PINK BOOK 1

Dimethiconol

CIR EXPERT PANEL MEETING
JUNE 28-29, 2010

Cosmetic Ingredient Review
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June 28, 2010

Memorandum

To: CIR Expert Panel

From: Wilbur Johnson, Jr.
Senior Scientific Analyst

Subject: Dimethiconol and its Esters and Reaction Products

At the April 5-6, 2010 CIR Expert Panel meeting, the Panel issued an insufficient data announcement with the following data requests: (1) Method of manufacture and impurities; (2) UV absorption; if there is absorption in the UVB/UVA band, then photoirritation and photosensitization data may be needed; and (3) Molecular weights or information about dermal absorption that can predict if dermal absorption can occur. If absorption occurs, then reproductive and developmental toxicity data may be needed. The Panel noted that, in order for dimethiconol/silsesquioxane copolymer to remain in this safety assessment, additional information on its composition is needed. The need for data on the composition of Dow Corning mixtures and FD80 and FD80/II polymers included in the safety assessment was also expressed. To date, there has been no response to the Panel's request for data.

A copy of the draft tentative report on these ingredients is included along with the following: CIR report history, minutes from the April 5-6, 2010 Panel meeting, literature search strategy, and comments from industry. The draft tentative report has been revised to include use concentration data from industry and studies on polymers FD 80 and FD 80/II from the SEHSC that were reviewed at the April 2010 Panel meeting. Data from the SEHSC are identified by a vertical line in the right margin of the report text. Additionally, the report now contains a table (table 2) on the composition of oil/butter sources of dimethiconol fatty acid moieties and excerpts from the summary and discussion of the published CIR final report on dimethicone and related compounds. At the Panel's request, the following ingredients have been deleted from the report text because of specific components that may raise different safety issues: dimethiconol fluoroalcohol dilinoleic acid, dimethiconol/IPDI copolymer, and trifluoropropyl dimethiconol.

After reviewing the available data, the Expert Panel needs to determine whether a tentative report with an insufficient data conclusion should be issued at this meeting.

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CIR History of:

Dimethiconol and its Esters and Reaction Products

The availability of a scientific literature review (SLR) on this group of ingredients was announced on December 16, 2009.

Data and comments from the Personal Care Products Council and Silicones Environmental, Health Safety Council (SEHSC) were subsequently received.

1st Review, Belsito and Marks Teams/Panel: April 5-6, 2010

Unpublished data received from the Personal Care Products Council and SEHSC have been added to the safety assessment.

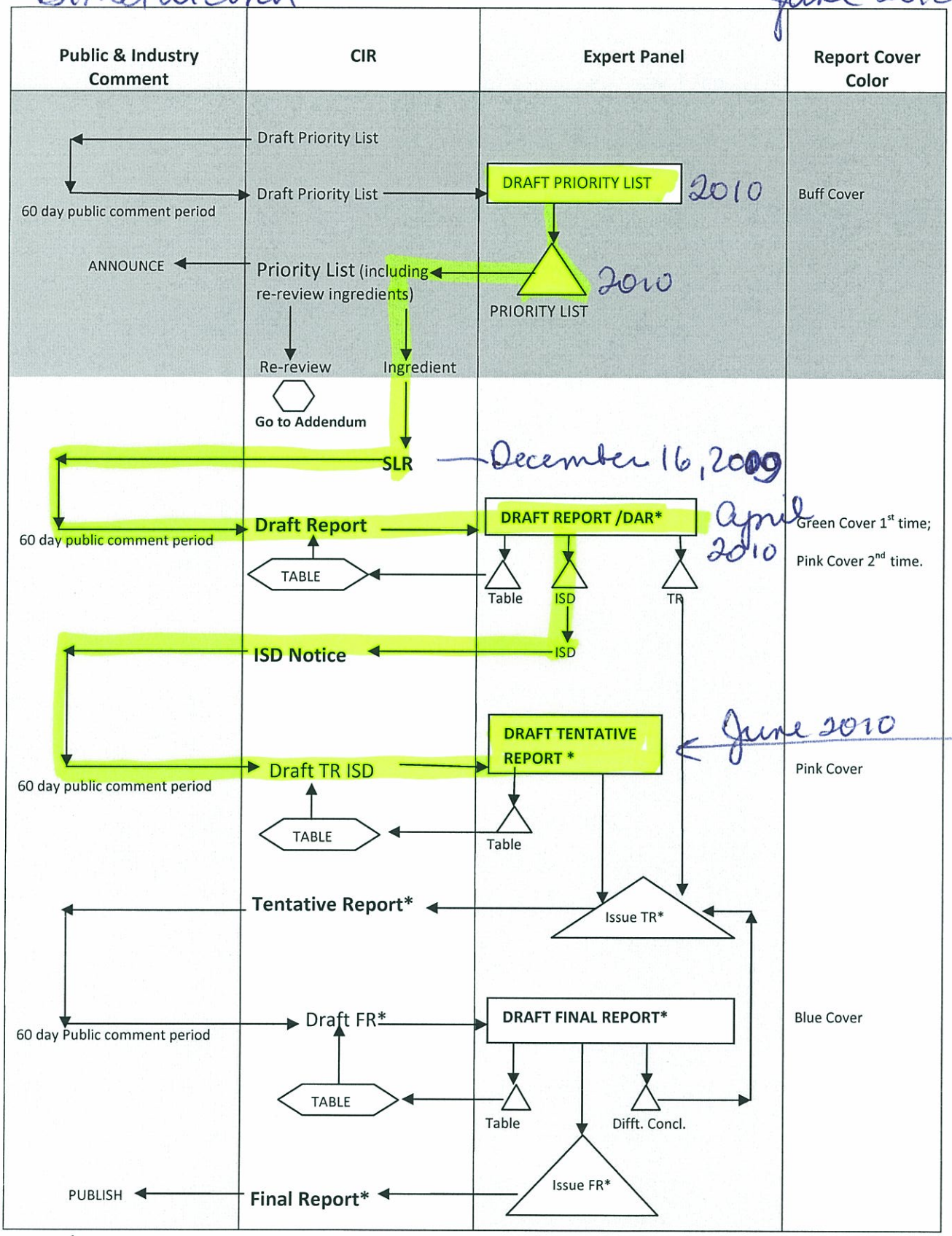
The Panel issued an insufficient data announcement with the following data requests: (1) Method of manufacture and impurities; (2) UV absorption; if there is absorption in the UVB/UVA band, then photoirritation and photosensitization data may be needed; and (3) Molecular weights or information about dermal absorption that can predict if dermal absorption can occur. If absorption occurs, then reproductive and developmental toxicity data may be needed. The Panel noted that, in order for dimethiconol/silsesquioxane copolymer to remain in this safety assessment, additional information on its composition is needed. The need for data on the composition of Dow Corning mixtures and FD80 and FD80/II polymers included in the safety assessment was also expressed.

2nd Review, Belsito and Marks Teams/Panel: June 28-29, 2010

The draft tentative report has been revised to include use concentration data from industry and studies on polymers FD 80 and FD 80/II from the SEHSC that were reviewed at the April 2010 Panel meeting. Data from the SEHSC are identified by a vertical line in the right margin of the report text. Additionally, the report now contains a table (table 2) on the composition of oil/butter sources of dimethiconol fatty acid moieties and excerpts from the summary and discussion of the published CIR final report on dimethicone and related compounds. At the Panel's request, the following ingredients have been deleted from the report text because of specific components that may raise different safety issues: dimethiconol fluoroalcohol dilinoleic acid, dimethiconol/IPDI copolymer, and trifluoropropyl dimethiconol.

SAFETY ASSESSMENT FLOW CHART

Dimethicone June 2010



* For ingredient groups originating as Re-Reviews, add word "Amended" before Report; (DAR: Draft Amended Report).

△ Expert Panel Decision

▭ Document for Panel Review

Ingre-dients	Toxline &PubMed	ChemIDplus	Multidatabase (See legend*)	DART	Household Products	Beilstein	Registry	Kosmet	Napralert	RTECS	CAplus
DM	135	1	0	0	1	0	1	27	0	0	515
DA	0	**0**	0	0	0	0	0	0	0	0	4
DB	0	0	0	0	0	0	0	1	0	0	3
DBE	0	0	0	0	0	0	0	0	0	0	3
DBO	0	0	0	0	0	0	0	0	0	0	0
DCA	0	0	0	0	0	0	0	0	0	0	0
DCN	0	0	0	0	0	0	0	0	0	0	0
DCY	0	0	0	0	0	0	0	0	0	0	1
DDB	0	0	0	0	0	0	0	0	0	0	0
DFD	0	0	0	0	0	0	0	0	0	0	0
DH	0	0	0	0	0	0	0	0	0	0	1
DIB	0	0	0	0	0	0	0	0	0	0	0
DIP	0	0	0	0	0	0	0	0	0	0	0
DI	0	0	0	0	0	0	0	0	0	0	0
DK	0	0	0	0	0	0	0	0	0	0	0
DL	0	0	0	0	0	0	0	0	0	0	0
DMF	0	0	0	0	0	0	0	0	0	0	0
DM	0	0	0	0	0	0	0	0	0	0	0
DMS	0	0	0	0	0	0	0	0	0	0	0
DMB	0	0	0	0	0	0	0	0	0	0	0
DP	0	0	0	0	0	0	0	0	0	0	28
DSB	0	0	0	0	0	0	0	0	0	0	0
DSC	0	0	0	0	0	0	0	0	0	0	0
DSQ	2	1	0	0	1	0	0	0	0	0	0
DS	0	0	0	0	0	0	0	0	0	0	0
DSM	0	0	0	0	0	0	0	0	0	0	0
HC	0	0	0	0	0	0	0	0	0	0	0
ID	0	0	0	0	0	0	0	0	0	0	0
TD	0	0	0	0	0	0	0	0	0	0	4
TDC	2	1	0	0	0	0	0	0	0	0	0
ADA	0	0	0	0	0	0	0	0	0	0	0

*Data in Table: Publications used (Total no. in search); Multidatabase = HSDB, CCRIS, ITER, IRIS, Gene-Tox, and LacMed;

InitialSearch: 2-25-2010
Search Updated (PubMed+Toxline) on 5-19-2010. No useful information was found.

