GREEN

Safety Assessment of Tin Oxide as Used in Cosmetics

CIR EXPERT PANEL MEETING

SEPTEMBER 10-11, 2012

Cosmetic Ingredient Review
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August 16, 2012

Memorandum

To: CIR Expert Panel

From: Wilbur Johnson, Jr.
Manager/Lead Specialist

Subject: Draft Report on Tin and Tin Oxide

Per Team/Panel discussions at the June 11-12, 2012 Expert Panel meeting, the draft report was tabled to better focus on the form of tin used in cosmetics. The Panel suggested the removal of metallic tin from the safety assessment and a confirmation of the oxidation state of tin oxide tested in some of the studies. Accordingly, the draft report was revised in response to this decision, and to include data received from the Council since the June Panel meeting. Included for your review is the draft report, the CIR report history, Literature search strategy, Ingredient Data profile, 2012 FDA VCRP data, and minutes from the June 2012 Panel meeting. The unpublished data included with this report are:

1. Human skin irritation/sensitization data submitted on 7-2-2012 (data1 pdf file);
2. In vitro assay data, evaluating ocular irritation potential, submitted on 7-2-2012 (data 1 pdf file)
3. Updated use concentration data submitted on 7-2-2012 (data2 pdf file)

After reviewing the draft report, the Expert Panel needs to determine whether additional data are needed for completion of this safety assessment, or if the available data are sufficient for arriving at a conclusion on the safety of tin and tin oxide used in cosmetic products.

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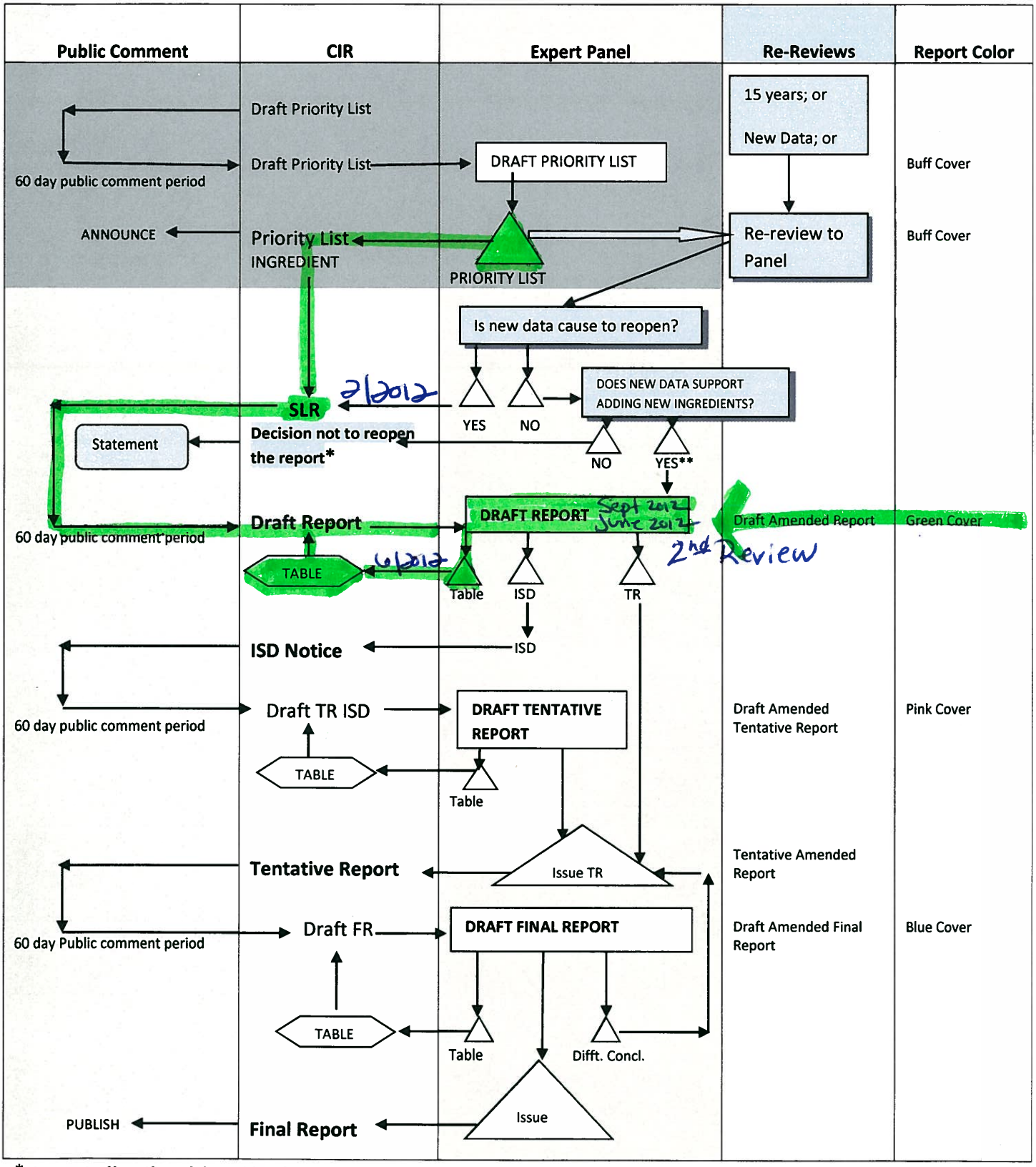
Titanium Dioxide

SAFETY ASSESSMENT FLOW CHART

Sept 2012



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

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

△ Expert Panel Decision

▭ Document for Panel Review

⇨ Option for Re-review

CIR History of:

Tin and Tin Oxide

A Scientific Literature Review (SLR) on these ingredients was issued in February of 2012. Use concentration and safety test data received from the Council were incorporated prior to announcement of the SLR.

1st Review, Belsito and Marks Teams/Panel: June 11-12, 2012

The following data on tin oxide (included in draft report) were received from the Council prior to announcement of the SLR: (1) RIPT on an eye shadow (0.3% tin oxide); (2) ophthalmological in-use safety evaluation of an eye shadow (0.3% tin oxide); (3) RIPT on a lipstick (0.5% tin oxide); RIPT on a lipgloss (0.35% tin oxide); and use concentration data on tin oxide.

2nd Review, Belsito and Marks Teams/Panel: September 10-11, 2012

Per Team/Panel discussions at the June 11-12, 2012 Expert Panel meeting, the draft report was tabled, pending removal of metallic tin from the safety assessment and efforts to confirm the oxidation state of tin oxide tested in some of the studies. Accordingly, the draft report was revised to reflect this decision, and, also, the following data received from the Council since the June Panel meeting have been included: (1) human RIPT data on an eye shadow containing 1.3% tin oxide and (2) in vitro assays evaluating the ocular irritation potential of an eye shadow containing 1.11% tin oxide. The report also contains a draft discussion for the Panel's review.

Tin Oxide Check List for September, 2012. Analyst – Wilbur Johnson																			
			Acute toxicity					Repeated dose toxicity				Irritation			Sensitization				
	Skin Penetration	Penetration Enhancement	ADME	Oral	Parenteral	Dermal	Inhale	Oral	Parenteral	Dermal	Inhale	Ocular Irritation	Dermal Irr. Animal	Dermal Irr Human	Sensitization Animal	Sensitization Human	Repro/Devel toxicity	Genotoxicity	Carcinogenicity	Phototoxicity
Tin Oxide								X			X	X		X		X		X		

Literature Search on Tin and Tin Oxide*

Ingredients	Toxline &PubMed	ChemIDplus	Multidatabase (See legend*)	DART	SciFinder	RTECS
Tin	2920	1	3	18	127,283	
Tin Oxide	1962	1	1	6	37,151	

*Data in Table: Publications found; Multidatabase = HSDB, CCRIS, ITER, IRIS, Gene-Tox, and LacMed

Searches Performed on12/22/2011
Search Performed on 2/24/2012
Search updated on 7/29/2012

Ingredients/Search Terms

Tin Oxide
Tin Dioxide
18282-10-5
1332-29-2

Tin
7440-31-5

Search Strings (NLM databases)

Tin Oxide OR Tin Dioxide OR 18282-10-5 OR 1332-29-2
Tin OR 7440-31-5

SciFinder Search Terms

18282-10-5
7440-31-5

Transcript

Day 1 of the June 11-12, 2012 CIR Expert Panel Meeting – Dr. Marks' Team

Tin (IV) Oxide and Tin

Tin oxide and tin. This is the first time we've seen this draft report on these ingredients, first time we've looked at these ingredients, and so the first question is, do we need any data? Or can we move forward with a safe conclusion?

Tom, Ron, from your perspective?

DR. SHANK: I don't have any data needs for tin oxide. For tin itself we may need sensitization data.

DR. MARKS: Yeah.

DR. SHANK: But it's not used, so maybe it would be -- could be considered just to drop it from the report.

MR. HILL: Yeah, and just a general question while we're thinking about it, really directly related to that is, we have a bunch of toxicology data in here for stanus fluoride, stanus chloride, stanus -- what was the citrate, I think it was? Where there was high solubility and availability and so forth. And I wondered if any of that was really relevant? I mean, do we have any information that suggests that anything that bio-available could be generated from tin oxide because we -- I don't guess we could throw this data out, but yet we need to cast it in such a way that this is really not very relevant to tin oxide, or tin metal, for that matter.

MR. JOHNSON: Even though we don't have our IPT data on tin, there's an allergenicity section on page 7, so there's limited data relating to the allergenicity of metallic tin powder.

