Safety Assessment of Camellia Sinensis-Derived Ingredients as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	February 21, 2014
Panel Meeting Date:	March 17-18, 2014

The 2014 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A. Hill, 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 Lillian C. Becker, Scientific Analyst/Writer.

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

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MEMORANDOM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: February 21, 2014

Subject: *Camellia sinensis* – Derived Ingredients As Used In Cosmetics

This is the Draft Tentative Report of Camellia sinensis-derived ingredients. An insufficient data announcement was issued at the December, 2013 meeting. The data needs were:

- Method of manufacture, including removal of impurities and constituents of concern (such as linalool)
- Composition data for camellia sinensis root extract, seedcoat powder, flower extract, and flower/leaf/stem juice
- Concentration of use data for camellia sinensis root extract, seedcoat powder, flower extract, flower/leaf/stem juice, and the catechins
- Human repeated insult patch test (HRIPT) on camellia sinensis leaf (100%), camellia sinensis stem/leaf extract (3%), and camellia sinensis catechins (at use concentrations)
- Confirmation that camellia sinensis leaf water is only used as a fragrance ingredient
- Information on the difference between leaf oil and leaf essential oil

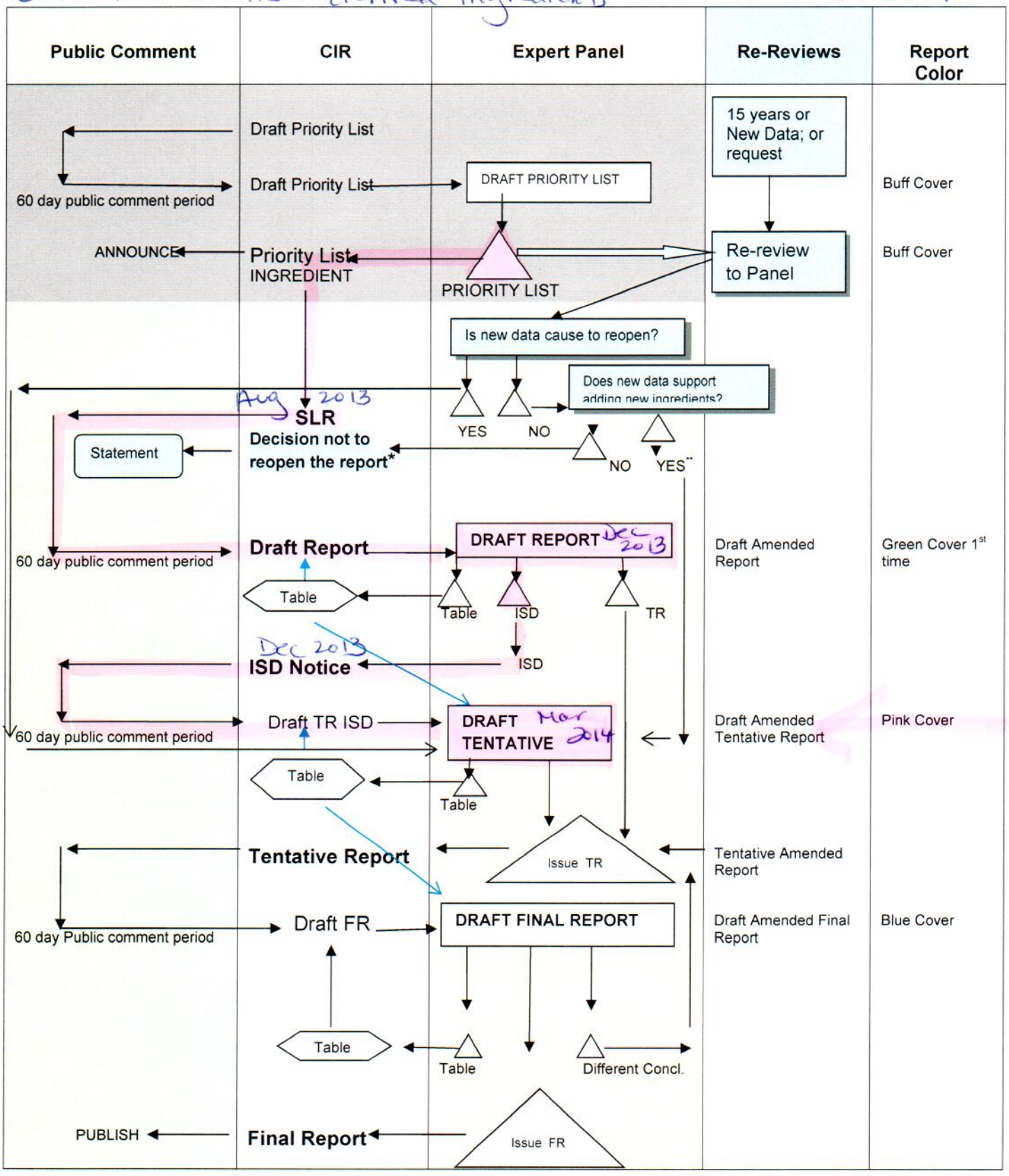
Data addressing some of these issues have been submitted, including HRIPTs of cosmetic products containing camellia sinensis leaf extract at 0.86%. A new concentration of use survey reports that camellia sinensis leaf is no longer used in tea bags for the eyes at 97% but at a maximum of 0.5% in bubble baths. The leaf powder, however, is used up to 50% in face and neck products. No additional concentration of use data were submitted for the root extract, seedcoat powder, or flower extract. There has been no new information on composition of these ingredients, the differences between oil and essential oil or if the only use for camellia sinensis leaf water is as a fragrance. No data on the method of manufacture were submitted.

The requested data on the photo effects of *C. sinensis* have been added to the report.

The Panel is to review the presented data and decide if there is sufficient information to meet the requirements of the insufficient data announcement. If so, then the Panel is to issue a conclusion of safe, not safe or safe with qualifications. If not, then the Panel is to issue a conclusion of insufficient data and list the data needs. The Panel is to develop the basis for the Discussion and issue a Tentative Report.

SAFETY ASSESSMENT FLOW CHART

Camellia Sinensis-derived ingredients Mar 2014



History
***Camellia Sinensis*-Derived Ingredients**

August, 2013 – SLR posted for comment.

December, 2013 – An insufficient data announcement was issued. The data needs were:

- Method of manufacture, including removal of impurities and constituents of concern (such as linalool)
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- Human repeated insult patch test (HRIPT) on camellia sinensis leaf (100%), camellia sinensis stem/leaf extract (3%), and camellia sinensis catechins (at use concentrations)
- Confirmation that camellia sinensis leaf water is only used as a fragrance ingredient
- Information on the difference between leaf oil and leaf essential oil

Camellia sinensis seed oil was removed from the report because it was included in the oils report.

March, 2014 - Panel is to examine the draft report with the additional data and updated concentration of use information. A Tentative Report should be issued.

Camellia Sinensis-Derived Ingredients Data Profile for December, 2013. Writer - Lillian Becker																		
	ADME			Acute toxicity			Repeated dose toxicity			Irritation			Sensitization					
	Dermal Penetration	Log K_{ow}	Use	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Irritation	Dermal Irr. Animal	Dermal Irr Human	Sensitization Animal	Sensitization Human	Repro/Devel toxicity	Genotoxicity	Carcinogenicity	Phototoxicity
Camellia Sinensis Leaf Extract	X		X								X			X	X		X	X
Camellia Sinensis Catechins	X									X	X	X	X		X	X	X	X
Camellia Sinensis Flower Extract																		
Camellia Sinensis Flower/Leaf/Stem Juice																		
Camellia Sinensis Leaf			X															
Camellia Sinensis Leaf Oil			X															
Camellia Sinensis Leaf Powder			X															
Camellia Sinensis Leaf Water			X									X		X				
Camellia Sinensis Root Extract																		
Camellia Sinensis Seedcoat Powder																		
Camellia Sinensis Seed Extract																		
Camellia Sinensis Seed Oil *REMOVED*																		
Camellia Sinensis Seed Powder																		
Hydrolyzed Camellia Sinensis Leaf																		
Hydrolyzed Camellia Sinensis Seed Extract																		

Camellia sinensis-Derived Ingredients
Search Strategy

SciFinder – "camellia sinensis dermal" culled for toxicity and relevant terms. 17 results

Internet Search – "Camellia sinensis". Tea Association information; Committee on Diet, Nutrition, and Cancer; European Medicines Agency; FDA Drug application and GRAS submission; and IARC.

SciFinder – "camellia sinensis" and "UV". 19 hits ordered
And "inhalation". Papers on using *C. sinensis* to treat pulmonary MRSA.

Camellia sinensis-Derived Ingredients
December 2013 Transcripts

Dr. Marks' Team

DR. MARKS: And so, this is camellia sinensis, is that right? I said sinensis. Who's the botanist in here?

DR. ANSELL: Sinensis. Sinensis.

DR. MARKS: Sinensis.

DR. BERGFELD: Sinensis.

DR. MARKS: And then how about is the first correct, the camellia? Okay. Tea is easy. These are ingredients derived from green, black, and oolong tea. And so this is the first time we've seen this report. You know that, Tom. I'll bring up Ron's in a second. I think he had a lot of the same ideas that I did when I looked at this.

So, yeah, the first thing was I had, Tom, what about the oral tox? There was some question whether we could deal with that.

DR. SLAGA: Well, to me, the oral tox, it's already a GRAS substance, and there's been a tremendous amount of study saying it's safe, you know, in drinking. So I thought that the oral tox, that there was no data needs, and it's "safe as used."

DR. MARKS: Okay. Okay. I'll read what -- thanks. One of the questions was did we remove the seed oil. That was in a previous report. That's a judgment call. It was "safe." And then the other, of course, do we include the leaf water. There is a question whether that's a – I don't have to bring out my cell phone.

DR. SLAGA: I had that down, too, but until we really know for sure, I'd leave it in.

DR. MARKS: Lillian, do you know? Did we get any clarification whether the leaf water was a fragrance?

MS. BECKER: No, we did not.

DR. MARKS: So I guess we'll leave it in at this point, particularly if we're going to come to a "safe" conclusion. If we're going to have otherwise, then maybe we would defer.

How about the seed oil since that was in a previous report? Would you leave it in or take it out?

DR. SLAGA: Well, it would be nice having it all combined in one, wouldn't it?

DR. BERGFELD: That's what I thought.

DR. MARKS: Yeah, I agree. We have boilerplates on page 13. Here we go. And I think this is the same that Ron had. I had do we need the manufacs for cosmetics. That's on page 12 of their report. We have manufacturing for GRAS, so let me see. Ron Shank says, "Discussion. Need method manufacturing of purity data to be certain that cosmetic grade ingredients are chemically the same as food grade ingredients." Okay.

DR. SLAGA: I agree with that. That's important. There was no information on that.

DR. MARKS: So, Jay, can you comment on that at all?

DR. ANSELL: This would be the relationship between the cosmetic grade and tea grade.

DR. MARKS: Yes, exactly.

DR. ANSELL: I have no information on that.

DR. MARKS: Okay. So I guess Ron Shank has it in a discussion. If we don't have any data, can we in the discussion handle this? We'll change the conclusion. And I have some insufficient data anyway, so we'll get to that in a minute. So I would put that in one of the potential needs or at least address. And, Jay, maybe the PCPC can alleviate that.

Lillian, I have in here -- so I'll go back to Ron Shank says. "It seems that the leaf and leaf extract would be substantially different from the extracts of the flower, root, and seed. This prevents read-across from the compounds and the toxicity database, the leaf, leaf extract." So just deleting the following materials: Flower, root, seed powder, seed extract, seed oils. Of course we can't remove seed oil if we have a previous report which is safe.

What do you think, Tom, about the read-across?

DR. SLAGA: I have no problem with the read- across.

DR. MARKS: Yeah, neither did I. I didn't put that as an issue also. So what we can do is when we have the discussion, we'll see what the Belsito team does. I feel a little lonely, Tom. I'm the only team member here of our team. The Belsito team, the only one missing is Dan.

DR. SLAGA: But you have lovely Wilma with you.

DR. MARKS: I know, exactly. Wilma was kind enough to join me so I wouldn't feel all alone here. So at any rate, we'll bring that up as a discussion. I have it here in my notes, and I'll mention that tomorrow. Do we need the manufacturer for cosmetics.

Lillian, on page 12, I have linalool concentration, 198,000 parts per million. Is that right? And if it is, that means it's like 19 percent of the tea is linalool?

DR. GILL: Page 12 of the PDF.

DR. SLAGA: Well, the (inaudible) 20 to 30 percent, but I didn't think there was anything else that high.

DR. MARKS: Well, let me see what I have highlighted. I'll go to that page. Maybe I read it incorrectly, Lillian. Oh, yeah, there it is. If you see under constituents of concern.

MS. BECKER: Yes.

DR. MARKS: And if you look under leaf essential oil, it has 198,400 parts per million of linalool. So that seems mighty high.

DR. ANSELL: Well, we do suggest that the seed oil be removed from the report for a couple of reasons, including that it's already been reviewed, but also that it's --

MS. BECKER: It's different.

DR. ANSELL: It's different, yeah.

DR. MARKS: Okay. So that's easy since it's already been removed. It's interesting. Since it's different, how do you mean, Jay?

DR. ANSELL: Different composition, triglycerides, than the rest of the ingredients in the report.

DR. MARKS: Okay. Tom, what do you think about that? It's already been --

DR. SLAGA: Yeah.

DR. MARKS: Let me see if Ron Shank has removed them or anything. Yeah, Ron mentions again page 13, impurities. So let me go back, Lillian. Do you think it's that high for linalool? Do you see what I'm looking at,

Jay? Page 12 of the PDF, and it's under "constituents of concern." It's the first sentence where it has linalool, and you see under leaf essential oil, it ranges up to 198,400 parts per million, so potentially close to 20 percent of the constituent could be linalool. And I didn't look up under the fragrance, but, boy, that's very high I would think. And this is a fragrance sensitizer. Although when I go back, I'll give you my needs in a second.

So, Lillian, I might ask you to just check that.

Ms. BECKER: I'm doing it now.

DR. MARKS: Yes.

DR. HELDRETH: I understand the Council's contention that the seed oil would be primarily triglycerides, but that doesn't make it different from all the ingredients in this report. We also have a leaf oil, and that would be triglycerides as well.

MS. BECKER: And this is also the correct according to the statement.

DR. BERGFELD: Which is correct?

MS. BECKER: The high amounts in the essential oil.

DR. BERGFELD: So you're saying it's the same.

MS. BECKER: Right, but this is the plant, essential oil --

DR. BERGFELD: Right.

MS. BECKER: -- that might be very different for what they actually use in cosmetics after processing.

DR. BERGFELD: Right.

DR. MARKS: Well, we'll be reassured when we have the sensitization study, so I just want to be sure that even -- let me see if this thing will respond here. Oh, good.

So let's go back up to the seed oil. So I have, Tom, you are fine with not having it included. Ron Shank didn't mention anything. Jay, you would like it removed because of the triglycerides, but, Bart, you say the other ingredients have triglycerides.

DR. HELDRETH: At least one.

DR. MARKS: Yeah. Would you remove it just because it's already in another report, Tom?

DR. SLAGA: Yeah, I'd remove it.

DR. MARKS: Okay. So let me see what else. Impurities, ocular. So I'll let you, Lillian, Ron Shank had a question on page 19, third paragraph under ocular. Which is it, 0.093 or 0.1? But again, that can be -- those are editorial comments. My concern was the leaf extract has 1,700 uses, so it's got a lot of uses.

The leaf itself is applied to eyelids at 97 percent. So it sounds like what they do is put the whole leaf there. They probably have little else.

So I felt we needed an HRIPT on both of these at use concentration. So the extract has used up to three percent, and then I wanted to see leaf meet HRIPT. And what we have now is we don't have HRIPT at those concentrations. So I would put it as an insufficient data announcement with the needs of the HRIPT on the leaf extract and the leaf --

Ron Shank didn't mention that, Tom.

DR. SLAGA: I didn't have any -- I would go with the -- it's the first time.

DR. MARKS: Yeah, exactly, and this is just an announcement. This is not an insufficient data.

DR. SLAGA: Right. I would go with that.

DR. MARKS: Okay. Wilma, do you have any comments? I don't know whether you noticed that when you reviewed it.

DR. BERGFELD: I wrote and said it needs irritation and sensitization.

DR. MARKS: Yeah, which would be gotten with the HRIPT.

DR. BERGFELD: Yeah, right.

DR. MARKS: Okay. So let me see. Who does this tomorrow? It'll Don, and we'll see how that works out. But right now, we'll remove the seed oil. We'll leave the water in for the time being. I'm going to call it now the botanicals boilerplate because that includes pesticides, metals, and aflatoxin. We need the method of manufacture, or we need the method of manufactures for cosmetics addressed.

And then it looks like the linalool concentration actually is 19 percent based on that.

MS. BECKER: So maybe needs method of extracting that.

DR. MARKS: Yeah. Yeah, exactly. And then the HRIPTs. Okay.

DR. BERGFELD: What are you going to do about the use of the GRAS food data? Are you going to from this team say you accept it?

DR. MARKS: Yes.

DR. BERGFELD: Okay.

DR. MARKS: I go with Tom. Tom said --

DR. BERGFELD: You have to say that, I think.

DR. MARKS: Okay. Let me put that up here.

DR. BERGFELD: The aflatoxins that are described in the impurity data, you're just going to put the boilerplate in to cover that.

DR. MARKS: Yes. Yeah.

DR. BERGFELD: Okay.

DR. MARKS: Oil tox, okay. Where am I? Thank you, Wilma.

DR. BERGFELD: Now, I was quite taken with the fact that if you drink too much of this tea, you can have liver damage.

MS. BECKER: Yeah.

DR. MARKS: Okay. So I guess the moral to that story is don't drink it or put it on your skin, or don't drink too much. Like everything else it's in moderation.

DR. BERGFELD: Well, people drink a lot of black tea.

DR. MARKS: Yeah, exactly. It's in moderation. Okay, Tom, does that sound good to you?

DR. SLAGA: Yeah. When I'm drinking tea and it drips on my skin, it kind of hurts.

(Laughter.)

DR. MARKS: So I'm going to put here oral tox, using that is okay. Remove the seed oil. We still don't know about the leaf water, the boilerplate, the manufacture of cosmetics. It looks like there's a high linalool concentration, and I'll see what Don's team says. And then the irritation sensitization and HRIPT on the leaf extract, the highest use, three percent, and on the leaf.

Okay. Any other comments?

DR. SLAGA: No.

DR. MARKS: Good. Thanks, Tom. Thanks, Lillian.

MS. BECKER: You're welcome.

DR. MARKS: Okay, let's see. They make quite a few comments, so I'm going to give you this. This is Ron Shank's. Oh, good. You have it.

MS. BECKER: He made copies.

Dr. Belsito's Team AND Combined Session

DR. BELSITO: Okay, so Camellia sinensis, leaf ingredient, so this is basically tea leaves. Hey, Dan.

DR. LIEBLER: Sure. I'm on the line.

DR. BELSITO: Okay. So we've dispensed with the infant skin absorption. We're moving into the last five ingredients. We just did phytosterols safe as used. Curt pointed out a genetic deficiency in some individuals that we're going to capture in the metabolism, the summary, and basically saying the discussion is not relevant to cosmetics. So with phytosterols we're going with a safe as used.

DR. LIEBLER: Good.

DR. BELSITO: Okay. We voted on that, so I gather you're voting in favor of that. Because we're doing sort of a combined team and then final right now.

DR. LIEBLER: Okay.

DR. BELSITO: Okay. People have already told you not to go to the airport, right?

DR. LIEBLER: Yeah, that's right.

DR. BELSITO: Okay. So now we're --

SPEAKER: A minor detail.

DR. BELSITO: Yeah. We're moving on to Camellia sinensis. So we've relied -- since this is, you know, a tea leaf that we drink, we've done the usual thing of dispensing with a lot of the oral toxicity and focusing more on the dermal applications. Counsel recommended that we remove the seed oil since it was reviewed previously as part of the plant oils and was found to be safe. And so the question is whether these ingredients that we have before us are -- where they're at.

So I thought the leaf extracts were safe as used. I didn't have a problem with that. The catechin sensitize at 5 percent, but not at 0.1 percent, and we don't have a concentration of use for them. So I said we could say they were safe at.1 percent because we have composition, but we couldn't say safe as used since we didn't know

how they were used.

The seed oil was previously done and I don't have a problem removing that from the report. But as with other botanicals that we've reviewed, we don't know what's in the root, we don't know what's in the seed coat powder, the seed extract, the seed powder, the hydrolyzed seed extract, the flower, the flower-leaf-stem juice, and they don't appear to be used. So I thought they were all insufficient for both composition and concentration of use.

And then they are photo-absorbers, but we had a negative phototoxicity study except one where, for reasons that I don't know, they exposed the animals to UVC, which, of course, is going to give you some erythema. Craziest phototox study I ever saw.

And I can talk about what I put in the discussion, but basically leaf extract, safe; catechin, safe to.1 percent; seed oil removed, previously reviewed; and all the others, insufficient.

DR. BERGFELD: Any discussion from the Belsito team regarding this?

DR. EISENMANN: So this is an insufficient data announcement. This is the first review.

DR. BELSITO: Right. Right. So it's going to be insufficient for root, seed coat powder, seed extract, so everything on the seed, everything on the flower, everything on the stem. We need composition and we need concentration reviews. And if industry wants a level higher than .1 percent for catechins, they have to provide us with data at where you can go between .1 and 5 percent and not sensitize.

DR. LIEBLER: I agree with all of that.

DR. BERGFELD: Okay. Anybody? Paul, Curt, anything?

DR. KLAASSEN: I agree.

DR. SNYDER: I agree.

DR. BERGFELD: So is that a motion?

DR. BELSITO: A motion that this be insufficient for the reasons that I asked, it go out as a data request.

DR. BERGFELD: And Jim?

DR. MARKS: Our team has insufficient, also, although I was concerned about not only what you said, Don, but the leaf extract has 1,700 uses and we didn't have an HRIPT at 3 percent, which is the top use concentration. So I wanted to see an HRIPT on the leaf extract at 3 percent and I wanted to see it on a leaf at neat (phonetic) since it's used on the eyelids at 97 percent.

DR. BELSITO: But we had one where they actually put the leaves on the eyes and there was nothing. That would have been --

SPEAKER: Leaf water.

DR. MARKS: That was leaf water, yes. The (inaudible) I don't -- that's not the same. The water has less in it, presumably, than the leaf itself and certainly less than the leaf extract. So I agree with your other -- I think we can --

DR. BELSITO: Well, I mean, as long as we're going insufficient, I mean -- so you're saying in addition to everything I said, you would like to see sensitization and irritation at 3 percent --

DR. MARKS: For the leaf extract and neat for the leaf itself.

DR. BELSITO: I'm okay with that.

DR. BERGFELD: Okay. So that is in addition to the insufficient list.

DR. BELSITO: Yeah.

DR. BERGFELD: So you're accepting that, Don?

DR. BELSITO: Yeah, sure.

DR. BERGFELD: All right. And so that's a second?

DR. MARKS: Yes.

DR. BERGFELD: Any comments?

DR. HILL: Could you read your list again? Because my flag was on method of manufacture, but, in reality, maybe what you have is capturing what I was concerned about.

DR. BELSITO: Well, we want sensitization and irritation at 100 percent on the leaf because it's used as an eye compress, right, the leaf itself? Is that --

DR. MARKS: Yes.

DR. BELSITO: Yeah. And then we want sensitization and irritation on the leaf water or leaf extract?

DR. BERGFELD: You said extract.

DR. MARKS: Leaf extract.

DR. BELSITO: At 5 percent.

DR. MARKS: And Ron Hill, thanks for bringing --

DR. BERGFELD: I think it was 3 percent.

DR. BELSITO: At 3 percent.