Ingredients

DM – Dimethiconol OR dyhydroxyplydmethylsiloxane OR 31692-79-2 OR 70131-67-8
DA – Dimethiconol arginine
DB – Dimethiconol beeswax OR 227200-35-3
DBE – Dimethiconol behenate OR 227200-34-2
DBO – Dimethiconol borageate OR 226994-45-2
DCA – Dimethiconol candelillate
DCN – Dimethiconol carnaubate
DCY – Dimethiconol cysteine
DDB – Dimethiconol dhupa butterate OR 243981-39-7
DFD – Dimethiconol fluoroalcohol dilinoleic acid
DH – Dimethiconol hydroxystearate OR 133448-13-2
DIB – Dimethiconol illipe butterate
DIP – Dimethiconol/IPDI copolymer OR 193281-67-3 OR 193281-67-3
DI – Dimethiconol isostearate OR 133448-14-3
DK – Dimethiconol kokum butterate OR 226994-48-5
DL – Dimethiconol lactate OR 227200-33-1

DMF – Dimethiconol meadowfoamate
DM – Dimethiconol methionine
DMS – Dimethiconol/methylsilanol/silicate cross polymer OR 68956-02-6
DMB – Dimethiconol mohwa butterate OR 225233-88-5
DP – Dimethiconol panthenol
DSB – Dimethiconol sal butterate
DSC – Dimethiconol/silica cross polymer
DSQ – Dimethiconol/silsesquioxane copolymer OR 68554-67-6
DS – Dimethiconol stearate OR 130169-63-0
DSM – Dimethiconol/stearyl methicone/phenyl trimethicone copolymer
HC – Hydrolyzed collagen PG-propyl dimethiconol
ID – Isopolyglyceryl-3 dimethiconol
TD – Trifluoropropyl dimethiconol
TDC – Trimethylsiloxysilicate/dimethiconol crosspolymer OR 68440-70-0
ADA – Acrylates/dimethiconol acrylate copolymer

Dimethiconol OR 227200-35-3 OR 227200-34-2 OR 226994-45-2 OR 243981-39-7 OR 133448-13-2 OR 193281-67-3 OR 193281-67-3 OR 133448-14-3 OR 226994-48-5 OR 227200-33-1 OR 68956-02-6 OR 225233-88-5 OR 68554-67-6 OR 130169-63-0 OR 68440-70-0

Dimethiconol Group

DR. BELSITO: Dimethiconol. This is the first time that we're looking at this ingredient. We got quite a bit of data, but unfortunately not all of the data that we needed to make a safety assessment. We felt that we needed manufacturing and impurities and UV absorption data, and, if UV absorption, photosensitization and photoirritation data may be needed.
Dermal absorption data are needed, and if we have dermal absorption, then reproductive toxicity data may be needed. We also received some data on a polymer that was labeled FD80 and FD80/2 and we wanted clarification as to what exactly was the composition of that polymer. It wasn't clear to our group. Those were the data needs.
Then there were other compounds to consider along with dimethiconol. Of that list, some of them were plant-derived fatty acids and

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seed oils, and we look forward to Christina's report to tell us exactly what the composition of those were, things like the borageate and dhupa butterate, et cetera. Some were amino acids and we felt that those could stay in the report as well as the fatty acids, pending a decision as to the composition of those. There were a couple though that we felt should come out of the report, specifically, the isophorone diisocyanate copolymer. It had no uses and I think it would be an issue in terms of isocyanate, both IGE-mediated sensitization respiratory-wise and also delayed-type hypersensitivity skin-wise, so that we would recommend that that dimethiconol IPDI copolymer be removed.
Also there were two fluorinated compounds that we felt should be removed from the list, the dimethiconol fluoroalcohol dilinoleic acid and the trifluoropropyl dimethiconol. One compound that we didn't want to delete at this point, but we did feel we needed more information on the dimethiconol silsesquioxane copolymer. So

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moving ahead with an insufficient and deleting three ingredients, the two fluoros and the diisocyanate, and requesting if we're going to keep the silsesquioxane copolymer in, more information on exactly what that was.
DR. BERGFELD: So you're making a motion?
DR. BELSITO: I'm making a motion.
DR. BERGFELD: And the motion is to go insufficient?
DR. BELSITO: It is to go insufficient and delete those three ingredients.
DR. BERGFELD: Is there a second?
DR. MARKS: Second.
DR. BERGFELD: Is there any further discussion?
DR. MARKS: Yes. We had similar concerns. We felt if we knew the molecular weight, the dermal absorption data may not be necessary. If it's a large enough molecule it wouldn't be absorbed. The safety of these ingredients is dependent on what was in that Dow

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mixture and we'd like to know what is in the Dow mixture. I think that's it from our team's point of view.
DR. BERGFELD: Dr. Liebler?
DR. LIEBLER: My point is very similar to the one Jim just said, that a lot of the safety data that's cited in the report just refers to a Dow proprietary designation and doesn't tell us what part of this dimethiconol chemical space is represented by those compounds so that it would be helpful if the report were annotated with information from the manufacturer that would better describe what the materials are.
DR. BERGFELD: Is there any other discussion? Dr. Slaga? Dr. Hill, anything? Dr. Klaassen, Dr. Snyder, nothing? I'll call for the vote then. It's been seconded. All those in favor of going for an insufficient? Approved. We'll go insufficient with those data needs.

to move on? What time is it?

MS. BECKER: It's 20 minutes until lunch.

DR. MARKS: Pardon?

MS. BECKER: It's only 20 minute until lunch.

DR. MARKS: Twenty minutes until lunch?

SPEAKER: Yes, we can get a break then.

DR. MARKS: You can get a break at lunchtime. The next is the dimethiconal, if I'm saying that correctly, group, and this is the first time the panel has seen this report. It's in the Green Book 1. So my sense, Lillian, was the team to move on until lunch.

MS. BECKER: (inaudible) just laying it out.

DR. MARKS: Oh, it's esters and reaction products. Are we going to get into the name structure, INCI, IUPAC. Shall we just save -- table it right now until we -- okay.

This is the first review, and I think the first question on page 20, we probably should

go over is on the report is, yeah, page 20. Oh, yeah. I went to page 20, because I went right to the structures here, Bart, and we had these end-capped homopolymers and the copolymers.

If you look at the top of Figure 1, we have dimethicone, which the panel has already reviewed it declared safe. That's on the left-hand side; on the right-hand side, we have the amodimethicone, which again was approved and found safe by the CIR.

And then we go at the bottom, and you see at the left-hand side a whole list of ingredients, and on the right- hand side another whole list of ingredients under the copolymers, and I think the first thing should be are there any alerts of ones that we should eliminate, and it gets back into since this is the first time we've seen it, it's not a no-brainer elimination.

We've got to eliminate for some reason. And if I'm correct, a number of these on both sides, like the dimethiconol beeswax, the dimethiconol behenate, have already been reviewed

and found safe; is that correct from page -- on Table 1, if you look on page 11 and 12, a number of these have been reviewed and declared safe in their conclusion.

So, in processing this as the first, do we really mean all those and then just combined into one report?

DR. HILL: Aren't those notations in Figure or in Table 1 referring to, well, to use the first example, beeswax had been reviewed, not the silicone product, just beeswax, and the next line down, behenyl alcohol, had been reviewed.

DR. MARKS: Okay. Thank you, Ron. So, is there anything that we should see chemically when you look at these, assuming that it is the INCI chemical that we're looking at, is there anything in here that doesn't -- that we should include and a good reason?

Does this make sense the way these have been divided into the end-capped homopolymers and the copolymers? I defer to Ron and Ron to that.

DR. SHANK: If you're asking about

removing any of these listed, I have three that I felt did not belong. Dimethiconol fluoroalcohol, dilinoleic acid seems not to fit with the others.

SPEAKER: Would you repeat them?

DR. SHANK: Dimethiconol fluoroalcohol, dilinoleic acid.

The fluoroalcohol could be a problem. The second one was dimethiconol IPDI Copolymer, and the third one was trifluoropropyl dimethiconol. I would delete those from the list.

DR. MARKS: And the reasons, Ron, you just didn't think that it fit in this group of chemicals.

DR. SHANK: Yes, the halogens could change the biological activity.

DR. MARKS: What was the third one again? I missed that. That was on the topolymers; correct; oh, the trifluoropropyl. Okay. The first one was the dimethiconol fluoro. Yes.

Ron Hill, any ones that you would like to eliminate from the list?

DR. HILL: I think these probably all need to be kept, depending on -- I'm not sure about that last three that he mentioned. I agree with what he said about the halogens. But I'm not sure. My general sense of this is that the data that would be relied -- that this is going to come to an insufficient data, and that pairing down the list is not going to change that. That's my general sense from reading the whole thing, because there's a lot of data in here that seems to relate to dimethoxy silicone that I don't see how that relates to these compounds at all.

And so there's a lot of data in here cited as toxicology that I'm not at all sure how that relates to the compounds that were looking at.

So I think we're going to -- I believe we're going to come to an insufficient data, and I don't see any reason to be removing very many compounds from this compilation.

But there may be a lot further discussion needed on that.

DR. MARKS: Okay. Again, this isn't -- doesn't meet the threshold of a no-brainer. The ingredient could be included if there are toxicologic problems with it or that it's we're seeing this for the first time.

So even though these halogenated products change the biologic activity, do you think that's a reason it should be removed from the whole -- the ingredient review or should you -- should we keep it in and just say there are problems with this. Unless we have very specific data, Ron -- Ron Shank -- that we couldn't rule on these being sufficient if we get to that point that are safe. What's your feeling or do you think it should be a -- actually a separate report of these halogenated products?

DR. SHANK: Yeah, I would expect that their toxicology could be different, and all of the -- most of the toxicology data we have is on a mixture from Dow Corning, and I'd like the chemists to tell me if that's -- if that mixture represents the cosmetic ingredients that we're

reviewing.

But the fluorinated compounds would be quite -- could be quite different.

So I would just take them out at the beginning.

DR. HILL: Let me give you my take on this and then maybe the audience members, if their -- have any opinions on this could comment is that we're here -- we're talking about a bunch of high molecular weight polymers. So my feeling was that really whatever is on the ends of those polymers could affect sensitization responses and uniquely, or we've got a big group of polymers that simply don't trigger any of the sensitization responses and so it kind of doesn't matter what's on the and other than do they get cleaved off in vivo in a way that might be of concern, because, otherwise, yeah, then you can rely on the toxicology of those caps; and, if they're cleaved in vivo, then you know in most cases something about them excepts perhaps these fluorinated alcohols that would make them separate.

But if really the whole issue is presenting to cells where sensitization is going to occur, then either the whole class is such that it almost never happens or it's every compound that is presented to the antigen-generated cells; what's on the end caps would matter greatly. I was wondering if somebody would come to the microphone and get.

DR. MARKS: Okay. I guess not, Ron. So we'll propose to delete those three halogenated compounds; the toxicology will be significantly different in those three ingredients.

And let's go then to now, since this is the first look at this, can we use the dimethicone and the (inaudible) methicone safety reports to help support this? Do we need more safety data?

MS. BERGFELD: Can I ask a question? Jay, I wonder if you could respond to my question, is the supplier for dimethicone Dow Chemicals only or are there other suppliers?

MS. GUERRERO: Hi. This is Tracy Guerrero from the Silicone Environmental Health

and Safety Council, and to answer that question, I'd have to go back to our members -- we -- as far as the actual suppliers go. We have a number of members who provided data, which were sent in, but I can't answer that specifically without going back to them.

This is not a primary group of materials that our association deals with as a whole. So I would need more information from them.

DR. MARKS: So data needs?

DR. SHANK: I think we need an explanation. Most of the toxicology data were on Dow Corning mixtures, and I'd like to have someone tell me what's the similarity between those mixtures and the cosmetic ingredients.

DR. MARKS: It doesn't sound like we are going to get that, at least today.

DR. SHANK: Okay. I think we also need absorption data.

DR. MARKS: Yes.

DR. SHANK: Skin absorption data on representative compounds.

DR. HILL: Well, or alternatively, some better idea about the molecular weights, because if they're all 5,000 molecular, I'm not sure we're going to be worried too much about skin absorption.

DR. MARKS: Do we need UV?

DR. SHANK: No.

DR. MARKS: No. And there is a mixture of irritation sensitization, but what I saw it looked like there really was little toxicity from an irritation and sensitization standpoint. I think your point, Ron, is exactly correct, which is how similar is the Dow mixture to the ingredients in cosmetics.

DR. SLAGA: Yeah, we need to have what's in that mixture and so we can interpret. To me, the only thing we can do is table it until -- because really everything else is kind of negative with the mixture, so.

DR. HILL: And on that score, Mr. Heldreth and Wilbur, I'm not sure that on your Figure 1 structures that that right-hand side

figure sufficiently encapsulates the list of compounds that are below it. In fact, I'm confident it does not.

So you've -- we've got basically one or two structures there, but looking at the list of what below -- on the right-hand side, not the left-hand side.

What's on the right-hand side I don't think your structure there encompasses, encapsulates, illustrates what those compounds are that are listed down below. There's a lengthy list of compounds. I don't think it gets it.

DR. BRESLAWEC: I'm not sure that it was intended to.

DR. HILL: No, I don't think it was.

DR. BRESLAWEC: I think it was an example.