DR. MARKS: One of the problems I had, Ron, going back to the skin is that the RIPT for tin oxide was at.5 percent, 0.5 percent. That was fine, that's on page 7 or Panel Book page 13. But then when I look, it's used up to 5 percent in a leave-on product. So, I would actually feel that we have insufficient sensitization data and we need an RIPT for 5 percent if we're going to say in the present use and concentration.

DR. SHANK: Good point.

DR. MARKS: So, I would put that as an insufficient, at least for that. And then the question is, are there other things -- particularly I think you were hitting onto that, Ron, as the metabolic fade of tin and/or tin oxide when applied to the skin. Did you have any concerns?

MR. HILL: I don't have any concerns at all. So, I guess my thinking is, I mean, even it's in a lipstick or something. The amount of tin we're talking about is just not in an available form. I think people are putting metallic tin in there to put tin oxide -- I don't think it's going to be converted to tin chloride or anything soluble in the gut. I am pretty sure it just passes through.

DR. SLAGA: Or if you put it on the skin --

MR. HILL: Or it should -- yeah, I mean, I think nothing will happen to it. Even if I'm sweating profusely, I don't think anything will happen to that tin oxide. I don't think it will be absorbed, I don't think it will go anywhere where it would cause -- but, you know, there's not all that much information about it here, but we have a lot -- about any of that, but then we have a lot of toxicology for stanus citrate, stanic citrate, stanic chloride, things I'm not sure there's much relevant at all.

Certainly have to somehow capture that, but we need to be clear that it's probably not relevant somehow.

DR. ANDERSEN: I think on -- actually, there is an opportunity at this stage. I mean, this is the first time you're seeing this report, and arguably when we put together the scientific literature review we grabbed onto a lot of data. And if those data really don't inform the decision, I'm not sure I have a problem with you suggesting that they be taken out.

I mean, let's focus this on the data that are really relevant. If that makes it shorter, so be it. At Stage 1 when we're just pulling it all together, we would almost always err on the side of being inclusive, but you have the opportunity now to say, you know, as Ron has said that doesn't really inform the decision. So, take it out.

MR. HILL: Unless we have some piece of information that causes us to believe that that tin oxide in any process of formulating finished cosmetic product or in any process on the

skin or mucous membranes or, you know, in any way is likely to be converted to something bioavailable, then it doesn't seem very relevant. I've never heard of such a thing, but.

MR. STEINBERG: Tin oxide is in use. In fact, I think it's almost its only use is as a pacifying agent. And if it's converted to anything inside, it's no longer a pacifying agent. So, basically it's formulated to stay in the tin oxide form.

MR. HILL: I think actually there's fairly vigorous chemistry that's required to get it out of that form and into something more bioavailable. That was my point. Just sitting there in heavy sweat wouldn't do it, anything I could think of in terms of putting that into a finished cosmetic formulation, I can't envision that happening.

MR. ANSELL: So, how would that inform the RIPT? It's only use -- the HRIPT at half-percent with a use concentration in an eye shadow at 5 percent if the material really isn't soluble or convertible? Would we feel that repeating the HRIPT would be needed?

MR. HILL: I don't know enough about the potential mechanisms by which such a substance could cause sensitization, to answer that question myself. I personally think we wouldn't see anything, but.

DR. MARKS: It has to be, obviously, absorbed in the skin.

DR. SHANK: It would not.

DR. MARKS: So the point is, we have -- theoretically it shouldn't be absorbed? Do you --

MR. HILL: I think that's probably true, and I kind of doubt we'd need the RIPT --

DR. SHANK: Okay, I think --

MR. HILL: But we have to explain in the discussion why we don't think we need it.

DR. MARKS: Okay.

MR. HILL: And Don may have another answer.

DR. MARKS: Okay, so with that in mind -- thank you, Jake, for bringing -- and to Ron. So, if it's not absorbed we shouldn't need the sensitivity, exactly. Though it's interesting when you look at the patch testing with tin alone on a coating, that gave positive patch test at 100 percent. So, is that reassuring or not? That's back on page --

DR. SHANK: Seven.

DR. MARKS: Yeah, page 7 or page 13 of the Panel Book. If you look under tin, there's an interesting -- they had positive -- now, they took nickel-sensitive individuals, so they were metal-sensitive. So, as a sub-set of individuals already sensitive to nickel, they took these discs that were plated with tin and positive reactions were seen in six, and presumably that was to the tin and not to the copper disc that it was coated on.

So, is that?

MR. HILL: But tin is not used -- tin metal is not used as a cosmetic ingredient.

DR. MARKS: No, but I'm talking about the absorptions.

MR. HILL: I mean, it's there but it's --

DR. MARKS: Somehow the tin got from that coating into the skin and caused the allergy. So, you know, do we still feel comfortable.

MR. ANSELL: Tin is more reactive?

DR. MARKS: I don't know. So, we still feel comfortable that tin oxide would not be absorbed? Do we have data in here?

DR. SLAGA: There's no data for absorption.

DR. MARKS: Right.

DR. SLAGA: I mean, we can ask for it because it would not be absorbed.

DR. MARKS: It would not be absorbed, okay.

MR. HILL: There's probably more known about the nickel sensitivity mechanism, and we have a doubt of the sensitivity of nickel -- the reaction to nickel stables, but you know.

DR. MARKS: Okay, so it --

MR. HILL: But my point is, something happens different with the metal, it's probably getting conjugated to thioles or something like that, resulting in sensitization. But if the metal is not being used as an ingredient in anything, then I don't think any of that's applicable to

tin oxide because I think once it's in the oxide state it's stable.

DR. MARKS: Okay, so we would move safe to mark? So we would issue a draft tentative report with a conclusion of safe. And it can be handled in the discussion that even though the RIPT that we have is not up to 5 percent, that the tin oxide is not absorbed. That would be under the discussion. Therefore, would not cause sensitivity. Plus, it wouldn't cause a lot of other toxic affects, would it?

MR. ANSELL: So you're basing that on the molecular weight? Why that would not be absorbed? Is that?

MR. HILL: Tin oxide is so insoluble as to be -- I mean, and even if it were to dissolve, it just wouldn't penetrate the skin. Even damp skin, it wouldn't go anywhere.

DR. SLAGA: Lesions of some sort.

DR. MARKS: Okay.

MR. HILL: The only question I have before we escape all of this is, there are no reported uses for tin in cosmetics, but yet tin is in the Cosmetic Ingredient Dictionary. I mean, why is that? I guess is what I'm asking, because I'm not sure the conclusion is --

DR. LORETZ: The same reason there's so many others in there.

MR. HILL: Yeah, okay.

SPEAKER: Someone applied for it.

DR. LORETZ: Yeah, somebody once upon a time wanted to name.

MR. HILL: So if we say safe in current manner of use and there are no uses of tin, are we covered? I guess that's what I'm asking. Because there could be sensitivity to tin, metal, I think.

DR. MARKS: That's shown.

MR. HILL: Yeah.

DR. MARKS: We presume it was the tin, not the copper. Okay, well, since it's not being used that's -- and we won't get into why it's in -- as you already stated, there are a number of ingredients. It sounds like the process, somebody applies for it included in the dictionary and then it gets included.

MR. ANSELL: That's it. There's no safety criteria. It's purely identification.

MR. HILL: Yeah.

MR. ANSELL: Whether it ever gets used or not is really beside the point.

And let me point out that I think apropos of also the botanical discussion this morning, these reports are always -- the conclusion is always predicated on the report itself. You can't separate that conclusion from the entire report, so it's always safe as used.

MR. HILL: I know. I mean, just in practicality -- and we talked about practicality when we did Brazilian blow- out -- is that practicality, given that there are mom and pop cosmetic companies out there. You know, I mean, it's incumbent upon them to know what you just said. But on the flip side, do we have the language in the discussion and conclusions to make sure that they realize that? I guess is the best way of putting that. Because a lot -- yeah. If they just read the discussion and conclusion, or maybe even get only the conclusion, you know, is it clear to them? Or do we -- you know, that's all I ask. And the kinds of education initiatives that Halyna was talking about to me, that would increasingly help them.

MR. ANSELL: Yeah. There's three fundamental parts and they can't be separated. You can't take the CIR and remove from it manufacturer responsibility. You can't --

MR. HILL: No, in fact that's fundamental to the whole thing, right? I mean --

MR. ANSELL: And FDA enforcement.

MR. HILL: Yeah.

MR. ANSELL: So, you know, the three parts all fit to make a kind of total quality system.

MR. HILL: And I agree with the FDA enforcement. It's just that you'd like it not to have to be from bad events, you know, after the fact as much as possible.

MR. ANSELL: Right. So, that's where.

DR. SHANK: Let me make sure I understand. We're not saying elemental tin is safe as used, but it isn't used. That's why it's safe? (Laughter) I don't care for that.

I would either say, insufficient for tin and you need sensitization data, or take it out of the report altogether..

MR. HILL: What about just taking it out of the report altogether, given that it's not being used? Alan?

DR. ANDERSEN: It cuts the productivity for this report in half. (Laughter) But --

MR. HILL: I don't care about that. (Laughter)

DR. ANDERSEN: I'm not sure I can figure out a way to craft the conclusion so that Ron's comments that the emperor appears to have no clothes can be avoided.

I could argue that we do ingredients that are not in current use all the time, and we put the caveat that says, oh, by the way for those that aren't in use we would expect their use to be similar to the others in the group.

Now in that case, that would say for tin it would be used at levels no greater than 5 percent in leave-on cosmetics. Would you be comfortable if tin appeared at 5 percent in leave-on cosmetics? If not, then I think taking it out or saying insufficient is where to go. I'm not sure I care which, but since it's not in use, taking it out would seem to be a perfectly reasonable approach.