DR. MARKS: And actually we have some, also, data we'd like to see. Now I was reading off a paper, now I brought up the computer, so, Ron Hill, you were right on.

Ron Shank, you -- and actually I was concerned about the method of manufacture that's in the document is not cosmetics. And we wanted to have reassurance that the same method of manufacture as in the document is being used for cosmetics.

DR. HILL: And plus, a lot of what's in there was for the oil. And if we're taking that -- are we taking that out?

DR. BELSITO: The seed oil, yeah.

DR. MARKS: Yes.

DR. HILL: Yeah. So then that wipes out a good bit of that section.

DR. MARKS: And then, Don, just as further clarification, is the leaf water a fragrance of not? Do you know?

DR. BELSITO: I haven't -- I don't know. I mean, we haven't gotten that answer back from (inaudible).

DR. MARKS: And then the only other thing when I reviewed the document, Don, and, again, it won't change our insufficient data announcement, is a linalool concentration, if you look at page 12, was up to close to 20 percent concentration range. It was 198,400, I think, parts per million and that stood out. Linalool being a sensitizer that would it actually be that high? And at our meeting this morning (inaudible) just wanted to clarify that. But I don't think, you know, we --

DR. BELSITO: If the concentration of linalool is that high, this is in the leaf water? Yeah, I mean, it's probably a pure fragrance ingredient.

MS. BECKER: It's in the leaf essential oil, but this is also the leaf essential oil of the plant, not the manufactured, gone through processing essential oil.

DR. MARKS: That was on page 12.

MS. BECKER: Twelve.

DR. MARKS: Yeah, and take a look there, Don, and you'll see.

DR. HILL: And that's a percentage of the essential oil? I mean, it's not percentage of the total, it's percentage of the oil, right?

MS. BECKER: Right, correct.

DR. HILL: Yeah.

MS. BECKER: And it's only from the plant, not the product.

DR. LIEBLER: Aren't we dropping the leaf essential oil?

DR. BELSITO: Yeah, we are.

DR. BRESLAWEC: This is the leaf. This is the essential oil. Did I get that right?

DR. EISENMANN: I thought you were dropping the seed oil --

SPEAKER: Seed oil.

DR. BELSITO: Seed oil.

DR. EISENMANN: -- which is (inaudible) non- essential oil.

DR. BELSITO: Right, because the seed oil has been reviewed. And I said the insufficiency for -- we don't have a concentration of use for the seed oil.

DR. BRESLAWEC: We're removing the seed oil because that's --

DR. BELSITO: I mean for the --

SPEAKER: (inaudible) review.

DR. BRESLAWEC: Well, do we want to include the leaf oil in this?

DR. BELSITO: Right, we don't have a concentration of use for the leaf oil, do we?

DR. EISENMANN: No, it's not shown in the table, so I didn't get anything.

DR. BELSITO: Right. So, I mean, I think the leaf oil is going to be very different from what we're seeing for everything else. So although we know what's in the leaf, we don't know what the composition of the -- well, we do know the composition of the leaf oil. It's very high in linalool.

DR. MARKS: That's what it says here.

DR. HELDRETH: It says that that's the high concentration of the essential oil, which may or may not be the same thing as the ingredient that's listed here.

DR. BELSITO: I mean, I think that we can go -- I mean, we can always decide to drop the oil or say it's insufficient, but, at this point, I think we need to know what the composition and concentration of use of the leaf oil is.

DR. HELDRETH: Yeah, exactly, and then maybe clarify what is leaf essential oil versus what's leaf oil? Because that was my -- I mean, when you see that magnitude of difference, although even with the shoot -- of course we aren't talking about the shoot in this, but it goes up to 10,300 parts per million of linalool. So it gives us time with the insufficient data announcement to work out these.

DR. BERGFELD: So we have a motion that's been seconded. Do you have another comment, Ron?

DR. LIEBLER: Yeah, one more thing that I had flagged here since I wasn't here this morning for that discussion, so I guess I'm cheating, but while we're at it there's a section on wound healing and the header says Camellia sinensis leaf extract, then it says leaf water extract in the actual text. But I wondered if we had any further information. And I didn't get a chance to look up that, but I wondered if anybody else noticed that. I mean, wound healing is, theoretically, a good thing, but it would be nice to know what the nature of the effect was.

DR. BRESLAWEC: Could you tell me where that is?

DR. HILL: Yeah, sure, on the PDF it's page 15, so I'm just tossing that out there for people to have another look at and I also flagged it.

DR. MARKS: Tom, are you on? Tom Slaga, are you on conference call, too?

DR. BERGFELD: Mm-mm, just Ron Liebler.

DR. MARKS: I know.

SPEAKER: Do they have his phone number?

DR. BRESLAWEC: I have a concern about, again, the heading "Wound Healing." That suggests an effect that I don't think we should be suggesting. You know, it's data that should be included in the report, but, you know, when you say something like "wound healing," that suggests effectiveness which we aren't evaluating.

DR. HILL: I looked at it just in terms of biochemistry and pharmacology. It's causing an effect. Is it relevant to any of the all of the rest of this at the concentrations tested? I can't answer that right at this very moment. I really just wanted people to pay a little attention to that before the next round.

DR. BRESLAWEC: I mean, likewise, the section on anti-phototoxicity could be combined with phototoxicity.

DR. BERGFELD: Any other comments? Edit? Seeing none, I'll call for the question. Now, as I understand it, it is safe?

SPEAKER: No, insufficient.

DR. BERGFELD: Insufficient.

DR. BELSITO: Insufficient.

DR. BERGFELD: Except for --

DR. BELSITO: The only on that we're saying is safe is catechins at a level of.1 percent.

DR. BERGFELD: .1, 0.1 percent. So that portion is safe; the rest is insufficient. And the list we've defined as?

DR. BELSITO: Method of manufacturing clarified, we want -- what?

DR. MARKS: Go ahead.

DR. BELSITO: We want sensitization and irritation at 100 percent for the leaf and 3 percent for the stem/leaf extract. And then for the remaining ingredients -- the leaf (inaudible), the roots, seed coat powder, seed extract, seed powder, hydrolyzed seed extracts, flower, flower-leaf-stem juice -- all insufficient for composition and concentration of use.

DR. LIEBLER: I will just further comment that one of the --

DR. BERGFELD: Go ahead.

DR. HILL: -- that one of the things I was trying to get at with -- because we have this impurity section which almost didn't make sense to me. I mean, I know what kind of information we'd like to capture, but given the nature of the ingredients, so what I was really more interested from the method of manufacture is the source of artifacts that might show up because the impurity section, even the presence of it is -- I'm not sure it makes the greatest of sense for this category, but.

MS. BECKER: Okay. So we're not putting method of manufacture in the insufficient list?

DR. BERGFELD: No, we are.

MS. BECKER: We are.

DR. BERGFELD: We are, but this is a clarification what the point of it is.

MS. BECKER: Okay.

DR. HILL: But not impurities. That was the point of that comment, I guess.

MS. BECKER: Okay.

DR. MARKS: So Don, I want to be clear, on page 21 of the document, in the summary, I guess this is, right before the discussion, it's the third paragraph before the discussion it says that catechins was a sensitize or had 0.1 percent, so that was a guinea pig.

DR. BELSITO: Oh, wait a minute, then I misread that.

DR. MARKS: Yeah. So you said safe at --

DR. BELSITO: But that may be a typo because I --

DR. BERGFELD: Where are you?

DR. MARKS: I'm in the summary section. Maybe I didn't go -- I looked through the others, but is that a --

DR. BELSITO: Well, that's what I'm checking because I thought it was --

DR. MARKS: Let me see, catechins --

DR. BELSITO: I got was a sensitizer, so I'm sorry, I just totally misread it. So yeah, catechins are insufficient for sensitization as well.

DR. MARKS: Yes, yeah.

DR. BELSITO: Thank you, Jim.

DR. MARKS: You're welcome.

DR. BERGFELD: So you're adding that?

DR. BELSITO: Yeah.

DR. BERGFELD: So that gives us how many items that we're asking for?

SPEAKER: A lot.

DR. BERGFELD: I know. Maybe something like --

DR. BELSITO: So for catechins we're asking for sensitization.

DR. BERGFELD: And catechin sensitization is in your (inaudible)?

SPEAKER: Mm-hmm.

DR. BERGFELD: Okay, so four specific requests.

DR. MARKS: And I -- that's not being used as a cosmetic ingredient in my notes --

DR. BELSITO: Right.

DR. MARKS: -- so we're probably not going to get that.

DR. BERGFELD: Okay.

DR. MARKS: So I think we could still move forward and where we'd have to at least in the discussion mention that because the others may be used at a concentration similar and we can't use the same conclusion --

DR. BELSITO: Right.

DR. MARKS: -- and the presence use and concentration.

DR. BERGFELD: All right. If there's no other comment, then we'll move the question. This ingredient is going insufficient. We've discussed the needs. All those in favor indicate by raising your hand. Fine, thank you very much.

DR. MARKS: Dan, did you raise your hand?

DR. BERGFELD: Are you raising your hand, Dan? Yes?

DR. LIEBLER: (inaudible)

DR. BERGFELD: Good, I saw it.

(Laughter)

DR. BELSITO: Okay.

DR. BERGFELD: I think we better proceed.

Safety Assessment of Camellia Sinensis-Derived Ingredients as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	February 21, 2014
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The 2014 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A. Hill, 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 Lillian C. Becker, Scientific Analyst/Writer.

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

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ABSTRACT

The Abstract will be edited and further developed at the March, 2014 Panel meeting.

Cosmetic ingredients derived from *Camellia sinensis* (tea) plant parts have functions that include antioxidant, and skin-conditioning agent – humectant and miscellaneous. The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed relevant animal and human data related to these ingredients and issued an insufficient data announcement. The *C. sinensis*-derived ingredients in this safety assessment are from consumable plant sources and exposures to these ingredients in beverages results in much larger systemic exposures than would result from cosmetic uses. Therefore, the oral toxicity potential of these cosmetic ingredients will not be addressed in this report. Because formulations may contain more than one botanical ingredient, caution was urged to avoid reaching levels of toxicity for constituents. Industry should use the good manufacturing practices to limit impurities. The Panel concluded…[*A conclusion will be developed at the March, 2014 Panel meeting*.]

INTRODUCTION

This is a safety assessment of cosmetic ingredients derived from *Camellia sinensis* (tea) plant parts. The functions of these ingredients include: antifungal agent; antimicrobial agent; antioxidant; cosmetic astringent; fragrance ingredient; light stabilizer; oral care agent; skin protectant; skin-conditioning agent – emollient; skin-conditioning agent – humectant; and skin-conditioning agent – miscellaneous (Table 1). The 14 ingredients in this report are:

- camellia sinensis leaf extract
- camellia sinensis catechins
- camellia sinensis flower extract
- camellia sinensis flower/leaf/stem juice
- camellia sinensis leaf
- camellia sinensis leaf oil
- camellia sinensis leaf powder
- camellia sinensis leaf water
- camellia sinensis root extract
- camellia sinensis seedcoat powder
- camellia sinensis seed extract
- camellia sinensis seed powder
- hydrolyzed camellia sinensis leaf
- hydrolyzed camellia sinensis seed extract

It is not known if camellia sinensis leaf water is solely used as a fragrance ingredient. If so, it will not be included in this report because the safety of fragrance ingredients is reviewed by the Research Institute for Fragrance Materials (RIFM).

Camellia sinensis seed oil was included in a 2011 Cosmetic Ingredient Review (CIR) safety assessment of plant based oils with the conclusion that it was safe in the present practices of use and concentration.[1]

The *C. sinensis*-derived ingredients in this safety assessment are from consumable plant sources and exposures to these ingredients in beverages results in much larger systemic exposures than would result from cosmetic uses. Therefore, the oral toxicity potential of these cosmetic ingredients will not be addressed in this report. While data on the potential for reproductive toxicity, genotoxicity, and carcinogenicity are presented, the primary focus of this report is on the potential for irritation and sensitization.

CHEMISTRY

Definition and Description

The definitions and functions of *Camellia sinensis*-derived ingredients are provided in Table 1.

CAMELLIA SINENSIS

There are four varieties of the *C. sinensis* plant: *sinensis*, *assamica*, *pubilimba*, and *dehungensis*. The first two are most commonly used to prepare tea for human consumption. The type of tea (i.e., white, green, oolong, black) depends on time of year harvested, age of leaves when harvested, location/soil/climate, and processing after harvest. The processing of tea for a beverage is referred to as fermentation, because it was originally believed that the leaves were fermented, but the process actually involves an enzymatic oxidation.[2,3] It is not known which of these teas or which specific processes are used to produce cosmetic ingredients.

The *C. sinensis* is native to East, South and Southeast Asia.[3-5] However, it is also cultivated in other tropical and subtropical regions. The leaves of this evergreen shrub can be lanceolate to obovate, up to 30 cm long (usually 4 - 15 cm) and 2 - 5 cm broad, pubescent, sometimes becoming glabrous, serrate, acute, or acuminate. The plant has a strong taproot. The 3 – 5 cm, yellow/white flowers are globular and have a delicate fragrance.

These plants are not the source of, nor are they related to, tea tree oil, which is derived from *Malaleuca alternifolia*.

CONSTITUENTS

The constituent groups of fresh green leaf *C. sinensis* are provided in Table 2. The constituent group having the highest concentrations is the flavanols (25.0% dry weight), which is followed by proteins (15.0%) and polysaccharides (13.0%).[3]

Other constituent groups found in *C. sinsensis* plant parts include:

Amino acids – The most abundant amino acid is one not typically found in proteins, theanine (5-*N*-ethylglutamine).[3,6]

Carotenoids – These are present in low levels in the leaves. They include neoxanthin, violaxanthin, lutein, chlorophylls a and b, and β-carotene.[3,7,8] Seventy-nine pigments, 41 chlorophylls and 38 other carotenoids have been detected.[9]

Enzymes – Fresh *C. sinensis* leaves contain high levels of the enzyme polyphenol oxidase.

Methylxanthines - Theobromine can range from 0.16% - 0.2% of a dry-weight leaf.[3,10,11] Dried leaves contain not less than 2% caffeine (dried weight). Increased use of nitrogen fertilizer can increase caffeine content by up to 40%. Theophylline is present at < 0.04% dry leaf weight.

Flavonoids – These include flavonols, flavanols, and glycosides. Flavanols include catechins, which are present in small amounts, and may occur as flavonols and glycosides.[3,12,13] Flavonols reported to be in leaf extract are kaempferol, quercetin, and myricetin.[3,14]

Catechins - These polyphenolic molecules are a subgroup belonging to the flavanol family.[3,15-17] They make up 20% - 30% of the weight of tea leaves. Catechins are especially concentrated in green tea which account for 30% - 40% of the dry weight of the leaves. The most abundant type of catechin in green tea is epigallocatechin gallate (EGCG; 12%). The other catechins are catechin (C), epicatechin (EC), gallocatechin (GC), epigallocatechin (EGC), catechin gallate (CG), gallocatechin gallate (GCG), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG) (Figure 1).

Minerals and elements - Potassium is the greatest mineral element present at 40% of the total mineral element content. The leaves are rich in fluoride and they accumulate aluminum and manganese.[3,18,19] Other minerals present include calcium, magnesium, sodium, phosphorus, and sulfur. Minor elements include boron, barium, chromium, copper, iron, molybdenum, nickel, rubidium, strontium, and zinc.[18] Trace elements include silver, arsenic, beryllium, bismuth, cadmium, cerium, cobalt, cesium, mercury, indium, lithium, lead, rare earth elements, antimony, selenium, tin, tellurium, thallium, uranium, vanadium, ytterbium, and zirconium.

Volatiles – There are a large number of volatile constituents in fresh leaves. *Trans*-2-hexenal and *cis*-3-hexenol are present in the greatest amounts.[3,13,20,21]

Climatic conditions during cultivation may affect the composition of theanine, standard α-amino acids (i.e., isoleucine, leucine, valine, alanine, threonine, and glutamine), quinic acid, EC, EGC, EGCG and caffeine levels in *C. sinensis* leaf extract (as green tea).[22,23] Soil conditions and cultivation methods affect mineral levels.[18]

Constituents reported to be predominately in *C. sinensis* seeds include caffeine, glucothea saponin, stearic acid, theasponin, and theobromine.[24]

Constituents reported to be in *C. sinensis* seed coat include caffeine and theobromine.[24]

CONSTITUENTS OF CONCERN

Linalool and several compounds containing linalool (i.e., (R)-linalool, linalool-oxide-(*cis*-furanoid), linalool-oxide-(*cis*-pyranoid), linalool-oxide-(*trans*-pyranoid), linalool-β-D-glucopyranoside, and linalool-oxides) have been reported in the leaves (6 -1984 ppm), leaf essential oil (31800 – 198 400 ppm), and shoot (600 – 10300 ppm) of *C. sinensis* (Table 3).[24]

Quercetin and several compounds containing quercetin (i.e., quercetin-glucosides) have been reported in the leaf (760 - 10000 ppm), plant, and shoot of *C. sinensis* (Table 3).

Climatic conditions during cultivation may affect the composition of theanine, standard α-amino acids (i.e., isoleucine, leucine, valine, alanine, threonine, and glutamine), quinic acid, EC, EGC, EGCG and caffeine levels in *C. sinensis* leaf extract (as green tea).[22,23] Soil conditions and cultivation methods affect mineral levels.[18]

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Constituents reported to be in *C. sinensis* seed coat include caffeine and theobromine.[24]

SAMPLE ANALYSIS

Constituents in medical grade *C. sinensis* extract include methylxanthines, flavanols (10% - 25%), flavonols, flavones, phenolic acids, amino acids (including theanine, 3%), terpene saponins, polysaccharides, proanthocyanidins, vitamins, and minerals (Table 4).[15,25-29]

Analyses of three lots of *C. sinensis* catechins (each prepared as a food additive) indicated 28% - 90% total catechin monomers and 37% - 100% polyphenols.[30]

CHARACTERIZATION

As herbal supplements, extracts are characterized by the drug/extract ratio (DER), which is the ratio of the quantity of herbal substance used in the manufacture of an herbal preparation (given as a range) to the quantity of the herbal preparation obtained in the finished product.[31] The specifications for *C. sinensis folium* as an herbal supplement in the European Union (EU) for the dry extract, purified (DER 45-56:1, extraction solvent: water) corresponds to 55% - 72% (-) epigallocatechin-3-*O*-gallate.[25,31] The decaffeinated dry extract (DER 6:1 to 10:1, solvents such as alcohol, methanol,

acetone, or water or mixtures of these solvents) contains not less than 60% of polyphenols, calculated as (-)-epigallocatechin-3-*O*-gallate, not less than 40% of (-)-epigallocatechin-3-O-gallate, and not more than 0.1% of caffeine, calculated on the anhydrous basis.

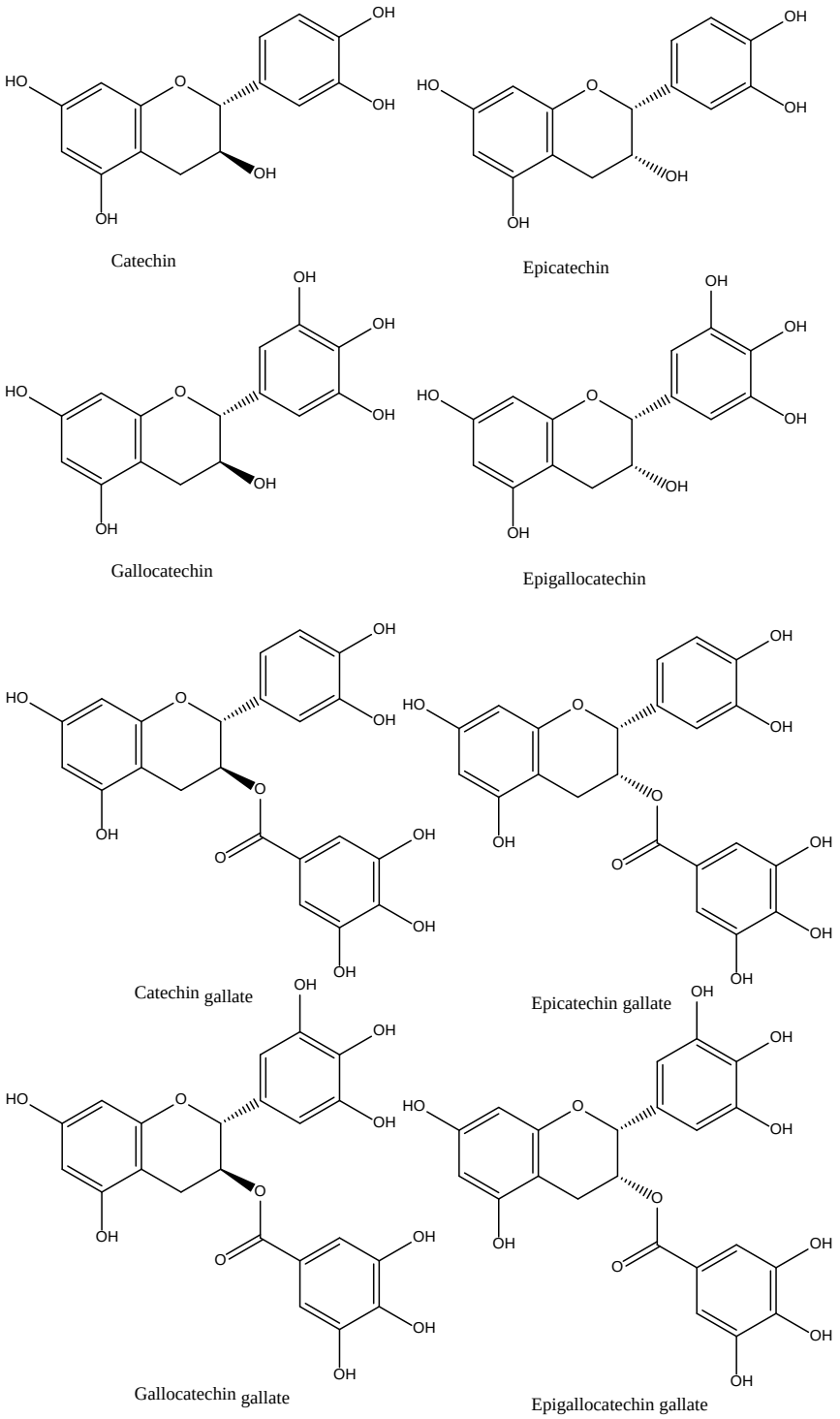

Figure 1. Catechins from *Camellia sinensis*

Physical and Chemical Properties

C. sinensis catechins have an astringent taste and are soluble in water.[3,15]

Three lots of oolong tea with *C. sinensis* catechins were stable for 18 months in unopened packaging at -20°C.[30] Total catechin monomers were reduced from 100% to 97% and 98% after 6 months of storage at 25°C in polyethylene terephthalate (PET) bottles and steel cans, respectively. At 37° for 2 months, catechin content was reduced to 96% in both types of containers.

A sunscreen with *C. sinensis* (2%, 3%, 4%, or 5%) in the form of green tea extract was stable for up to 6 months.[32]

Method of Manufacture

No information on the method of manufacture for *C. sinensis*-derived cosmetic ingredients was discovered or submitted. The methods below are general to the processing of *C. sinensis* for food or food ingredients and it is unknown if they apply to cosmetic ingredients. The makeup of the *C. sinensis* extract will differ with the manufacturing process.

C. sinensis leaf in the form of green tea consists of whole or cut young, unfermented, rapidly heat-dried leaves.[16,25] The fresh leaves are processed by a method designed to prevent the enzymatic oxidation of catechins. The enzymes are inactivated by heat (pan-fried or steam).