DR. HILL: It says example, but I think we need to find a way to add structures, expand or make multiple figures, or whatever, inasmuch as is possible based on what's known about the structures of those compounds, which I could just

look at them and scribble and have a -- yeah, but, of course, the industry could supply you with I think something that would be.

DR. MARKS: Are there --

DR. HILL: Except if it's proprietary, and they can't divulge whatsoever, but even there, I think it's pretty clear.

DR. MARKS: Prior to getting the Dow mixture ingredients, are there any toxicologic issues or alerts with this, meaning we want the UV -- I mean the absorption or the molecular weight. Is there anything that stood out as being a toxicologic issue? No.

DR. SLAGA: Not to me.

DR. MARKS: Okay. So the real issue, and I get the sense, then, is to table to find out what's in the Dow mixture and how does that compare to the cosmetic ingredients we are reviewing and the motion would be to table it tomorrow.

DR. HILL: And, of course, there's an acrylate copolymer here, but we're looking at

those anyway; right? So a separate review; so I mean that -- we can rely on other review information.

DR. MARKS: Yes.

DR. HILL: We all pretty much asked how much monomer might be there, but, yeah.

DR. ANDERSEN: I think the -- I wouldn't lose, Jim, in your presentation -- if you can manage to get it in just before you move to table that there is a clear need for molecular weight information here, because there's no reason for us to come back at a later point and then raise that for the industry. Folks ought to know that that's an issue now and if it can be resolved and we get the clarification on just what does the Dow data refer to, then all those --

DR. HILL: Because I think in this case, for me, sensitization is going to be the major issue and what one would really like to know is across this group of compounds how consistently are they presented to antigen-generating cells and are they processed similarly? If we have a

representative sample, which I don't think we necessarily have, based on what's in the report, can we know that they'll be pretty consistent across the group, and I think we could, easily, but there needs to be a representative sample of.

DR. ANDERSEN: But if it all sits on the surface of the skin and never --

DR. HILL: Then it doesn't matter.

DR. ANDERSEN: -- then it doesn't matter.

DR. HILL: That was my first comment.

DR. MARKS: Any other comments. I'll move -- we'll table it. We really want to know what the molecular weight is, because we probably aren't going to get the absorption on all these. We want to know what is in the Dow mixture and then we're going to remove the three halogenated ingredients. Does that capture it? Did we make lunch?

MS. BECKER: Right there.

DR. MARKS: Right there. Okay.

(Whereupon, at 12:00 p.m., a

DR. BAILEY: Well, you know, I think we'll take this issue back to our science and support committee too because they bring a lot of experience and perspective on this to help us figure out how to present this, so.

DR. BELSITO: Just -- you know, I think that we have all the data. If we're going to be able to reach a conclusion we're not asking for anything more, we're just asking that the data be presented in a clearer fashion that really helps us, you know, set the restrictions on the impurities.

Okey-doke, so we're tabling it and everyone knows what they're doing and no one who's doing it is happy doing it.

Okay, dimethiconal, okay. It's the first time we're seeing this and we've got a decent amount of data and we've gotten comments from the SEHSC that it looks to me like you pretty much have incorporated, Wilbur, their comments.

MR. JOHNSON: Well, their comments haven't been incorporated but the actual data --

DR. BELSITO: The data has been incorporated, yes, that's what I meant. Okay.

So, I guess, the first thing is, this is the first time we're looking at it and so there were other ingredients that could be added to dimethiconal and its esters and reaction products, so before we even look at it, it goes to Dan to tell us whether he thinks all of these additional ingredients that Bart and CIR have added in are reasonable ingredients and those are listed in Table 1 starting on page 11.

DR. LIEBLER: I don't see a note to myself that says there's something wrong with that.

I don't have a concern about it written down, so.

DR. BELSITO: So then we need to look at we're adding in here in terms of whether it's been reviewed. Arginine we've not reviewed, right? Is that correct?

MS. BURNETT: Correct.

DR. BELSITO: Beeswax?

MS. BURNETT: Yes, (inaudible) they're in there.

DR. BELSITO: Safe as used, okay. Behenate, safe as used. Borage (inaudible) oil we've not reviewed, so that's -- and that's going to be a botanical, obviously, with all the issues of a botanical. So do we even want to go with borageate? I would probably delete that.

MS. BURNETT: (inaudible)

DR. BELSITO: I understand, but do we know what the fatty acids from borageate (inaudible) seed oil are?

SPEAKER: No, I haven't looked that one up yet.

MS. BURNETT: No, (inaudible) not familiar with (inaudible).

DR. BELSITO: Pardon?

MS. BURNETT: We're in the process of reviewing oils. I could tell you offhand.

DR. BELSITO: Okay. So if we were to keep it, we'd need to know what the fatty acids are in borago oil.

Candelillate, candelilla wax has been reviewed, so that's okay.

Cannauba wax, that's been reviewed. Cysteine we haven't reviewed. Does anyone have problems with arginine and cysteine? Okay. Dhupa butter. Dhupa butter, D-H? I never heard of that combination of two consonants together. Dhupa butterate. So it's the fatty acids from dhupa butter. Do we know what dhupa butter is? So we'd need to know the composition.

Okay. Fluorinated alcohol containing 6 to 20 carbons. I'm not sure we want to go there, do we, in fluoroalcohol.

DR. LIEBLER: I don't see any reason to.

DR. BELSITO: Are there even any cosmetic uses? Okay, the stearates we've reviewed. Illipe butterate, again, I think we need to know what the fatty acids in illipe butter are.

Here's what I have a problem with, dimethiconol and diisocyanate, isophorone diisocyanate. Isophorone diisocyanate is a really

strong sensitizer both for respiratory asthma and for cutaneous contact dermatitis, and I don't know that we need to get involved in those issues in this report, so I would get rid of that.

DR. KLAASSEN: Right. Right. It's an analogue of Bhopal, India.

DR. BELSITO: Of what, Kurt?

DR. KLAASSEN: The big blow up in Bhopal, India, 20, 30 years ago.

DR. BELSITO: Yeah, I remember that. Okay, so the next one, the siloxanes we've reviewed, that's okay. Same question here, what are the fatty acids in kokum butter?

Lactate is okay. Meadow foamate, again, what are the fatty acids? Methionine, okay. Silicate crosspolymers, we've done silicate, no?

DR. SNYDER: Well, we're doing it. We're in the process, right?

DR. BELSITO: I thought we finished off on that, no? So that's okay. Mohwa butter, we need the fatty acids; panthenol's okay; sal butter, we'd need to know what the fatty acids

are; silica, again, we should have passed off on that, so we need the reference. Trimethoxysilate, does anyone want to comment on that, this silsesquioxane copolymer, siloxane with siloxane.

DR. KLAASSEN: I don't think it should be included unless we can find something --

DR. LIEBLER: It's not a silica, it's --

DR. KLAASSEN: It's a misnomer?

DR. LIEBLER: Yeah.

DR. BELSITO: So, do we cross it out? Need a little more information?

DR. KLAASSEN: I'd say more information.

DR. BELSITO: Okay, stearate, we've reviewed. So, this trimethicone copolymer we've reviewed. Hydrolyzed collagen PG -- we've reviewed hydrolyzed collagen, no?

DR. EISENMANN: I think so.

DR. LIEBLER: Should be just a bunch of amino acids.

DR. BELSITO: All right. Isopolyglyceryl 1-3, dimethiconol --

DR. SNYDER: Falls under this

(inaudible).

DR. BELSITO: It's a --

DR. SNYDER: It's (inaudible).

DR. BELSITO: Mm-hmm.

DR. BAILEY: It's pretty closely related.

DR. BELSITO: Right. Trifluoropropyl, again, I don't think we should be looking at fluoro groups. Trimethylsiloxysilicate --

DR. BAILEY: That's pretty closely related.

DR. LIEBLER: Yup, it is.

DR. BELSITO: Okay, and then the acrylates. That's it. So, okay, so we are deleting -- or we're asking for the composition in the fatty acids for all of the plant products. We're deleting the fluoroalcohol, the diisocyanate and the trifluoropropyl dimethiconol and asking for clarification of the dimethiconol silsesquioxane copolymer.

MS. BURNETT: Dr. Belsito?

DR. BELSITO: Yes.

MS. BURNETT: I could get you -- I could possibly get you the fatty acid information on borago oil.

DR. BELSITO: It's no rush, I mean, because this is the first time we're looking at it.

MS. BURNETT: I have a spreadsheet I can pull up. Did you say you needed meadowfoamate?

DR. BELSITO: Yeah, we needed all the -- we needed borageate, we need --

MS. BURNETT: I only have a couple of them --

DR. BELSITO: -- mohwa, sal --

MS. BURNETT: Meadowfoam, I think is in cocoamidopropyl betaine, actually. (inaudible) composition.

DR. BELSITO: Okay. We need the dhupa butterate, we need the illipe butterate, we need the meadowfoamate, we need the mohwa butterate, we need the kokum, we need the sal butterate --

MS. BURNETT: Meadowfoam is in the CAPB report.

DR. BELSITO: Okay.
MS. BURNETT: So, it just needs to be brought into this report.
DR. BELSITO: Okay.
MS. BURNETT: So, basically all the ones that are plants we need the fatty acid compositions.
DR. BELSITO: Okay, so we have our list. In terms of what we don't have, we don't have UV absorption on these.
DR. SNYDER: Impurity (inaudible).
DR. BELSITO: Yeah. We don't have method of manufacturing and impurities. We don't have absorption metabolism rate in (inaudible).
We have no -- we have bacterial, but we have no mammalian genotox, but we do have a negative 36 month implantation study and a one year oral study, so the question is whether we needed anymore toxicity data on these ingredients. And except for the (inaudible) do -- if we -- do we need anything?
DR. SNYDER: Well, it's not absorbed.

DR. BELSITO: It's not absorbed. Right. So, I mean, that's really all we need would be absorption.
DR. SNYDER: I mean, the feeding study in the rat was only like.05 percent, so we can take that into consideration.
DR. BELSITO: Right, but I mean, it's not likely that these are going to be absorbed. It would be nice to -- I mean, if we just got some absorption data it would negate the need, I think, for reproductive or any more animal studies.
We have some sensitization and irritation, but at this point we don't have concentration of use, so it makes it hard to put that into --
DR. EISENMANN: You've got --
DR. SNYDER: We do. It hasn't been incorporated yet. John provided it in a memo, right?
DR. EISENMANN: But I got it in the back (inaudible).
DR. SNYDER: It's right here in that

last memo in the back.
DR. LIEBLER: Oh, in the supplemental?
DR. SNYDER: Way in the back of this report.
DR. EISENMANN: Somehow they managed to get this one in where they didn't (inaudible).
DR. SNYDER: It hasn't been added in yet, though.
SPEAKER: Which one is that?
DR. BELSITO: The --
DR. SNYDER: Right there.
DR. BELSITO: Yeah, okay. I missed it again. Concentration of use.
So, it has hairspray uses, so we'd need a hairspray boilerplate. Okay, so what we need are method of manufacturing and impurities. So, absorption would be nice. In the absence of absorption then we'd need some reproductive toxicity and we need UV. And then I have to go back and look at sensitization and irritation depending upon how that compares to the concentration of use because it wasn't somehow in

there, unfortunately. Then we have that (inaudible) sensitization --
DR. SNYDER: Well, we've got some human negative but I don't know what level that is.
DR. BELSITO: Five percent in the water emulsion, guinea pigs, did not induce sensitization. Humans, RIPT, 1.1 percent, 16 percent.
MR. JOHNSON: And in that list, data submission, I think, was called Wave 2. You actually received sensitization data on polymer FD-80 and that was tested at concentrations of 50 percent and 100 percent in the guinea pig sensitization test.
DR. BELSITO: And on page 7, Wilbur, the dimethiconol beeswax, there's no listed concentration. Was that known?
MR. JOHNSON: Use concentration?
DR. BELSITO: Yeah.
MR. JOHNSON: Oh, what page?
DR. BELSITO: Page 8, dimethiconol beeswax. It says, "the skin sensitization

potential of a test product identified as dimethiconol beeswax was evaluated in an RIPT using 102 subjects with no significant active skin pathology." It never says the percentage. If you could check and see what that was.