MR. ANSELL: If the data on tin in here we feel is insufficient, I mean --

MR. HILL: Look, basically --

MR. ANSELL: We kind of blew through all the tin data saying it's not relevant. Well, maybe we need to go back and look at all the tin data again. You know, because there is.

MR. HILL: Well, there's data for metallic tin, which is what Dr. Marks was talking about, and then there's data for a lot of tin salts that are highly soluble. The ones that I was arguing were not relevant were the highly soluble tin salts where we administer them orally and we get a good bit of absorption and we see accumulation in bone, et cetera, et cetera. I'm saying that's basically not relevant to tin oxide in cosmetic use.

DR. ANDERSEN: I think the question here is, can we use the pattern of use of tin oxide to cover a potential pattern of use for tin, which is vague and uncertain because it's not in current use? And I'm sensing some discomfort with doing that, so I would take tin out.

DR. SLAGA: I agree.

DR. ANDERSEN: Now, since we're going to have to write a discussion of all of this, that that issue doesn't really bother me. But there's another issue in here that you haven't talked about that is of concern, and that is pneumoconiosis. Tin oxide is clearly linked if it's inhaled at high levels.

MR. ANSELL: Occupational.

DR. ANDERSEN: But I think you need to tell me that you're comfortable or tell Wilbur that you're comfortable with the unlikelihood of exposures from cosmetic use that would lead to the kind of inhalation toxicity that is of concern for pneumoconiosis. So, I think it's pretty obvious, but I want you to say it.

DR. MARKS: Ron? Sound good?

DR. SHANK: And with that, least importantly? Because there are inhalation in uses -- not inhalation uses, potential inhalation exposures.

MR. HILL: It was pointed out to me and I will relay it that it wouldn't function as an opacifier if the particle size were so small as to allow for appreciable inhalation.

DR. SHANK: That's right.

MR. HILL: But definitely the discussion is going to capture that, yes --

DR. MARKS: The inhalation boilerplate would cover this. Is that -- Ron?

MR. HILL: But I think you have to mention that specific issue and then explain why it's not of concern to us.

DR. ANDERSEN: Thank you.

DR. MARKS: And that was which page of the Panel Book?

DR. ANDERSEN: The data are on -- primarily on page --

MR. HILL: Panel Book page 14.

DR. MARKS: Fourteen. Okay, so tomorrow I'm going to move that we issue a draft tentative report for tin oxide. That it's safe as used, and when presumably that's seconded and during the discussion phase I'll mention that we should have the inhalation boilerplate included in the discussion to cover the issue of pneumoconiosis.

Any other comments?

MR. JOHNSON: Yes, Dr. Marks. Before in terms of the accounting of the discussion, you had said that even though the RIPT data are not up to 5 percent --

DR. MARKS: Right, that'll be the second discussion.

MR. JOHNSON: That'll be in there also?

DR. MARKS: Tin oxide is not absorbed, it's not soluble so we don't need an RIPT up to 5 percent use concentration.

MR. JOHNSON: Okay.

DR. MARKS: Thanks, Wilbur.

MR. JOHNSON: Okay. You're welcome.

DR. MARKS: Any other comments about tin oxide, since we're deleting tin? None? Okay. Let's move on to chlorphenesin. It's Green Book, also. This is also --

MR. HILL: Big Green Book.

DR. MARKS: A substantial Green Book, and that's not even -- don't have way too many in here, so we'll see if we have it. There are lots of uses --

MR. JOHNSON: Excuse me, Dr. Marks, before we conclude with tin oxide. We did receive some Wave 2 data on tin oxide, so I just want to confirm that you want those data incorporated into the safety assessment. We just have acute orotox, acute parental toxicity data, and additional data relating to non-cosmetic use. All on tin oxide.

DR. MARKS: That seems certainly to be relevant.

MR. HILL: I was going to say, why would we not put it in?

DR. MARKS: Yes.

Day 1 of the June 11-12, 2012 CIR Expert Panel Meeting – Dr. Belsito's Team

Tin (IV) Oxide and Tin

DR. BELSITO: Right. Okay. Tin oxide and tin. It's so funny that she mentioned tin in her presentation this morning, which incidentally was a great presentation. I would have liked to -- I almost wanted to ask her what do you know about tin that I don't know? But I figured you'd all tell me when we got to this report.

So this is the first time we're seeing this. And it's two ingredients -- tin and tin oxide. We've got some data and we need to decide where we are with this. We also got some Wave 2 data with acute oral and parental toxicity, a memorandum from the FDA. I mean, overall, when I looked at this I thought it was okay except that it's used around the eye at 5 percent and I had no data to support the safety in terms of irritation of tin when it was used at that amount around the eye area, particularly since it's tin oxide. And I don't know a lot about tin oxide, but things like zinc oxide, titanium oxide oftentimes are more irritating than other things compounded with those metals. So I thought it was insufficient for irritation at -- tin oxide, the irritation at 5 percent. But otherwise, I was happy with the data.

DR. LIEBLER: Okay. This is one I had a lot of problems with and I think it has to do with there really were two issues. The first is I'm not sure why tin is in this because there are no uses for it. So there's only uses listed for tin oxide. And tin itself, it could have -- if there uses and if we were to review it, then we've got a problem because I don't think we have any data for the form of tin that would be used in a cosmetic product if it were used in a cosmetic product. And we do have some data that Wilbur found for carcinogenicity where they looked at pieces of tin foil implanted. They had little cylinders of pure tin or little pieces of tin needs and so on. None of those I'm sure are the form that tin would be used in a cosmetic product. If it were to be used it would probably be some kind of powder, but I would suspect based on what's known about the chemistry of tin that if it was made into a powder it would be too susceptible to oxidation and therefore would be too unstable to be used successfully in a cosmetic product. So I have a feeling that tin is not -- tin itself is probably not reviewable and there may be a lot of practical reasons why it's not used. I'm not sure if it's in the dictionary, why it's in the dictionary, but that's nothing I can do anything about. But I think it may not be reviewable for us. Tin oxide is reviewable.

And that gets to my second problem, which is that the different types of -- this is typical of inorganic materials. There's a term called speciation which has to do with the oxidation state and the other atoms that are present in the compound. So, you know, there's tin(II), there's tin(IV), the two oxidation states that you described in the report. And you can have tin(II) oxide, SnO, and tin(IV) oxide, which is SnO2. And it's the latter that's used as a cosmetic ingredient.

Nevertheless, there are data cited in the report for tin oxide, as well as -- tin(II) oxide, as well as tin(IV) oxide. I think that tin(II) oxide cannot be considered equivalent chemically or biologically to tin(IV) oxide. So the data that you would have for tin(II) oxide is probably not relevant. It's arguably irrelevant. And the same can be said for the compound they have the most data for in the entire repot, which is tin(II) chloride. And tin(II) chloride is one of the most stable commonly used forms of tin. It's not used as a cosmetic ingredient, but it's well studied and it is encountered in other contexts, which is why you've got a lot of data for it. But I think it's not possible to justify that as a surrogate for the effects of tin(IV) in tin(IV) oxide.

So, essentially, the issue of speciation is really important here, and it's unusually important in inorganic materials. Another great example of speciation really driving the biology and toxicology is with arsenic. Now, I'm not suggesting that arsenic and tin are nearly equivalent in toxicity, but arsenate, which is the +5 oxidation state of arsenic is relatively less toxic than arsenite, which is the +3 oxidation state. And, you know, there is evidence in the body that those can be interconverted, or at least arsenite can be oxidized to arsenate. We don't really know about the tins but the issue here is tin(IV). And I think if you took out all the things that aren't tin(IV), you would have actually very little data. Most of the data that you would be left with are data that suggest that tin(IV) is safe as used. But this report has a lot of incidences, spots in it where I flagged it. It simply says tin oxide and you can't tell if it's tin(II) or tin(IV). And it might not even be possible to tell from the original source literature that you reviewed, but you might need to go

back and double-check those. I think the tin(II) chloride data is not relevant. The tin data is not relevant to tin oxide. And the SNO, the tin(II) oxide data is not relevant to tin(IV) oxide.

So I'm not sure what you need to do. My suggestion is that you might need to table this report to go back and get this onto a single chemical species to evaluate because I don't think there's any other compound that's an appropriate surrogate for tin(IV) oxide other than tin(IV) oxide. And I don't know if it's possible, but I would suggest that we delete tin from this report.

DR. BELSITO: Yes, I would largely agree with the tin oxide. One of the tins that there has been some work on is actually tin fluoride because that's what stannous fluoride and stannic fluoride is that you brush your teeth with. But that's different form this. So I basically agree that we need to cut this down just to this one compound.

DR. SNYDER: So what were you thinking -- your impression is in those datasets you'll be able to pull out what is actually reflected in what was actually studied regarding the form of tin in these particular studies?

MR. JOHNSON: For studies in which tin oxide was tested, I can basically go back to the original publication and determine whether or not the oxidation state, you know, was specified.

DR. SNYDER: Because I'm particularly interested in the absorption data because it just says tin. And so I had already found this to be insufficient for irritation data at 5 percent but it sounds like at this point probably the better part of valor is to table it and get rid of all the data that cannot be verified as SN204.

DR. LIEBLER: SM204.

DR. BELSITO: Which is the valence that's used in cosmetics.

DR. LIEBLER: That's right. SM204 is correct.

DR. BELSITO: And let us look at what's left when it's just SN204 or if it's just labeled as tin oxide.