There are different harvesting and manufacturing processes for white, green, black and oolong teas for drinking.[16,18,25,33] White tea is made from very young leaves and leaf buds. Green tea is made from new, fully-formed leaves. These two teas are minimally processed, steamed, and dried. Black tea and oolong tea are made from older, fully-formed leaves. Oolong tea is withered, and rolled during "fermentation", then fired and dried. Black tea is withered, crushed, and rolled during "fermentation" then fired and dried. Phenolics content typically differs substantially between green and black teas (Table 5).

Catechins are isolated through an initial hot water extraction with ethyl acetate, and then separation by chromatography, followed by spray-drying.[34] The spray-dried catechins may be recrystallized. Two other processes for the extraction of catechins from *C. sinensis* leaves are conducted with or without enzymatic treatment with tannase. The initial extract is further extracted with water and ethanol, and then filtered through multiple media. The product of the process without tannase is sterilized above 100°C., whereas the product obtained with the tannase treatment is sterilized below 100°C.

The presence of minerals and elements in an extract depends on the extent of entrapment in the organic matrix, the degree of solubility/choice of solvent, the duration of extraction, temperature, pH, and agitation.[18] Most elements, especially the metals, are complexed with the flavonols, catechols, tannins, and polyphenols.

The oil may be directly expressed from the source (seed or pulp) followed by solvent extraction. *Bailey's Industrial Oil and Fat Products* states that the removal of pigments and polar materials is mandatory for most cosmetic applications.[35] The process used for refining oil used for foods may be adequate for this purpose, or additional steps may be required. Special refining methods to yield colorless and odorless oils are used by the cosmetic industry and include proprietary adsorption chromatography and supercritical fluid extractions.

Oils are produced either from mechanical extraction or solvent extraction, or a hybrid of both methods, known as prepress solvent extraction.[36] In solvent extraction, hexane is the most commonly used solvent, because it is economical and easily removed from the extracted oil. Seeds that are rich in oil can be cold pressed to extract oil without the use of solvents.[37]

After the initial extraction, the crude (degummed) oil is often refined.[36] The first step is treating the oil with caustic soda to neutralize free fatty acids, hydrolyze phosphatides, and remove some colored pigments and unsaponifiable materials. Soap stock is usually a by-product of this step. The next step involves treating the neutralized oil with activated earth to further adsorb pigments. The last major step in refining oil is deodorizing, usually by steam distillation, which is intended to remove all oxidative cleavage products that impart odor or flavor to the oil. Deodorization also removes tocopherols, sterols, and other minor free fatty acids and undesirable materials.

After deodorization, oils can be further processed by hydrogenation, which makes the oils more resistant to oxidative and thermal damage, and by winterization, in which the oil is slowly cooled to promote the formation of crystals that cause cloudiness, and then filtered to remove the crystals.

Cosmetic grade fatty acid plant oils may include a physical refining step that involves heating crude oil under a vacuum.[37] This step removes volatile components such as color compounds, odor compounds, and free fatty acids, which give the refined oil a lighter color, less odor, and lower acid values.

Impurities

No published data on impurities of these cosmetic ingredients were discovered and no unpublished data were submitted. The information below applies to impurities found in *C. sinensis* as a food or food ingredients.

Analysis of twelve *C. sinensis* catechins lots extracted as food ingredients showed that arsenic, cadmium, lead, and tin were below levels of detection.[30] Three lots of *C. sinensis* catechins were analyzed for other components: caffeine (≤7%), organic acids (≤10%), protein and amino acids (≤10%), saccharide (≤12%), fiber (≤1%), fat (≤1%), and ash (≤5%). No microbial contamination was detected.

Ten commercial *C. sinensis* teas for drinking were analyzed for metals.[38] The ranges for metal content were: zinc 1.05 – 3.21 mg/kg; iron, 5.47 - 8.41 mg/kg; manganese, 1.27 – 2.73 mg/kg; copper, 0.01 – 0.93 mg/kg; nickel, 0.01 – 0.64 mg/kg; lead, 0.26 – 1.25 mg/kg; and cadmium, 0.01 – 0.05 mg.kg. The authors concluded that the differences in the contents of the samples were attributable to differences in geographic region of cultivation.

Aflatoxigenic molds and aflatoxins have been reported to be present on *C. sinensis* teas for drinking.[39] In a sampling of 27 commercial black teas (7 branded, 20 nonbranded), aflatoxigenic molds were detected in one branded and 6 unbranded (25.9%) tea samples. Only one of the samples (nonbranded) had detectable aflatoxins (19.2 µg/kg). In black teas that had been spiked with aflatoxins, most of the aflatoxins residue was still present in the leaves after boiling in water, but only 30.6% was present in the final beverage.

It was reported that levels of 712 – 1530, 166 – 280, 1.7 – 7.5, and 1.51 – 2.63 µg/g for aluminum, iron, chromium, and lead, respectively, were found in commercial tea samples (n = 2) using electrothermal atomic absorption spectrometry (ETAAS) and inductively coupled plasma atomic emission spectrometry (ICP-AES; Table 6).[40] For two types of green tea, the ranges were 605 – 620, 1486 – 1550, 4.5 – 4.7, 2.20-2.34 µg/g, respectively. For infusions of these teas, the levels for aluminum, iron, copper, and zinc were 149 – 367, 7.6 – 11.0, 0.7 – 3.2, and 36 - 50 µg/g, respectively. For green tea infusions, these values were 124-127, 22 – 23, 0.2 – 0.5, 31-32 µg/g, respectively.

USE

Cosmetic

Data on ingredient usage are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP; Table 7).[41] A survey was conducted by the Personal Care Products Council (Council) of the maximum use concentrations for these ingredients.[42,43]

Data were available from both the VCRP and the Council for the following ingredients:

- Camellia sinensis leaf extract was reported to be used in 1011 leave-on, 710 rinse-off, and 35 bath cosmetic products.[41] There are reported uses in every exposure type (Table 7). Usage of cosmetic ingredients called "green tea" and "green tea extract" were also reported in the VCRP. Since these are technical names for camellia sinensis leaf extract, the VCRP numbers for these three listings were combined. Camellia sinensis leaf extract was reported to be use up to 2% in leave-on products (the highest concentrations in body and hand products) and up to 1% in rinse-off products (the highest concentration in bath soaps and detergents).[42] It is also reported to be used in products diluted in the bath at up to 0.1% (the highest concentration in bubble baths).
- Camellia sinensis leaf was reported to be used in 38 leave-on, 14 rinse-off, and 1 bath product.[41] Camellia sinensis leaf was reported to be used up to 0.05% in bubble baths.[42] A previously reported product of tea bags for the eyes at 97% is no longer sold.[42,44]
- Camellia sinensis leaf powder was reported to be used in 7 leave-on and 8 rinse-off products.[41] Camellia sinensis leaf powder was reported to be used up to 50% in leave-on products (the highest concentration in face and neck products) and up to 0.01% in rinse-off products (highest concentration in bath soaps and detergents).[42]
- Camellia sinensis leaf water was reported to be used in 26 leave-on and 11 rinse-off products.[41] Camellia sinensis leaf water was reported to be used up to 30% in mascara.[42]

Data were available only on the frequency of use (VCRP) for the following ingredient:

- Camellia sinensis leaf oil was reported to be used in 24 leave-on products and 9 rinse-off products.[41]

Data were available only on concentration of use for the following ingredient:

- Camellia sinensis seed extract was reported to be used in leave-on products up to 0.1% (highest concentration in moisturizing creams and lotions) and in rinse-off products up to 0.0013% (highest concentration in bath soaps and detergents).[42]

There were no frequency of use or concentration of use data reported for:

- Camellia sinensis catechins
- Camellia sinensis flower extract
- Camellia sinensis flower/leaf/stem juice
- Camellia sinensis root extract
- Camellia sinensis seedcoat powder
- Camellia sinensis seed powder
- Hydrolyzed camellia sinensis leaf
- Hydrolyzed camellia sinensis seed extract

Non-Cosmetic

Tea, under the previous name *Thea sinensis*, is generally regarded as safe (GRAS) by the FDA. (21 CFR 582.20)

In Europe, *C. sinensis* preparations are used to treat asthenia and as an adjuvant treatment in weight loss/control.[25]

Preparations are also used in cutaneous treatment of external genital and perianal warts (condylomata acuminata) in immune-compromised patients.[25,45]

In the United States, green tea products are used as dietary supplements (nutraceuticals), primarily for purported weight loss and antioxidant properties.[16,17,46-55] Other health benefits attributed to green tea include prevention and/or control of atherosclerosis, hypertension, coronary heart disease, diabetes, metabolic syndrome, obesity, and cancer as well as antibacterial, antiviral, antifungal, and neuroprotective effects.

Annual tea consumption varies from country to country, ranging from negligible to approximately 3 kg per person.[56] Worldwide average consumption is approximately 0.5 kg per person.

In 2012, over 79 billion servings of tea were consumed in the United States (over 3.60 billion gallons).[57] Of this, Americans consumed approximately 84% black tea, 15% green tea, and the rest oolong and white tea.

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Dermal/Percutaneous

CAMELLIA SINENSIS CATECHINS

When camellia sinensis leaf extract (0.32, 0.68, 1.03, 1.35 mg/cm in methanol; as green tea) was applied to full thickness pig ear skin using a Franz cell, there was a dose-dependent penetration of the catechins EGCG, EGC, and EC.[58] Saturated solutions of camellia sinensis were formulated using water, polyethylene glycol 400, citrate/phosphate buffer (pH 5.5), and a 50:50 mixture of polyethylene glycol 400 and the buffer. The solutions were applied to drug-in-adhesive patches under occlusion in methanol and applied to the pig skin. The receptor cell was sampled periodically for 48 h.

Penetration by the catechins was fastest in the buffer solution and slowest in PEG-400 solution. In the buffer solution, EGCG permeated the skin at 1.37 ± 0.40 and 1.88 ± 0.45 μg/cm^2 at 24 and 48 h, EGC permeated at 0.189 ± 4.10 x 10^2 and 0.342 ± 7.48 x 10^{-2} μg/cm^2, EC permeated at 32.4 ± 11.3 and 71.2 ± 35.2 μg/cm^2, respectively. In the mixed solution, EGCG permeated the skin at 1.27 ± 0.38 and 1.62 ± 0.18 μg/cm^2 at 24 and 48 h, EGC permeated at 0.128 ± 1.71 x 10^{-3} and 0.392 ± 0.004 μg/cm^2, EC permeated at 22.2 ± 17.3 and 40.2 ± 43.8 μg/cm^2, respectively. In PEG-400 solution, EGCG permeated the skin at 1.37 ± 0.40 and 1.88 ± 0.45 μg/cm^2 at 24 and 48 h, EGC permeated at 0.189 ± 4.10 x 10^2 and 0.342 ± 7.48 x 10^{-2} μg/cm^2, EC permeated at 32.4 ± 11.3 and 71.2 ± 35.2 μg/cm^2, respectively. In water, EGCG permeated the skin at 0.27 ± 0.15 and 0.66 ± 0.30 μg/cm^2 at 24 and 48 h, EGC permeated at 0.06 ± 0.02 and 0.10 ± 0.03 μg/cm^2, EC permeated at 1.32 ± 0.22 and 2.34 ± 0.34 μg/cm^2, respectively.

Caffeine in the buffer solution permeated at 0.32 ± 0.05 and 0.49 ± 0.01 μg/cm^2 at 24 and 48 h; 173 ± 24.6 and 368 ± 52.9 μg/cm^2 in the mixed solution; 46.8 ± 3.43 and 88.9 ± 0.08 μg/cm^2 in the PEG-400 solution; and 28.4 ± 2.46 and 50.2 ± 1.54 μg/cm^2 in water, respectively.[58]

When EGCG was dermally applied in a transdermal gel (50 mg/kg; 28.6 μg/cm^2) to female SKH-1 mice (n = 4, 5, or 6), EGCG was detected in the skin, plasma, liver, small intestines, and colon for at least 24 h.[59] The test material was administered once. Over the next 24 h, blood was collected under anesthesia and dorsal skin was removed, fractioned into epidermis and dermis, and analyzed. Liver, small intestine, and colon tissues were removed and analyzed.

In the total plasma, the C_{max} was 44.5 ± 8.4 ng/mL, the $t_{1/2}$ was 94.4 ± 13.2 h, and the $AUC_{0\rightarrow24}$ was 881.5 ± 123.4 ng/mL/h. The C_{max} for the epidermis and dermis were 1365.7 ± 613.8 ng/mL and 411.2 ± 21.5 ng/mL, respectively; the $AUC_{0\rightarrow24}$ was 5978.3 ± 2779.9 and 1729.5 ± 259.4 ng/g/h, respectively. The $t_{1/2}$ was 9.3 ± 4.3 and 10.9 ± 1.6 h, respectively.

The C_{max} of EGCG in the liver was 164.8 ± 83.0 ng/g with a $t_{1/2}$ of 74.6 ± 20.1 h and an $AUC_{0\rightarrow24}$ 2494.8 ± 673.6 ng/g/h. The C_{max} in the small intestine was 203.1 ± 64.0 ng/g with a $t_{1/2}$ of 26.8 ± 5.6 h and an $AUC_{0\rightarrow24}$ 2802.8 ± 588.5 ng/g/h. The C_{max} in the colon was 77.0 ± 22.4 ng/g with a $t_{1/2}$ of 21.3 ± 3.2 h and an $AUC_{0\rightarrow24}$ 715.0 ± 107.3 ng/g/h. The C_{max}, $t_{1/2}$, $AUC_{0\rightarrow24}$ for EGCG in the urine were 177 ng/mL, 3427.9 ng/mL/h, and 70.0 h, respectively.[59]

Inhalation

No published inhalation toxicokinetic data on these cosmetic ingredients were discovered and no unpublished data were submitted.

Antimicrobial Activity

CAMELLIA SINENSIS LEAF EXTRACT

The decaffeinated methanolic extract of the leaves of *C. sinensis* exhibited in vitro antimicrobial properties against 111 bacteria comprising 2 genera of Gram positive and 7 genera of Gram negative bacteria.[60] The extract was active in the range of 10 - 50 μg/ml. A few strains were sensitive at lower concentrations (5 μg/ml). In decreasing order of sensitivity, the bacterial groups were: *Staphylococcus aureus*, *Vibrio cholerae*, *Escherichia coli*, *Shigella* spp., *Salmonella* spp., *Bacillus* spp., *Klebsiella* spp. and *Pseudomonas aeruginosa*.

When the above extract (30, 60 μg/mouse) was intraperitoneally administered to a Swiss strain of white mice (n =

20; control = 60), the mice were protected from a challenge of a medium lethal dose injection of *S. typhimurium*.[60] In the control group, 48 mice died. In the low-dose group, 4 mice died and no mice died in the high-dose group.

Dermal Effects

CAMELLIA SINENSIS LEAF EXTRACT

There was reduced healing time and no adverse effects in burned rabbits (n = 5) administered an aqueous camellia sinensis leaf extract (100%; 0.05 mL) compared to controls.[61] The rabbits were burned with a heated glass rod applied to shaved skin, then the extract, antibiotic, or nothing was administered. The rabbits were observed for 5 weeks. The size of the wounds reduced faster with the extract and the antibiotic compared to controls. Closure time for the treatment groups was 8 – 10 days for antibiotics and 7 – 9 days for the extract. At five weeks, the wounds were almost healed in the treated groups (0.25 ± 0.02 cm^2) while the average size of the wound in the control group was 0.92 ± 0.15 cm^2. Hair growth also began sooner in both of the treated groups. Microscopic examination showed skin with a more normal appearance in the camellia sinensis leaf extract group compared to the antibiotic and controls groups.

Anti-Inflammatory Effects

CAMELLIA SINENSIS CATECHINS

When saponins (0, 50, 100, 200 mg/kg) extracted from *C. sinensis* leaf were orally administered to rats prior to a subcutaneous injection of carrageenan (1%; 0.5 mL) in a rat hind-paw edema assay, edema in response to carrageenan was mitigated in a dose-dependent manner.[62]

Cytotoxicity and Cellular Effects

CAMELLIA SINENSIS EXTRACT

Camellia sinensis extract (10, 50, 100 μg/mL) was not cytotoxic to rat pheochromocytoma (PC12) cells when exposed in vitro for 24 h.[33] However, at higher concentrations (250, 500, 100 μg/mL), the extract was cytotoxic with < 40% viability at the two highest concentrations. When the cells were incubated with the extract and hydrogen peroxide (250 μM), hydrogen peroxide poisoning was mitigated by the extract at 5, 100, and 250 μM.

Camellia sinensis water extract (as Korean green tea) had a 50% inhibitory dose (ID_{50}) of 2.05% (0.28 mg/mL dry matter) in the inhibition of protein synthesis in Sprague-Dawley rat hepatic cells.[63] The 25% effective dose (ED_{25}) for lactate dehydrogenase (LDH) release was 1.84% (0.25 mg/mL). Camellia sinensis extract (in the form of black tea) had an ID_{50} of 2.50% (0.46 mg/mL) for protein synthesis and an ED_{25} for LDH release of 5.11% (0.94 mg/mL).

CAMELLIA SINENSIS LEAF EXTRACT

In a 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl-tetrazolium bromide (MTT) test (n = 6), camellia sinensis leaf extract (0, 0.00013%, 0.0006%, 0.0032%, 0.016%, 0.08%, 0.4%, 2%, and 10%) was cytotoxic at 2% and 10% to human keratinocytes.[64] Morphological modifications of the cells were observed at 0.4%. The test substance was a cold extract of green tea using water/propylene glycol (10% dry plant material) prepared in the same manner as that used to prepare tea for drinking.

When human keratinocytes were incubated in camellia sinensis leaf extract (0.05% and 0.1%) there was a 43% protection against oxidation when the cells were exposed to UV radiation (312 nm; 160 mJ/cm^2; time not provided).[64]

CAMELLIA SINENSIS CATECHINS

EGCG induced apoptosis at 400 and 800 μmol/L in neonatal human dermal fibroblasts.[65] At 200 μmol/L EGCG, a decrease in the proportion of cells in the S and G_2/M phases of the cell cycle and an increase in the proportion of cells in the G_0/G_1 phase was observed. Regulation of the expression of pNF-κB was concentration dependent but EGCG did not affect NF-κB expression. cDNA microarray analysis revealed that EGCG (200 μmol/L) down-regulated cell cycle-related genes. A/B cyclins and cyclin-dependent kinase 1 was reversibly effected by EGCG (200 μmol/L).

TOXICOLOGICAL STUDIES

The *C. sinensis*-derived ingredients in this safety assessment are from consumable sources and exposure to these ingredients in beverages would result in much greater systemic doses than those from exposures from use of cosmetic products. Consequently, their oral toxicity potential is not addressed in this report. Though data are presented on the potential for reproductive toxicity, genotoxicity, and carcinogenicity, the focus in this report is primarily on the potential for irritation and sensitization.

Acute Toxicity

Oral – Non-Human

When camellia sinensis leaf extract (2 g/kg; 1.94 mL/kg) was orally administered to Sprague-Dawley (SPF) rats (n = 5/sex), it was concluded that the minimum lethal dose is > 2 g/kg.[66] The test substance was administered after 16 h on a hydric diet. After administration, the rats were observed for 6 h for clinical signs and then followed for 14 days. There were

no effects on weight gains and there were no mortalities. Necropsy was unremarkable. The test substance was a cold extract of green tea using water/propylene glycol (10% dry plant material) and prepared in the same manner as that used to prepare tea for drinking.

The above experiment was repeated with an extract of black tea (2 g) provided to the laboratory as a brown powder with the same conclusion.[67] Reduced motility and ptosis of the eyelids was observed in all rats 1 h after administration. Necropsies were unremarkable.

Dermal – Non-Human

CAMELLIA SINENSIS CATECHINS

The dermal LD_{50} of EGCG (2000 mg/kg extract; 1860 mg EGCG/kg; 4 mL/kg) was > 1860 mg/kg for HanBrl:WIST (SPF) rats (n = 5/sex).[34] The acute dermal toxicity test was conducted in accordance with the Organization for Economic Co-operation and Development (OECD) guideline number 402 under semi occlusion. The day before the study, the backs of the rats were clipped with an electric clipper exposing approximately 10% of the total body surface. The dressing covering the test site was removed at 24 h and flushed with lukewarm tap water and dried. The rats were observed twice daily for 15 days. Macroscopic examination of all animals was performed at day 15.

There were no signs of systemic toxicity in any of the rats. A slight to moderate erythema was observed in all treated rats after removal of the dressing, which persisted for up to 5 days. Body weights were within standard range for this strain and age of rat. No abnormal macroscopic findings were observed at necropsy.[34]

Repeated Dose Toxicity

Inhalation - Human

There were no adverse effects, such as respiratory tract obstruction, allergic bronchial spasm, or skin eruption, including laboratory changes observed when subjects suffering from cerebrovascular diseases (n = 36) inhaled catechins (3.7 mg/mL in saline; 2 mL; 43% of catechins composed of EGCG) or the vehicle (n = 33) three times/day for 7 days.[68] The test substance was delivered by a handheld nebulizer. The sputum of the subjects all tested positive for methicillin-resistant Staphylococcus aureus (MRSA). Total catechin content was 73.0% (31% (-)-EGCG, 21% (-)-EGC, 8.6% (-)-EC, 8.6% (-)-ECG, 2.9% (-)-GCG, and 0.8% (-)-CG.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

CAMELLIA SINENSIS LEAF EXTRACT

There were no adverse effects when pregnant Wistar rats (n = 6) were orally administered camellia sinensis extract (0, 84, 167, 501, and 1336 mg/mL/d; in the form of black tea).[69] The caffeine content was 4.14% (865 mg for the highest dose). The test material was administered either on gestation days 1 – 7, 8 – 14, or 15 – 21. Internal examinations of the dams were conducted by laparoscopy under anesthesia. Pups were examined daily. The test doses were calculated to be equivalent to 1.5, 3, 9, and 24 cups of tea. There were no mortalities. There were no differences in number of pregnancies, number of uterine implants, number of viable implants, implantation index, pre-implantation loss, post-implantation loss, gestation index, number of pups born, litter index, live birth index, and viability index compared to controls. There were no differences in length of the implants/fetus, gestation duration, cranial length, cranial diameter, and tail length of pups. There were no differences in time taken to open eyes, eruption of incisors and appearance of fur. There were no gross morphological birth abnormalities observed.

CAMELLIA SINENSIS CATECHINS

Unpublished studies were submitted to the FDA for the approval of a topical ointment as a drug that contains up to 15% camellia sinensis catechins to treat warts.[70] These studies are summarized in Table 8. In oral studies, there were increased resorptions at 1000 mg/kg/d in rats. In subcutaneous studies, the test substance was not well tolerated; subcutaneous lesions with necrosis developed. There were spontaneous abortions, increased resorptions, and increased fetal malformations at doses as low as 12 mg/kg/d. Intravaginal administrations up to 0.15 ml/d yielded fewer adverse effects.

When camellia sinensis catechins (1400, 4200, 14000 ppm in feed; EGCG 90%, ECG ≤3.01%, GCG ≤0.12%, other catechins ≤0.54%) were administered to pregnant Wistar (SPF) rats (n = 25) on gestation days 6 - 20, there were no adverse effects observed.[71] All rats survived treatment and there were no clinical signs. There was a transient reduction in feed consumption in the high-dose group and an increase in water consumption in the mid- and high-dose groups. There were no treatment-related macroscopic findings in the dams. There was no effect to embryo/fetal survival, fetal weights, or sex ratios.

In a two generation study of camellia sinensis catechins (1200, 3600, 12000 ppm in feed) using Sprague-Dawley rats (n = 30/sex), there were no adverse effects in either generation. The rats were treated for 10 weeks and then paired for mating. The diet continued through gestation until after weaning. The dams were killed and necropsied after weaning. The pups were culled to 25/sex and the above treatment repeated with mating taking place after 8 weeks.

