	Shampoos (noncoloring)	0.0001%
Citrus Nobilis (Mandarin Orange) Oil	Dentifrices	0.035%
Citrus Nobilis (Mandarin Orange) Oil	Bath soaps and detergents	0.0009-0.0017%
Citrus Nobilis (Mandarin Orange)	Shampoos (noncoloring)	0.0005%
Citrus Nobilis (Mandarin Orange)	Bath soaps and detergents	0.0005%
Citrus Reticulata (Tangerine) Extract	Permanent waves	0.00013%
Citrus Reticulata (Tangerine) Extract	Shampoos (noncoloring)	0.005%
Citrus Reticulata (Tangerine) Extract	Tonics, dressings and other hair grooming aids	0.0051%
Citrus Reticulata (Tangerine) Extract	Face and neck products Not spray	 0.00016%
Citrus Reticulata (Tangerine) Extract	Moisturizing products Not spray	 0.00016%
Citrus Reticulata (Tangerine) Extract	Night products Not spray	 0.00016%
Citrus Tangerina (Tangerine) Extract	Other bath preparations	0.0005%
Citrus Tangerina (Tangerine) Extract	Colognes and toilet waters	0.0005%
Citrus Tangerina (Tangerine) Extract	Hair conditioners	0.00035%
Citrus Tangerina (Tangerine) Extract	Shampoos (noncoloring)	0.00001-0.00035%
Citrus Tangerina (Tangerine) Extract	Tonics, dressings and other hair grooming aids Not spray	0.00001% 0.0000025%
Citrus Tangerina (Tangerine) Extract	Bath soaps and detergents	0.0001%
Citrus Tangerina (Tangerine) Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00025%
Citrus Tangerina (Tangerine) Extract	Face and neck products Not spray	 0.0001-0.0045%
Citrus Tangerina (Tangerine) Extract	Body and hand products Not spray	 0.0005%

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

**The Dictionary defined Citrus Tangerina (Tangerine) Extract as " the extract of the tangerine, *Citrus tangerina*", rather than as an extract of the whole plant.

Information collected 2015-2016

Table prepared February 10, 2016

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: December 9, 2015

SUBJECT: Comments on the Draft Report: Safety Assessment of *Citrus* Plant- and Seed-Derived Ingredients as Used in Cosmetics (draft prepared for the December 2015 CIR Expert Panel meeting)

Chemistry, Definition and General Characteristics - It would be helpful to state that the citrus seed oils are fixed oils.

Constituents/Composition - This section should contain published information on the composition of these ingredients. Although there may not be information on the "whole plant" preparations, general information on composition of seed oils should be presented and there is likely information on specific seed preparations such as:

Akpata MI, Akubor PI. 1999. Chemical composition and selected functional properties of sweet orange (Citrus sinensis) seed flour. *Plant Food Hum Nutr* 54(4): 353-362.

Kim TW, Kim KK, Kang YH, et al. 2015. Fatty acid analysis of citron (Citrus junos Sieb. ex TANAKA) seed oil and its regulation effects on nitric oxide production, lipid accumulation, and leptin secretion. *The FASEB Journal* 29(Suppl): (meeting abstract)

Cosmetic Use, Summary - The European limit for furocoumarin is not presented correctly. It is now a regulation and should be cited to Annex II of the cosmetic regulations not to the 2005 SCCP opinion (reference 13). The listing in Annex II (entry 358) is for furocoumarins, it is not specifically about citrus-derived ingredients. Annex II entry 358 prohibits the use of "Furocoumarines (e.g. trioxysalen (INN), 8-methoxypsoralen, 5-methoxypsoralen) except for normal content in natural essences used. In sun protection and in bronzing products, furocoumarines shall be below 1 mg/kg."

Both the Use section and the Summary indicate that citrus aurantium (bitter orange) oil was not included in the 2013 use survey. The other ingredients not included in the 2013 use survey should also have been mentioned.

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