DR. LIEBLER: Sorry, it's not SM204; it's SnO2.

DR. BELSITO: SnO2.

DR. LIEBLER: SnO2, which is tin(IV).

DR. BELSITO: Okay. SnO2 and if it's just labeled as tin oxide, perhaps we can put those studies in but indicate that we don't know the valency of the tin in those cases. Is that fair or what?

DR. LIEBLER: I would be okay with leaving those in, but they need to be clearly labeled.

DR. BELSITO: Right. So labeled as to when it's SnO2 and tin oxide unknown.

DR. LIEBLER: Right.

DR. BELSITO: But if it's SN0, we don't want it in there.

DR. LIEBLER: Right.

DR. BELSITO: And if it's just tin, we don't want it in there.

DR. LIEBLER: Right. So I'd recommend we delete tin itself.

DR. BELSITO: Okay.

DR. LIEBLER: Tin metal.

DR. BELSITO: So our recommendations are delete tin metal. Table, get rid of what is not SnO2 or what is -- get rid of what clearly is tin and SN0 and label clearly what is SnO2 and SN0 valency unknown and separate those out and let us look at what we have because there may be insufficiencies beyond irritation at that point.

DR. LIEBLER: Right. This is just an area where we really can't do read-across with these inorganic species. They're really different and hard to predict.

Day 2 of the June 11-12, 2012 CIR Expert Panel Meeting – Full Panel

Tin (IV) Oxide and Tin

DR. BERGFELD: Then moving on to the next green document which is the tin oxide and tin. Dr. Marks?

DR. MARKS: This is the draft report we reviewed. It's the first time we've seen these two cosmetic ingredients tin and tin oxide. The first thing that our team felt is we wanted to delete tin from this report and have the report focus on tin oxide. We felt tin oxide was safe as used and moved to issue a tentative report with that conclusion safe as used for tin oxide.

DR. BERGFELD: That's a motion. Is there a second or discussion?

DR. BELSITO: Discussion, and I'll let Dan lead this. We agreed to delete tin and the question was the valiancy of the tin oxide that was used in cosmetic products, and I'll let Dan further elaborate.

DR. LIEBLER: We totally agreed about tin, and with tin oxide and with the other forms of tin that were cited in the report for safety data, the issue is one of speciation for inorganics, the oxidation state and substituents for the tin. The cosmetic ingredient is tin(IV) oxide (SnO_2). In some cases, SnO tin(II) oxide was cited, in other cases, tin chloride $SnCl_2$ was cited. Unlike many organics that we consider, we felt that the concept of read across is dicey at best with these inorganics because they can have significantly different effects. It wasn't clear in the report the speciation of some of the forms of tin cited in some of the references and it might not even be clear from the source literature, although Wilbur is going to go have to go back and look. What we felt was that there is so much data that was cited in support of tin oxide, even if you throw away the tin, that it is unclear relevance because speciation isn't clear, I suggested that the report be tabled until all of that can be resolved, sift out the stuff that's not really relevant to tin(IV) oxide and then take another look at it. I don't suspect that we're going to have a problem, I think we're going to end up safe as used, but I think the supporting data at this point are kind of a mess and we just need to go back and clear that up before we can draw a conclusion.

DR. BERGFELD: Is there a motion to table?

DR. MARKS: I'll withdraw my motion to move forward with safe and certainly we can table to clear up the report. We felt that tin oxide would be safe also because it's not absorbed and it's not soluble, so other than I think housekeeping and getting the document as you suggested, Dan, I think we'll be moving forward.

DR. BERGFELD: Is there a second to table?

DR. MARKS: I'm fine with tabling. I withdraw the motion.

DR. BERGFELD: We need the motion.

DR. BELSITO: We're fine with tabling. I'd say as an FYI there was one other issue that our group had and that is it's used in an eye product at 5 percent and we were concerned about potential irritation given the reports of ocular irritation at that level so that as this gets tabled and cleared up, just a note to industry that we would like to see some data at 5 percent.

DR. BERGFELD: There has been a second to table. We need to vote. All those in favor of tabling this ingredient please raise your hand. Unanimous. Are there any other discussion points? Alan?

DR. ANDERSEN: I want to make sure that everybody is comfortable with adding the traditional caveat for ocular irritation if available.

DR. BELSITO: I'm not talking about doing an ocular study. I'm talking about dermal irritation at 5 percent because it's used in an eye product.

DR. ANDERSEN: Thank you.

DR. MARKS: The only other which we noted and Alan pointed out is the issue of pneumoconiosis and we felt we could handle that in the discussion with the inhalation boilerplate.

DR. BERGFELD: Is there anything else? Seeing none, we'll move forward then. Thank you very much for that.

Report

Safety Assessment of Tin(IV) Oxide as Used in Cosmetics

Status: Draft Report for CIR Expert Panel Review
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The 2012 Cosmetic Ingredient Review Expert Panel members are: Chair, 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 F. Alan Andersen, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Manager/Lead Specialist.

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INTRODUCTION

The safety of tin(IV) oxide and tin as used in cosmetics is reviewed in this safety assessment. Tin(IV) oxide functions as an abrasive, bulking, and opacifying agent and tin functions as a surface modifier in cosmetic products.[1]

CHEMISTRY

Definition and Structure

Tin(IV) oxide (CAS Nos. 1332-29-2 and 18282-10-5), dioxide of tin, is an inorganic oxide that conforms to the following structure:

Other names for this chemical include: stannic oxide, white tin oxide, tin dioxide, stannic anhydride, and flowers of tin.[1,2]

Physical and Chemical Properties

Tin is a silver-white metal that is malleable and somewhat ductile. It has a highly crystalline structure and exists in two allotropic forms at normal pressures. Gray tin exists below 13.2 °C and has a cubic structure. At 13.2 °C, gray tin is converted to white tin, which has a tetragonal structure.[3,4] The white form is better known as the common, stable form at room temperature.[5] In compounds, tin can exist in the +2 or +4 oxidation state:[3,4] Divalent and tetravalent oxidation states are designated as stannous and stannic, respectively. The Stock Oxidation-Number system denotes the oxidation state using Roman numerals in parentheses following the metal's name: tin(II) and tin(IV).[6] The cosmetic ingredient, tin oxide, is tin(IV) oxide.

Chemical and physical properties of tin(IV) Oxide are found in Table 1.

Method of Manufacture

The earth's crust contains approximately 2 to 3 ppm tin, comprising 0.0006% of the earth's crust.[2,7] The most important tin-containing mineral is cassiterite, also known as SnO_2. Other tin minerals are stannite, teallite, cylindrite, and canfieldite. After tin-containing ores are mined, they undergo further separation processing, resulting in concentrates containing 70–77% tin by weight, almost pure cassiterite, and are ready for smelting.[8] Elemental tin is obtained from cassiterite by reduction with coal in a reverberatory furnace.[5] Although tin(IV) oxide occurs naturally in mineral form, this is not the source of the commercial product. It is manufactured directly from tin metal by thermal oxidation (from mined or recycled tin), either by exposing molten tin to air in a furnace at elevated temperatures, or by blowing tin powder in a stream of air through a furnace at approximately 700 °C.

According to one source, the commercial production of tin(IV) oxides yielded the following grades: average particle size of 0.3 µm (bulk density = 0.72 g/cm^3), average particle size of 0.4 µm (bulk density = 1.15 g/cm^3), and average particle size of 0.5 µm (bulk density = 1.35 g/cm^3).[9] Each grade is > 99.0% pure and has a specific gravity of 6.9.

Impurities

Data on tin(IV) oxide impurities were not found in the published literature. However, commercially available metallic tin is approximately 99.8% pure.[5] As stated above, tin(IV) oxide is manufactured directly from tin metal.

USE

Cosmetic

Tin(IV) oxide functions as an abrasive, bulking, and opacifying agent and tin functions as a surface modifier in cosmetic products.[1] According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2011(Table 2), tin(IV) oxide was being used in 1,098 cosmetic products.[10] Results from a survey of ingredient use concentrations provided by the Personal Care Products Council (also included in Table 2) in 2012 indicate that tin(IV) oxide was being used at concentrations up to 0.4% in rinse-off products (max. concentration in non-coloring shampoos) and at concentrations up to 1.3% in leave-on products (max. concentration in eye shadow).[11]

Cosmetic products containing tin(IV) oxide may be applied to the skin and hair, or, incidentally, may come in contact with the eyes and mucous membranes. Products containing these ingredients may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

Tin(IV) oxide is used in dusting powders (up to 0.03%), body and hand cosmetic sprays (up to 0.06%), and other fragrance preparations (up to 0.08%), and could possibly be inhaled. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm.[12,13,14,15] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[12,13]

Noncosmetic

Tin(IV) oxide is used in a variety of manufacturing applications, including polishing glass and other metals.[2] Elemental tin is present mainly in solder alloys used in the electronics industry, and is also used as a protective coating for other metals, especially those used for food containers.[16]

According to a memorandum on food contact substance notification (FCN) No. 000431, the intended use of Tin (IV) oxide is, in combination with silicon dioxide and titanium dioxide, as a colorant for food-contact polymers, paper and paperboard, coatings, and in printing inks applied to non-food-contact surfaces of food-contact articles.[17] The food contact surface will be used at a level not to exceed 6% of the total colorant weight. The finished food-contact articles may contact all food types with no temperature limitation.