The offspring of the high-dose group had reduced growth rates, and there was an increase in pup loss. A growth effect among pups was also observed at 3600 ppm, but only in the second generation. Both sexes of the F_1 generation in the high-dose group showed reduced absolute kidney and liver weights. The F_1 males had reduced spleen and prostate weights,

but the females' spleens were normal. Histological examination revealed no abnormalities. The lowest dose was considered the overall NOAEL. The authors derived a NOAEL of 200 mg/kg body weight per day EGCG preparation. Because dams consumed twice the amount of feed during the crucial lactation period, during which effects occurred, twice the lowest dose (i.e., 2 x 100 mg/kg/d) was estimated to be the NOAEL.[71]

GENOTOXICITY

In Vitro

CAMELLIA SINENSIS CATECHINS

Catechins were not mutagenic in multiple in vitro and in vivo assays including Ames tests (up to 5000 µg/plate), mouse micronucleus assays (up to 2000 mg/kg), and micronucleus assays. A polyphenol mixture was lethal at 2000 mg/kg/d to mice. Mixed results were reported in a mouse lymphoma assay at concentrations > 100 µg/mL (Table 9).[70,72-74]

CARCINOGENICITY

CAMELLIA SINENSIS LEAF EXTRACT

In 1997, the International Agency of Research in Cancer (IARC) listed green tea in group 3, meaning that it is not classifiable according to its carcinogenicity to humans.[56]

Camellia sinensis extract (125, 250, 500 mg/kg/d; as green tea; 85% - 95% catechins w/w, 55% EGCG) did not increase the incidence of neoplastic or non-neoplastic lesions in the organs and tissues of p53 transgenic heterozygous mice (n = 25).[70] The mice were treated daily for 26 weeks. p-Cresidine and water served as controls.

Anti-Carcinogenicty

The catechins in *C. sinensis*, especially EGCG, have been shown to have preventive and treatment effects in cancer cell lines related to cancers of the prostate, lung, skin, pancreas, breast, and ovaries.[17]

In a population-based case-control study of residents of southern Arizona (n = 404, males = 238, females = 166; mean age 66.6 ± 10), subjects who consumed black tea within the last year had fewer instances of squamous cell carcinoma (SCC) of the skin (odds ratio 0.60) than controls, residents of Tucson, (n = 391, males = 226, females = 165; average age 66.2 ± 11.1 y).[75] Arizona was chosen because it has one of the highest risks of skin SCC worldwide. Variables were controlled for tanning ability, antioxidant intake, education, gender, smoking, and average sun exposure.

When female SKH-l mice (n = 28, 29) were orally administered *C. sinensis* as lyophilized green tea (0.3%, 0.9%; 3, 9 mg of tea solids/mL) in place of drinking water and exposed to UVB (30 mJ/cm^2) twice per week for 35 weeks, there was a decrease in the number of tumors per mouse by 35% and 94%, respectively, compared to controls exposed to UVB without *C. sinensis* treatment.[76] The tumor volume per mouse was decreased by 49% and 97%, respectively. The composition of the green tea polyphenol fraction was: (-)-epigallocatechin gallate (49.5%), (-)-epigallocatechin (11.5%), (-)-epicatechin gallate (11.4%), caffeine (7.6%), (-)-epicatechin (6.1%), (+)-catechin (0.5%), and gallic acid (0.4%).

When female SKH-1 mice (n = 29) were orally administered *C. sinensis* (as green tea for their drinking water; 1.25 g steeped in100 mL hot water; ~4 mg tea solids/mL) UVB-induced complete carcinogenesis was inhibited. This was not the case with decaffeinated green tea. The *C. sinensis* extract was administered for 2 weeks before and concurrently with twice per week treatment with enhanced UVB (280-320 nm; 75% - 80% total energy; 30 mJ/cm^2 for 25 – 30 s) exposure. There were increases in apoptosis in the epidermis observed, but no effect in non-UVB treated normal epidermis. The authors concluded that administration of green tea and caffeine may inhibit UVB-induced carcinogenesis, at least in part, by enhancing UVB-induced apoptosis.

Oral administration of *C. sinensis* (1.25% as green or black tea leaf extract; 1.25 g of tea leaf steeped in100 mL water; 4.0 or 4.4 mg tea solids/ml) as the drinking water to the UVB-treated mice decreased the number of tumors per mouse by 51% and 41%, respectively. Tumor volume/mouse was decreased by 79% and 70%, respectively. The mice were treated with gradually increasing doses of the test substances for 2 weeks before the start of the twice/week treatment with UVB for 40 weeks. The mice were killed 4 weeks after the end of the UVB administration. Decaffeinated green or black *C. sinensis* leaf extracts (1.25%) containing 3.6 or 3.9 mg of tea solids/mL, respectively, were less effective than regular green or black tea extracts, and decaffeinated black tea was less effective than decaffeinated green tea at inhibiting the formation of skin tumors. Adding 0.36 mg of caffeine/mL to the decaffeinated extracts either fully or partially restored the inhibitory effects on UVB-induced tumorigenesis.[76]

IRRITATION AND SENSITIZATION

Irritation

Dermal – Non-Human

CAMELLIA SINENSIS LEAF EXTRACT

When camellia sinensis leaf extract (100%; 0.5 mL) was dermally administered to the clipped skin of albino New Zealand rabbits (n = 3), there were no signs of irritation.[77] The test substance was a cold extract of green tea using water/propylene glycol (10% dry plant material) and prepared in the same manner as that used to prepare tea for drinking. It

was provided to the laboratory as a brown liquid. The test substance was applied to a 2.5-cm^2 gauze pad, which was then kept in contact with the skin for 24 h using hypoallergenic adhesive tape. The test site was examined within 1 h of removal and at 24 and 72 h after removal.

The above experiment was repeated with an extract of black tea (0.5 g), provided to the laboratory as a brown powder, with a conclusion that the test substance was a slight irritant.[78] A slight to definite erythema was observed on all treated rabbits. Cutaneous dryness and a slight decrease in skin suppleness were observed. The test sites were observed at 1, 25, and 72 h after removing the pad.

CAMELLIA SINENSIS CATECHINS

There were no signs of irritation when EGCG (0.47 g in 3 ml distilled water) was administered to the clipped flanks of male New Zealand White rabbits (n = 3) for 4 h under semi-occluded patch.[34] The tests were conducted according to the EC Commission Directive 92/69/EEC, B.4, ''Acute Toxicity—Skin Irritation'' and OECD guideline number 404 (1992). The dorsal fur of three male rabbits was removed with electric clippers 24 h before the administration of the test material. Each rabbit was treated with 0.5 g of EGCG preparation (93.4% EGCG) dissolved in 0.3 ml distilled water and applied to the skin of one flank using a semi-occlusive patch. After removing the patch, the skin was cleaned with water. Skin reactions and irritation effects were assessed at approximately 1, 24, 48 and 72 h after patch removal. Adjacent areas of untreated skin from each animal served as controls. There were no signs of toxicity observed.

In a preliminary study for a guinea pig maximization test, an intradermal injection of 0.09% EGCG was found to be the greatest tolerable dose.[34] A grade 3 erythema was produced, but not necrosis. At 48 h of dermal exposure, there was no reaction in the preliminary test at concentrations up to 50%.

Dermal – Human

CAMELLIA SINENSIS LEAF WATER

In a patch test (n = 10) of a mascara containing camellia sinensis leaf water (30%), there were no signs of irritation at 30 min, and 24 and 48 h after the removing the patch.[79] The test substance was administered to the inner side of the upper arm for 24 h.

In a trial of an ointment containing camellia sinensis catechins (10% and 15%) for the treatment of anogenital warts, there was no irritation or other adverse effects, reported.[80] The ointment was administered three times per day for up to 16 weeks. No adverse effects were reported during treatment, or during the 12-week follow-up, and the ointment was reported to be well tolerated.

When *C. sinensis* preparations (DER ranging from 1/1000 - ≥1/10; 0.1% - >10%) were used in dermal applications, the following were among the adverse effects: erythema, pruritus, irritation/burning, pain, ulcer, edema, induration, and vesicles.[25] A full list of reported effects is provided in Table 10.

Mucosal

CAMELLIA SINENSIS CATECHINS

Intravaginal administration of an ointment containing camellia sinensis catechins (15%) to pregnant SD rats (n = 25) from gestation day 6 to the end of lactation caused ulceration and erosion of the vaginal mucosa with inflammation for the duration of treatment.[70] The control group (no catechins) did not exhibit damage to the vaginal mucosa. The effects resolved when treatment stopped.

Ocular

CAMELLIA SINENSIS LEAF EXTRACT

Camellia sinensis leaf extract (100%; 0.1 mL) administered to the lower conjuctival sac of the right eye of albino New Zealand rabbits (n = 3) was a slight ocular irritant.[81] There was slight irritation of the conjuctiva at 1 h; there were no iris lesions. Two rabbits had a very slight superficial epithelial attack of the cornea. All signs of irritation were resolved within 24 h. The test substance was a cold extract of green tea using water/propylene glycol (10% dry plant material) and prepared in the same manner as that used to prepare tea for drinking. It was provided to the laboratory as a brown liquid. The eyes were examined 1 h after instillation and 1, 2, and 3 days later.

The above experiment was repeated with an extract of black tea (0.1 g), provided to the laboratory as a brown powder, with the same conclusion.[82] There was a slight irritation of the conjuctiva observed at 1h; there were no lesions of the iris. All rabbits had a slight epithelial attack of the cornea. All signs of irritation were resolved within 48 h.

CAMELLIA SINENSIS CATECHINS

The administration of EGCG preparation (0.093 g EGCG; 0.1 g total) into the eye of a single female New Zealand White rabbit resulted in moderate to severe irritation including reddened conjunctivae and sclera, discharge and chemosis.[34] A slight to moderate corneal opacity affecting the whole area of the cornea was observed up to 72 h after administration of the test material. No damage to the iris, and no corrosion or staining of the eye by EGCG was observed throughout this study. The test was done in compliance with OECD guideline number 405. Both eyes of the rabbits were examined at the

beginning of the study. The lids were briefly held together after administration; the eyes were not rinsed. The animal was observed for ocular irritancy for 17 days. Because EGCG was suspected to be an ocular irritant, a single animal was treated first and observed to recovery. Based on the results from this preliminary study, no additional rabbits were tested.

Sensitization

Dermal – Non-Human

CAMELLIA SINENSIS CATECHINS

In a sensitization assay using female GOHI (SPF) guinea pigs (n = 6), camellia sinensis catechins (5%, 10%, 30% in ethanol; 100 µL/8 cm^2; 4%, 8%, 24% EGCG) was sensitizing at challenge (1%, 3%, 5%, and 10%) as well as at a second challenge (0.1%, 0.5%, 1%, 3%, 5% and 10%) two weeks later.[34] The skin sensitization assay was performed using a procedure adopted from OECD guideline number 406 (OECD, 1992b). During the induction phase of the assay, an EGCG preparation (80% EGCG) was applied to the shaved right flanks of the guinea pigs 5 days/week for 4 weeks. Control animals were treated with ethanol. Treatment sites were left open between applications. During induction, new treatment sites were chosen whenever the irritation became considerable. Immediately following the induction period, the guinea pigs were challenged with EGCG (25 µL/2 cm^2 on the left flank). During the induction period the guinea pigs were observed for signs of erythema and edema on each test site. Challenge reactions were assessed at 24 and 48 h after application.

Irritation responses increased throughout the induction period starting with the fifth application; the 30% group had the greatest frequency of reactions. Erythema became evident in the 10% and 5% groups after the 13th and 16th administrations, respectively. In the 10% group, a slight erythema was observed in 2/6 guinea pigs after the 13th application, with all guinea pigs showing similar signs by the 16th application. For the 5% group, erythema was observed only for 3 days in 1/6 guinea pigs. Both EGCG preparation elicited positive effects in the test groups during the challenges.

Control animals showed no response after the first challenge; one or two of the six control guinea pigs had slight or well defined erythema after the second challenge with 0.8% or higher EGCG. Although there was a positive dose–response effect for the challenge, it did not clearly correlate to the induction doses. There were a greater number of reactions in the 5% induction group (6 at 24h, 5 at 48 h) than in the 30% induction group (2 at 24 h, 1 at 48 h). No mortalities or symptoms of systemic toxicity were observed in any of the guinea pigs, and body weights of the test animals were in the same range as those of the controls during the study period.[34]

In a maximization test using female Himalayan strain albino guinea pigs (n = 10; control n = 5), camellia sinensis catechins (0.1% in distilled water; 0.1 ml; 90% EGCG) was a sensitizer.[34] All guinea pigs had grade 3 or 4 erythema following challenge by intradermal injection of the test material and/or Freund's Complete Adjuvant. Grade 1 erythema was observed following the first test challenge in 3/10 in the test group and 0/5 in the control group. In a second challenge 1 week later, 9/10 in the test group showed stronger (grade 2) erythema. No mortalities or signs of systemic toxicity were observed in any of the guinea pigs and body weights of the test group were in the same range as those of the controls during the study period.

Dermal – Human

CAMELLIA SINENSIS LEAF EXTRACT

A facial line filler treatment product containing camellia sinensis leaf extract (0.86%; 150 µL) was not irritating or sensitizing in an HRIPT (n = 101).[83] The test substance was administered nine times on a 2 x 2 cm absorbent pad under occlusion. No reactions were observed in any of the 106 to complete the induction phase. No reactions were observed in any of the 101 to complete the challenge phase.

An eye cream containing camellia sinensis leaf extract (0.86%) was not irritating or sensitizing in an HRIPT (n = 638). The test substance was administered under occlusion.[84]

CAMELLIA SINENSIS LEAF WATER

In an HRIPT (n = 110) of a mascara containing camellia sinensis leaf water (30%), there were no signs of irritation or sensitization.[85]

Phototoxicity

CAMELLIA SINENSIS LEAF EXTRACT

There were no signs of erythema on treated sites on the forearms of subjects (n = 6) treated with camellia sinensis leaf extracts (10%; in the form of green or black tea) then exposed to UVA, B, and C.[86] Freeze-dried green and black tea extracts were used to make gels with 1% carbomer solution and sodium hydroxide. These were administered to a 4 cm^2 area. The controls were an untreated area and an area treated with just the gel. The arms were then exposed to UVA/UVB/UVC (UVA 4550 µW/cm^2; UVB = 2800 µW/cm^2; UVC = 500 µW/cm^2) for 2.5 min. Erythema was observed in the control and carbomer treated sites but not the treatment sites.

Photo Effects

CAMELLIA SINENSIS LEAF EXTRACT

A sunscreen containing various concentrations of camellia sinensis leaf extract (0, 2%, 3%, 4%, 5%; in the form of green tea) protected against photoaging and photoimmunology-related biological measurements in female human subjects (n = 20); especially at 3%.[32] The melanoma index decreased in a dose-dependent manner until 4%; effectiveness decreased at 4% and 5%. The same pattern was observed for the thickness of the stratum cornium and total epidermis measurements. Cytokeratins CK5/6, CK16 were overexpressed on the site irradiated with or without the base cream; the reduced effect followed the same pattern as the other markers. Matrix metalloproteinases MMP-2 and MMP-9 were slightly to moderately expressed on unirradiated skin. Expression of MMP-2 and MMP-9 was decreased on the 2%, 3%, and 4% sites.

The sunscreen was applied 30 min before each irradiation at 1.5 x each individual's minimal erythemal dose (MED) and 6, 24, and 48 h after the last irradiation. The subjects' backs were irradiated on four consecutive days (duration of treatment was not provided). The MED of the subjects ranged from 25 to 40 mJ/cm^2, with an average of 32.46mJ/cm^2. Punch biopsies were obtained from all the seven sites 72 h after the last UVR exposure and analyzed. Standardized photographs were taken with a digital camera before each procedure and at the follow-up examinations.[32]

CAMELLIA SINENSIS CATECHINS

Topical treatment with green tea polyphenols (3 mg/2.5 cm^2 in acetone) on human skin reduced the UVB induction of cyclobutane pyrimidine dimer formation and erythema in a dose-dependent manner.[87] The polyphenols consisted of EC at 6%, EGC at 5%, EGCG at 65%, and ECG at 24%. Green tea polyphenols were administered to the buttocks of Caucasian subjects (n = 6) 20 min before the skin was exposed to 0.5%, 1.0%, 2.0%, or 4.0% of the previously established minimal erythema dose. The test sites were examined and skin punch biopsies taken 24 h after UVB treatment. Cyclobutane pyrimidine dimers and erythema were reduced in the treated sites exposed to 1.0%, 2.0, and 4.0% of a minimal erythema dose of UVB in a dose-dependent manner.

Metalloproteinase activity in cultured fibroblasts and keratinocytes decreased when incubated in EGCG (0.01, 0.1 µM in propylene glycol:ethanol 3:7) for 24 h before exposure to UVA radiation.[88] This indicated possible protection of the cells by EGCG from oxidative stress from UVA exposure. An artificial skin was prepared using human keratinocytes and dermal fibroblasts on a lattice of bovine type I collagen. The skin was incubated in EGCG for 24 h and washed. The skin was exposed to UVA (340 – 400 nm; 20 J/cm^2; duration not provided) 6 h later. Supernatant was collected 24 h after irradiation and analyzed.

The dermal administration of either EGCG (1 mg/cm^2 in a hydrophilic ointment ; >98% pure) or green tea catechins (0.2% in a hydrophilic ointment ; > 86% catechins) to female SKH-1 hairless mice (n = not provided) prevented single and multiple UV (180 mJ/cm^2) exposure-induced depletion of catalase activity and prevented the depletion of antioxidant enzymes (e.g., glutathione peroxidase, catalase, and glutathione).[89] Treatment also inhibited UVB-induced oxidative stress when measured in terms of lipid peroxidation and protein oxidation. The test substances were administered to the backs of the mice either once or daily for 10 consecutive days prior to UVB (290 – 320 nm) and UVA exposure. The mice were killed 24 h after the last UV exposure and the skin was biopsied. The green tea catechins were composed of: EC, 10.4%; EGC, 8.3%; EGCG, 55.8%; GCG, 4.4%; and ECG, 6.9%.

Female SKH-1 hairless mice were administered green tea catechins (0.2% in drinking water) for 10 days before and during UV exposure as described above. Treatment with green tea catechins prevented single or multiple UVB irradiation-induced depletion of antioxidant enzymes, oxidative stress, and phosphorylation of proteins. However, the photoprotective efficacy was less than that of topical treatments of EGCG and green tea catechins. The authors stated that this may be due to less bioavailability in skin target cells.[89]

Green tea catechins at 70 and 140 mg/L were reported to protect human retinal pigment epithelial (RPE) cells, in vitro, from the cytotoxic effects of UVB radiation.[90] The protective effect observed at these concentrations was suggested to be the result of the attenuation of the UVB-induced suppression of survivin gene expression and resultant suppression of mitochondrion-mediated apoptosis. However, 700 and 1400 mg/L appeared to have a toxic rather than protective effect on the UVB-irradiated cells. RPE cells were treated with green tea catechins for 2 h before or after exposure to UVB (100 µw/cm2) for 2 h. Viability of UVB-irradiated RPE cells decreased by 49.2% compared with unirradiated controls. The protective effects of catechin pretreatment were more effective than post-treatment. Viability of RPE cells was assessed by 3,(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) assay. Survivin gene expression was examined by real-time PCR analysis. Ultrastructure of RPE cells was examined by transmission electron microscopy. The composition of the catechins was: GC, 44.38; EGC, 85.47; C 14.09; EGCG, 344.73; GCG, 42.49; ECG 103.37; CG 8.80 mg/g.

CLINICAL USE

Case Studies

A 51-year-old man was diagnosed with hypersensitivity pneumonitis (HP) after undergoing catechin inhalation therapy for 1 month.[91] The diagnosis was based on the clinical course, bronchoscopy, and a challenge test. The subject was being treated for tuberculosis and had been administered the catechin inhalation therapy when MRSA was observed in his sputum. He was administered catechin-rich green tea extract solution (2 mL) dissolved in distilled water (50 mg/ml) once or

twice daily using a handheld nebulizer. There were no initial symptoms, but the subject later noticed that he coughed frequently during and after inhalation of the extract.

OTHER REVIEWS

In a safety assessment of *C. sinensis* as green tea used in dietary supplement products, the U.S. Pharmacopeia Dietary Supplement Information Expert Committee concluded that when supplements containing concentrated green tea extracts are used and formulated appropriately, there are no significant safety issues with the caveat that a caution statement be included in the labeling section.[92] The caution statement warns of the potential of liver damage when concentrated green tea supplements are consumed on an empty stomach. This does not apply to *C. sinensis* as a beverage.

There are several reviews regarding the protective effects of green tea extracts and its catechins, especially EGCG, against chemical carcinogens.[48,93-96]

According to Yang *et al*.[94], there are more than 133 studies published from 1991 to 2008 on this topic (Table 11). Inhibitory effects of tea and/or tea constituents on lung, oral, stomach, intestine, dermal, prostrate, breast, liver, bladder, pancreas, and thyroid cancers were found.

SUMMARY

This is a safety assessment of *Camellia sinensis* (tea)-derived cosmetic ingredients. These ingredients function mostly as antioxidants and skin-conditioning agents – miscellaneous. Because tea is ingested in food and drink, this safety assessment does not address systemic toxicity but is primarily focused on the potential for irritation and sensitization.

The constituents of *C. sinensis* include amino acids, carotenoids, catechins, enzymes, flavonoids (including flavanols and flavonols), and glycosides. The concentrations of these constituents in plant parts is influenced by growing conditions, geographical location, soil conditions, and processing.

Camellia sinensis leaf extract was reported to be used in 1011 leave-on, 710 rinse-off, and 35 bath cosmetic products; it was used up to 3% in leave-on products, 1% in rinse-off products, and up to 0.1% in bath products. Camellia sinensis leaf was reported to be used in 38 leave-on, 14 rinse-off, and 1 bath product; it was used up 0.05% in bubble baths. Camellia sinensis leaf powder was reported to be used in 7 leave-on and 8 rinse-off products; it was used up to 50% in leave-on products and up to 0.01% in rinse-off products. Camellia sinensis leaf water was reported to be used in 26 leave-on and 11 rinse-off products; it was used up to 30% in mascara. Camellia sinensis leaf oil was reported to be used in 24 leave-on products and 9 rinse-off products. Camellia sinensis seed extract was reported to be used in leave-on products up to 0.1% and in rinse-off products up to 0.0013%.

The FDA considers *C. sinensis* to be GRAS for use as a food additive.

Catechins from camellia sinensis leaf extract penetrated pig ear skin as did caffeine. EGCG penetrated mouse skin.

Camellia sinensis leaf extract exhibited antimicrobial properties towards multiple bacterial species and wound-healing properties.

Camellia sinensis extract was not cytotoxic to rat pheochromocytoma cells up to 100 µg/mL but induced apoptosis to neonatal human dermal fibroblasts at 400 and 800 µmol/L.

The oral LD_{50} for rats was > 2 g/kg for camellia sinensis leaf extract as both green and black tea. The dermal LD_{50} of EGCG was > 1860 mg/kg for rats. There was slight to moderate erythema observed.

Reproduction and developmental studies of an ointment that contained up to 15% camellia sinensis catechins were conducted. In oral studies, there were increased resorptions at 1000 mg/k/d in rats. In subcutaneous studies, the test substance was not well tolerated; subcutaneous lesions with necrosis developed. There were spontaneous abortions, increased resorptions, and increased fetal malformation as low as 12 mg/kg/d. Intravaginal administration up to 0.15 mL/d had fewer adverse effects.

Camellia sinensis extract had no adverse effects when orally administered to pregnant rats up to 1336 mg/mL/d in drinking water. In a two-generation study, camellia sinensis catechins up to 12000 ppm in feed caused no clinical signs and no effects to embryo/fetal survival, fetal weights, or sex ratios. The offspring of the high-dose group had reduced growth rates, and there was an increase in pup loss. While there were some reduced organ weights, histological examination revealed no abnormalities. The NOAEL was 200 mg/kg/d EGCG.