DR. LIEBLER: We've got irritation and sensitization on one, sort of lipid derivative, because these are mostly basically silica polymers and then a big group of these natural product-derived ones are lipid or fatty acid derivatives. So, we probably ought to make sure that we're covered with some data on representative fatty acid derivatised compounds as well as just the silica polymers.

DR. BELSITO: Well, we may be covered once we find out what the fatty acids are. We may have already reviewed them.

DR. LIEBLER: Right, but I mean, just that the silica polymer with the fatty acid on it, that molecule may have different biological properties than just the dimethiconol itself without the fatty acid baggage and even if the

fatty acid piece by itself has been reviewed, I don't know that that means that we know how the dimethiconol with the fatty acid chains will necessarily behave.

DR. BELSITO: So, what additional information? Do you want metabolism on those?

DR. LIEBLER: No, not necessarily, but I just would like to make sure that we have representative data from that type of compound as well. As I scroll through this I see that we've got dimethiconol beeswax and behenate in the skin irritation and sensitization. And then we have -- scroll up -- in the animal -- or, let's see -- yeah, in the animal studies we have just the stearate, I believe.

DR. SNYDER: That supplemental (inaudible) had a whole bunch more sensitization data in it.

DR. LIEBLER: Okay. I don't remember if that includes the studies --

MR. JOHNSON: One study.

DR. SNYDER: One study was all?

MR. JOHNSON: Yeah, but you had acute dermal, acute oral --

DR. SNYDER: Right.

MR. JOHNSON: Ocular irritation also.

DR. SNYDER: Right.

DR. EISENMANN: So, (inaudible) compound is --

DR. LIEBLER: Yeah, and it's just to represent that part of this chemical space.

DR. EISENMANN: So, can you tell me what (inaudible)?

DR. LIEBLER: Oh, I see. An example compound could be the stearate derivatives of the represented dimethiconols.

DR. EISENMANN: So, dimethiconol stearate or hydroxyl stearate? One of those?

DR. LIEBLER: Something like that.

DR. EISENMANN: Okay.

DR. BELSITO: Okay, so let me reiterate where we are. Insufficient method of manufacturing and impurities. UV absorption, yes? No?

DR. SNYDER: Yes.

DR. BELSITO: Okay. Cutaneous absorption, dermal absorption, and if not, then we need a dermal reproductive toxicity study. Do we need anything else? We're satisfied with a feeding study and the (inaudible) study to serve for our other tox needs? And then we're asking for sensitization and irritation on one of the fatty acids? Or, what do you need on fatty acids, Dan?

DR. LIEBLER: Sensitization and irritation on fatty acid derivative or representative fatty acid derivative dimethiconol.

DR. BELSITO: Anything else on a representative fatty acid derivative? Dermal absorption? Reproductive toxicity?

DR. LIEBLER: I wouldn't expect these things to be absorbed very well, but do we want to have the data?

DR. BELSITO: I mean, I'm not sure why you would be concerned that the -- I mean, if anything, if they don't break down into their

constituents, dimethiconol and fatty acid, they're going to be so large I don't think they would be a sensitizer if they're not going to get through. But if they do break down then I think that sensitization irritation data for the fatty acids, once we know what they are, that we've reviewed will be adequate.

DR. LIEBLER: I guess I have less of a feel for what's going to be irritating and sensitizing than you guys do, so I'll defer if you feel it's not necessary.

DR. BELSITO: Fatty acids are rarely irritating or sensitizing, even at 100 percent.

DR. LIEBLER: Okay. I was only concerned that this silica polymer with the fatty acid ornamentation could cause a problem.

DR. EISENMANN: And there is a little bit -- there's a primary irritation study --

DR. BELSITO: Right.

DR. EISENMANN: -- done with dimethiconol stearate. And high irritation.

DR. LIEBLER: Okay, so I'll back off on

that.

DR. BELSITO: Okay, so then if we back off on that we're left with manufacturing, impurities, UV, dermal absorption, or in the absence of dermal absorption, reproductive -- dermal reproductive toxicity.

DR. SNYDER: And UV (inaudible) phototox.

DR. BELSITO: And UV, right, if positive photo.

DR. SNYDER: Yeah. It's the standard.

DR. BELSITO: And are there any of these add-ons? Fatty acids we're not going to be concerned about UV absorption. The -- what about the amino acids? They're going to absorb down in this UVC. They're going to be like 250-something, right?

DR. LIEBLER: There are no aromatics --

DR. BELSITO: No, so we're not really --

DR. LIEBLER: -- (inaudible) sustained.

DR. BELSITO: Yeah, they're all going to be around 250, right?

DR. LIEBLER: Oh, no, well lower than that.

DR. BELSITO: So, we don't have any concerns there, so there's no real represent -- just show us some data on dimethiconol and that'd be nice.

That's it. Right?

MR. JOHNSON: Can I just make one comment, Dr. Belsito. I know (inaudible) team expressed concern over the data on Dow Corning materials that were submitted, as to whether or not those data are representative of the dimethiconol ingredients as named in this report. So, you know, specifically, you know, what is the composition of the Dow Corning materials in these studies that are included, just to make sure that these data are actually, you know, on the -- can be used to support the safety of the cosmetic ingredients named in the safety assessment. That's why we say we have data. We don't know whether or not those data are actually, you know, data on dimethiconol and the other chemicals as

named in the safety assessment.

DR. BELSITO: Assuming they are. So, I mean, we've never questioned when the industry has given us data other than to sometimes ask is it the same manufacturing or the same product that was used for drug use or whatever, so what are they asking you to do?

DR. SNYDER: Was there some specific thing that they were concerned about in the --

DR. BELSITO: Throw out those reports. Go back to Dow Corning and ask them to --

MR. JOHNSON: Well, they're actually asking Dow to provide data on the composition of the materials for which data were submitted.

For example, that wave two data --

DR. BELSITO: Right.

MR. JOHNSON: Those were on polymer FD80 and polymer FD80/II.

DR. BELSITO: Right.

MR. JOHNSON: So, just knowing whether or not those data are really -- relate to the ingredients that are named in the safety

assessment.

DR. BELSITO: And they didn't say what those were in that report?

MR. JOHNSON: All we know is that all those Dow Corning materials are associated with the CAS number 70131-67-8.

DR. BAILEY: That should be the same then, I would think.

DR. SNYDER: I'd say the CAS number gives you more confidence in that.

DR. BELSITO: Yeah.

DR. BAILEY: It's as close as you're going to get.

DR. BELSITO: Yeah.

DR. EISENMANN: But the second batch of material isn't Dow Corning, right? It's another company.

DR. BELSITO: But if it gets us the CAS number, that's much more specific than we have ever had.

DR. EISENMANN: It didn't come in --

DR. BELSITO: Before we just had verbal

reports that this unknown product contained 6.2 percent of what we're looking at. I mean, that's -- I don't know how much better you can get if you know the CAS number.

MR. JOHNSON: We have the sponsor's name, I think it was Wacker --

DR. EISENMANN: Right.

DR. BAILEY: Right, this is the Hazelton.

MR. JOHNSON: Hazelton Laboratories, yeah.

DR. EISENMANN: So, you have Dow Corning and -- you have two suppliers that provided --

MR. JOHNSON: Two different ones, yes.

DR. BELSITO: And we have CAS numbers for them, so what else -- I mean --

MS. BRESLAWEC: I think the issue Wilber's raising is that the other group was concerned that this was an issue that he would like you to discuss it to see --

DR. BELSITO: If we have CAS numbers it's a nonissue.

MS. BRESLAWEC: That's your due.

DR. BELSITO: And in fact do we have CAS numbers for them?

MR. JOHNSON: Well, we have two CAS numbers that are supposed to --

DR. BELSITO: In the --

MR. JOHNSON: No.

DR. BELSITO: I don't have my computer, so in the second wave of what was sent --

MR. JOHNSON: We don't have --

DR. BELSITO: -- how were the products identified?

MR. JOHNSON: Just as polymer FD80 and polymer FD80/II.

DR. BELSITO: But I thought that you said just before that they were associated with a CAS number?

MR. JOHNSON: No, that referred to the data provided by the Silicones Environmental Health and Safety Council, all those data that were received initially.

DR. SNYDER: Oh, okay. I see.

DR. BELSITO: In the second wave, how are -- do you have it printed out there?

MR. JOHNSON: Yeah.

DR. BAILEY: (inaudible) trade magazine.

DR. BELSITO: Polymer FD80 (inaudible).

DR. EISENMANN: (inaudible) get to the back.

DR. BAILEY: That's all right, I mean, just for them to confirm the CAS number or identity. Because it is polymer FD80.

DR. LIEBLER: I think even though these have CAS numbers assigned to them, the CAS number isn't the very specific definition of the molecule in the way the CAS number for aspirin would be, for acetylsalicylic acid.

DR. BAILEY: It's ranges, though.

DR. LIEBLER: But, I mean, this CAS number is for polysiloxane dimethyl hydroxyl terminated, and those could be big, big guys, or little, little guys, or mixtures thereof, and those are generically similar but actually a variety and different. And the Dow nomenclature,

their naming conventions, probably describe mixtures of chemical substances that have been characterized at least at Dow and perhaps the concern is that information is not available to us to allow us to map those test compounds to this product --

DR. BELSITO: Yeah. In fact, we don't even know what it is. So, yes, that -- we definitely need to go back to Hazelton or to Wacker who sponsored these studies. Second wave came from Hazelton and was sponsored by a West German -- at that point, West German company, and they just have polymer FD80. We don't know what polymer FD80 is --

DR. LIEBLER: What it means, right.

DR. BELSITO: So, yes. We need clarification of what's in polymer FD80 and what's in polymer FD80/II.

DR. SNYDER: So, did they supply that at your request, John, or -- who -- how did we get that data?

DR. BAILEY: The silicones SCHSC were --

was aware that this review was coming and provided it --

DR. SNYDER: So, we didn't get a cover memo explaining what the data represented?

DR. EISENMANN: No, it didn't (inaudible) sent it directly.

DR. SNYDER: Okay.

MR. JOHNSON: So, we need to send a cover memo.

DR. BELSITO: Okay, anything else? Okey-doke. Pelargonic acid. Okay. Also known as nonanoic acid, its esters and diesters. The last meeting we went insufficient with potential for dermal sensitization and irritation at current concentration of use of isodecyl isononanoate at 80 percent, and now this time we find that it's not used at 80 percent anymore, ethylhexyl is the highest use. And what happened? How did that come about? They decided they didn't want to support it at 80 percent or it was a miscalculation? Because it went from 80 to 8.

DR. SNYDER: Twenty-three.

One. So we have one against and four. Thank you very much. That was very worthwhile.

Moving on to the next ingredient, dimethiconol. Dr. Belsito?

DR. BELSITO: Dimethiconol. This is the first time that we're looking at this ingredient. We got quite a bit of data, but unfortunately not all of the data that we needed to make a safety assessment. We felt that we needed manufacturing and impurities and UV absorption data, and, if UV absorption, photosensitization and photoirritation data may be needed.

Dermal absorption data are needed, and if we have dermal absorption, then reproductive toxicity data may be needed. We also received some data on a polymer that was labeled FD80 and FD80/2 and we wanted clarification as to what exactly was the composition of that polymer. It wasn't clear to our group. Those were the data needs.