Tin (IV) oxide is not regulated in 21 CFR but is the subject of threshold of regulation (TOR) exemption 98-004, for the use of tin oxide at a maximum level of 1.1% by weight in colorants otherwise composed of mica and titanium dioxide, provided that the maximum loading rate for the colorant in the food-contact material does not exceed 3% by weight for polymers, 5% for paper and paperboard, 15% for coatings, or 30% for ink formulations. Tin(IV) oxide is a constituent of the food contact surface that is the subject of FCN 235 (Use of tin antimony oxide [also known as antimony gray cassiterite] as a pigment for all polyolefins for food contact applications).[17]

TOXICOKINETICS

Data on the absorption, distribution, metabolism, and excretion of tin(IV) oxide were not found in the published literature. However, the International Commission on Radiological Protection (ICRP) has provided classifications for clearance of inhaled tin compounds in the respiratory tract, for use in an inhalation model.[18,19] Sulfides, oxides, hydroxides, halides, and nitrates of tin, and stannic phosphate were classified as Type M (M = moderate lung absorption). With Type M compounds, approximately 70% of the tin deposited in alveolar interstitial regions is eventually transferred to the blood, approximately 10% of the tin deposited in the bronchi and bronchioles is absorbed rapidly, and 5% of the tin is deposited in the gastrointestinal tract.

TOXICOLOGY

Acute Oral Toxicity

An acute oral LD_{50} of > 20 g/kg has been reported for tin(IV) oxide in mice and rats (strains and ages not stated).[20] If available, study details will be included after this study has been translated.

Acute Intraperitoneal Toxicity

Following i.p. dosing of rats and mice (numbers and strains not stated) with tin(IV) oxide, an acute LD_{50} of > 0.6600E + 4 mg/kg was reported.[20] If available, study details will be included after this study has been translated.

Repeated Dose Toxicity

Groups of 10 males and 10 females were fed diets containing 0, 0.03, 0.10, 0.30, or 1.0% tin(IV) oxide for 28 days.[21] Endpoints monitored included: mortality, growth, food consumption and utilization, hematology, urinalysis, serum biochemistries, and gross and microscopic pathology. No compound-related adverse effects were observed among rats fed tin(IV) oxide during the 4-week feeding period.

Ocular Irritation

The ocular irritation potential of an eye shadow containing 0.3% tin oxide [tin(II) or tin(IV) not stated] was evaluated using 34 female subjects (18 to 65 years old), 3 of whom withdrew for reasons unrelated to conduct of the study.[22] The participants were instructed to use the test material at least once daily for 4 weeks. A comprehensive ocular examination was performed at the end of the 4-week period. There were no adverse events, and all ophthalmologic examinations remained within normal limits. Study results did not indicate a potential for ocular irritation or hypersensitivity.

In an *in vitro* study, the ocular irritation potential of an eye shadow containing 1.11% tin oxide was evaluated using the chorioallantoic membrane vascular assay (CAMVA-14 day) and the bovine corneal opacity and permeability test (BCOP).[23] In the CAMVA-14 day assay, 2 groups of 10 White Leghorn eggs were dosed (40 µl or 40 mg) with the eye shadow at concentrations of 100% and 50% (effective concentration ≈ 0.6%), respectively. The 14-day incubation period was followed by an additional 30 ± 5 minutes of incubation. The CAM was then observed for signs of vascular hemorrhage, capillary injection, or ghost vessels (all positive responses), and the RC_{50} was determined. The RC_{50} is defined as the concentration at which 50% of the treated eggs show a positive response. Positive responses were not observed in treated eggs (RC50 > 100%). In the BCOP assay, 5 corneas were dosed with 0.75 ml of a 20% (effective concentration ≈ 0.2%) solution of the eye shadow in minimal essential media. Opacity measurements and sodium fluorescein permeability were determined. The corrected mean opacity score was 0.6, and the corrected mean optical density (permeability) was -0.003. In the study conclusion, it was stated that the *in vitro* score, as calculated, was 0.56 (0.6 + 15 (-0.003) = 0.56).

Skin Irritation and Sensitization

The skin irritation and sensitization potential of a powder eye shadow containing 0.3% tin oxide [likely tin(IV) oxide] was evaluated in a repeated insult patch test (RIPT) using 111 male and female subjects (18 to 75 years old), 98 of whom completed the study.[24] Withdrawal from the study was not related to application of the test material. A 1" x 1" semi-occlusive patch containing 0.2 g of the test material was applied to the upper back (between the scapulae) of each subject 3 times per week for a total of 9, 24 h induction applications. After a 2-week non-treatment period, challenge patches were applied for 24 h to a new test site. Reactions were scored at 24 h and 72 h post-application. No reactions were observed, and it was concluded that the test material did not have skin irritation or allergic contact sensitization potential.

The skin irritation and sensitization potential of a lipstick containing 0.5% tin oxide [likely tin(IV) oxide] was also evaluated in an RIPT (similar procedure) using 112 male and female subjects (16 to 79 years old), 103 of whom completed the study. Withdrawal from the study was not related to application of the test material. No reactions were observed, and it was concluded that the test material did not have the potential for causing dermal irritation or allergic contact sensitization.[25] In another study, the skin irritation and sensitization potential of a lipgloss product containing 0.35% tin oxide [likely tin(IV) oxide] was evaluated in an RIPT (amount per patch not stated) using 112 male and female subjects (18 to 70 years old), 108 of whom completed the study.[26] The test protocol was identical to that used in the preceding test, with the exception that

challenge sites were evaluated at 24 h, 48 h, and 72 h post-application. No reactions were observed, and it was concluded that the test material did not demonstrate a clinically significant potential for eliciting dermal irritation or sensitization.

Except for use of a 3/4" x 3/4" semiocclusive patch and the evaluation of challenge reactions at 24 h and 48 h only, the same RIPT procedure in the preceding study was used to evaluate the primary or cumulative irritation and/or allergic contact sensitization potential of an eye shadow containing 1.3% tin oxide.[27] The initial study group consisted to 232 subjects (16 to 79 years old), 209 of whom completed the study. Withdrawal from the study was not related to product application. It was concluded that test results for the eye shadow did not indicate a potential for dermal irritation or allergic contact sensitization.

Occupational Studies/Case Reports

Two-hundred fifteen workers (ages not stated) were exposed to tin(IV) oxide fumes at a plant, 95% of whom had at least 3 years of service.[28] Of the 215 workers that received chest X-rays, 121 had changes identified as pneumoconiosis. None of the X-ray films was suggestive of massive fibrosis or significant emphysema, and there was no evidence of massive fibrosis or nodulation. There were no differences in the following between the 121 pneumoconiotic workers and 94 non-pneumoconiotic workers: respiratory symptoms, vital capacity, chest expansion, loss time due to chest illness, and incidence of tuberculosis.

A clinical study of 19 male employees (most < 30 years old) exposed to tin(IV) oxide dust and fumes at a plant was performed.[29] Impairment of pulmonary function was not observed in any of the subjects, and there were no reports of work disability from any clinical cause. Physical examinations did not reveal any abnormal lung findings or significant findings in general. All of the values for vital capacity, maximal breathing capacity, resting minute volume, and respiratory reserve were within normal limits. The absence of alteration in these ventilatory tests indicae that there was no significant degree of obstructive emphysema or of diffuse pulmonary fibrosis. Based on the methods used, it was noted that the only type of pulmonary function alteration that could have escaped detection would have been impaired diffusion of the alveolo-capillary block type, which is found in cases of asbestosis and berylliosis.

Based on chest roentgenograms, one subject was classified as completely normal, 8 were classified as stannosis suspects, and 10 were classified as having tin oxide pneumoconiosis. It was noted that subjects with less than 3 years of exposure may be classified as either normal or suspects, but do not present with pulmonary nodulation. After 3 years of exposure to tin(IV) oxide, nodular stenosis was found in all cases, and advanced stages occurred with increasing frequency as the years of exposure increased. Of the 10 employees with roentgenographic changes classified as stannosis, 6 had been exposed to tin oxide fume. The most advanced changes were observed in 4 of these 6 employees. One of the 4 subjects probably had been exposed exclusively to tin(IV) oxide dust and had first stage stannosis, and the remaining 3 subjects (exposure to dust and fumes) had varying degrees of change. Six of the 10 employees with lung changes were asymptomatic and the following signs were reported for the remaining 4: moderate anorexia (2 subjects), cough with serious expectoration (1 subject), and scapular pain (1 subject). For the 10 cases of stannosis, the hemograms and sedimentation rates were within normal limits. Traces of albumin in the urine were reported for 3 of the cases, and the blood Kahn reaction was normal in all cases. The authors noted that the results of this study corroborate the conclusion that tin oxide fume, and not tin oxide dust, is more likely to be the cause of stannosis.[29]

Stannosis is the form of pneumoconiosis (non-fibrotic form) that results from the inhalation of tin in the form of tin(IV) oxide fumes or dust. Tin(IV) oxide accumulates in the pulmonary parenchyma. Lung radiography results for a man (age not stated) who had worked in the smelter of a tin mine for 26 years revealed moderately profuse small nodules, some of which were metallic in density.[30] The patient was asymptomatic and clinically normal. Lung function tests were not performed. Results 8 years later revealed an increase in the profusion of small opacities, particularly in the left mid-zone of the lung. The patient remained asymptomatic. Another case report involved a 55-year-old male employee of a detinning plant for 15 years. He was exposed to tin(IV) oxide fumes as well as clouds of coal dust on the job, and lung function test results yielded a forced vital capacity of 90% and a forced expiratory volume that was 96% of predicted values. Lung radiography results revealed very profuse bilateral nodules (~ 3 mm in diameter). At lung biopsy, focal aggregations of macrophages containing dust particles (black particles) were observed in some of the air spaces and in the perivascular and peribronchiolar connective tissue. Electron probe analysis results indicated that tin was present in the dust.[30]

A 50-year-old female (non-smoker) with stannosis was exposed to tin(IV) oxide fumes for 33 years.[31] There were also exposures to biomass fuels and asbestos. A chest X-ray revealed common nolular lesions and thorax high resolution computed tomography revealed widespread interlobular thickening and peribronchial thickening. Subpleural nodules with metallic density were observed in the upper and middle lobe of the right lung. Bronchial lavage cytology was defined as

class II, and histiocytic cells and focal fibrosis were detected on transbronchial lung biopsy. The patient died 6 months later due to respiratory failure.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Data on the reproductive and developmental toxicity of tin(IV) oxide were not found in the published literature.