Catechins were not mutagenic in multiple in vitro and in vivo assays including Ames test (up to 5000 µg/plate), mouse micronucleus assays (up to 2000 mg/kg), and micronucleus assays. A polyphenol mixture was lethal at 2000 mg/kg/d to mice. Mixed results were reported in a mouse lymphoma assay at concentrations > 100 µg/mL.

Camellia sinensis extract at 500 mg/kg/d was not carcinogenic to pS3 mice after 26 weeks.

Camellia sinensis leaf extracts, that contained 10% dry green or black tea, were not dermally irritating to rabbits. Camellia sinensis leaf extract at 100% caused no adverse effect to the skin of burned rabbits. Camellia sinensis catechins were not irritating to rabbits with intact skin at 0.47 g.

There were no adverse effects in a patch test of mascara containing camellia sinensis leaf water at 30%. There were no adverse effects in a trial of an ointment containing camellia sinensis catechins at 10% and 15%.

C. sinensis preparations with > 10% plant material caused erythema, pruritus, irritation/burning, pain, ulcer, edema, induration, and vesicles in dermal tests.

The intravaginal administration of an ointment containing camellia sinensis catechins at 15% caused ulceration and erosion of the vaginal mucosa with inflammation for four weeks.

Camellia sinensis leaf extracts from green or black tea were slight ocular irritants. The administration of a preparation containing 0.093% EGCG into the eye of a single rabbit resulted in moderate to severe irritation including reddened conjunctivae and sclera, discharge and chemosis.

Camellia sinensis catechins were sensitizing to guinea pigs at 5%. In another guinea pig test, camellia sinensis catechins was a sensitizer at 0.1%.

Camellia sinensis leaf extract was not irritating or sensitizing in two HIRPTs conducted on two cosmetic products that contain this ingredient at 0.86%. In an HRIPT of a mascara product containing camellia sinensis leaf water at 30%, there were no signs of irritation or sensitization

There was no sign of erythema at treatment sites on the forearms of subjects treated with 10% camellia sinensis leaf extract in the form of green or black tea then exposed to UVA and B. Topical treatment with green tea polyphenols at 3 mg/2.5 cm^2 to human skin reduced the UVB induction of cyclobutane pyrimidine dimer formation and erythema in a dose-dependent manner. Metalloproteinase activity in cultured fibroblasts and keratinocytes decreased when incubated in EGCG at 0.01 and 0.1 μM for 24 h before exposure to UVA radiation. Multiple in vitro and in vivo studies demonstrated UV-protective effects of camellia sinensis catechins.

DISCUSSION

The Discussion will be edited and further developed at the March, 2014 Panel meeting.

Tea, under the previous name *Thea sinensis*, is a GRAS substance. The *C. sinensis*-derived ingredients in this safety assessment are from consumable sources and exposure to these ingredients in beverages would result in much greater systemic doses than exposures from use of cosmetic products. Consequently, their oral toxicity potential is not addressed in this report. Though data are presented on the potential for reproductive toxicity, genotoxicity, and carcinogenicity, the focus of the Panel was primarily on the potential for irritation and sensitization.

Linalool and several compounds containing linalool have been reported in the leaves ranging from 6 to 1984 ppm and in the leaf essential oil ranging from 31800 to 198 400 ppm in *C. sinensis* plants. Linalool is a dermal sensitizer that has been found to be safe up to 4.3%. Also, quercetin and several compounds containing quercetin have been reported in the leaf, plant, and shoot ranging from 760 to 10000 ppm. A positive genotoxic effect in an Ames assay has been reported and genotoxicity in in vitro tests and in some in vivo studies of i.p. exposures, but results were consistently nongenotoxic in oral exposure studies using mice and rats.

The Panel has noted that linalool and quercetin are found in *C. sinensis* leaves and essential oil and acknowledges that, depending on growing conditions and methods of manufacture, these constituents may or may not be found in the cosmetic ingredients. The Panel further noted that the use of other botanical ingredients that may contain linalool and quercetin in combination with *C. sinensis*-derived ingredients in a single formulation, or in formulations that are used at the same time or in close time proximity, could result in exposures that exceed levels of toxicological concern. Thus, cosmetic products containing one or more botanical ingredient(s) should be formulated to ensure concentrations of linalool and quercetin do not exceed the limit set by the Panel, and that total exposures to such constituents remain below the levels of toxicological concern, whether these products typically are used simultaneously or sequentially.

The Panel recognized that every extract would likely be somewhat different and that the characterization of the composition of the plant-derived ingredients addressed in this safety assessment is broad. Nonetheless, the available composition data represent what would be found commonly in ingredients prepared in the manner described. The Panel assumes that the manufacturing process is the same for oral consumption and cosmetics. The conclusion regarding safety, therefore, is valid only for ingredients prepared in a manner that produces a chemical profile similar to that described in this report. Extracts not prepared in a manner that produces similar chemical profiles, could be considered safe only if they have similar safety test profiles.

The Panel expressed concern about pesticide residues and heavy metals that may be present in botanical ingredients.

Aflatoxins have been detected in dried C. sinensis leaves for drinking. The Panel believes that aflatoxins will not be present at levels of toxicological concern in C. sinensis-derived ingredients. The Panel recognizes the USDA designation of ≤ 15 ppb as corresponding to “negative” aflatoxin content. They stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

These ingredients are photoabsorbers. However, there were several studies showing photoprotective, not phototoxic effects. Therefore, the Panel is not concerned that phototoxicity is a problem.

CONCLUSION

The Conclusion will be developed at the March, 2014 CIR Expert Panel meeting.

TABLES AND FIGURES

Table 1. Definitions and functions of *Camellia s.*-derived ingredients in this report.[97]

Ingredient CAS No.	Definition	Function
Camellia Sinensis Leaf Extract 84650-60-2	The extract of the leaves of *Camellia sinensis.*	Antifungal agent; antimicrobial agent; antioxidant; cosmetic astringent; fragrance ingredient; light stabilizer; oral care agent; skin protectant; skin-conditioning agent – emollient; skin-conditioning agent – humectant; skin-conditioning agent - miscellaneous
Camellia Sinensis Catechins	A mixture of catechins obtained from the leaves of *Camellia sinensis.*	Antioxidants
Camellia Sinensis Flower Extract	The extract of the flowers of *Camellia sinensis.*	Skin-conditioning agents – miscellaneous
Camellia Sinensis Flower/Leaf/Stem Juice 1196791-49-7	The juice expressed from the flowers, leaves and stems of *Camellia sinensis.*	Antioxidant
Camellia Sinensis Leaf	The leaf of *Camellia sinensis.*	Skin-conditioning agent – miscellaneous
Camellia Sinensis Leaf Oil 68916-73-4	The oil derived from the leaves of *Camellia sinensis.*	Antioxidant; skin-conditioning agent - miscellaneous
Camellia Sinensis Leaf Powder	A powder derived from the dried, ground leaves of *Camellia sinensis.*	Exfoliant
Camellia Sinensis Leaf Water	An aqueous solution of the steam distillate obtained from the leaves of *Camellia sinensis.*	Fragrance ingredient
Camellia Sinensis Root Extract	The extract of the roots of *Camellia sinensis.*	Skin-conditioning agent – miscellaneous
Camellia Sinensis Seedcoat Powder	The powder obtained from the dried, ground seedcoats of *Camellia sinensis.*	Skin conditioning agent – miscellaneous
Camellia Sinensis Seed Extract	The extract of the seeds of *Camellia sinensis.*	Skin-conditioning agent – humectant
Camellia Sinensis Seed Powder	The powder obtained from the dried, ground seeds of *Camellia sinensis.*	Antioxidant; skin-conditioning agent – miscellaneous
Hydrolyzed Camellia Sinensis Leaf	The hydrolysate of Camellia Sinensis Leaf (q.v.) derived by acid, enzyme or other method of hydrolysis.	Skin-conditioning agent – humectant
Hydrolyzed Camellia Sinensis Seed Extract	The hydrolysate of Camellia Sinensis Seed Extract derived by acid, enzyme or other method of hydrolysis.	Antioxidant; skin protectant; skin-conditioning agent - miscellaneous

Table 2. Constituent groups of fresh green *C. sinensis* leaf.[3]

Constituent	% of dry weight
Flavonols	25.0
Flavonols and flavonol glycosides	3.0
Polyphenolic acids and depsides	5.0
Other polyphenols	3.0
Caffeine	3.0
Theobromine	0.2
Amino acids	4.0
Organic acids	0.5
Monosaccharides	4.0
Polysaccharides	13.0
Cellulose	7.0
Protein	15.0
Lignin	6.0
Lipids	3.0
Chlorophyll and other pigments	0.5
Ash	5.0
Volatiles	0.1

Table 3. Constituents of concern in *C. sinensis*.

Constituent	Effects	Reference
Linalool	Dermal sensitizer. Safe at up to 4.3% (20% in a consumer fragrance)	[98]
Quercetin	Positive genotoxic effect in an Ames assay	[99]
	Consistently genotoxic in in vitro tests and in some in vivo studies of i.p. exposures, but was consistently nongenotoxic in oral exposure studies using mice and rats.	[100]

Table 4. Constituent groups in medical grade *Camellia sinensis* leaf extract.[15,25-29]

Constituent group	Constituent	Concentration (%)
Methylxanthines	Caffeine	2.5-4.2
	Theophylline	0.02-0.04
	Theobromine	0.15-0.2
Flavanols (flavan-3-ols)		10-25
	Monomers (catechins)	
	(-)-epicatechin (EC)	
	(-)-epicatechin-3-*O*-gallate (ECG)	
	(-)-epigallocatechin (EGC)	
	(-)-epigallocatechin-3-*O*-gallate (EGCG)	
	Dimers (theaflavins)	
	Theaflavin	
	Theaflavin 3-gallate	
	Theaflavin 3-*O*-gallate	
	Theaflavin3,3-*O*-digallate	
Flavonols		
	Quercetin (and its glycosides)	
	Kaempferol (and its glycosides)	
	Myricetin (and its glycosides)	
Flavones		
	Apigenin	
	Luteolin	
Phenolic acids		
	Chlorogenic acid	
	Gallic acid	
	Theogallin	
Amino acids	Theanine (5-N-ethyl glutamine)	3
	18 other amino acids	
Therpene saponins (theafolia saponins)	Aglycones	
	Barringtogenol C	
	R1-barringenol	
	And others	
Polysaccharides		13
Proanthocyanidins (tannins)		
Vitamins		
	Ascorbic acid	
	α-Tocopherol	
Other compounds		
	Fluoride	
	Chlorophyll	
	Organic acids	
Constituent group	**Constituent**	**Concentration (ppm)**
Elements		
	Copper	270
	Iron	13040
	Nickel	1340
	Sodium	1.800
	Potassium	262
	Magnesium	30,800
	Calcium	13,750
	Zinc	630.0
	Chromium	10.0

Table 5. Phenolic composition of green and black tea.[54]

Constituent	Green tea (%w/w)	Black tea (%w/w)
Catechins	30-42	3-10
Flavonols	5-10	6-8
Other flavonoids	2-4	-
Theagallin	2-3	-
Gallic acid	0.5	-
Quinic acid	2.0	-
Theanine	4-6	-
Methylxanthines	7-9	8-11
Theaflavins	-	3-6
Thearubigins	-	12-18

Table 6. Trace elements in commercial teas and their infusions.[40]

Tea	Na (μg/g)	K (mg/g)	Rb (μg/g)	Ca (mg/g)	Mg (mg/g)	Al (μg/g)	Fe (μg/g)	Mn (μg/g)	Cu (μg/g)	Zn (μg/g)	Cr (μg/g)	Pb (μg/g)
Dried tea leaves												
Unbranded 1	75±5	17±1.6	50±2.3	4.50±0.21	6.23±0.31	757±28	211±20	420±37	32.3±2.1	87±6	5.8±0.4	1.51±0.14
Unbranded 2	84±4	14.5±0.7	41.5±1.8	4.42±0.23	2.34±0.15	712±36	185±15	372±29	21.4±1.7	93±8	3.6±0.1	1.82±0.16
Unbranded 3	65±5	11.3±0.4	43±1.7	6.24±0.35	3.52±0.20	925±44	187±21	738±53	40.3±3.4	97±7	7.5±0.3	2.00±0.13
Red Label	81±6	16.2±0.8	46.7±2.4	5.31±0.38	2.81±0.08	1530±67	280±24	864±47	33.6±2.8	96±10	3.5±0.1	1.58±0.17
Tata Gold	48±4	17.0±1.5	42.8±1.9	2.44±0.08	3.95±0.32	891±51	190±13	1130±96	21.9±2.3	111±8	5.7±0.3	2.63±0.14
Society	39±2	17.4±1.4	43.4±2.1	6.25±0.47	5.76±0.30	713±41	166±9	258±18	29.5±0.8	85±6	1.7±0.1	166±0.20
Tetley Green 1	18±0.8	10.2±0.4	17.2±0.7	3.87±0.28	1.97±0.10	605±29	1550±74	1120±65	8.2±0.2	80±7	4.5±0.2	2.20±0.19
Tetley Green 2	21±1	11.3±0.5	19.3±0.8	3.20±0.31	2.31±0.09	620±38	1486±82	1030±82	7.3±0.3	78±5	4.7±0.2	2.34±0.23
Aqueous infusion (percentage of total leached into the infusion)												
Unbranded 1	68 (90)	11.6 (68)	37 (74)	0.20 (5)	1.31 (21)	196 (26)	8.5 (4.3)	168 (40)	0.7 (2.2)	36 (42)	-	-
Unbranded 2	90 (107)	10.1 (70)	30 (75)	0.18 (4)	0.56 (24)	149 (21)	9.6 (5.2)	122 (33)	1.0 (5)	40 (43)	-	-
Unbranded 3	51 (73)	7.6 (67)	32 (74)	0.37 (6)	1.09 (31)	278 (30)	7.6 (4.1)	273 (37)	3.2 (8)	43 (44)	-	-
Red Label	78 (96)	11.3 (70)	33 (71)	0.27 (5)	0.76 (27)	367 (24)	11.0 (4.7)	259 (30)	2.3 (7)	40 (42)	-	-
Tata Gold	41 (85)	12.4 (73)	32 (75)	0.17 (7)	1.03 (26)	196 (22)	9.3 (4.9)	452 (41)	1.8 (8)	30 (45)	-	-
Society	42 (108)	12.0 (69)	30 (70)	0.31 (5)	1.44 (25)	192 (27)	7.6 (4.6)	80 (31)	1.2 (4)	38 (45)	-	-
Tetley Green 1	14 (77)	6.6 (65)	4.1 (23)	0.12 (3)	0.57 (29)	127 (21)	22 (1.4)	380 (34)	0.2 (3)	32 (41)	-	-
Tetley Green 2	19 (95)	7.5 (66)	4.8 (25)	0.10 (3)	0.72 (31)	124 (20)	23 (1.5)	360 (35)	0.5 (7)	31 (40)	-	-

Table 7. Frequency of use according to duration and exposure of *C. sinensis*-derived ingredients.[41-43]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Camellia sinensis leaf extract[1]		**Camellia sinensis leaf**		**Camellia sinensis leaf oil**		**Camellia sinensis leaf powder**	
Total/range	**1756**	**0.00002-2**	53	**0.05**	33	**NR**	16	**0.005-50**
Duration of use								
Leave-on	**1011**	**0.00002-2**	**38**	**NR**	**24**	**NR**	**7**	**0.005-50**
Rinse-off	**710**	**0.00002-1**	**14**	**NR**	**9**	**NR**	**8**	**0.01**
Diluted for (bath) use	**35**	**0.0001-0.1**	**1**	**0.05**	**NR**	**NR**	**NR**	**NR**
Exposure type								
Eye area	129	0.0002-0.87	6	NR[f]	NR	NR	1	0.3
Incidental ingestion	31	0.001-0.14[d]	NR	NR	5	NR	NR	NR
Incidental Inhalation-sprays	76	0.0005[a]; 0.00008-2[b]; 0.0001-0.0055[c]	1	NR	NR	NR	1	0.005-50[g]
Incidental inhalation-powders	10	0.00008-2[b]; 0.0003-0.0037[c];	NR	NR	1	NR	NR	0.005-50[b]
Dermal contact	1412	0.00002-2	51	0.05	20	NR	16	0.005-50
Deodorant (underarm)	9	0.0055[a, e]; 0.0055-0.023[b]	NR	NR	NR	NR	NR	NR
Hair-noncoloring	263	0.000055-0.0063	2	NR	8	NR	NR	NR
Hair-coloring	42	0.003-0.006	NR	NR	NR	NR	NR	NR
Nail	1	0.00002-0.53	NR	NR	NR	NR	NR	NR
Mucous Membrane	364	0.0001-1	1	0.05	10	NR	9	0.01
Baby	5	NR	NR	NR	1	NR	NR	NR

	Camellia sinensis leaf water		**Camellia sinensis seed extract**			
Total/range	**37**	**30**	NR	**0.001-0.1**		
Duration of use						
Leave-on	**26**	**30**	**NR**	**0.001-0.1**		
Rinse-off	**11**	**NR**	**NR**	**0.001-0.0013**		
Diluted for (bath) use	**NR**	**NR**	**NR**	**NR**		
Exposure type						
Eye area	5	**30**	NR	NR		
Incidental ingestion	NR	NR	NR	NR		
Incidental Inhalation-sprays	NR	NR	NR	0.1[c]		
Incidental inhalation-powders	NR	NR	NR	NR		
Dermal contact	36	NR		0.001-0.1		
Deodorant (underarm)	NR	NR	NR	NR		
Hair-noncoloring	1	NR	NR	NR		
Hair-coloring	NR	NR	NR	NR		
Nail	NR	NR	NR	NR		
Mucous Membrane	NR	NR	NR	0.0013		
Baby	NR	NR	NR	NR		

[1] "Green tea" and "green tea extract" are not INCI names of cosmetic ingredients but were listed in the VCRP. Since these are technical names for camellia sinensis leaf extract, these total were combined with this ingredient.
NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.
[a] Aerosol product(s)
[b] Not aerosol product(s)
[c] Not reported if an aerosol product(s) or not
[d] Ingestible oral hygiene product – 0.14%
[e] Deodorant pump spray – 0.0055%
[f] Tea bags for the eyes (97%) is no long sold
[g] 50% in a professional product that is diluted with water for use

Table 8. Reproductive and developmental studies submitted to the FDA for the approval of an ointment containing 15% polyphenols.[70]

Species (n); administration	Results
Oral	
Pregnant rats (6-7); 0, 125, 250, 500, 750, 1000 mg/kg ointment in water (assume by gavage) on gestation days 6-15	Complete resorptions in 2/6 dams in the highest dose group. No other treatment related effects.
Sprague-Dawley (27); 0, 250, 500, 1000 mg/kg ointment on gestations days 6-18 by gavage	Body weight gains were reduced in all treatment groups compared to controls (14%, 7%, 10%, respectively). No effects on fertility, embryo/fetal development.
Rabbits (not provided); 0, 62.5, 125, 250, 500, 1000 mg/kg ointment on gestations days 6-18 by gavage	No treatment related effects observed.
White rabbits (not provided); 0, 100, 300, 1000 mg/kg ointment on gestations days 6-18 by gavage	Mortality due to gavage trauma. Body weight gains were reduced in the low- and high-treatment groups (-31%, +10%, 84%, respectively). Feed consumption was reduced in the high-dose group. No effects on fertility, embryo/fetal development.
Subcutaneous	
Rabbits (6); 0, 37.5, 150 mg/kg/d on gestation days 6-19	High-dose group- irritation with severe subcutaneous lesions/necrosis at injection sites. Treatment was discontinued after 6 days. One rabbit aborted. There was body weight loss, reduced feed consumption, and embryonic resorptions. Two fetuses from separate litters had umbilical hernia (one with hyperflexed limb), one fetus had a short tail. Low-dose group-Local irritation, reduced body weight gain. Increased early and late resorptions, Decreased corpora lutea, implants, litter size. No effect to fetal weights.
Rabbits (at least 6); 0,4, 12, 36 mg/kg/d on gestation days 6-19	High-dose group-severe local irritation at injection sites, reduced weight gain and feed consumption, reduced fetal weight. Abortions on gestation day 26. Reduced fetal weights. There were 3 malformed fetuses from 2 litters. Number of corpora lutea, pre-implantation loss, number of implantations, and sex ratios were similar to controls. Mid-dose group- one abortion on last day of gestation. 6 fetuses (from 5 litters) were malformed. One aborted fetus had a domed head. Number of corpora lutea, pre-implantation loss, number of implantations, and sex ratios were similar to controls. Low-dose group- Seven fetuses (from 4 litters) were malformed. Control group had 3 malformed fetuses from 2 litters. Blood tests show no accumulation of EGCG in the plasma during treatment.
Intravaginal	
Sprague-Dawley rats (25); 0.15 ml administered 4 days before mating through gestation day 17	No adverse effect on reproductive ability or embryo/fetal development. There were no mortalities. There were no differences in feed consumption.
Rats (25); 0.05, 0.10, 0.15 mL/d administered gestation day 6 - weaning	4 rats in the high-dose group and 3 in the mid-dose groups died possibly due to parturition complications. Dam in high-dose group killed after both pups died. There were no clinical signs observed. High-dose group-Increased stillborn pups (23 from 6 dams). There was reduced litter size and live birth index. There were no other treatment-related effects on pre- and –postnatal development. Controls-5 stillborn pups from 3 dams
Rats (25); 0, 0.05. 0.10, 0.15 mL/rat/d administered gestation day 6 – weaning. F1 generation were paired (25) and were mated untreated	F_0 - High-dose group-4 dams killed due to possible parturition complications. 20 dams delivered successfully with 23 stillborn pups from 2 litters. Mid-dose group-3 dams killed due to possible parturition complications. 22 dams delivered successfully with 9 stillborn pups from 7 litters Low-dose group-22 dams delivered successfully Controls-5 stillborn pups from 3 litters. F_1 – No mortalities. One male in the mid-dose group was missing the tip of his tail and one female had dental abnormalities. No clinical signs, body weight gains, pinna unfolding, incisor eruption, eye opening, surface righting, gripping pupillary and auditory reflex, age of vaginal opening, and balano-preputial separation were normal. Water maze field tests were normal. All mating and fertility parameters were normal.

Table 9. Mutagenicity studies of *C. sinensis* extracts and constituents.