Then there were other compounds to consider along with dimethiconol. Of that list, some of them were plant-derived fatty acids and

seed oils, and we look forward to Christina's report to tell us exactly what the composition of those were, things like the borageate and dhupa butterate, et cetera. Some were amino acids and we felt that those could stay in the report as well as the fatty acids, pending a decision as to the composition of those. There were a couple though that we felt should come out of the report, specifically, the isophorone diisocyanate copolymer. It had no uses and I think it would be an issue in terms of isocyanate, both IGE-mediated sensitization respiratory-wise and also delayed-type hypersensitivity skin-wise, so that we would recommend that that dimethiconol IPDI copolymer be removed.

Also there were two fluorinated compounds that we felt should be removed from the list, the dimethiconol fluoroalcohol dilinoleic acid and the trifluoropropyl dimethiconol. One compound that we didn't want to delete at this point, but we did feel we needed more information on the dimethiconol silsesquioxane copolymer. So

moving ahead with an insufficient and deleting three ingredients, the two fluoros and the diisocyanate, and requesting if we're going to keep the silsesquioxane copolymer in, more information on exactly what that was.

DR. BERGFELD: So you're making a motion?

DR. BELSITO: I'm making a motion.

DR. BERGFELD: And the motion is to go insufficient?

DR. BELSITO: It is to go insufficient and delete those three ingredients.

DR. BERGFELD: Is there a second?

DR. MARKS: Second.

DR. BERGFELD: Is there any further discussion?

DR. MARKS: Yes. We had similar concerns. We felt if we knew the molecular weight, the dermal absorption data may not be necessary. If it's a large enough molecule it wouldn't be absorbed. The safety of these ingredients is dependent on what was in that Dow

mixture and we'd like to know what is in the Dow mixture. I think that's it from our team's point of view.

DR. BERGFELD: Dr. Liebler?

DR. LIEBLER: My point is very similar to the one Jim just said, that a lot of the safety data that's cited in the report just refers to a Dow proprietary designation and doesn't tell us what part of this dimethiconol chemical space is represented by those compounds so that it would be helpful if the report were annotated with information from the manufacturer that would better describe what the materials are.

DR. BERGFELD: Is there any other discussion? Dr. Slaga? Dr. Hill, anything? Dr. Klaassen, Dr. Snyder, nothing? I'll call for the vote then. It's been seconded. All those in favor of going for an insufficient? Approved. We'll go insufficient with those data needs.

DR. MARKS: This is the first time we've seen this first draft report. Scientific Literature Review has sent out for the methyl

Draft Tentative Report on the Safety Assessment of the Cosmetic Ingredient Review Expert Panel

On the Safety Assessment of Dimethiconol and its Esters and Reaction Products

June 28, 2010

The 2010 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 F. Alan Andersen, Ph.D. This report was prepared by Wilbur Johnson, Jr., Senior Scientific Analyst.

Cosmetic Ingredient Review

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INTRODUCTION

This safety assessment includes dimethiconol and its esters. These reaction products can be categorized into two types:

1) end-capped homopolymers: dimethiconol arginine, dimethiconol beeswax, dimethiconol behenate, dimethiconol borageate, dimethiconol candelillate, dimethiconol carnaubate, dimethiconol cysteine, dimethiconol dhupa butterate, dimethiconol, dimethiconol hydroxystearate, dimethiconol illipe butterate, dimethiconol isostearate, dimethiconol kokum butterate, dimethiconol lactate, dimethiconol meadowfoamate, dimethiconol methionine, dimethiconol mohwa butterate, dimethiconol panthenol, dimethiconol sal butterate, and dimethiconol stearate; and

2) 2) copolymers: hydrolyzed collagen PG-propyl dimethiconol, dimethiconol/methylsilanol/silicate crosspolymer, dimethiconol/silica crosspolymer, dimethiconol/silsesquioxane copolymer, dimethiconol/stearyl methicone/phenyl trimethicone copolymer, isopolyglyceryl-3 dimethiconol, trimethylsiloxysilicate/dimethiconol crosspolymer, and acrylates/dimethiconol acrylate copolymer.

The end-capped homopolymers consist of polymers chains made from dimethyl siloxyl monomers, wherein each end of the polymer chain is capped with an ester side chain (e.g, dimethiconol behenate, a dimethyl siloxyl polymer which terminates on each end with the behenate ester). The copolymers consist of two monomers polymerized together. The skin conditioning agent/hair conditioning agent function in personal care products is associated with most of these ingredients.

Of the 28 ingredients that are being reviewed in this safety assessment, the following 9 are reported to the Food and Drug Administration as being used in personal care products: dimethiconol, dimethiconol arginine, dimethiconol beeswax, dimethiconol cysteine, dimethiconol meadowfoamate, dimethiconol methionine, dimethiconol panthenol, dimethiconol stearate, and trimethylsiloxysilicate/dimethiconol crosspolymer. Current use concentration data from the Personal Care Products Council also indicate that, while not reported to the VCRP, the following ingredients are also being used in cosmetic products: dimethiconol behenate, dimethiconol/silsesquioxane copolymer, and acrylates/dimethiconol acrylate copolymer.

The CIR Expert Panel has reviewed the safety of similar chemicals, dimethicone and amodimethicone, in cosmetics and concluded that both are safe as used in cosmetic products.[1] Excerpts from the summary and discussion in this safety assessment are included.

Most of the toxicity data included in this safety assessment are related to α,ω-dihydroxydimethyl-polysiloxanes associated with CAS No. 70131-67-8, from Dow Corning. These hydroxy-terminated dimethyl siloxane (silicone) polymers are often listed in the CAS Registry and various literature references as siloxanes and silicones, dimethyl, hydroxy-terminated; or dimethoxy silicone/silane, hydroxy-terminated. The data herein refers specifically to Dow Corning chemicals associated with the CAS No. 70131-67-8 at concentrations of $\geq$ 95%. Siloxanes and silicones, dimethyl, hydroxy-terminated and CAS No. 70131-67-8 are listed among the other chemical names/identification numbers for dimethiconol in the *International Cosmetic Ingredient Dictionary and Handbook*; however, the name dimethiconol is not mentioned in any of the toxicity studies. Additionally, the name dimethiconol is not associated in the CAS Registry with CAS No. 70131-67-8. Instead, dimethiconol is associated with CAS No. 31692-79-2. As both CAS Registry files describe hydroxy-terminated dimethyl siloxane, the discrepancy is likely an error.

CHEMISTRY

DEFINITION AND STRUCTURE

Chemical definitions, other chemical names, and cosmetic ingredient functions for the ingredients reviewed in this safety assessment are included in Table 1.[2] The ingredient moieties that have been reviewed by the CIR Expert Panel are also identified. Because the dimethiconol fatty acid (FA) moieties are of botanical origin by definition, information on the composition of oil/butter sources of these FAs is included in Table 2. Chemical structures for dimethiconol[3] and its representative siloxanes are included in Figure 1A. The chemical structures for 3 dimethiconol polymers are included in Figure 1B.

Data provided by the Personal Care Products Industry [4] indicate that dimethiconol stearate and dimethiconol beeswax are supplied at approximately 100% active. Similar information on the remaining ingredients included in this review were not provided.

CHEMICAL AND PHYSICAL PROPERTIES

Dimethiconol and the copolymers have a reactive hydroxyl group on the terminal portion of the molecule. The hydroxyl group is bonded directly to the silicon atom in a silicon-oxygen bond. These compounds condense, under acid or alkaline catalysis, and also undergo ethoxylation. When these compounds undergo condensation reactions in the presence of an acid or base, the molecular weight is increased (i.e., an increase in the n value) and water is released.

The limited available data on the properties of dimethiconol, dimethiconol Beeswax, dimethiconol behenate, and Dimethiconol/silsequioxane copolymer (5%) and dimethiconol (20%) in anionic surfactant emulsion, are included Table 3; information on the remaining compounds was not found**.** Neither UV absorption data nor octanol-water partition coefficients for dimethiconol or any of the other compounds reviewed in this safety assessment were found in the published literature. As indicated in Table 4, the composition of many of the substances comprising the test materials evaluated in this safety assessment remains unknown.

ANALYTICAL METHODS

Dimethiconol has been analyzed via infrared spectroscopy.[5] The same method has been used to analyze dimethiconol (60%) in anionic surfactant emulsions[6] and dimethiconol/silsequioxane copolymer (5%) and dimethiconol (20%) in anionic surfactant emulsions.[7]

USE

PURPOSE IN COSMETICS

Most of the ingredients reviewed in this safety assessment function either as a skin conditioning agent or hair conditioning agent in personal care products (Table 1)[2].

SCOPE AND EXTENT OF USE IN COSMETICS

According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2009,[8] the following ingredients are being used in personal care products: dimethiconol (935 products), dimethiconol arginine (4 products), dimethiconol beeswax (13 products), dimethiconol cysteine (6 products), dimethiconol meadowfoamate (9 products), dimethiconol methionine (4 products), dimethiconol panthenol (6 products), dimethiconol stearate (9 products), and trimethylsiloxysilicate/dimethiconol crosspolymer (2 products). These data are summarized in Table 5. Independent of these data, the results of a survey of current ingredient use concentrations that was conducted by the Personal Care Products Council in 2009 are also summarized in Table 5.[9] For example**,** dimethiconol is used in 55 of the 1,744 body and hand creams, lotions, and powders reported to the VCRP, and results from the separate industry survey indicate use of this ingredient at concentrations ranging from 0.004% to 36% in these products. This concentration range is inclusive of the highest and lowest reported use concentrations of ingredients reviewed in this safety assessment. In other cases, e.g. dimethiconol arginine, uses are reported to the VCRP, but use concentration data are not available.

Current use concentration data from the Personal Care Products Council also indicate that, while not reported to the VCRP, the following ingredients are also being used in cosmetic products: dimethiconol behenate, dimethiconol/silsesquioxane copolymer, and acrylates/dimethiconol acrylate copolymer.

The use of amodimethiconol in personal care products is also being reported to the FDA;[8] however, amodimethiconol is not listed in the *International Cosmetic Ingredient Dictionary and Handbook* [2] and data on this ingredient were not found in the published literature. Amodimethiconol is not included in this assessment.

Personal care products containing these ingredients may be applied to the skin, nails, or 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, nails, or hair for variable periods following application. Daily or occasional use may extend over many years.

NONCOSMETIC USE

The insecticidal activity of dimethoxy silicone/silane, hydroxy-terminated has been reported.[10]

ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION

Information on absorption, distribution, metabolism and excretion of the ingredients reviewed in this safety assessment were not identified in the published literature.

ANIMAL TOXICOLOGY

The following data are included in this section: acute inhalation toxicity, acute oral toxicity, acute dermal toxicity, ocular irritation, skin and mucous membrane irritation, skin sensitization, and chronic toxicity/tumorigenicity. Some of the studies (unpublished data summaries) were provided by the Silicones Environmental, Health and Safety Council of North America (SEHSC), and all of the SEHSC studies are on chemicals that contain ≥ 95% CAS No. 70131-67-8 (polysiloxanes, di-Me, hydroxy-terminated).[11] *However, in the Chemical Abstract Service's Registry database,*[12] *CAS No. 31692 -79-2, but not CAS No. 70131-67-8, is listed as the CAS No. for dimethiconol (dihydroxypolydimethylsiloxane).*

The published literature was not found to contain short-term toxicity, subchronic toxicity, reproductive toxicity, or phototoxicity/photosensitization data on the ingredients reviewed in this safety assessment.

ACUTE INHALATION TOXICITY

The acute inhalation toxicity[13] of a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl (20%) was evaluated using groups of 10 Hilltop-Wistar rats (5 males, 5 females/group). The animals were exposed to vapor substantially saturated with the test material for 6 hours. None of the animals died, and neither signs of toxicity nor remarkable necropsy findings were observed.