GENOTOXICITY

Tin(IV) oxide was administered to rats through the trachea, and cytological preparations were made at various intervals in order to determine effects on micronucleus frequency and karyorrhexis of rat bone marrow cells and lung macrophages.[32] Results indicated that tin(IV) oxide can induce micronuclei and karyorrhexis in bone marrow cells. On the first and tenth day, the frequency of karyorrhexis was higher than that of micronuclei, and differed significantly from that of the control, and vice versa, on the 20^{th} and 30^{th} days. Tin(IV) oxide also can induce micronuclei and karyorrhexis in lung macrophages. On the 10^{th} and 20^{th} days, the frequency of karyorrhexis was the same as that in bone marrow cells.

CARCINOGENICITY

Data on the carcinogenicity of tin(IV) oxide were not found in the published literature.

SUMMARY

The safety of tin(IV) oxide (dioxide of tin) and elemental tin in cosmetics is reviewed in this report. Elemental tin is obtained from cassiterite by reduction with coal in a reverberatory furnace. Tin oxide is manufactured directly from tin metal by thermal oxidation. According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2012, tin oxide was being used in 1,098 cosmetic products. Furthermore, results from a survey of ingredient use concentrations provided by the Personal Care Products Council in 2011 indicate that tin oxide was being used at concentrations up to 0.4% in rinse-off products (max. concentration in non-coloring shampoos) and up to 1.3% in leave-on products (max. concentration in eye shadow).

Data on tin(IV) oxide impurities were not found in the published literature. However, commercially available metallic tin is approximately 99.8% pure. Tin(IV) oxide is manufactured directly from tin metal.

Data on the absorption, distribution, metabolism, and excretion of tin(IV) oxide were not found in the published literature. However, the ICRP has provided classifications for clearance of inhaled tin compounds in the respiratory tract, for use in an inhalation model. Sulfides, oxides, hydroxides, halides, and nitrates of tin, and stannic phosphate were classified as Type M (M = moderate lung absorption). With Type M compounds, approximately 70% of the tin deposited in alveolar interstitial regions is eventually transferred to the blood, approximately 10% of the tin deposited in the bronchi and bronchioles is absorbed rapidly, and 5% of the tin is deposited in the gastrointestinal tract.

An acute oral LD_{50} of > 20 g/kg has been reported for tin(IV) oxide in mice and rats. Following i.p. dosing of rats and mice with tin(IV) oxide, an acute LD_{50} of > 0.6600E + 4 mg/kg was reported. No test substance-related adverse effects were observed in rats fed tin(IV) oxide at concentrations up to 1.0% in the diet for 28 days.

An eye shadow containing 0.3% tin oxide [likely tin(IV) oxide] not stated did not cause ocular irritation in 31 subjects who participated in a 4-week product use study (daily applications). In vitro assay results relating to the ocular irritation potential of an eye shadow containing 1.11% tin oxide were negative when the product was diluted to concentrations of 0.6% and 0.2% prior to testing. Results of In repeated insult patch tests, neither a lipstick (0.5% tin oxide, 103 subjects), lipgloss product (0.35% tin oxide, 108 subjects), powder eye shadow (0.3% tin oxide, 98 subjects), nor another eye shadow (1.3% tin oxide, 209 subjects) induced skin irritation or allergic contact sensitization.

In occupational settings, stannosis, a form of pneumoconiosis, has been observed in workers exposed to tin(IV) oxide fumes.

Tin(IV) oxide administered intratracheally induced micronuclei and karyorrhexis in rat bone marrow cells *in vivo*. Data on the carcinogenicity or reproductive and developmental toxicity of of tin(IV) oxide were not found in the published literature.

DISCUSSION

Because tin(IV) oxide was reported to be used in products that may be sprayed, the Panel discussed the issue of incidental inhalation exposure. In the absence of typical inhalation toxicity studies, the Panel considered other pertinent data that were available, i.e., occupational exposure data. Stannosis, a form of pneumoconiosis, has resulted from occupational exposure to tin(IV) oxide dust/fumes, but the Panel agreed that this level of exposure to tin(IV) oxide would not result from cosmetic use. The Panel noted that 95% – 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. The potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. Inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects depending on their chemical and other properties. However, coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. Acute or repeated dose toxicity following exposure to tin(IV) oxide via other routes was not a concern, based on relatively high oral and i.p. LD_{50} values reported for rats and mice and negative results (rats) in a 28-day oral feeding study.

The Panel recognizes the absence of carcinogenicity and reproductive and developmental toxicity data on tin(IV) oxide, but agreed that these data would not be needed because tin(IV) oxide is insoluble and, theoretically, should not be absorbed across the skin. Based on the results of studies on product formulations containing tin oxide [likely tin(IV) oxide], there is no indication that this ingredient would have any irritation or sensitization potential at use concentrations up to 1.3% in cosmetic products.

Table 1. Properties of Tin(IV) Oxide and Tin[33]

Chemical	Form	Molecular Weight	logP	Density	Water Solubility	Boiling Point	Melting Point
Tin(IV) Oxide	Gray tetragonal crystals	150.71	NA*	6.85 g/cm^3	Insoluble	NA	1630ºC

*NA = Not Available

Table 2. Frequency and Concentration of Use According to Duration and Type of Exposure Provided in 2012[10,11]

	Tin(IV) Oxide		
	# of Uses	Conc. (%)	
Exposure Type			
Eye Area	272	0.003 to 1.3	
Incidental Ingestion	381	0.008 to 0.2	
Incidental Inhalation-sprays	35	0.0005 to 0.08	
Incidental Inhalation-powders	53	0.0005 to 1	
Dermal Contact	650	0.000003 to 1	
Deodorant (underarm)	NR	NR	
Hair - Non-Coloring	9	0.0008 to 0.4	
Hair-Coloring	NR	0.04	
Nail	52	0.002 to 1	
Mucous Membrane	443	0.0005 to 0.2	
Baby Products	NR	NR	
Duration of Use			
Leave-On	1030	0.000003 to 1.3	
Rinse off	67	0.0003 to 0.4	
Diluted for (bath) use	1	NR	
Totals*/Conc. Range**	1098	0.000003 to 1.3	

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 be equal to sum total uses.

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Data

2012 FDA VCRP Data
Tin Oxide

02D - Other Bath Preparations	1
03A - Eyebrow Pencil	1
03B - Eyeliner	44
03C - Eye Shadow	208
03D - Eye Lotion	3
03F - Mascara	6
03G - Other Eye Makeup Preparations	10
04A - Cologne and Toilet waters	2
04B - Perfumes	3
04C - Powders (dusting and talcum, excluding aftershave talc)	14
04E - Other Fragrance Preparation	23
05A - Hair Conditioner	1
05F - Shampoos (non-coloring)	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	4
05I - Other Hair Preparations	2
07A - Blushers (all types)	34
07B - Face Powders	39
07C - Foundations	21
07D - Leg and Body Paints	1
07E - Lipstick	381
07F - Makeup Bases	5
07G - Rouges	25
07H - Makeup Fixatives	1
07I - Other Makeup Preparations	56
08D - Nail Extenders	1
08E - Nail Polish and Enamel	51
10A - Bath Soaps and Detergents	22
10E - Other Personal Cleanliness Products	39
12A - Cleansing	2
12C - Face and Neck (exc shave)	10
12D - Body and Hand (exc shave)	14
12F - Moisturizing	58
12G - Night	2
12H - Paste Masks (mud packs)	1
12J - Other Skin Care Preps	4
13B - Indoor Tanning Preparations	7
Total	**1,098**

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 2, 2012

SUBJECT: Safety Data on Products Containing Tin Oxide

Consumer Product Testing Co. 2012. Repeated insult patch test of an eye shadow containing 1.3% Tin Oxide.

MB Research Laboratories. 2012. Chlorioallantoic membrane vascular assay and bovine corneal opacity and permeability test of an eye shadow containing 1.11% Tin Oxide.

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Eye shadow containing
1.11% tin oxide – IVO Report

MB Research Laboratories

PROJECT NUMBER : [redacted]
TEST ARTICLE :
SPONSOR :
STUDY TITLE : Chorioallantoic Membrane Vascular Assay (CAMVA-14 Day) and Bovine Corneal Opacity and Permeability Test (BCOP)
PROTOCOL # : [redacted]

OBJECTIVE

To determine the potential for ocular irritation using an alternative to the Draize methodology. The methodology is based on that described in *An improved CAM Method for Predicting Ocular Irritation*, Bagley, D.M., Rizvi, P.Y., Kong, B.M., and De Salva, S.J. (1988), Alternative Methods in Toxicology, Vol. 6, Progress in *In vitro Toxicology, pp. 131-138*, and Bovine Corneal Opacity and Permeability Test: An *In Vitro* Assay of Ocular Irritancy, (1992); Gautheron, Pierre; Dukic, Martine; Alix, Danielle and Sina, Joseph F.; Fundamental and Applied Toxicology 18, 442-449 and includes an analysis based on OECD Guideline for the Testing of Chemicals #437, adopted September 7, 2009.