Assay	Ingredient/constituent (concentration)	Results	Reference
	In vitro		
Ames test (*S. typhimurium* strains TA98, TA100, TA1535, TA1537 and *E. coli* WP2*uvr*A);	Polyphenol mixture containing 51.4% EGCG and 4 other catechins (0-5000 µg/plate in sterile water); Metabolic activation at 4% and 10%	Not mutagenic with or without metabolic activation. Not cytotoxic.	[72]
Ames test (*S. typhimurium* strains TA97, TA98, TA100, TA102)	Camellia sinensis flower extract (0.008, 0.04, 0.1, 1.0, 5.0 mg/plate; water extract) with and without metabolic activation	Not mutagenic with or without metabolic activation.	[74]
Ames test (*S. typhimurium* strains TA97, TA98, TA100, TA102, TA1535)	EGCG (88.1%-95% pure) (50-5000µg/plate) with and without metabolic activation	Not mutagenic with or without metabolic activation.	[73]
Mouse lymphoma assay	Polyphenol mixture containing 51.4% EGCG and 4 other catechins (0-625 µg/mL in sterile water)	Not mutagenic with or without metabolic activation. Cytotoxic at ≥375 µg/mL.	[72]
Mouse lymphoma assay	Polyphenol mixture containing 51.4% EGCG and 4 other catechins (0-500 µg/mL without; 0-625 with metabolic activation in sterile water)	Mutagenic at ≥164 µg/mL without metabolic activation; mutagenic at ≥375 µg/mL with metabolic activation. Cytotoxic at ≥500 µg/mL.	[72]
Mouse lymphoma assay	EGCG (77% pure) with and without metabolic activation	Not mutagenic without metabolic activation up to 100 µg/mL; mutagenic ≥ 125 µg/mL with metabolic activation	[73]
Mouse lymphoma assay	Polyphenol mixture (0, 87, 155, 276, 492, 878, 1568, 2800, 5000 µg/mL) with and without metabolic activation	Not mutagenic with or without metabolic activation.	[70]
	In vivo		
Mouse micronucleus assay (n = 5/sex)	Polyphenol mixture containing 51.4% EGCG and 4 other catechins (0-1500 mg/kg) by gavage	Not mutagenic	[72]
Mouse micronucleus assay (n = 5/sex)	EGCG (91.9% pure) (500, 1000, 2000 mg/kg) by gavage	Not mutagenic	[73]
Big blue mutation assay Swiss-Webster mice (n = 7/sex)	Polyphenol mixture containing 51.4% EGCG and 4 other catechins (0, 500, 1000, 2000 mg/kg/d for 28 d) by gavage. Necropsied 28 days after final dose. Tissues analyzed for mutations.	No increase in cII mutant frequencies in the livers, lungs, and spleen tissues at 500 and 2000 mg/kg. Mice died during treatment in the 2000 mg/kg group and were not analyzed.	[72]
Micronucleus assay diet study using CD-1 mice (6/sex)	EGCG (80% pure) (4200, 8400, 12600 ppm in feed)	No increase in frequency of micronucleated polychromatic erythrocytes	[73]
Micronucleus assay intravenous study using Wistar rats (5/sex)	EGCG (92.6% pure) (15, 25, 50 mg/kg/d intravenously for 2 days	No increase in frequency of micronucleate polychromatic erythrocytes	[73]
Micronucleus assay intraperitoneal study using Sprague-Dawley rats (7/sex)	Polyphenol mixture (0, 8500 mg/kg). Bone marrow sampled 24 and 48 h after treatment	No increase in frequency of micronucleate polychromatic erythrocytes	[70]

Table 10. Dermal reactions to *C. sinensis* leaf (aqueous extract or dried leaves) application in ointments for dermal treatment of genital and perianal warts.[25]

DER	Very common	Common	Uncommon
≥ 1/10	Local reactions at the application site including erythema, pruritus, irritation/burning, pain, ulcer, edema, induration and vesicles		
≥1/100 – 1/10		Local reactions at the application site including exfoliation, discharge, bleeding and swelling	
≥1/1,000 - ≤100			Local reactions at the application site including discoloration, discomfort, dryness, erosion, fissure, hyperesthesia, anesthesia, scar, nodule, dermatitis, hypersensitivity, local necrosis, papules, and eczema
≥1/1,000 - ≤100			Application site infection, application site pustules, herpes simplex, infection, pyoderma, staphylococcal infection, urethritis, vaginal candidiasis, vulvovaginitis and vulvitis

DER = drug/extract ratio

Table 11. The number of published studies discovered in a PubMed search (1965-2008) for the carcinogenicity inhibitory effect of green tea extracts and its catechins in animal models.[94]

Organ/tissue	Inhibitory effect (xenograft studies)	No inhibitory effect
Lung	20 (1)	2
Oral cavity	6	0
Esophagus	4	0
Stomach	9	0
Small intestine	8	1
Colon	11 (3)	6
Skin	27 (1)	0
Prostate	4 (5)	0
Breast	10 (8)	0
Liver	7	1
Bladder	3 (1)	0
Pancreas	2 (2)	0
Thyroid	1	0

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MEMORANDOM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: February 21, 2014

Subject: Data Submitted for *Camellia sinensis* – Derived Ingredients

To address the insufficient data announcement that was issued at the December, 2013 meeting, the Council has submitted new data. These data include:

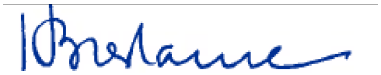
- Updated concentration of use survey
- Irritation and sensitization test of a facial product containing 0.86% camellia sinensis leaf extract
- HRIPTs on an eye cream containing 0.86% camellia sinensis leaf extract

The new concentration of use survey reports that camellia sinensis leaf is no longer used in tea bags for the eyes at 97%. There has been no new information on composition of these ingredients, the differences between oil and essential oil or if the only use for camellia sinensis leaf water is as a fragrance. No HRIPT on camellia sinensis leaf at 100% or camellia sinensis catechins at use concentrations were submitted. No data on the method of manufacture were submitted.

Personal Care Products Council
Committed to Safety, Quality & Innovation

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

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



DATE: January 16, 2014

SUBJECT: Updated Concentration of Use by FDA Product Category: Camellia sinensis-Derived Ingredients

Concentration of Use by FDA Product Category - *Camellia sinensis*-Derived Ingredients

Camellia Sinensis Catechins
Camellia Sinensis Flower Extract
Camellia Sinensis Flower/Leaf/Stem Juice
Camellia Sinensis Leaf
Camellia Sinensis Leaf Extract
Camellia Sinensis Leaf Oil
Camellia Sinensis Leaf Powder
Camellia Sinensis Leaf Water
Camellia Sinensis Root Extract
Camellia Sinensis Seedcoat Powder
Camellia Sinensis Seed Extract
Camellia Sinensis Seed Oil
Camellia Sinensis Seed Powder
Hydrolyzed Camellia Sinensis Leaf
Hydrolyzed Camellia Sinensis Seed Extract

Ingredient	**FDA Code†**	**Product Category**	**Maximum Concentration of Use**
Camellia Sinensis Leaf	02A	Bath oils, tablets and salts	0.05%
Camellia Sinensis Leaf Extract	02A	Bath oils, tablets and salts	0.0001%
Camellia Sinensis Leaf Extract	02B	Bubble baths	0.005-0.1%
Camellia Sinensis Leaf Extract	03B	Eye liner	0.1%
Camellia Sinensis Leaf Extract	03C	Eye shadow	0.005%
Camellia Sinensis Leaf Extract	03D	Eye lotion	0.001-0.87%
Camellia Sinensis Leaf Extract	03E	Eye makeup remover	0.00002-0.01%
Camellia Sinensis Leaf Extract	03F	Mascara	0.0007-0.005%
Camellia Sinensis Leaf Extract	03G	Other eye makeup preparations	0.02-0.2%
Camellia Sinensis Leaf Extract	04A	Colognes and toilet waters	0.0004-0.0055%
Camellia Sinensis Leaf Extract	04B	Perfumes	0.0001-0.005%
Camellia Sinensis Leaf Extract	04C	Powders (dusting and talcum)	0.0037%
Camellia Sinensis Leaf Extract	05A	Hair conditioners	0.000055-0.0063%
Camellia Sinensis Leaf Extract	05B	Hair sprays pump spray	 0.0005%
Camellia Sinensis Leaf Extract	05D	Permanent waves	0.00023%
Camellia Sinensis Leaf Extract	05E	Rinses (noncoloring)	0.0003%
Camellia Sinensis Leaf Extract	05F	Shampoos (noncoloring)	0.000055-0.0055%
Camellia Sinensis Leaf Extract	05G	Tonics, dressings and other hair grooming aids	0.0004-0.005%
Camellia Sinensis Leaf Extract	05I	Other hair preparations (noncoloring)	0.005-0.0063%

Camellia Sinensis Leaf Extract	06A	Hair dyes and colors (all types requiring caution statement and patch test)	0.003%
Camellia Sinensis Leaf Extract	06F	Hair lighteners with color	0.006%
Camellia Sinensis Leaf Extract	07A	Blushers (all types)	0.0002-0.02%
Camellia Sinensis Leaf Extract	07B	Face powders	0.0003-0.001%
Camellia Sinensis Leaf Extract	07C	Foundations	0.0003-0.05%
Camellia Sinensis Leaf Extract	07E	Lipstick	0.001-0.01%
Camellia Sinensis Leaf Extract	07F	Makeup bases	0.00011-0.005%
Camellia Sinensis Leaf Extract	07H	Makeup fixatives	0.01%
Camellia Sinensis Leaf Extract	08A	Basecoats and undercoats (manicuring preparations)	0.00002%
Camellia Sinensis Leaf Extract	08B	Cuticle softeners	0.01-0.092%
Camellia Sinensis Leaf Extract	08E	Nail polish and enamel	0.00014%
Camellia Sinensis Leaf Extract	08G	Other manicuring preparations	0.005-0.53%
Camellia Sinensis Leaf Extract	09A	Dentifrices (aerosol, liquid, pastes and powders)	0.01%
Camellia Sinensis Leaf Extract	09C	Other oral hygiene products	0.14%[b]
Camellia Sinensis Leaf Extract	10A	Bath soaps and detergents	0.003-1%
Camellia Sinensis Leaf Extract	10B	Deodorants not spray pump spray	 0.0055-0.023% 0.0055%
Camellia Sinensis Leaf Extract	10E	Other personal cleanliness products	0.0005-0.0055%
Camellia Sinensis Leaf Extract	11A	Aftershave lotions	0.0006-0.99%
Camellia Sinensis Leaf Extract	11D	Preshave lotions (all types)	0.01%
Camellia Sinensis Leaf Extract	11E	Shaving cream (aerosol, brushless and lather)	0.00006-0.01%
Camellia Sinensis Leaf Extract	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0006-0.44%
Camellia Sinensis Leaf Extract	12B	Depilatories	0.03%

Camellia Sinensis Leaf Extract	12C	Face and neck products not spray	 0.0001-2%
Camellia Sinensis Leaf Extract	12D	Body and hand products not spray spray	 0.00008-3% 0.0005%
Camellia Sinensis Leaf Extract	12E	Food powders and sprays spray	 0.22%
Camellia Sinensis Leaf Extract	12F	Moisturizing products not spray	 0.0007-0.5%
Camellia Sinensis Leaf Extract	12G	Night products not spray	 0.001-0.02%
Camellia Sinensis Leaf Extract	12H	Pastes masks and mud packs	0.001-0.1%
Camellia Sinensis Leaf Extract	12J	Other skin care preparations	0.002-0.87%
Camellia Sinensis Leaf Extract	13A	Suntan products not spray pump spray	 0.18-0.2% 0.07%
Camellia Sinensis Leaf Extract	13B	Indoor tanning preparations	0.001%
Camellia Sinensis Leaf Powder	03F	Mascara	0.3%
Camellia Sinensis Leaf Powder	10A	Bath soaps and detergents	0.01%
Camellia Sinensis Leaf Powder	12C	Face and neck products not spray	 0.015-50%[c]
Camellia Sinensis Leaf Powder	12D	Body and hand products not spray	 0.005-7%
Camellia Sinensis Leaf Water	03F	Mascara	30%
Camellia Sinensis Seed Extract	07C	Foundations	0.001%
Camellia Sinensis Seed Extract	10A	Bath soaps and detergents	0.0013%
Camellia Sinensis Seed Extract	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.001%
Camellia Sinensis Seed Extract	12F	Moisturizing creams, lotions and powders	0.1%
Camellia Sinensis Seed Extract	12H	Paste masks and mud packs	0.001%
Camellia Sinensis Seed Oil	05A	Hair conditioners	0.001%
Camellia Sinensis Seed Oil	05F	Shampoos (noncoloring)	0.001%

Camellia Sinensis Seed Oil	10E	Other personal cleanliness products	1%
Camellia Sinensis Seed Oil	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.01%
Camellia Sinensis Seed Oil	12C	Face and neck products not spray	0.01%
Camellia Sinensis Seed Oil	12D	Body and hand products not spray	0.01%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.
†Product category codes used by FDA

[b]Ingestible
[c]Product containing 50% Camellia Sinensis Leaf Powder is a professional product that is diluted with water before use

Information collected in 2013
Table prepared: May 31, 2013
Updated January 16, 2014 - deleted 97% Camellia Sinensis Leaf Product, no longer being sold

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: January 16, 2014

SUBJECT: HRIPTs on Products Containing Camellia Sinensis Leaf Extract

Product Investigations, Inc. 2006. Determination of the irritating and sensitizing propensities of a facial product (containing 0.86% Camellia Sinensis Leaf Extract) on Human Skin.

Clinical Research Laboratories, Inc. 2012. Repeated insult patch test of an eye cream containing 0.86% Camellia Sinensis Leaf Extract.

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

PRODUCT INVESTIGATIONS, INC.

151 East Tenth Avenue
Conshohocken, PA 19428
610-825-5855 • fax 610-825-7288

REPORT: [redacted]

DETERMINATION OF THE IRRITATING AND SENSITIZING PROPENSITIES OF [redacted] ON HUMAN SKIN

Facial product containing 0.86 % Camellia Sinensis Leaf Extract

PREPARED FOR

[redacted]

6 July 2006

[redacted]

[redacted]

[redacted]

TABLE OF CONTENTS

[redacted]

DETERMINATION OF THE IRRITATING AND SENSITIZING PROPENSITIES OF [redacted] HUMAN SKIN

1.00 OBJECTIVES:

.01 To identify and characterize the skin-damaging propensities that [redacted] can be induced to exercise under the conditions of this modified patch test procedure.

.02 To adjudge whether the exercise of such propensities under the ions contraindicates the kind of skin contact that would be occasioned during the appropriate use of the product.

2.00 DESIGN:

.01 A modified version of the Repeated Insult Patch Test [redacted] was conducted under double blind conditions on a panel composed of more than one hundred subjects at the outset.

.02 The regimen comprised nine sequential 24-hour induction applications and two concurrently conducted 24-hour challenge applications, one on the initial induction site and one on a naive site.

.03 During the initial phase, the skin of the contact sites was graded and the grades recorded on Wednesdays, Fridays (i.e. twenty-four hours after patches had been removed), and Mondays (i.e. forty-eight hours after patches had been removed).

.04 During the challenge phase, the skin of the contact sites was graded within moments after the patches had been removed and again twenty-four and forty-eight hours later. Follow-up examinations were conducted thereafter only if adverse effects were present.

.05 This study was conducted in compliance with the standards of good clinical practices generally applicable for the protection of the privileges and well-being of individuals who participate in patch test procedures.

3.00 SPONSOR:

[redacted]

Project Director:

Authorization:

4.00 STUDY PRODUCT:

Type of Product:	Facial Line Filler Treatment
Sponsor Identification:	[redacted]
Date received:	5/19/06
Quantity rec'd:	> 600 g. gross wt.
Form used in study:	as supplied
PI Nº	[redacted]

5.00 SITE OF STUDY:

Product Investigations, Inc.
142 North Ninth Street
Modesto, CA 95350

Study Personnel:

Medical Director:	Morris V. Shelanski, MDCM
Dir. Derm. Services:	Joseph E. Nicholson III
CA. Physician:	Clinton E. Prescott Jr., MD
Sr. Technician:	Lisa A. Cortez
Quality Assurance:	Samuel J. Charles III

6.00 DATES OF STUDY:

Started:	22 May 2006
Completed:	28 June 2006

[redacted]

7.00 SELECTION OF SUBJECTS:

.01 RECRUITING:

Prospective subjects were recruited from surrounding localities via phone, posters and personal contact.

.02 INFORMED CONSENT:

All individuals who expressed interest in participating were given an informed consent document to read. This document, which each candidate had to read and sign before being entered into the study, presented the following information:

a. How many subjects were to be enrolled in the study;
b. The intended use of the product;
c. Why the product was being tested;
d. How the test was to be performed;
e. That the regimen was not intended to benefit a subject's health, well being, or quality of life.
f. The different ways that participation may be detrimental to a subject's health, well being, or quality of life.
g. That not all detrimental effects could be foreseen and made known at the time the informed consent was presented for the prospective subject's signature.
h. What commitments a subject had to make to be in compliance; and
i. What considerations a subject was entitled to receive and the conditions for receiving them.

.03 DETERMINATION OF ELIGIBILITY:

Information concerning a prospective subject's qualifications was obtained from the answers the subject gave in filling out a medical history form and in responding to specific questions. Those who did not meet the following criteria were rejected.

a. Inclusion Criteria: Satisfaction of all the following items was obligatory:

i. The candidate was at least eighteen years old, and
ii. agreed to comply fully with the scheduled study regimen, and
iii. expressed awareness that a participant would incur risks that would affect her/his well-being, and
iv. denied that the amount of the stipend had induced her/him to participate against her/his better judgement, and
v. had read the informed consent agreement, and
vi. had assured the interviewer that she/he had no questions about the informed consent's contents that had not been answered to her/his satisfaction, and
vii. had signed the consent form willingly and without reservation.

b. Exclusion Criteria: Any one of the following items was cause for rejection:

i. The candidate had an illness that contraindicated participation; or
ii. a condition that rendered the skin unsuitable for use in this study; or
iii. was using dosages of medications that could alter the skin's tolerance; or
iv. had a documented history of intolerance to the category of products submitted for study; or
v. was a female who was pregnant or was breast feeding an infant.

.04 PANEL INFORMATION:

a. Panel №: [redacted]

b. Demographics:

SEX	Number	Age Range
Female	70	18 - 70
Male	40	19 - 63

c. Dedication: The subjects in this panel were simultaneously engaged in the study of products submitted by sponsors other than [redacted]

8.00 SITE INFORMATION:

.01 LOCATION:

[redacted] was assigned Band #2 on the left upper arm of each subject.

.02 IDENTIFICATION OF A CONTACT SITE:

At each visit the skin around the contact site was marked to facilitate examinations after the device was removed and positioning of subsequently-applied devices as precisely as was feasible on the same site.

[redacted]

9.00 PATCHING DEVICES:

.01 TYPE OF DEVICE:

Partially-occlusive patching devices consisting of a 2 cm x 2 cm absorbent pad centered on the adhesive-coated surface of a 2 cm x 4 cm plastic film were used to convey and maintain the product on the skin.

.02 PREPARATION OF A PATCHING DEVICE:

a. The webril pad of a patching device was infused with 150µl of the test material.

.03 POSITIONING AND REMOVING A PATCHING DEVICE:

a. A prepared device was positioned on its designated site on each subject with the product-treated surface of the pad in contact with the skin.
b. Firm pressure was applied to the backing of the device to effect intimate contact of the pad with the skin and to bond the flanges of the device securely to the skin.
c. When the time came for removing the device, the device was peeled off the skin as gently as was feasible under the circumstances.

10.00 DATA ACQUISITION:

.01 GRADING PROCEDURE:

a. Examinations of the contact sites to grade the effects elicited by the product were conducted on Mondays, Wednesday and Fridays. When a subject came in on a scheduled examination day, the technician examined the skin of the contact site.
   i. If no adverse effect was detected, a "0" was recorded in the subject's Case Report Form.
   ii. If an adverse effect was detected, the technician entered a grade indicating her assessment of the response's intensity.
b. The subject was then sent into the patching room where the site was examined again by a second technician to ascertain independently whether or not the site should be used again. If she disagreed with the first technician's assessment, the application was held in abeyance until the issue could be resolved with the help of the supervisor and/or the investigator.
c. The supervisor or the investigator was called in not only when a disagreement had to be resolved, but also to validate substantial sudden changes, e.g. when a response is deemed to merit a grade ≥3 or when a response has been judged to have decreased by two or more points from the previous day's status.

.02 CRITERIA FOR GRADING RESPONSE INTENSITY:

The following scale was used in this procedure to designate the intensities of those gross skin changes that may be occasioned by exposing the surface of the skin to a product.

Morphology	Visible Change	Grade
Subclinical Stage	None	0
Inflammation		
Vascular Dilation:	Faint redness with poorly defined margins	1
	Redness with well-defined margins	2
Infiltration:	Redness plus well-defined edema	3
	Redness plus papules, or vesicles or ulceration	4

.04 SITE CHANGES:

a. **Switch to a Naive Site:**
   i. If the product had elicited a Grade 2 response on a subject, application of the product would have been switched immediately to a naive site on the subject.
b. **Discontinuation of Applications:**
   i. If the product had elicited a second Grade 2 on a subject, application of the product would have been discontinued immediately for the remainder of the initial phase on the affected subject.
   ii. If the product had elicited a Grade 3 response on a subject, application of the product would have been discontinued immediately for the remainder of the initial phase on the affected subject.

[redacted]

11.00 OVERVIEW OF STUDY REGIMEN:

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week #1	Apply	Remove	Rem/Gr/Apply	Remove	Rem/Gr/Apply	(Removed)	--
Week #2	Holiday	Grade/Apply	Rem/Gr/Apply	Remove	Grade/Apply	(Removed)	--
Week #3	Grade/Apply	Remove	Grade/Apply	Remove	Grade/Apply	(Removed)	--
Week #4	Grade	--	--	--	--	--	--
Week #6	Apply	Remove/Grade	Grade	Grade*	Grade*	--	--

*If necessary

12.00 STUDY REGIMEN:

.01 INITIAL/INDUCTION PHASE-

Week #1:

Monday:

i. As each subject presented herself/himself at the clinic, the skin of the contact site assigned to the product submitted for study was examined and ascertained to be suitable before applications were begun.
ii. A freshly-prepared patching device was applied on its assigned site.
iii The skin around the device was marked and the subject was instructed to return on Tuesday.

Tuesday:

i. As each subject returned, the site-identifying marks were reinforced.
ii.. The patching device was removed by a technician and the subject was instructed to return on Wednesday.

Wednesday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii.. A freshly-prepared patching device was applied on the same site.
iii. The site-identifying marks were reinforced and the subject was instructed to return on Thursday

Thursday:

i. As each subject returned, the site-identifying marks were reinforced.
ii.. The patching device was removed by a technician and the subject was instructed to return on Friday.

Friday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared patching device was applied on the same site.
iii The site-identifying marks were reinforced.
iv. The subject was dismissed with instructions to remove the patching device on Saturday, to record the time of removal, and to return to the clinic on the following Tuesday for resumption of the regimen.

Week #2 / Week #3:

Monday (Week 2): Memorial Day Holiday, clinic was closed.

Monday (Week 3) and Tuesday (Week 2):

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii.. The time at which the patch was removed on Saturday was recorded.
iii. A freshly-prepared patching device was applied on the same site.
iv.a The site-identifying marks were reinforced and the subject was instructed to return on Wednesday (Wk. 2).
iv.b The site-identifying marks were reinforced and the subject was instructed to return on Tuesday (Wk. 3).

Tuesday: (Week 3)

i. As each subject returned, the site-identifying marks were reinforced.
ii.. The patching device was removed by a technician and the subject was instructed to return on Wednesday.

Wednesday,

i. As each subject returned, the site-identifying marks were reinforced. The patching device was removed by a technician and the skin of the contact site was graded. The grade was recorded (Wk. 2)
i. As each subject returned, the skin of the contact site was graded. The grade was recorded (Wk. 3)
ii.. A freshly-prepared patching device was applied on the same site.
iii. The subject was dismissed with instructions to return on Thursday

Thursday, Friday:

The same procedures followed during Week 1 were followed during Weeks 2 and 3.

[redacted]

Week #4:

Monday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii a) If the subject had undergone all nine induction applications, she/he was dismissed after being instructed as follows:
i) to report back to the clinic on the following Monday to receive the challenge applications, and
ii) to notify the investigator without delay should any significant changes occur in the skin of the contact site before Monday of the challenge week.
b) If the subject had not received the required number of induction applications and was deficient without valid reason, applications were continued. As many as two missed applications could be made up during this week. When the subject had undergone the required number of make up applications, she/he was dismissed after being instructed as in sections ii(a), above.

.02 HIATUS/MAKE UP PHASE-

Week #'s 4 and 5:

After the examination on Monday of Week 4, no procedures were scheduled during this period except make-up applications.

.03 CHALLENGE PHASE-

Week #6:

Monday:

i. As each subject returned, the skin of the initial induction site was examined and ascertained to be free of any conditions that would have rendered it unfit for undergoing the challenge applications.
ii. A prepared device was applied on the initial induction site.
iii A second prepared device was applied on a naive site.
iv. The skin around both devices was marked and the subject was instructed to return on Tuesday.