ACUTE ORAL TOXICITY

In 4 acute oral toxicity studies (rats), none of the animals died, and there were no signs of toxicity.

The acute oral toxicity[13] of a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl (20%) was evaluated using groups of 10 Hilltop-Wistar albino rats (5 males, 5 females/group). The test substance was administered by stomach tube up to a dose of 16.0 ml/kg. None of the animals died and there were no signs of toxicity. Mottled lungs (red or pink and dark red) were noted at necropsy. The LD50 was > 16.0 ml/kg.

An acute oral toxicity study summary on a suspension containing Dow Corning® 60,000CSt, NO CO-SOLVENT in corn oil (20% w/v) (containing ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) was provided by the SEHSC.[11] A single dose of the test substance (2 g/kg body weight) was administered to 10 sprague-Dawley rats by gavage. None of the animals died and there were no overt signs of toxicity during the 14-day observation period. Lesions were not observed at gross necropsy. The LD50 was > 2 g/kg body weight.

The acute oral toxicity of polymer FD 80 (composition not stated) was evaluated using Sprague-Dawley rats (5 males, 5 females). The test substance was administered by gavage at a dose of 2009 mg/kg, and necropsy was performed after day 14. None of the animals died and there was no evidence of pathological clinical signs. The LD50 was > 2009 mg/kg[14].

Dimethiconol Stearate

The acute oral toxicity of dimethiconol stearate was evaluated using 10 fasted, Wistar-derived albino rats (5 males, 5 females).[15] Following dosing by gavage (dose = 5 g/kg body weight), feed and water were provided *ad libitum*. Dosing was followed by a 14-day observation period. Dimethiconol stearate was classified as non-toxic (LD50 > 5 g/kg).

ACUTE DERMAL TOXICITY

While acute dermal toxicity studies have either local irritation reactions or not, in all cases the LD_{50} values were >2g/kg, indicating low acute dermal toxicity.

The acute dermal toxicity[13] of a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl) (20%) was evaluated using groups of 8 New Zealand White rabbits (4 males, 4 females/group). The test substance was applied (doses up to 16.0 ml/kg; 24 h period) under impervious plastic sheeting to clipped, intact skin of the trunk. Skin irritation was not observed. One male rabbit and 2 female rabbits died (all at 16 ml/kg dose). Mottled lungs (males) and mottled livers/lungs (females) were noted at necropsy. There were no remarkable necropsy findings in surviving animals. LD50s were > 16.0 ml/kg for males and females.

In another study,[16] the acute dermal toxicity of siloxanes and silicones, dimethyl, hydroxy-terminated (22 wt. %) in Dow Corning ® 2-1845 microemulsion (remaining composition not stated) was evaluated using 12 (6 males, 6 females) New Zealand White rabbits of the Hra:(NZW)SPF strain. The undiluted test substance was applied (under an occlusive wrap) to clipped dorsal skin at a dose of 2,000 mg/kg (dose volume = 1.9741 ml/kg) for approximately 24 hours. The following reactions (all test substance-related) were observed at the application site: erythema and desquamation (6 rabbits), erythema and edema (1 rabbit), and desquamation (1 rabbit). None of the animals died during the 14-day study, and there were no test substance-related effects on body weight gain. Macroscopic findings were not observed at necropsy. It was concluded that the Dow Corning ® 2-1845 microemulsion was non-toxic (LD50 > 2,000 mg/kg).

An acute dermal toxicity study summary on Dow Corning® 60,000CSt, NO CO-SOLVENT was provided by the SEHSC.[11] The test substance was applied to the skin of each of 10 (5 males, 5 females) New Zealand white rabbits for 24 h. Erythema was observed at application sites, having cleared by day 7. None of the animals died and there were no signs of systemic toxicity during the 14-day observation period. An acute dermal LD50 of > 2 g/kg body weight was reported.

The acute dermal toxicity of polymer FD 80 (composition not stated) was evaluated using Sprague-Dawley rats (5 males, 5 females). The test substance was applied to the skin at a dose of 2009 mg/kg, and necropsy was performed after day 14. None of the animals died and there was no evidence of pathological clinical signs. The LD50 was > 2009 mg/kg.[17]

SUBCHRONIC ORAL TOXICITY

Neither mortalities nor test substance-related findings were reported in a subchronic oral study in which rabbits were fed a basal diet containing 0.05% Dow Corning special polymer (polymerized siloxane) for 8 months.

In an 8-month feeding study,[18] 6 of 18 rabbits were fed 0.05% Dow Corning special polymer 5-26-64, a polymerized siloxane containing siloxanes and silicones, dimethyl, hydroxy-terminated, in a basal diet. The remaining 12 rabbits comprised the control group (basal diet only). Both groups had equal numbers of males and females. None of the animals died during the feeding period, and all animals were killed after 8 months.

In both groups, signs of nasal/ocular irritation included nasal exudates, sneezing, and iridial inflammation for 1 to 2 h after feeding. There were no significant changes in weight (increases or decreases) in either group, and hematologic determinations revealed no abnormalities. Elevated serum cholesterol values were not test substance-related, and biochemical determinations indicated no effects on liver or biliary function. Additionally, urinalyses revealed no significant findings. At necropsy, there was no evidence of treatment-related effects in the abdominal viscera. However, all treated males had gross changes that were associated with the gonads, including one with a

prostate described as soft and practically gelatinous. Microscopic findings in the liver and kidneys of treated and untreated rabbits did not differ significantly. Incomplete testicular development was noted in 2 treated males. This finding is frequently observed in laboratory rabbits, although it was not observed in the study's concurrent control males. It was concluded that there was no evidence that test substance administration caused any adverse effects in rabbits.[18]

OCULAR IRRITATION

Some studies report an absence of ocular toxicity, but others demonstrate ocular irritation and/or corneal injury. The Dow Corning® 35 emulsion containing siloxanes and silicones, dimethyl, hydroxy-terminated at a concentration of 13% was the highest test concentration that did not induce ocular irritation.

The ocular irritation potential of an emulsion (Dow Corning® 35 emulsion)[19] containing siloxanes and silicones, dimethyl, hydroxy-terminated at a concentration of 13% and another emulsion (Dow Corning® 22 emulsion) containing siloxanes and silicones, dimethyl, hydroxy-terminated at a concentration of 38% was evaluated using 2 groups of 10 albino rabbits (1 per test substance). Two drops of either emulsion were instilled into the right conjunctival sac, followed by rinsing. Two drops were also instilled into the left eye (not rinsed). Following instillation, the eyes were observed for conjunctival and corneal responses for up to 48 h, or as long as 9 days post-instillation, if warranted. The Dow Corning® 35 emulsion did not induce a significant ocular response in rinsed or unrinsed eyes. The Dow Corning® 22 emulsion elicited slight, transient conjunctivitis only in the unrinsed eye and appeared to elicit appreciable pain.

The ocular irritation potential of a mixture[13] containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl) (20%) was evaluated using groups of 6 New Zealand White rabbits (3 males, 3 females). The test substance was instilled into the lower conjunctival sac of one eye per animal per group at volumes up to 0.1 ml. Six eyes were dosed per test volume. Dose volumes of 0.005, 0.01, and 0.1 ml induced moderate, persistent corneal and conjunctival injury (in all rabbits per group). Moderate iritis was also observed at a dose volume of 0.1 ml. All reactions had cleared by day 21 post-instillation.

An ocular irritation study summary on Dow Corning® 60,000CSt, NO CO-SOLVENT was provided by the SEHSC.[11] The undiluted test substance was instilled (0.1 ml) into the right eye of each of 3 female New Zealand white rabbits. Conjunctival erythema, chemosis, and discharge were observed in all rabbits, having cleared by 72 h post-instillation. Lesions of the cornea or iris were not observed. The test substance was classified as a non-irritant.

The SEHSC[11] also provided an ocular irritation study summary on Dow Corning® PA Fluid. Direct contact with the test substance resulted in very slight redness in the unrinsed rabbit eye through 48h. The rinsed eye was clear at 24 h post-exposure.

The ocular irritation potential of polymer FD 80/II (composition not stated) was evaluated using 6 albino rabbits. The test substance (0.1 ml or 100 mg) was instilled into the inferior conjunctival sac of one eye, and ocular reactions were evaluated for up to 72 h post-instillation. Polymer FD 80/II was classified as a slight ocular irritant.[20]

Dimethiconol Stearate

The ocular irritation potential of dimethiconol stearate was evaluated using 6 healthy, young adult New Zealand albino rabbits.[21] The test substance (0.1ml) was instilled into the one eye of each animal; contralateral eyes served as controls. Ocular lesions were evaluated according to the Draize scale (0 to 110). An ocular irritation score of 0 was reported for each rabbit, and dimethiconol stearate was classified as nonirritating to the eyes of rabbits.

SKIN IRRITATION

The following t*ested ingredients were non-irritating in studies involving rabbits: a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl) (20%); Dow Corning®, No Co-Solvent; and dimethiconol stearate.*

The skin irritation potential of a mixture[13] containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl) (20%) was evaluated using 6 New Zealand White rabbits (3 males, 3 females). The test substance was applied (0.5 ml, 4-h application) under a gauze patch to clipped, intact skin. The patch was covered with impervious sheeting. Reactions were scored according to the following Draize scale: 0 (no erythema) to 4 (severe erythema). Skin irritation was not observed in any of the rabbits.

A skin irritation data summary on Dow Corning®, No Co-Solvent was provided by the SEHSC.[11] The undiluted test substance (0.5 g) was applied to clipped/shaved skin of the back of each of 3 female New Zealand white rabbits. The application site was covered with a cotton gauze patch secured with porous tape for 4 h. Reactions were scored for up to 72 h post-removal. None of the rabbits had signs of dermal irritation or corrosivity, and the test substance was classified as a non-irritant.

Dimethiconol Stearate

The skin irritation potential of dimethiconol stearate was evaluated using 6 healthy, New Zealand albino rabbits.[22] The test substance (0.5 g under a 2.5 cm^2 patch) was applied to intact and abraded skin sites on the trunk, clipped free of hair. The entire trunk was wrapped with a rubberized elastic cloth during the 24 h application period. Reactions were scored at 24 h and 72 h according to the following scales: 0 (no erythema) to 4 (severe erythema to slight eschar formation) and 0 (no edema) to 4 (extreme edema). Skin irritation was not observed in any of the animals tested (primary irritation index [PII] = 0).

MUCOUS MEMBRANE IRRITATION

The following tested ingredients were non-irritating to mucosal memberanes: Dow Corning® 4-2797 and 3 Dow Corning materials containing 82.1% siloxanes and silicones, dimethyl, hydroxy-terminated.

The mucous membrane irritation potential of 3 Dow Corning materials (TX-102A, TX-102B, and TX-102C)[23] containing 82.1% siloxanes and silicones, dimethyl, hydroxy-terminated (remaining composition unknown) was evaluated using 6 dogs (2 dogs per test material). Each material (amounts ranging from 8 to 18 g) was maintained in contact with the hard palate for 7 h, using an aluminum mold previously shaped to the contour of the roof of the mouth. At the end of the contact period, the oral cavity was examined for evidence of irritation or lesions. The animals were killed on day 8, and punch biopsy specimens of the hard palate were obtained and examined microscopically. Test materials TX-102A and TX-102B did not induce irritation of the hard palate. Test material TX-102-C induced slight edema of the hard palate in both dogs; the edema had cleared by the end of the 8-day observation period. Results of microscopic examinations were not reported. However, according to the SEHSC, microscopic examinations were considered normal for all samples in this study.[24]

A mucous membrane irritation study summary on Dow Corning® 4-2797 (X7-9192), dimethylsiloxane hydroxy-terminated fluid was provided by the SEHSC.[11] Following application of the test substance (0.5 g) to the vaginal mucosa of each of 6 New Zealand white rabbits, there were no signs of irritation, weight loss, or clinical signs of toxicity during the 72-h observation period.