CAMVA - ABSTRACT

Method Synopsis: Based on the results of a preliminary screen, the chorioallantoic membrane (CAM) of twenty White Leghorn eggs, incubated for 14 days, was dosed with 40 µl or 40 mg of [redacted] A total of two concentrations were used, one per group. The dosed eggs were then incubated for another 30 ± 5 minutes after which the CAM was observed for signs of vascular hemorrhage, capillary injection, or ghost vessels. The RC_{50} was determined.

Summary: There were no positive responses to the one dilution in corn oil or the undiluted test article.

Concentration (%)	# of Eggs	# of Positive Responses
50	10	0/10
100	10	0/10

Conclusion: The RC_{50} is greater than 100%.

BCOP - ABSTRACT

Method Synopsis: Five corneas were dosed with 0.75 ml of a 20% solution of [redacted] in Minimum Essential Media (MEM). Opacity measurements and sodium fluorescein permeability were determined.

Summary: The corrected mean opacity score was 0.6. The corrected mean optical density (permeability) score was -0.003.

Conclusion: The *in vitro* score, as calculated, was 0.56.

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phone: (215) 536-4110 fax: (215) 536-1818

GOOD LABORATORY PRACTICES COMPLIANCE STATEMENT

This study was conducted in accordance with the Good Laboratory Practices regulations of the EPA (40 CFR Part 160) and the FDA (21 CFR Part 58) with the following exception:

Prior to study initiation, the study director was not supplied with the test article characterization information. The effect of the lack of test article characterization cannot be fully assessed. However, considering the short duration of this assay, no adverse impact is expected.

Final report:

Dana Wolfinger, B.S.
Study Director

10 Jun 2012
Date

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[redacted]

QUALITY ASSURANCE EVALUATION

The Quality Assurance Unit (QAU) has determined that the methods and results contained herein accurately reflect the raw data.

The QAU inspected a critical phase of the study on 17 May 2012, audited the raw data on 24 May 2012 and audited the report.

Quality Assurance Unit — Date

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RESULTS FOR CAMVA

CONCENTRATION: 50%[a, b]	EGG NUMBER									
OBSERVATIONS	21	22	23	24	25	26	27	28	29	30
Normal	X	X	X	X	X	X	X	X	X	X

CONCENTRATION: 100%[a, b]	EGG NUMBER									
OBSERVATIONS	11	12	13	14	15	16	17	18	19	20
Normal	X	X	X	X	X	X	X	X	X	X

a = Test Article physically removed from CAM

b = CAM washed with distilled water

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RESULTS FOR BCOP

INDIVIDUAL CONTROL SCORES FOR BCOP

Cornea #:	Pretest	4 Hours	O.D. Scores
C3	1	2	0.033
C4	1	2	0.044
MEAN	1	2	0.039
Corrected Mean Control Opacity Score[1]	1		

INDIVIDUAL TEST SCORES

CORNEA #	PRETEST SCORES				4 HOUR SCORES				O.D. SCORES
1	C3	-4	C4	-4	C3	-2	C4	-2	0.042
2	C3	-4	C4	-5	C3	-2	C4	-2	0.028
3	C3	-3	C4	-4	C3	-2	C4	-2	0.032
4	C3	-5	C4	-5	C3	-3	C4	-4	0.030
5	C3	-4	C4	-5	C3	-4	C4	-4	0.046

CALCULATED SCORES

Cornea #	Corrected Opacity Scores				Corrected O.D.
	4 Hour Scores				
1	C3	2	C4	2	0.003
2	C3	2	C4	3	-0.011
3	C3	1	C4	2	-0.007
4	C3	2	C4	1	-0.009
5	C3	0	C4	1	0.007
Corrected Mean Optical Density =					-0.003
Corrected Mean Opacity Score[2] =					0.6

Calculated In Vitro Score
0.6 + 15 (-0.003)
0.6 + (-0.045)
0.56

IN VITRO = 0.56

[1]Corrected Mean Control Opacity Score = 4 hour mean score minus pretest mean score
[2]Corrected Mean Opacity Score = mean treated opacity score minus corrected mean control opacity score

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Consumer Product Testing Co.

EST 1975

Tin Oxide 1.3% RIPT (0/209)

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Repeated Insult Patch Test

TEST MATERIAL: [redacted] Loose Eye Shadow [redacted]

Contains 1.3% Tin Oxide

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRC, CCRA
Director, Clinical Evaluations

Approved by: Joy Frank, R.N. [redacted]
Executive Vice President, Clinical Evaluations

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co.

QUALITY ASSURANCE UNIT STATEMENT

Trial Number: [redacted]

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

Quality Assurance Representative

3/30/12
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

[redacted]

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: Two hundred thirty-two (232) qualified subjects, male and female, ranging in age from 16 to 79 years, were selected for this evaluation. Two hundred nine (209) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] and over.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: Loose Eye Shadow [redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
20120049	February 3, 2012	March 15, 2012
20120055	February 8, 2012	March 22, 2012
20120057	February 13, 2012	March 22, 2012

[a]With parental or guardian consent

[redacted]

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 3/4" x 3/4" absorbent pad portion of an adhesive dressing. This pad was moistened with several drops of water to ensure adherence of the test material. This was then applied to the appropriate treatment site to form an occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy two hours post-application.

[redacted]

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	**=**	**No visible skin reaction**	**E**	**=**	**Edema**
0.5	**=**	**Barely perceptible**	**D**	**=**	**Dryness**
1	**=**	**Mild**	**S**	**=**	**Staining**
2	**=**	**Moderate**	**P**	**=**	**Papules**
3	**=**	**Marked**	**V**	**=**	**Vesicles**
4	**=**	**Severe**	**B**	**=**	**Bullae**
			U	**=**	**Ulceration**
			Sp	**=**	**Spreading**

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Adverse Events:

Subject [redacted] experienced a displacement of his artificial knee, which required hospitalization and subsequent surgery. It was the Principal Investigator's opinion that the relationship to the test material was unlikely.

Subject [redacted] experienced an episode of vertigo, which resulted in hospitalization for 3 days. It was the Principal Investigator's opinion that the relationship to the test material was unlikely.

Amendments:

There were no amendments.

Deviations:

Due to a holiday weekend, subjects on [redacted] may have experienced a delay in patch applications during the Induction Phase. It is the Principal Investigator's opinion that this would have no effect on the final results, since the appropriate number of applications were maintained.

Results:

The results of each participant are appended (Table 1).

Observations remained within normal limits throughout the test interval.

Subject demographics are presented in Table 2.

Summary:

Under the conditions of this study, test material, Loose Eye Shadow [redacted] did not indicate a potential for dermal irritation or allergic contact sensitization.

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	DID NOT COMPLETE											
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0.5	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	DID NOT COMPLETE											
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	DID NOT COMPLETE				
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	DID NOT COMPLETE					
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
59	0	0	0	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0	0	0	0
61	0	0	0	0	0	0	0	0	0	0	--DNC--	
62	0	0	0	0	0	0	0	0	0	0	0	0
63	0	0	0	0	0	0	0	0	0	0	0	0
64	0	0	0	0	0	0	0	0	0	0	0	0
65	0	0	0	0	0	0	0	0	0	0	0	0
66	0	0	0	0	0	0	0	0	0	0	0	0
67	0	0	0	0	0	0	0	0	0	0	0	0
68	0	0	0	0	0	0	0	0	0	0	--DNC--	
69	0	0	0	0	0	0	0	0	0	0	0	0
70	0	0	0	0	0	0	0	0	0	0	0	0
71	0	0	0	0	0	0	0	0	0	0	0	0
72	0	0	0	0	0	0	0	0	0	0	0	0
73	0	0	0	0	0	0	0	0	0	0	0	0
74	0	0	0	0	0	0	0	0	0	0	0	0
75	0	0	0	0	0	0	0	0	0	0	0	0
76	0	0	0	0	0	0	0	0	0	0	0	0
77	0	0	0	0	0	0	0	0	0	0	0	0
78	0	0	0	0	0	0	0	0	0	0	0	0
79	0	0	0	0	0	0	0	0	0	0	0	0
80	0	0	0	0	0	0	0	0	0	0	--DNC--	
81	0	0	0	0	0	0	0	0	0	0	0	0
82	0	0	0	0	0	0	0	0	0	0	0	0
83	0	0	0	0	0	0	0	0	0	0	0	0
84	0	0	0	0	0	0	0	0	0	0	0	0
85	0	0	0	0	0	0	0	0	0	0	0	0
86	0	0	0	0	0	0	0	0	0	0	0	0
87	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
DNC = Did not complete study