Tuesday: (**Note:** If a subject was absent on Monday, she/he was patched on Tuesday.)

i. As each subject returned, the site-identifying marks around both contact sites were reinforced.
ii. Both patching devices were removed by a technician.
iii The skin of both contact sites was graded; the grades were recorded.
iv. The subject was instructed to return on Wednesday.

Wednesday:

i. As each subject returned, the skin of both contact sites was graded; the grades were recorded.
ii. If follow-up was indicated, the subject was instructed to return on Thursday, otherwise the subject was dismissed from the study of this material..

.04 FOLLOW-UP PHASE:

Week No. 7 and Week No. 8:

During the two weeks following the exit examination, the subjects were given the opportunity to relay any information concerning effects that were relevant to the characterization of the product as well as to communicate the need for treatment of persistent or newly-occurring responses.

13.00 PROCEDURE DEVIATIONS:

Monday of Week two was the Memorial Day Holiday and the laboratory was closed for business. The application scheduled for Monday of Week 2 was applied on the following day for the normal contact period of 24 hours. The results of this 24 hour application were assessed and graded on Wednesday.

The normal schedule of conduct was resumed on Wednesday of Week 2.

[redacted]

14.00 COMPLIANCE:

PHASE	No. Of AEC's Required	EXCUSED	COMPLIANT YES	COMPLIANT NO
Induction	8	0	101	9
Challenge	1/1	0	101	9

101 of the 110 Subjects were in compliance with the number of required application/examination cycles during induction.
101 of the 110 Subjects were in compliance with the number of required application/examination cycles during challenge.

15.00 INCIDENCE OF RESPONSES:

GRADE	TYPE OF RESPONSE	INDUCTION PHASE	CHALLENGE PHASE	
			Original Contact Site	Naive Contact Site
0	No visible change	106 subjects	101 subjects	101 subjects
1	Faint redness, undefined border	0 "	0 "	0 "
2	Intense redness, defined border	0 "	0 "	0 "
3	Redness + definite edema	0 "	0 "	0 "
4	Redness + papules, or vesicles, etc.	0 "	0 "	0 "
[redacted]	No. of Responders	0 subjects	0 subjects	0 subjects
[redacted]	No Data Acquired	4 subjects	9 subjects	9 subjects

16.00 SIGNIFICANCE OF THE RESPONSES:

.01 INITIAL/INDUCTION PHASE:

No responses were noted on any of the 106 subjects who participated in all or part of this study. The absence of responses characterize the product as one which is devoid of clinically significant skin-irritating propensities.

.02 CHALLENGE PHASE:

a. **Original Contact Sites:**
No responses were noted on any of the 101 subjects who participated in this phase of the study. The absence of responses characterize the product as one which is devoid of clinically significant skin sensitizing propensities.

b. **Naive Contact Sites:**
No responses were noted on any of the 101 subjects who participated in this phase of the study. The absence of responses characterize the product as one which is devoid of clinically significant skin sensitizing propensities.

[redacted]

17.00 CONCLUSIONS:

.01 [redacted] was found to be neither a clinically significant skin irritant nor a skin sensitizer under the conditions of this study.

.02 [redacted] is not contraindicated for usages entailing repeated applications on human skin under conditions appropriate for such products.

PRODUCT INVESTIGATIONS, INC.

7/6/06
Date

Joseph E. Nicholson III
Director, Clinical Studies

18.00 COMPLIANCE WITH GOOD QUALITY ASSURANCE STANDARDS :

I have audited the results presented in this report and believe that, to the best of my knowledge, they accurately reflect the raw data acquired during the course of this study.

Samuel Charles
Director, Quality Assurance

[redacted]

[redacted]

Site: L2

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE WEEK					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
001	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
002	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
003	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
004	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
005	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
006	B/0		Dropped																							
007	B/0		Dropped																							
008	B/0		Dropped																							
009	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
010	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
011	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
012	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
013	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
014	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
015	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
016	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
017	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
018	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
019	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
020	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
021	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
022	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
023	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
024	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
025	B/0		0		0		0	A		0	0		0		0	0		0			B/0	0/0	0/0			
026	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
027	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
028	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
029	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
030	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			

[redacted]

Site: L2

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE WEEK					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
031	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
032	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
033	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
034	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
035	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
036	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
037	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
038	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
039	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
040	B/0		0		0		0	0		0	A		A		Dropped											
041	B/0		0		0		0	0		0	A		A		Dropped											
042	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
043	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
044	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
045	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
046	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
047	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
048	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
049	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
050	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
051	B/0		0		0		0	A		Dropped																
052	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
053	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
054	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
055	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
056	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
057	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
058	B/0		0		0		0	0		0	A		A		Dropped											
059	B/0		0		0		0	0		0	A		A		Dropped											
060	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			

[redacted]

Site: L2

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE WEEK					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
061	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
062	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
063	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
064	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
065	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
066	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
067	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
068	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
069	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
070	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
071	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
072	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
073	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
074	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
075	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
076	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
077	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
078	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
079	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
080	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
081	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
082	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
083	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
084	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
085	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
086	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
087	B/0		Dropped																							
088	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
089	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
090	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			

[redacted]

Site: L2

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE WEEK					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
091	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
092	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
093	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
094	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
095	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
096	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
097	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
098	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
099	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
100	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
101	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
102	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
103	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
104	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
105	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
106	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
107	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
108	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
109	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			
110	B/0		0		0		0	0		0	0		0		0	0					B/0	0/0	0/0			

LEGEND

A = Absent
D = Dropped

<u>Monday week 6</u>: Only if any reactions on the last Friday week 5 (challenge week)

Clinical
Research
Laboratories, Inc.

[redacted]

Final Report

Repeated Insult Patch Test

CLIENT:

ATTENTION:

[redacted]

TEST MATERIAL: Eye Cream

CRL STUDY NUMBER: CRL59312 (N=600) containing 0.86% Camellia Sinensis Leaf Extract

AUTHORIZED SIGNATURES:

Bruce E. Kanengiser, M.D.
President/Medical Director

Michael J. Muscatiello, Ph.D.
Executive Vice President/COO

Anita Lee Cham, M.D.
Dermatologist

[redacted]

REPORT DATE: August 24, 2012

371 Hoes Lane, Suite 100 • Piscataway, NJ 08854 • (732) 981-1616 • FAX (732) 981-0520

Clinical
Research
Laboratories, Inc.

Good Clinical Practice
Quality Assurance Audit Statement

Clinical Study Number: CRL59312 (N=600)

Start Date: May 14, 2012

Completion Date: August 3, 2012

The clinical study listed above was conducted in accordance with Clinical Research Laboratories, Inc. Standard Operating Procedures, which incorporate the principles of Good Clinical Practice defined by applicable guidelines and regulations established by U.S. Regulatory Agencies. The conduct of the study was monitored for compliance, and the associated records, including source documents or raw data, were reviewed for documentation practices and accuracy by a Project Manager/Study Director and/or a Quality Assurance Representative. Standard Quality Assurance audit procedures for this final report and study related documents were conducted, as indicated below.

Signature of QA Auditor

8/24/12
Date

Clinical Research Laboratories, Inc.

FINAL REPORT

REPEATED INSULT PATCH TEST

PURPOSE

The purpose of this study was to determine the dermal irritation and sensitization potential of a test material.

INVESTIGATIVE SITE

Clinical Research Laboratories, Inc.
371 Hoes Lane Suite 100
Piscataway, New Jersey 08854
732-981-1616

TEST MATERIAL

The following test material was provided [redacted] and was received by Clinical Research Laboratories, Inc. on May 14th, 2012:

Test Material	Test Condition	Patch Type
[redacted] Eye Cream	Test as received.	Occlusive*

The test material was coded with the following CRL identification number:

CRL59312 (N=600)

STUDY DATES

This study was initiated on May 14, 2012 and was completed on August 3, 2012.

* Occlusive Strip with Flexcon® (Brady Medical, Mesquite,TX)

Clinical Research Laboratories, Inc.

PANEL SELECTION

Each subject was assigned a permanent CRL identification number. All subjects signed an Informed Consent Form in compliance with 21 CFR Part 50: "Protection of Human Subjects" and a HIPAA Authorization Form in compliance with 45 CFR Parts 160 and 164. All subjects completed a Subject Profile/Medical History Form provided by Clinical Research Laboratories, Inc. prior to the study (Subject Demographics - Appendix I). Subjects who met the following Inclusion Criteria and none of the Exclusion Criteria were impaneled:

Inclusion Criteria

a. Male and female subjects between the ages of 18 and 70 years;

b. Subjects who do not exhibit any skin diseases which might be confused with a skin reaction from the test material;

c. Subjects who agree to avoid exposure of the test sites to the sun and to refrain from visits to tanning salons during the course of this study;

d. Subjects willing to sign an Informed Consent in conformance with 21CFR Part 50: "Protection of Human Subjects;"

e. Subjects who have completed a HIPAA Authorization Form in conformance with 45CFR Parts 160 and 164;

f. Subjects in generally good health who have a current Subject Profile/Medical History on file;

g. Subjects who are dependable and able to follow directions as outlined in the protocol.

Exclusion Criteria

a. Female subjects who are pregnant or nursing;

b. Subjects who are currently using any systemic or topical corticosteroids, anti-inflammatory drugs, or antihistamines on a regular basis;

c. Subjects exhibiting any skin disorder, sunburn, scars, excessive tattoos, etc. in the test area.

Clinical Research Laboratories, Inc.

TEST METHOD

Prior to the application of the patch, the test area was wiped with 70% isopropyl alcohol and allowed to dry. The test material, which was prepared as described in the Test Material section of the report, was applied to the upper back (between the scapulae) and was allowed to remain in direct skin contact for a period of 24 hours.

Patches were applied to the same site on Monday, Wednesday, and Friday for a total of 9 applications during the Induction Period. This schedule may have been modified to allow for missed visits or holidays. If a subject was unable to report on an assigned test date, the test material was applied on 2 consecutive days during the Induction Phase and/or a makeup day was added at the end of the Induction Phase.

The sites were graded by a CRL technician for dermal irritation 24 hours after removal of the patches by the subjects on Tuesday and Thursday and 48 hours after removal of the patches on Saturday, unless the patching schedule was altered as described above.

The sites were graded according to the following scoring system:

Dermal Scoring Scale

0 No visible skin reaction
± Barely perceptible erythema
1+ Mild erythema
2+ Well defined erythema
3+ Erythema and edema
4+ Erythema and edema with vesiculation

If a "2+" reaction or greater occurred, the test material was applied to an adjacent virgin site. If a "2+" reaction or greater occurred on the new site, the subject was not patched again during the Induction Phase but was challenged on the appropriate day of the study. At the discretion of the Study Director, patch sites with scores less than a "2+" may have been changed.

Following approximately a 2-week rest period, the challenge patches were applied to previously untreated test sites on the back. After 24 hours, the patches were removed by a CRL technician and the test sites were evaluated for dermal reactions. The test sites were re-evaluated at 48 and 72 hours. Subjects exhibiting reactions during the Challenge Phase of the study may have been asked to return for a 96-hour reading.

Clinical Research Laboratories, Inc.

RESULTS

This study was initiated with 672 subjects. Thirty-four subjects discontinued study participation for reasons unrelated to the test material. A total of 638 subjects completed the study.

Individual dermal scores recorded during the Induction and Challenge Phases appear in Table I.

CONCLUSION

Based on the test population of 638 subjects and under the conditions of this study, the test material identified as [redacted] Eye Cream did not demonstrate a clinically significant potential for eliciting dermal irritation or sensitization.

RETENTION

Test materials and all original forms of this study will be retained by Clinical Research Laboratories, Inc. as specified in CRL Standard Operating Procedures 30.6 and 30.6C, unless designated otherwise by the Sponsor.

[redacted]

Clinical Research Laboratories, Inc.

TABLE I

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
1A	0	0	0	0	0	0	0	0	0	0	0	0
2A	0	0	0	0	0	0	0	0	0	0	0	0
3A	0	0	0	0	0	0	0	0	0	0	0	0
4A	0	0	0	0	0	0	0	0	0	0	0	0
5A	0	Discontinued										
6A	0	0	0	0	0	0	0	0	0	0	0	0
7A	0	0	0	0	0	0	0	0	0	0	0	0
8A	0	0	0	0	0	0	0	0	0	0	0	0
9A	0	0	0	0	0	0	0	0	0	0	0	0
10A	0	0	0	0	0	0	0	0	0	0	0	0
11A	0	0	0	0	0	0	0	0	0	0	0	0
12A	0	0	0	0	0	0	0	0	0	0	0	0
13A	0	0	0	0	0	0	0	0	0	0	0	0
14A	0	0	0	0	0	0	0	0	0	0	0	0
15A	0	0	0	0	0	0	0	0	0	0	0	0
16A	0	0	0	0	0	0	0	0	0	0	0	0
17A	0	0	0	0	0	0	0	0	0	0	0	0
18A	0	Discontinued										
19A	0	0	0	0	0	0	0	0	0	0	0	0
20A	0	0	0	0	0	0	0	0	0	0	0	0
21A	0	0	0	0	0	0	0	0	0	0	0	0
22A	0	0	0	0	0	0	0	0	0	0	0	0
23A	0	0	0	0	0	0	0	0	0	0	0	0
24A	0	0	0	0	0	0	0	0	0	0	0	0
25A	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted] Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
26A	0	0	0	0	0	0	0	0	0	0	0	0
27A	0	0	0	0	0	0	0	0	0	0	0	0
28A	0	0	0	0	0	0	0	0	0	0	0	0
29A	0	0	0	0	0	0	0	0	0	0	0	0
30A	0	0	0	0	0	0	0	0	0	0	0	0
31A	0	Discontinued										
32A	0	0	0	0	0	0	0	0	0	0	0	0
33A	0	0	0	0	0	0	0	0	0	0	0	0
34A	0	0	0	0	0	0	0	0	0	0	0	0
35A	0	0	0	0	0	0	0	0	0	0	0	0
36A	0	0	0	0	0	0	0	0	0	0	0	0
37A	0	0	0	0	0	0	0	0	0	0	0	0
38A	0	0	0	0	0	0	0	0	0	0	0	0
39A	0	0	0	0	0	0	0	0	0	0	0	0
40A	0	0	0	0	0	0	0	0	0	0	0	0
41A	0	0	0	0	0	0	0	0	0	0	0	0
42A	0	0	0	0	0	0	0	0	0	0	0	0
43A	0	0	0	0	0	0	0	0	0	0	0	0
44A	0	0	0	0	0	0	0	0	0	0	0	0
45A	0	0	0	0	0	0	0	0	0	0	0	0
46A	0	0	0	0	0	0	0	0	0	0	0	0
47A	0	0	0	0	0	0	0	0	0	0	0	0
48A	0	0	0	0	0	0	0	0	0	0	0	0
49A	0	0	0	0	0	0	0	0	0	0	0	0
50A	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
51A	0	0	0	0	0	0	0	0	0	0	0	0
52A	0	0	0	0	0	0	0	0	0	0	0	0
53A	0	0	0	0	0	0	0	0	0	0	0	0
54A	0	0	0	0	0	0	0	0	0	0	0	0
55A	0	0	0	0	0	0	0	0	0	0	0	0
56A	0	0	0	0	0	0	0	0	0	0	0	0
57A	0	0	0	0	0	0	0	0	0	0	0	0
58A	0	Discontinued										
59A	0	0	0	0	0	0	0	0	0	0	0	0
60A	0	0	0	0	0	0	0	0	0	0	0	0
61A	0	0	0	0	0	0	0	0	0	0	0	0
62A	0	0	0	0	0	0	0	0	0	0	0	0
63A	0	0	0	0	0	0	0	0	0	0	0	0
64A	0	0	0	0	0	0	0	0	0	0	0	0
65A	0	0	0	0	0	0	0	0	0	0	0	0
66A	0	0	0	0	0	0	0	0	0	0	0	0
67A	0	0	0	0	0	0	0	0	0	0	0	0
68A	0	0	0	0	0	0	0	0	0	0	0	0
69A	0	0	0	0	0	0	0	0	0	0	0	0
70A	0	0	0	0	0	0	0	0	0	0	0	0
71A	0	0	0	0	0	0	0	0	0	0	0	0
72A	0	0	0	0	0	0	0	0	0	0	0	0
73A	0	0	0	0	0	0	0	0	0	0	0	0
74A	0	0	0	0	0	0	0	0	0	0	0	0
75A	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
76A	0	0	0	0	0	0	0	0	0	0	0	0
77A	0	0	0	0	0	0	0	0	0	0	0	0
78A	0	0	0	0	0	0	0	0	0	0	0	0
79A	0	0	0	0	0	0	0	0	0	0	0	0
80A	0	0	0	0	0	0	0	0	0	0	0	0
81A	0	0	0	0	0	0	0	0	0	0	0	0
82A	0	0	0	0	0	0	0	0	0	0	0	0
83A	0	0	0	0	0	0	0	0	0	0	0	0
84A	0	0	0	0	0	0	0	0	0	0	0	0
85A	0	0	0	0	0	0	0	0	0	0	0	0
86A	0	0	0	0	0	0	0	0	0	0	0	0
87A	0	0	0	0	0	0	0	0	0	0	0	0
88A	0	0	0	0	0	0	0	0	0	0	0	0
89A	0	0	0	0	0	0	0	0	0	0	0	0
90A	0	0	0	0	0	0	0	0	0	0	0	0
91A	0	0	0	0	0	0	0	0	0	0	0	0
92A	0	0	0	0	0	0	0	0	0	0	0	0
93A	0	0	0	0	0	0	0	0	0	0	0	0
94A	0	0	0	0	0	0	0	0	0	0	0	0
95A	0	0	0	0	0	0	0	0	0	0	0	0
96A	0	0	0	0	0	0	0	0	0	0	0	0
97A	0	0	0	0	0	0	0	0	0	0	0	0
98A	0	0	0	0	0	0	0	0	0	0	0	0
99A	0	0	0	0	0	0	0	0	0	0	0	0
100A	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
101A	0	0	0	0	0	0	0	0	0	0	0	0
102A	0	0	0	0	0	0	0	0	0	0	0	0
103A	0	0	0	0	0	0	0	0	0	0	0	0
104A	0	0	Discontinued									
105A	0	0	0	0	0	0	0	0	0	0	0	0
106A	0	0	0	0	0	0	0	0	0	0	0	0
107A	0	0	0	0	0	0	0	0	0	0	0	0
108A	0	0	0	0	0	0	0	0	0	0	0	0
109A	0	0	0	0	0	0	0	0	0	0	0	0
110A	0	0	0	0	0	0	0	0	0	0	0	0
111A	0	0	0	0	0	0	0	0	0	0	0	0
112A	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
1B	0	0	0	0	0	0	0	0	0	0	0	0
2B	0	0	0	0	0	0	0	0	0	0	0	0
3B	0	0	0	0	0	0	0	0	0	0	0	0
4B	0	0	0	0	0	0	0	0	0	0	0	0
5B	0	0	0	0	0	0	0	0	0	0	0	0
6B	0	0	0	0	0	0	0	0	0	0	0	0
7B	0	0	Discontinued									
8B	0	0	0	0	0	0	0	0	0	0	0	0
9B	0	0	0	0	0	0	0	0	0	0	0	0
10B	0	0	0	0	0	0	0	0	0	0	0	0
11B	0	0	0	0	0	0	0	0	0	0	0	0
12B	0	0	0	0	0	0	0	0	0	0	0	0
13B	0	0	0	0	0	0	0	0	0	0	0	0
14B	0	0	0	0	0	0	0	0	0	0	0	0
15B	0	0	0	0	0	0	0	0	0	0	0	0
16B	0	0	0	0	0	0	0	0	0	0	0	0
17B	0	0	0	0	0	0	0	0	0	0	0	0
18B	0	0	0	0	0	0	0	0	0	0	0	0
19B	0	0	0	0	0	0	0	0	0	0	0	0
20B	0	0	0	0	0	0	0	0	0	0	0	0
21B	0	0	0	0	0	0	0	0	0	0	0	0
22B	0	0	0	0	0	0	0	0	0	0	0	0
23B	0	0	0	0	0	0	0	0	0	0	0	0
24B	0	0	0	0	0	0	0	0	0	0	0	0
25B	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
26B	0	0	0	0	0	0	0	0	0	0	0	0
27B	0	0	0	0	0	0	0	0	0	0	0	0
28B	0	0	0	0	0	0	0	0	0	0	0	0
29B	0	0	0	0	0	0	0	0	0	0	0	0
30B	0	0	0	0	0	0	0	0	0	0	0	0
31B	0	0	0	0	0	0	0	0	0	0	0	0
32B	0	0	0	0	0	0	0	0	0	0	0	0
33B	0	0	0	0	0	0	0	0	0	0	0	0
34B	0	0	0	0	0	0	0	0	0	0	0	0
35B	0	0	0	0	0	0	0	0	0	0	0	0
36B	0	0	0	0	0	0	0	0	0	0	0	0
37B	0	0	Discontinued									
38B	0	0	0	0	0	0	0	0	0	0	0	0
39B	0	0	0	0	0	0	0	0	0	0	0	0
40B	0	0	0	0	0	0	0	0	0	0	0	0
41B	0	0	0	0	0	0	0	0	0	0	0	0
42B	0	0	0	0	0	0	0	0	0	0	0	0
43B	0	0	0	0	0	0	0	0	0	0	0	0
44B	0	0	0	0	0	0	0	0	0	0	0	0
45B	0	0	0	0	0	0	0	0	0	0	0	0
46B	0	Discontinued										
47B	0	0	0	0	0	0	0	0	0	0	0	0
48B	0	0	0	0	0	0	0	0	0	0	0	0
49B	0	0	0	0	0	0	0	0	0	0	0	0
50B	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
51B	0	0	0	0	0	0	0	0	0	0	0	0
52B	0	0	0	0	0	0	0	0	0	0	0	0
53B	0	0	0	0	0	0	0	0	0	0	0	0
54B	0	0	0	0	0	0	0	0	0	0	0	0
55B	0	0	0	0	0	0	0	0	0	0	0	0
56B	0	0	0	0	0	0	0	0	0	0	0	0
57B	0	0	0	0	0	0	0	0	0	0	0	0
58B	0	0	0	0	0	0	0	0	0	0	0	0
59B	0	0	0	0	0	0	0	0	0	0	0	0
60B	0	0	0	0	0	0	0	0	0	0	0	0
61B	0	0	0	0	0	0	0	0	0	0	0	0
62B	0	0	0	0	0	0	0	0	0	0	0	0
63B	0	0	0	0	0	0	0	0	0	0	0	0
64B	0	0	0	0	0	0	0	0	0	0	0	0
65B	0	0	0	0	0	0	0	0	0	0	0	0
66B	0	0	0	0	0	0	0	0	0	0	0	0
67B	0	0	0	0	0	0	0	0	0	0	0	0
68B	0	0	0	0	0	0	0	0	0	0	0	0
69B	0	0	0	0	0	0	0	0	0	0	0	0
70B	0	0	0	0	0	0	0	0	0	0	0	0
71B	0	0	0	0	0	0	0	0	0	0	0	0
72B	0	0	0	0	0	0	0	0	0	0	0	0
73B	0	0	0	0	0	0	0	0	0	0	0	0
74B	0	0	0	0	0	0	0	0	0	0	0	0
75B	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted] Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
76B	0	0	0	0	0	0	0	0	0	0	0	0
77B	0	0	0	0	0	0	0	0	0	0	0	0
78B	0	0	0	0	0	0	0	0	0	0	0	0
79B	0	0	0	0	0	0	0	0	0	0	0	0
80B	0	0	0	0	0	0	0	0	0	0	0	0
81B	0	0	0	0	0	0	0	0	0	0	0	0
82B	0	0	0	0	0	0	0	0	0	0	0	0
83B	0	0	0	0	0	0	0	0	0	0	0	0
84B	0	0	0	0	0	0	0	0	0	0	0	0
85B	0	Discontinued										
86B	0	0	0	0	0	0	0	0	0	0	0	0
87B	0	0	0	0	0	0	0	0	0	0	0	0
88B	0	0	0	0	0	0	0	0	0	0	0	0
89B	0	0	0	0	0	0	0	0	0	0	0	0
90B	0	0	0	0	0	0	0	0	0	0	0	0
91B	0	0	0	0	0	0	0	0	0	0	0	0
92B	0	0	0	0	0	0	0	0	0	0	0	0
93B	0	0	0	0	0	0	0	0	0	0	0	0
94B	0	0	0	0	0	0	0	0	0	0	0	0
95B	0	0	0	0	0	0	0	0	0	0	0	0
96B	0	0	0	0	0	0	0	0	0	0	0	0
97B	0	0	0	0	0	0	0	0	0	0	0	0
98B	0	0	0	0	0	0	0	0	0	0	0	0
99B	0	0	0	0	0	0	0	0	0	0	0	0
100B	0	0	0	0	0	0	0	0	0	0	0	0