SKIN IRRITATION AND SENSITIZATION

The following tested materials were not irritants or sensitizers: Dow Corning® 2-1870 HV microemulsion containing 22 wt.% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning® 2-1845 microemulsion; Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated; Dow Corning® 60,000CSt, NO CO-SOLVENT in Dow Corning® 360 Medical Fluid (5% w/v), and polymer FD 80.

A primary irritation screen[25] on a microemulsion (Dow Corning® 2-1870 HV) containing 22 wt.% siloxanes and silicones, dimethyl, hydroxy-terminated (remaining composition not stated) in Dow Corning® 2-1845 microemulsion (composition not stated) was performed prior to the maximization test below. Ten guinea pigs were injected with the test article at concentrations ranging from 0.5 % to 5%. Four guinea pigs were patch-tested (24 h patch application) with concentrations ranging from 25% to 100%. Well-defined to severe erythema and slight to moderate edema at intradermal injection sites were observed at concentrations ranging from 2% to 5%. Very slight

to well-defined erythema at intradermal injection sites was observed at concentrations of 0.5% and 1.0%. Skin irritation was not observed at 24h or 48 h post-application of the test substance at concentrations up to 100%.

In the maximization test,[25] the preceding test substance was evaluated using the following groups of albino guinea pigs: 1 test group (20 males), 1 negative control group (10 males, cottonseed oil), and 1 positive control group (10 males, 2,4-dinitrochlorobenzene). The first of the 2 induction stages (sites in shoulder area) for the test article was described as follows: 1% Dow Corning® 2-1870 HV microemulsion in cottonseed oil (total volume = 0.1 ml) was injected intradermally. Also, 1% Dow Corning® 2-1870 HV microemulsion in cottonseed oil in Freund's complete adjuvant/0.9% sodium chloride (50/50) was injected intradermally (total volume = 0.1 ml).

On day 7 of the study (2nd induction stage, 1 week after injections), a 2 x 4 cm patch saturated with the test article (75% in cottonseed oil) was placed on the injection area. After a 2-week non-treatment period, the animals were challenged (left flank) with a lower concentration of the test article (50% in cottonseed oil). Sixteen of 20 guinea pigs in the test group had a sensitization reaction during the challenge phase. Sensitization reactions were not observed in the negative control group, but all positive control animals had a sensitization response. It was concluded that Dow Corning® 2-1870 HV microemulsion was a strong sensitizer in guinea pigs. The results of this study may not lead to a conclusion regarding the sensitization potential of siloxanes, silicones, dimethyl, hydroxy-terminated, given the low concentration of this ingredient relative to the remaining composition of Dow Corning® 2-1870 HV microemulsion.[25]

A skin irritation and sensitization data summary on Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated was provided by the SEHSC.[11] In the primary irritation test, the test substance (0.1 ml in H_20, under Finn chamber) was applied to the skin of each of 4 guinea pigs. Concentrations ranging from 25% to 100% were applied and reactions were scored for up to 72 h post-application. Skin irritation was not observed over the range of test concentrations. Skin sensitization test results are included below.

The sensitization potential of the test substance (5% in water emulsion) was evaluated in the maximization test using groups of 10 (5 males, 5 females) guinea pigs. Intradermal injections (0.1 ml) of the test substance were administered on day 0. On day 7 of induction, the test substance was applied under an occlusive patch for 48 h. During the challenge phase, initiated on day 21, the test substance was applied under an occlusive patch for 24 h. Reactions were scored on days 23 and 24. Sodium chloride (0.9%) and DNCB (0.1%) served as vehicle and positive controls, respectively. The test substance did not induce sensitization.[11]

A skin sensitization data summary on Dow Corning® 60,000CSt, NO CO-SOLVENT in Dow Corning® 360 Medical Fluid (5% w/v) was provided by the SEHSC.[11] The maximization test involved the following groups of male Hartley guinea pigs: 20 test, 10 vehicle controls (Dow Corning® 360 Medical Fluid), and 10 positive controls (DNCB in propylene glycol, 1% w/v). The first induction involved intradermal injections (0.1 ml per injection) of the undiluted test substance, vehicle control, and positive control in the respective groups. The second induction involved the 48 h application of a 2 x 4 cm pad saturated with each substance per group. At 2 weeks after the last induction, test animals were challenged with the undiluted test substance (0.3 ml), and both control groups were also challenged with respective materials. Positive responses were not observed in test or vehicle control animals, and the test substance was not considered a skin sensitizer.

Prior to the following maximization test, 3 preliminary studies (4 guinea pigs per study) were conducted to evaluate the skin irritation potential of polymer FD 80.[26] In study #1 (for induction), moderate irritation was observed in 4 guinea pigs at 24 h and 48 h after intradermal injection with 50% polymer FD 80 in liquid paraffin, and weak to moderate irritation was observed in these animals after injection at a concentration of 10%. In another study (study #2, for induction), undiluted polymer FD 80 (0.5 ml) and at a concentration of 50% in liquid paraffin were each applied to an 8 cm^2 area of skin for 48 h using occlusive patches. A weak irritant response was observed in one guinea pig patch tested with 50% FD 80 in study #2. In the final preliminary study (study #3, for challenge), skin irritation was not observed following a 24 h or 48 h occlusive patch application of undiluted or 50% FD 80 in liquid paraffin to a 4 cm^2 area of skin. It was concluded that polymer FD 80, as supplied, was a non-irritant.

The skin sensitization potential of polymer FD 80 (composition not stated) was evaluated in the maximization test using 2 groups of 20 Dunkin-Hartley albino guinea pigs, one of which was the control group. The induction phase consisted of 0.1 ml intradermal injections of 10% or 20% polymer FD 80 in liquid paraffin and 48 h

occlusive patch applications of undiluted polymer FD 80 (0.5 ml) to an 8 cm^2 area of skin. The challenge phase involved a 24 h occlusive patch application of undiluted polymer FD 80 (0.5 ml) to a 4 cm^2 area of skin. It was concluded that polymer FD 80 did not induce sensitization. Sensitization reactions also were not observed in control guinea pigs treated with liquid paraffin. [26]

GENOTOXICITY

The following tested ingredients were not genotoxic in bacterial assays: uncured and cured Dow Corning® X3-5040 sealant containing approximately 75% siloxanes and silicones, dimethyl, hydroxy-terminated; a mixture containing siloxanes and silicones, dimethyl, hydroxy-terminated; Dow Corning® 4-2797, dimethylsiloxane, hydroxy-terminated fluid; and Dow Corning® 60,000CST NO Co-Solvent.

In the Ames spot plate test and overlay plate test, [27] the mutagenicity of uncured and cured Dow Corning® X3-5040 sealant containing approximately 75% siloxanes and silicones, dimethyl, hydroxy-terminated was evaluated using the following *Salmonella typhimurium* strains with and without metabolic activation: TA98, TA100, TA1535, TA1537, and TA1538. The test substance was extracted with dimethylsulfoxide and doses up to 500 µl/plate were tested. The positive control for activation assays was 2-anthramine, and the nonactivation assay positive controls were sodium azide, 9-amino acridine, and 2-nitrofluorene. Dimethylsulfoxide was used as the solvent control. In both the spot and overlay plate tests, results for the test substance and solvent control were negative in all strains, both with and without metabolic activation, and the positive controls were mutagenic. The test material was considered nonmutagenic.

In another Ames plate test,[28] the mutagenicity of a mixture containing siloxanes and silicones, dimethyl, hydroxy-terminated (concentration not stated; solvent, acetone) was evaluated using the following *Salmonella typhimurium* strains with and without metabolic activation: TA98, TA100, TA1535, TA1537, and TA1538. Concentrations up to 150 µl/plate were tested. The positive control for activation assays was 2-anthramine in dimethylsulfoxide, and the nonactivation assay positive controls were: sodium azide, 2-nitrofluorene, and quinacrine mustard. Results for the test substance were negative in all strains, both with and without metabolic activation, and the positive controls were mutagenic. The test substance was considered nonmutagenic.

A mutagenicity data summary on Dow Corning® 4-2797, dimethylsiloxane, hydroxy-terminated fluid was provided by the SEHSC.[11] In the Ames test, the mutagenicity of this fluid (in DMSO, doses up to 5,000 µg/plate) was evaluated using the following bacterial strains with and without metabolic activation: *Salmonella typhimurium* strains TA97, TA98, TA100, and TA 1535, and *Escherichia coli* strain WP2. The following positive controls were used: sodium azide, 4-nitroquinoline-N-oxide, daunomycin, and N-methyl-N-nitro-N-nitrosoguanidine (with metabolic activation) and 2-anthramine and 2-aminofluorene (without metabolic activation). The test substance was not mutagenic to any of the strains tested. All positive controls were mutagenic.

The SEHSC[11] also provided a mutagenicity data summary on Dow Corning® 60,000CST NO Co-Solvent. Test substance doses up to 5,000 µg/plate were evaluated in the Ames test using the following bacterial strains with and without metabolic activation: *Salmonella typhimurium* strains TA98, TA100, Ta1535, TA1537 and *E. coli* strains WP2*uvr*A and WP2*uvr*A (pKM101). The following positive controls were used: 2-aminoanthracene (with metabolic activation), and sodium azide, 2-nitrofluorene, 9-aminoacridine, and methyl methanesulfonate (without metabolic activation). The test substance was not mutagenic to any of the strains tested. All positive controls were mutagenic. The complete study has been requested from the SEHSC.

CHRONIC TOXICITY/TUMORIGENICITY

The following tested ingredients were neither toxic or tumorigenic up to 36 months post-implantation: siloxanes and silicones, dimethyl, hydroxy-terminated (68%) in uncured DC 386 ; siloxanes and silicones, dimethyl, hydroxy-terminated (72%) in uncured DC 382; siloxanes and silicones, dimethyl, hydroxy-terminated (96%) in uncured DC 5392;and siloxanes and silicones, dimethyl, hydroxy-terminated (80%) in uncured Medical Adhesive Type A. Negative results were reported for Dow Corning special polymer (contains siloxanes and silicones, dimethyl, hydroxy-terminated) in a 1-year oral feeding study.

Chronic implantation studies of polysiloxanes were conducted using 38 pure-bred beagle dogs (~ 5 to 7 months old).[29] The 4 implanted materials were defined as follows: siloxanes and silicones, dimethyl, hydroxy-terminated (68%) in uncured DC 386 ; siloxanes and silicones, dimethyl, hydroxy-terminated (72%) in uncured DC 382; siloxanes and silicones, dimethyl, hydroxy-terminated (96%) in uncured DC 5392 ; and siloxanes and silicones, dimethyl, hydroxy-terminated (80%) in uncured Medical Adhesive Type A. The remaining compositions of the materials tested are unknown. The implants (intramuscular, intraperitoneal, and subcutaneous) were removed at intervals of 3, 9, 24, and 36 months. Neither gross nor microscopic findings revealed a pattern of polymer-induced systemic toxicity. The materials tested also did not induce any untoward chronic tissue reactions, and there was no evidence of tumorigenesis over a 3-year testing period.

A chronic feeding study on Dow Corning special polymer was conducted using 30 albino weanling rats.[30] Regarding the composition of the polymer tested, the only chemical substance listed was siloxanes and silicones, dimethyl, hydroxy-terminated. The test group consisted of 10 rats (5 males, 5 females), and these animals were fed a basal diet consisting of 0.05% Dow Corning special polymer for 1 year. The control group (10 males, 10 females) was fed basal diet only. The only reported deaths were 2 rats in the control group. There were no test substance-related effects on hematological or clinical chemistry values. Gross evidence of severe pulmonary disease was noted at necropsy. Inflammatory changes in the lungs or tubular degenerative changes in the kidneys were fairly common in test and control groups, and were not considered test substance-related. It was concluded that administration of the test substance did not induce adverse effects in rats.