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
88	0	0	0	0	0	0	0	0	0	0	0	0
89	0	0	0	0	0	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0	0	0	0	0	0
91	0	0	0	0	0	0	0	0	0	0	0	0
92	0	0	0	0	0	0	0	0	0	0	0	0
93	0	0	0	0	0	0	0	0	0	0	0	0
94	0	0	0	0	0	0	0	0	0	0	0	0
95	0	0	0	0	0	0	0	0	0	0	0	0
96	0	0	0	0	0	0	0	0	0	0	0	0
97	0	0	0	0	0	0	0	0	0	0	0	0
98	0	0	0	0	0	0	----------DID NOT COMPLETE----------					
99	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0
101	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0
107	0	0	0	0	0	0	0	0	0	0	0	0
108	0	0	0	0	0	0	0	0	0	0	0	0
109	0	0	0	0	0	0	0	0	0	0	0	0
110	0	0	0	0	0	0	0	0	0	0	0	0
111	0	0	0	0	0	0	0	0	0	0	0	0
112	0	0	0	0	0	0	----------DID NOT COMPLETE----------					
113	0	0	0	0	0	0	0	0	0	0	0	0
114	0	0	0	0	0	0	0	0	0	0	0	0
115	0	0	0	0	0	0	0	0	0	0	0	0
116	0	0	0	0	0	0	0	0	0	0	0	0
117	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0[m]	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	----------DID NOT COMPLETE----------					
11	0	0	0	0	0	0	----------DID NOT COMPLETE----------					
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	-	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	----------DID NOT COMPLETE----------							
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
m = Additional makeup day granted at the discretion of the clinic supervisor
- = Subject not present for supervised removal

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	----------DID NOT COMPLETE----------											
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	----------DID NOT COMPLETE----------						
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	----------DID NOT COMPLETE----------											
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	-	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	--DNC--	

24* = Supervised removal of 1st Induction and Challenge Patch
\- = Subject not present for supervised removal
DNC = Did not complete study

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	DID NOT COMPLETE											
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

[redacted]

Table 1
(continued)

[redacted]

Individual Results

Loose Eye Shadow [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	DID NOT COMPLETE									
32	0	0	0	0	0	0	0	DID NOT COMPLETE				
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	--DNC--	
35	0	0	0	0	DID NOT COMPLETE							
36	0	0	0	0	0	0	0	0	0	0	--DNC--	
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	DID NOT COMPLETE										
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
DNC = Did not complete study

[redacted]

Table 2

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
1	CAM	55	M
2	MJV	36	M
3	WCN	42	M
4	OFS	67	M
5	MTF	50	F
6	KAM	54	F
7	LPC	76	F
8	JRD	28	M
9	MMC	25	M
10	FPC	71	M
11	S-G	74	M
12	SKF	22	F
13	G-H	24	M
14	LCS	54	F
15	CSG	25	F
16	T-D	70	F
17	RFP	61	M
18	GSG	69	F
19	J-M	56	F
20	F-G	77	M
21	L-G	77	F
22	AJM	20	M
23	SMF	44	F
24	JFK	68	F
25	VCI	50	F
26	SJC	20	M
27	T-L	72	M
28	DAD	53	F
29	DLB	51	F

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
30	TPW	36	F
31	KTC	69	F
32	R-C	72	M
33	M-M	50	F
34	CJW	36	M
35	GDM	60	F
36	M-R	19	F
37	NVN	22	M
38	CJF	69	F
39	MCG	22	F
40	KJC	23	F
41	JGQ	33	F
42	LJC	53	F
43	MKS	32	F
44	GFM	70	F
45	RCM	69	M
46	CMW	59	F
47	MAW	79	F
48	DSM	68	M
49	JSN	39	F
50	REF	75	M
51	GJD	71	M
52	JBO	22	M
53	MLD	65	F
54	G-D	68	M
55	J-C	74	M
56	R-S	44	M
57	CAT	70	F
58	MEQ	40	F

[redacted]

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
59	JMQ	69	F
60	S-A	49	F
61	DMH	46	F
62	J-R	72	M
63	NAM	60	F
64	RWL	71	M
65	F-A	35	M
66	MEL	59	F
67	I-B	59	M
68	CRS	22	M
69	CEC	46	F
70	D-P	50	F
71	S-N	50	M
72	LMM	51	F
73	SSC	27	M
74	DLB	28	F
75	M-B	64	F
76	LEH	66	M
77	PAB	60	F
78	TFC	46	F
79	JWC	61	M
80	MJL	22	M
81	SMZ	20	F
82	LAC	18	M
83	AAM	65	F
84	KAI	50	M
85	SEG	47	F
86	MAS	68	F
87	AVM	47	M

[redacted]

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
88	EIB	76	F
89	RSG	54	M
90	MJP	18	F
91	GMV	46	F
92	SYC	45	F
93	WAS	74	M
94	AMS	70	F
95	TPC	25	F
96	DJD	52	F
97	C-R	53	F
98	S-R	51	F
99	RDE	24	F
100	CAC	29	F
101	RID	69	F
102	SKS	59	F
103	CBS	30	F
104	AOS	32	M
105	DJM	25	M
106	J-C	47	F
107	MAS	46	M
108	AFD	44	M
109	KMC	47	F
110	JJR	34	M
111	S-P	44	M
112	J-N	28	F
113	HJB	51	M
114	CAB	49	F
115	DJG	40	F
116	APS	18	F
117	DLS	48	F

[redacted]

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
1	C-S	20	M
2	JAH	18	F
3	JNW	18	F
4	M-D	74	M
5	DTC	17	M
6	CJF	31	F
7	WCM	40	M
8	KLJ	38	F
9	MMC	44	F
10	MFC	65	M
11	SOC	54	F
12	TJS	67	F
13	DCS	39	M
14	JFL	53	F
15	BMW	43	F
16	EJS	34	M
17	KTJ	16	M
18	MBL	31	F
19	FAB	35	F
20	N-G	62	F
21	SCR	37	F
22	RMV	56	F
23	LBP	41	F
24	TKR	24	F
25	R-S	63	F
26	OUL	16	M
27	G-M	55	F
28	D-D	58	M
29	D-D	62	F

[redacted]

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
30	DLJ	16	F
31	NCE	68	F
32	LAD	48	F
33	REM	59	M
34	LAT	46	F
35	DRA	22	M
36	L-M	53	F
37	NTC	41	F
38	J-M	66	F
39	CLK	66	M
40	EJK	67	F
41	BCT	62	F
42	LCL	28	F
43	CLD	41	F
44	WVO	72	M
45	EIW	79	F
46	BAH	78	F
47	A-G	76	F
48	N-P	67	M
49	JML	62	F
50	JEV	31	M
51	JLP	76	M
52	SLM	71	M
53	J-H	75	M
54	WEG	69	M
55	J-N	46	M
56	JSW	76	F
57	PLK	22	M
58	LJT	44	F

[redacted]

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
1	G-C	55	F
2	VJM	67	F
3	JAR	67	F
4	CAO	68	F
5	D-D	70	F
6	JMN	20	F
7	T-N	22	F
8	PRK	50	M
9	KAH	42	F
10	MH	60	F
11	LLA	53	F
12	USF	42	F
13	LES	34	M
14	EAH	43	F
15	SAF	63	F
16	RMD	52	M
17	R-S	51	F
18	EGL	49	M
19	G-P	47	F
20	P-G	58	F
21	WTS	64	M
22	M-M	54	F
23	AMQ	50	F
24	TTG	31	F
25	J-P	61	F
26	SLQ	27	F
27	RSW	57	F
28	A-R	67	F
29	GNR	42	F

[redacted]

Table 2
(continued)

[redacted]

Subject Demographics

Subject Number	Initials	Age	Sex
30	DJC	28	F
31	AST	18	F
32	A-G	40	M
33	S-M	35	M
34	GMS	40	F
35	DMJ	18	F
36	SAA	38	F
37	ACM	18	M
38	SMA	18	F
39	K-T	47	F
40	LTW	46	F
41	SMJ	49	F
42	F-B	60	F
43	SEC	67	F
44	TMC	39	F
45	R-D	49	F
46	DJB	50	F
47	TAM	67	F
48	EEL	69	F
49	TML	51	M
50	JVR	66	F
51	KAM	48	F
52	A-W	54	F
53	A-C	69	F
54	MJC	45	F
55	MMN	20	F
56	LDA	64	F
57	RNA	67	M

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 2, 2012

SUBJECT: Updated Concentration of Use by FDA Product Category: Tin Oxide

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

Concentration of Use by FDA Product Category
Tin Oxide

Product Category	Maximum Concentration of Use
Eyebrow pencil	0.01-0.03%
Eye liner	0.06-1.3%
Eye shadow	0.07-1%
Eye lotion	0.004-0.09%
Eye makeup remover	0.3%
Mascara	0.003-0.08%
Other eye makeup preparations	0.01%
Colognes and toilet waters	0.0005%
Powders (dusting and talcum)	0.0005-0.03%
Other fragrance preparations	0.04-0.08%
Hair conditioners	0.001-0.003%
Shampoos (noncoloring)	0.0008-0.4%
Tonics, dressings and other hair grooming aids	0.001-0.002%
Hair dyes and colors (all types requiring caution statement and patch testing)	0.04%
Blushers (all types)	0.02-0.3%
Face powders	0.03-1%
Foundations	0.01-0.1%
Leg and body paints	0.09%
Lipstick	0.008-0.2%
Makeup bases	0.03%
Rouges	0.005-0.3%
Other makeup preparations	0.000003-0.02%
Nail polish and enamel	0.002-1%

Bath soaps and detergents	0.0005-0.2%
Other personal cleanliness products	0.0005%
Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0003-0.006%
Depilatories	0.002%
Face and neck creams, lotions and powders not spray	 0.02-0.05%
Body and hand creams, lotions and powders not spray spray	 0.0009-0.05% 0.002-0.06%
Moisturizing creams, lotions and powders	0.00005-0.01%
Other skin care preparations	0.002-0.3%
Suntan gels, creams and liquids	0.02% (not sprays)

Information collected in 2011
Table prepared January 10, 2012
Updated July 2, 2012: eyeliner high concentration changed to 1.3%; eye shadow high concentration changed to 1%; lipstick high concentration changed to 0.2%; basecoats and undercoats deleted