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted] Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
101B	0	0	0	0	0	0	0	0	0	0	0	0
102B	0	0	0	0	0	0	0	0	0	0	0	0
103B	0	0	0	0	0	0	0	0	0	0	0	0
104B	0	0	0	0	0	0	0	0	0	0	0	0
105B	0	0	0	0	0	0	0	0	0	0	0	0
106B	0	0	0	0	0	0	0	0	0	0	0	0
107B	0	0	0	0	0	0	0	0	0	0	0	0
108B	0	0	0	0	0	0	0	0	0	0	0	0
109B	0	0	0	0	0	0	0	0	0	0	0	0
110B	0	0	0	0	0	0	0	0	0	0	0	0
111B	0	0	0	0	0	0	0	0	0	0	0	0
112B	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
1C	0	0	0	0	0	0	0	0	0	0	0	0
2C	0	0	0	0	0	0	0	0	0	0	0	0
3C	0	0	0	0	0	0	0	0	0	0	0	0
4C	0	0	0	0	0	0	0	0	0	0	0	0
5C	0	0	0	0	0	0	0	0	0	0	0	0
6C	0	0	Discontinued									
7C	0	0	0	0	0	0	0	0	0	0	0	0
8C	0	0	0	0	0	0	0	0	0	0	0	0
9C	0	0	0	0	0	0	0	0	0	0	0	0
10C	0	0	0	0	0	0	0	0	0	0	0	0
11C	0	0	0	0	0	0	0	0	0	0	0	0
12C	0	0	0	0	0	0	0	0	0	0	0	0
13C	0	0	0	0	0	0	0	0	0	0	0	0
14C	0	0	0	0	0	0	0	0	0	0	0	0
15C	0	0	0	0	0	0	0	0	0	0	0	0
16C	0	0	0	0	0	0	0	0	0	0	0	0
17C	0	0	0	0	0	0	0	0	0	0	0	0
18C	0	0	0	0	0	0	0	0	0	0	0	0
19C	0	0	0	0	0	0	0	0	0	0	0	0
20C	0	0	0	0	0	0	0	0	0	0	0	0
21C	0	0	0	0	0	0	0	0	0	0	0	0
22C	0	0	0	0	0	0	0	0	0	0	0	0
23C	0	0	0	0	0	0	0	0	0	0	0	0
24C	0	0	0	0	0	0	0	0	0	0	0	0
25C	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
26C	0	0	0	0	0	0	0	0	0	0	0	0
27C	0	0	0	0	0	0	0	0	0	0	0	0
28C	0	Discontinued										
29C	0	0	0	0	0	0	0	0	0	0	0	0
30C	0	0	0	0	0	0	0	0	0	0	0	0
31C	0	0	0	0	0	0	0	0	0	0	0	0
32C	0	0	0	0	0	0	0	0	0	0	0	0
33C	0	Discontinued										
34C	0	0	0	0	0	0	0	0	0	0	0	0
35C	0	0	0	0	0	0	0	0	0	0	0	0
36C	0	0	0	0	0	0	0	0	0	0	0	0
37C	0	0	0	0	0	0	0	0	0	0	0	0
38C	0	0	0	0	0	0	0	0	0	0	0	0
39C	0	0	0	0	0	0	0	0	0	0	0	0
40C	0	0	0	0	0	0	0	0	0	0	0	0
41C	0	0	0	0	0	0	0	0	0	0	0	0
42C	0	0	0	0	0	0	0	0	0	0	0	0
43C	0	0	0	0	0	0	0	0	0	0	0	0
44C	0	0	0	0	0	0	0	0	0	0	0	0
45C	0	0	0	0	0	0	0	0	0	0	0	0
46C	0	0	0	0	0	0	0	0	0	0	0	0
47C	0	0	0	0	0	0	0	0	0	0	0	0
48C	0	0	0	0	0	0	0	0	0	0	0	0
49C	0	0	0	0	0	0	0	0	0	0	0	0
50C	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
51C	0	0	0	0	0	0	0	0	0	0	0	0
52C	0	0	0	0	0	0	0	0	0	0	0	0
53C	0	0	0	0	0	0	0	0	0	0	0	0
54C	0	0	0	0	0	0	0	0	0	0	0	0
55C	0	0	0	0	0	0	0	0	0	0	0	0
56C	0	0	0	0	0	0	0	0	0	0	0	0
57C	0	0	0	0	0	0	0	0	0	0	0	0
58C	0	0	0	0	0	0	0	0	0	0	0	0
59C	0	0	0	0	0	0	0	0	0	0	0	0
60C	0	0	0	Discontinued								
61C	0	0	0	0	0	0	0	0	0	0	0	0
62C	0	0	0	0	0	0	0	0	0	0	0	0
63C	0	0	0	0	0	0	0	0	0	0	0	0
64C	0	0	0	0	0	0	0	0	0	0	0	0
65C	0	0	0	0	0	0	0	0	0	0	0	0
66C	0	0	0	0	0	0	0	0	0	0	0	0
67C	0	0	0	0	0	0	0	0	0	0	0	0
68C	0	0	0	0	0	0	0	0	0	0	0	0
69C	0	0	0	0	0	0	0	0	0	0	0	0
70C	0	0	0	0	0	0	0	0	0	0	0	0
71C	0	0	0	0	0	0	0	0	0	0	0	0
72C	0	0	0	0	0	0	0	0	0	0	0	0
73C	0	0	0	0	0	0	0	0	0	0	0	0
74C	0	0	0	0	0	0	0	0	0	0	0	0
75C	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

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TABLE I
(Continued)

Summary of Dermal Scores

Test Material: [redacted] Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
76C	0	0	0	0	0	0	0	0	0	0	0	0
77C	0	0	0	0	0	0	0	0	0	0	0	0
78C	0	0	0	0	0	0	0	0	0	0	0	0
79C	0	0	0	0	0	0	0	0	0	0	0	0
80C	0	0	Discontinued									
81C	0	0	0	0	0	0	0	0	0	0	0	0
82C	0	0	0	0	0	0	0	0	0	0	0	0
83C	0	0	0	0	0	0	0	0	0	0	0	0
84C	0	0	0	0	0	0	0	0	0	0	0	0
85C	0	0	0	0	0	0	0	0	0	0	0	0
86C	0	0	0	0	0	0	0	0	0	0	0	0
87C	0	0	0	0	0	0	0	0	0	0	0	0
88C	0	0	0	0	0	0	0	0	0	0	0	0
89C	0	0	0	0	0	0	0	0	0	0	0	0
90C	0	0	Discontinued									
91C	0	0	0	0	0	0	0	0	0	0	0	0
92C	0	0	0	0	0	0	0	0	0	0	0	0
93C	0	0	0	0	0	0	0	0	0	0	0	0
94C	0	0	0	0	0	0	0	0	0	0	0	0
95C	0	0	0	0	0	0	0	0	0	0	0	0
96C	0	0	0	0	0	0	0	0	0	0	0	0
97C	0	0	0	0	0	0	0	0	0	0	0	0
98C	0	0	0	0	0	0	0	0	0	0	0	0
99C	0	0	0	0	0	0	0	0	0	0	0	0
100C	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
101C	0	0	0	0	0	0	0	0	0	0	0	0
102C	0	0	0	0	0	0	0	0	0	0	0	0
103C	0	0	0	0	0	0	0	0	0	0	0	0
104C	0	0	0	0	0	0	0	0	0	0	0	0
105C	0	0	Discontinued									
106C	0	0	0	0	0	0	0	0	0	0	0	0
107C	0	0	0	0	0	0	0	0	0	0	0	0
108C	0	0	0	0	0	0	0	0	0	0	0	0
109C	0	0	0	0	0	0	0	0	0	0	0	0
110C	0	0	0	0	0	0	0	0	0	0	0	0
111C	0	0	0	0	0	0	0	0	0	0	0	0
112C	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
1D	0	0	0	0	0	0	0	0	0	0	0	0
2D	0	0	0	0	0	0	0	0	0	0	0	0
3D	0	0	0	0	0	0	0	0	0	0	0	0
4D	0	0	0	0	0	0	0	0	0	0	0	0
5D	0	0	0	0	0	0	0	0	0	0	0	0
6D	0	0	0	0	0	0	0	0	0	0	0	0
7D	0	0	0	0	0	0	0	0	0	0	0	0
8D	0	0	0	0	0	0	0	0	0	0	0	0
9D	0	0	0	0	0	0	0	0	0	0	0	0
10D	0	0	0	0	0	0	0	0	0	0	0	0
11D	0	0	0	0	0	0	0	0	0	0	0	0
12D	0	0	0	0	0	0	0	0	0	0	0	0
13D	0	0	0	0	0	0	0	0	0	0	0	0
14D	0	0	0	0	0	0	0	0	0	0	0	0
15D	0	0	0	0	0	0	0	0	0	0	0	0
16D	0	0	0	0	0	0	0	0	0	0	0	0
17D	0	Discontinued										
18D	0	0	0	0	0	0	0	0	0	0	0	0
19D	0	0	0	0	0	0	0	0	0	0	0	0
20D	0	0	0	0	0	0	0	0	0	0	0	0
21D	0	0	0	0	0	0	0	0	0	0	0	0
22D	0	0	0	0	0	0	0	0	0	0	0	0
23D	0	0	0	0	0	0	0	0	0	0	0	0
24D	0	0	0	0	0	0	0	0	0	0	0	0
25D	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
26D	0	0	0	0	0	0	0	0	0	0	0	0
27D	0	0	0	0	0	0	0	0	0	0	0	0
28D	0	0	0	0	0	0	0	0	0	0	0	0
29D	0	0	0	0	0	0	0	0	0	0	0	0
30D	0	0	0	0	0	0	0	0	0	0	0	0
31D	0	0	Discontinued									
32D	0	0	0	0	0	0	0	0	0	0	0	0
33D	0	0	0	0	0	0	0	0	0	0	0	0
34D	0	0	0	0	0	0	0	0	0	0	0	0
35D	0	0	0	0	0	0	0	0	0	0	0	0
36D	0	0	0	0	0	0	0	0	0	0	0	0
37D	0	0	0	0	0	0	0	0	0	0	0	0
38D	0	0	0	0	0	0	0	0	0	0	0	0
39D	0	0	0	0	0	0	0	0	0	0	0	0
40D	0	0	0	0	0	0	0	0	0	0	0	0
41D	0	0	0	0	0	0	0	0	0	0	0	0
42D	0	0	0	0	0	0	0	0	0	0	0	0
43D	0	0	0	0	0	0	0	0	0	0	0	0
44D	0	0	0	0	0	0	0	0	0	0	0	0
45D	0	0	0	0	0	0	0	0	0	0	0	0
46D	0	0	0	Discontinued								
47D	0	0	0	0	0	0	0	0	0	0	0	0
48D	0	0	0	0	0	0	0	0	0	0	0	0
49D	0	0	0	0	0	0	0	0	0	0	0	0
50D	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted] Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
51D	0	0	0	0	0	0	0	0	0	0	0	0
52D	0	0	0	0	0	0	0	0	0	0	0	0
53D	0	0	0	0	0	0	0	0	0	0	0	0
54D	0	0	0	0	0	0	0	0	0	0	0	0
55D	0	0	0	0	0	0	0	0	0	0	0	0
56D	0	0	0	0	0	0	0	0	0	0	0	0
57D	0	0	0	0	0	0	0	0	0	0	0	0
58D	0	0	0	0	0	0	0	0	0	0	0	0
59D	0	Discontinued										
60D	0	0	0	0	0	0	0	0	0	0	0	0
61D	0	0	0	0	0	0	0	0	0	0	0	0
62D	0	0	0	0	0	0	0	0	0	0	0	0
63D	0	0	0	0	0	0	0	0	0	0	0	0
64D	0	0	0	0	0	0	0	0	0	0	0	0
65D	0	0	0	0	0	0	0	0	0	0	0	0
66D	0	0	0	Discontinued								
67D	0	0	0	0	0	0	0	0	0	0	0	0
68D	0	0	0	0	0	0	0	0	0	0	0	0
69D	0	0	0	0	0	0	0	0	0	0	0	0
70D	0	0	0	0	0	0	0	0	0	0	0	0
71D	0	0	0	0	0	0	0	0	0	0	0	0
72D	0	0	0	0	0	0	0	0	0	0	0	0
73D	0	0	0	0	0	0	0	0	0	0	0	0
74D	0	0	0	0	0	0	0	0	0	0	0	0
75D	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	[redacted]	Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
76D	0	0	0	0	0	0	0	0	0	0	0	0
77D	0	0	0	0	0	0	0	0	0	0	0	0
78D	0	0	0	0	0	0	0	0	0	0	0	0
79D	0	0	0	0	0	0	0	0	0	0	0	0
80D	0	0	0	0	0	0	0	0	0	0	0	0
81D	0	0	0	0	0	0	0	0	0	0	0	0
82D	0	0	0	0	0	0	0	0	0	0	0	0
83D	0	0	0	0	0	0	0	0	0	0	0	0
84D	0	0	0	Discontinued								
85D	0	0	0	0	0	0	0	0	0	0	0	0
86D	0	0	0	0	0	0	0	0	0	0	0	0
87D	0	0	0	0	0	0	0	0	0	0	0	0
88D	0	0	0	0	0	0	0	0	0	0	0	0
89D	0	0	0	0	0	0	0	0	0	0	0	0
90D	0	0	0	0	0	0	0	0	0	0	0	0
91D	0	0	0	0	0	0	0	0	0	0	0	0
92D	0	0	0	0	0	0	0	0	0	0	0	0
93D	0	0	0	0	0	0	0	0	0	0	0	0
94D	0	0	0	0	0	0	0	0	0	0	0	0
95D	0	0	0	0	0	0	0	0	0	0	0	0
96D	0	0	0	0	0	0	0	0	0	0	0	0
97D	0	0	0	0	0	0	0	0	0	0	0	0
98D	0	0	0	0	0	0	0	0	0	0	0	0
99D	0	0	0	0	0	0	0	0	0	0	0	0
100D	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

Clinical Research Laboratories, Inc.

TABLE I
(Continued)

Summary of Dermal Scores

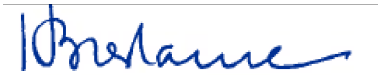
Test Material:	[redacted] Eye Cream

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
101D	0	0	0	0	0	0	0	0	0	0	0	0
102D	0	0	0	0	0	0	0	0	0	0	0	0
103D	0	0	0	0	0	0	0	0	0	0	0	0
104D	0	0	0	0	0	0	0	0	0	0	0	0
105D	0	0	0	0	0	0	0	0	0	0	0	0
106D	0	0	0	0	0	0	0	0	0	0	0	0
107D	0	0	0	0	0	0	0	0	0	0	0	0
108D	0	0	0	0	0	0	0	0	0	0	0	0
109D	0	0	0	0	0	0	0	0	0	0	0	0
110D	0	0	0	0	0	0	0	0	0	0	0	0
111D	0	0	0	0	0	0	0	0	0	0	0	0
112D	0	0	0	0	0	0	0	0	0	0	0	0

Personal Care Products Council
Committed to Safety, Quality & Innovation

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

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



DATE: January 31, 2014

SUBJECT: Updated Concentration of Use information for *Camellia sinensis*-Derived Ingredients

Concentration of Use by FDA Product Category - *Camellia sinensis*-Derived Ingredients

Camellia Sinensis Catechins
Camellia Sinensis Flower Extract
Camellia Sinensis Flower/Leaf/Stem Juice
Camellia Sinensis Leaf
Camellia Sinensis Root Extract
Camellia Sinensis Seedcoat Powder
Camellia Sinensis Seed Extract
Camellia Sinensis Seed Oil
Camellia Sinensis Leaf Extract
Camellia Sinensis Leaf Oil
Camellia Sinensis Leaf Powder
Camellia Sinensis Leaf Water
Camellia Sinensis Seed Powder
Hydrolyzed Camellia Sinensis Leaf
Hydrolyzed Camellia Sinensis Seed Extract

Ingredient	**FDA Code†**	**Product Category**	**Maximum Concentration of Use**
Camellia Sinensis Leaf	02A	Bath oils, tablets and salts	0.05%
Camellia Sinensis Leaf Extract	02A	Bath oils, tablets and salts	0.0001%
Camellia Sinensis Leaf Extract	02B	Bubble baths	0.005-0.1%
Camellia Sinensis Leaf Extract	03B	Eye liner	0.1%
Camellia Sinensis Leaf Extract	03C	Eye shadow	0.005%
Camellia Sinensis Leaf Extract	03D	Eye lotion	0.001-0.87%
Camellia Sinensis Leaf Extract	03E	Eye makeup remover	0.00002-0.01%
Camellia Sinensis Leaf Extract	03F	Mascara	0.0007-0.005%
Camellia Sinensis Leaf Extract	03G	Other eye makeup preparations	0.02-0.2%
Camellia Sinensis Leaf Extract	04A	Colognes and toilet waters	0.0004-0.0055%
Camellia Sinensis Leaf Extract	04B	Perfumes	0.0001-0.005%
Camellia Sinensis Leaf Extract	04C	Powders (dusting and talcum)	0.0037%
Camellia Sinensis Leaf Extract	05A	Hair conditioners	0.000055-0.0063%
Camellia Sinensis Leaf Extract	05B	Hair sprays pump spray	 0.0005%
Camellia Sinensis Leaf Extract	05D	Permanent waves	0.00023%
Camellia Sinensis Leaf Extract	05E	Rinses (noncoloring)	0.0003%
Camellia Sinensis Leaf Extract	05F	Shampoos (noncoloring)	0.000055-0.0055%
Camellia Sinensis Leaf Extract	05G	Tonics, dressings and other hair grooming aids	0.0004-0.005%
Camellia Sinensis Leaf Extract	05I	Other hair preparations (noncoloring)	0.005-0.0063%
Camellia Sinensis Leaf Extract	06A	Hair dyes and colors (all types requiring caution statement and patch test)	0.003%
Camellia Sinensis Leaf Extract	06F	Hair lighteners with color	0.006%

Camellia Sinensis Leaf Extract	07A	Blushers (all types)	0.0002-0.02%
Camellia Sinensis Leaf Extract	07B	Face powders	0.0003-0.001%
Camellia Sinensis Leaf Extract	07C	Foundations	0.0003-0.05%
Camellia Sinensis Leaf Extract	07E	Lipstick	0.001-0.01%
Camellia Sinensis Leaf Extract	07F	Makeup bases	0.00011-0.005%
Camellia Sinensis Leaf Extract	07H	Makeup fixatives	0.01%
Camellia Sinensis Leaf Extract	08A	Basecoats and undercoats (manicuring preparations)	0.00002%
Camellia Sinensis Leaf Extract	08B	Cuticle softeners	0.01-0.092%
Camellia Sinensis Leaf Extract	08E	Nail polish and enamel	0.00014%
Camellia Sinensis Leaf Extract	08G	Other manicuring preparations	0.005-0.53%
Camellia Sinensis Leaf Extract	09A	Dentifrices (aerosol, liquid, pastes and powders)	0.01%
Camellia Sinensis Leaf Extract	09C	Other oral hygiene products	0.14%[b]
Camellia Sinensis Leaf Extract	10A	Bath soaps and detergents	0.003-1%
Camellia Sinensis Leaf Extract	10B	Deodorants not spray pump spray	 0.0055-0.023% 0.0055%
Camellia Sinensis Leaf Extract	10E	Other personal cleanliness products	0.0005-0.0055%
Camellia Sinensis Leaf Extract	11A	Aftershave lotions	0.0006-0.01%
Camellia Sinensis Leaf Extract	11D	Preshave lotions (all types)	0.01%
Camellia Sinensis Leaf Extract	11E	Shaving cream (aerosol, brushless and lather)	0.00006-0.01%
Camellia Sinensis Leaf Extract	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0006-0.44%
Camellia Sinensis Leaf Extract	12B	Depilatories	0.03%
Camellia Sinensis Leaf Extract	12C	Face and neck products not spray	 0.0001-2%
Camellia Sinensis Leaf Extract	12D	Body and hand products not spray spray	 0.00008-1% 0.0005%
Camellia Sinensis Leaf Extract	12E	Food powders and sprays spray	 0.22%

Camellia Sinensis Leaf Extract	12F	Moisturizing products not spray	 0.0007-0.5%
Camellia Sinensis Leaf Extract	12G	Night products not spray	 0.001-0.02%
Camellia Sinensis Leaf Extract	12H	Pastes masks and mud packs	0.001-0.1%
Camellia Sinensis Leaf Extract	12J	Other skin care preparations	0.002-0.87%
Camellia Sinensis Leaf Extract	13A	Suntan products not spray pump spray	 0.18-0.2% 0.07%
Camellia Sinensis Leaf Extract	13B	Indoor tanning preparations	0.001%
Camellia Sinensis Leaf Powder	03F	Mascara	0.3%
Camellia Sinensis Leaf Powder	10A	Bath soaps and detergents	0.01%
Camellia Sinensis Leaf Powder	12C	Face and neck products not spray	 0.015-50%[c]
Camellia Sinensis Leaf Powder	12D	Body and hand products not spray	 0.005-7%
Camellia Sinensis Leaf Water	03F	Mascara	30%
Camellia Sinensis Seed Extract	07C	Foundations	0.001%
Camellia Sinensis Seed Extract	10A	Bath soaps and detergents	0.0013%
Camellia Sinensis Seed Extract	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.001%
Camellia Sinensis Seed Extract	12F	Moisturizing creams, lotions and powders	0.1%
Camellia Sinensis Seed Extract	12H	Paste masks and mud packs	0.001%
Camellia Sinensis Seed Oil	05A	Hair conditioners	0.001%
Camellia Sinensis Seed Oil	05F	Shampoos (noncoloring)	0.001%
Camellia Sinensis Seed Oil	10E	Other personal cleanliness products	1%
Camellia Sinensis Seed Oil	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.01%
Camellia Sinensis Seed Oil	12C	Face and neck products not spray	 0.01%
Camellia Sinensis Seed Oil	12D	Body and hand products not spray	 0.01%

*Ingredients included in the title of the table but not found in the table were included in the concentration

of use survey, but no uses were reported.
†Product category codes used by FDA

[b]Ingestible
[c]Product containing 50% Camellia Sinensis Leaf Powder is a professional product that is diluted with water before use

Information collected in 2013
Table prepared: May 31, 2013
Updated January 16, 2014 - deleted 97% Camellia Sinensis Leaf Product, no longer being sold
Updated January 31, 2014 - Camellia Sinensis Leaf Extract high concentration for Aftershave changed from 0.99% to 0.01%; high concentration of body and hand products changed from 3% to 1%