CLINICAL ASSESSMENT OF SAFETY

SKIN IRRITATION AND SENSITIZATION

Neither skin irritation nor sensitization were reported in patch tests or RIPTs involving the following ingredients/products: 16% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning XET-40002; body lotion containing dimethiconol; dimethiconol behenate; and dimethiconol beeswax.

The skin irritation and sensitization potential of cotton treated with 16% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning XET-40002 (remaining composition not stated) was evaluated using 200 human subjects.[31] The test protocol was not stated. Neither the test substance nor the untreated cotton control induced primary skin irritation or sensitization. This study is being included because data in the published literature relating to the skin irritation/sensitization potential of the ingredient siloxanes and silicones, dimethyl, hydroxy-terminated in the published literature are very limited.

Dimethiconol

In an RIPT,[32] the skin irritation and sensitization potential of a body lotion containing 1.125% dimethiconol (0.2 g per 1" x 1" patch) was evaluated using 104 subjects ranging in age from 17 to 74 years. The test substance was applied to the upper back of each subject for 24 h, using a semiocclusive patch, for a total of 9 induction patch applications. A 24-h challenge patch was applied at the end of a 2-week non-treatment period. Induction and challenge reactions were scored according to the following scale: 0 (no visible skin reaction) to 4 (severe erythema, possible edema, vesiculation, bullae and/or ulceration). There were no visible skin reactions in any of the subjects, and it was concluded that the body lotion did not indicate a potential for dermal irritation or allergic contact sensitization.

Dimethiconol Behenate

In another RIPT (occlusive patches, similar procedure),[33] the skin irritation and sensitization potential of lip product containing 0.5% dimethiconol behenate was evaluated using 50 subjects ranging in age from 18 to 70 years. The dose per cm^2 was not stated. There were no visible skin reactions in any of the subjects, and it was concluded that lip product did not demonstrate a potential for eliciting dermal irritation or sensitization.

Dimethiconol Beeswax

The skin sensitization potential of a test product identified as undiluted dimethiconol beeswax was evaluated in an RIPT using 102 subjects (29 males, 73 females; > 18 years old) with no significant active skin pathology.[34] During induction, the test material was applied to the back (0.025 g/cm^2 skin, 8 mm Finn chambers) of each subject, for a total of 10 occlusive patch applications. Each chamber remained in place for 48 h. Following a 12-day non-treatment period, an occlusive challenge patch was applied for 48 h to a new site on the back of each subject. Reactions were scored at 48 h and 96 h post-application according to the following scale: 0 (no reaction) to 4 (erythema, edema, and bullae). Dimethiconol did not induce skin irritation or sensitization in this study.

SUMMARY OF INFORMATION FROM EARLIER CIR SAFETY ASSESSMENT

Most of the data reviewed in the CIR safety assessment on dimethicone, amodimethicone, and related compounds are studies on dimethicone. These ingredients were found to be safe as used in cosmetics, with a concern in the discussion regarding inhalation exposure, which was addressed.

Dimethicone

Clinical and animal absorption studies generally reported that dimethicone was not absorbed following oral or dermal exposure. Dimethicone was not acutely toxic following oral exposure (mice, rats, and guinea pigs), and adverse effects were not observed in rats that received up to 10% dimethicone in the diet for 90 days.

The dermal LD50 for diemthicone was > 2 g/kg in rats and rabbits, and no adverse effects were found in rabbits, following short-term dermal dosing with 6% to 79% dimethicone. Most dermal irritation studies classified dimethicone as a minimal irritant. Studies that scored reactions according to the Draize scale reported PIIs of < 2.8 (with test samples containing 5% to 100% dimethicone). Most ocular irritation studies using rabbits classified dimethicone as a mild to minimal irritant. Dimethicone (tested undiluted and at 79%) was not a sensitizer in 4 assays using mice and guinea pigs. It also was not a sensitizer at a concentration of 5% in a clinical RIPT using 83 panelists.

Dimethicone was tested in numerous oral-dose (using rats) and dermal-dose (using rats, rabbits, and monkeys) reproductive and developmental toxicity studies. In a few studies, treated males had significantly decreased body weight and/or decreased testes or seminal vesicle weights. No treatment-related adverse findings were noted in dosed pregnant females or fetuses. Results for dimethicone were negative in all mutagenicity assays and in both oral (tested at 91%) and dermal (tested at unknown concentration) carcinogenicity assays using mice.

In the discussion of the safety assessment, the CIR Expert Panel did note a concern about inhalation exposure, which was addressed. Specifically, the Panel expects that the manufacturing process for cosmetic formulations in which dimethicone, amodimethicone, and related compounds are found and which may be inhaled would continue to produce particle size distributions that are not significantly respirable.

SUMMARY

The following ingredients are reviewed in this safety assessment: dimethiconol, dimethiconol arginine, dimethiconol beeswax, dimethiconol behenate, dimethiconol borageate, dimethiconol candelillate, dimethiconol carnaubate, dimethiconol cysteine, dimethiconol dhupa butterate, dimethiconol hydroxystearate, dimethiconol illipe butterate, dimethiconol isostearate, dimethiconol kokum butterate, dimethiconol lactate, dimethiconol meadowfoamate, dimethiconol methionine, dimethiconol/methylsilanol/silicate crosspolymer, dimethiconol mohwa butterate, dimethiconol panthenol, dimethiconol sal butterate, dimethiconol/silica crosspolymer, dimethiconol/silsesquioxane copolymer, dimethiconol stearate, dimethiconol/stearyl methicone/phenyl trimethicone copolymer, hydrolyzed collagen PG-propyl dimethiconol, isopolyglyceryl-3 dimethiconol, trimethylsiloxysilicate/dimethiconol crosspolymer, and acrylates/dimethiconol acrylate copolymer. The skin

conditioning agent/hair conditioning agent function in personal care products is associated with most of these ingredients.

Of the 28 ingredients that are being reviewed in this safety assessment, the following 9 are reported to the Food and Drug Administration as being used in personal care products: dimethiconol, dimethiconol arginine, dimethiconol beeswax, dimethiconol cysteine, dimethiconol meadowfoamate, dimethiconol methionine, dimethiconol panthenol, dimethiconol stearate, and trimethylsiloxysilicate/dimethiconol cross-polymer. Based on the results of an industry use concentration survey, the following 3 additional ingredients are also being used: dimethiconol behenate, dimethiconol/silsesquioxane copolymer, and acrylates/dimethiconol acrylate copolymer. Dimethiconol is being used in cosmetic products at concentrations ranging from 0.004% to 36%, and this range is inclusive of the highest and lowest reported use concentrations of ingredients reviewed in this safety assessment.

Most of the toxicity data included in this safety assessment are on siloxanes and silicones, dimethyl, hydroxy-terminated; dimethoxy silicone/silane, hydroxy-terminated; and Dow Corning materials containing 95% or greater CAS No. 70131-67-8 (polysiloxanes, di-Me, hydroxy-terminated). The CAS number for these chemical names is identified as 70131-67-8 in these studies. Siloxanes and silicones, dimethyl, hydroxy-terminated and CAS No. 70131-67-8 are listed among the other chemical names/identification numbers for dimethiconol in the *International Cosmetic Ingredient Dictionary and Handbook.*

In an acute inhalation toxicity study, neither deaths nor toxic signs were reported for rats exposed to vapor substantially saturated with a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl (20%) for 6 h. Similar results were reported for the same mixture in an acute oral toxicity study involving rats (LD50 > 16 ml/kg), for polymer FD 80 (LD50 > 2 g/kg, rats), and for a suspension containing Dow Corning® 60,000CSt, NO CO-SOLVENT in corn oil (20% w/v) (LD50 > 2 g/kg, rats). The latter test substance contains 95% or greater CAS No. 70131-67-8 (polysiloxanes, di-Me, hydroxy-terminated). Dimethiconol Stearate was also classified as non-toxic in an acute oral toxicity study involving rats (LD50 > 5 g/kg).

Following dermal application of a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl (20%), irritation was not observed at application sites and 3of 8 rabbits died (LD50 > 16 ml/kg). Both siloxanes and silicones, dimethyl, hydroxy-terminated (22 wt. %) in Dow Corning ® 2-1845 microemulsion and Dow Corning® 60,000CSt, NO CO-SOLVENT (contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) were non-toxic (LD50 > 2 g/kg) in acute dermal toxicity studies involving rabbits; skin irritation was observed at application sites. Polymer FD 80 was also classified as non-toxic (LD50 > 2 g/kg) in a dermal toxicity study.

Neither mortalities nor test substance-related findings were reported in a subchronic oral study in which rabbits were fed a basal diet containing 0.05% Dow Corning special polymer (polymerized siloxane) for 8 months.

Dow Corning emulsions containing siloxanes and silicones, dimethyl, hydroxy-terminated at concentrations of 13% (Dow Corning® 35 emulsion) and and 38% (Dow Corning® 22 emulsion) did not induce a significant ocular response in rabbits. Transient ocular irritation, not classified as moderate or severe, was observed following the instillation of Dow Corning® 60,000CSt, NO CO-SOLVENT or Dow Corning® PA Fluid (≥ 95% polysiloxanes, di-Me, hydroxy-terminated in both) into the eyes of rabbits. Dimethiconol stearate was classified as nonirritating to the eyes of rabbits. However, a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl) (20%) induced moderate, persistent conjunctival and corneal injury and iritis in rabbits. This mixture did not induce skin irritation in rabbits. Polymer FD 80/II was classified as a slight ocular irritant in rabbits.

Both a mixture containing dimethoxy silicone/silane, hydroxy-terminated (80%) and 1-propamine, 3-(trimethoxysilyl)-N-(3-trimethoxysiloyl propyl) (20%) and undiluted Dow Corning®, No Co-Solvent (contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) were not irritating to the skin of rabbits. The same was true for dimethiconol stearate.

Of the 3 Dow Corning materials (TX-102A, TX-102B, and TX-102C) containing 82.1% siloxanes and silicones, dimethyl, hydroxy-terminated that were maintained in contact with the hard palate of dogs, only one (TX-102) induced irritation (slight edema). Neither signs of vaginal mucosal irritation, weight loss, nor clinical signs of toxicity were observed in rats receiving an application of Dow Corning® 4-2797 (X7-9192), dimethylsiloxane hydroxy-terminated fluid (contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) to the vaginal mucosa.

A primary irritation screen on a microemulsion (Dow Corning® 2-1870 HV) containing 22 wt.% siloxanes and silicones, dimethyl, hydroxy-terminated was performed prior to a guinea pig maximization test. Slight to severe erythema (dose response) was observed at sites injected intradermally with concentrations ranging from 0.5% to 5%. However, patch test results (24 h application) were negative for concentrations up to 100%. In the maximization test, strong sensitization reactions were observed in guinea pigs challenged with 50% test substance in cottonseed oil. Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated (contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) was not a skin irritant in guinea pigs patch tested with concentrations up to 100% and, at a concentration of 5% in a water emulsion, also did not induce sensitization in the maximization test. Maximization test results for undiluted polymer FD 80 and Dow Corning® 60,000CSt, NO CO-SOLVENT in Dow Corning® 360 Medical Fluid (5% w/v) were also negative in guinea pigs. This Dow Corning material contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated.

Negative Ames test results were reported for the following chemicals: uncured and cured Dow Corning® X3-5040 sealant containing ~ 75% siloxanes and silicones, dimethyl, hydroxy-terminated (doses up to 500 µl/plate); a mixture containing siloxanes and silicones, dimethyl, hydroxy-terminated (up to 150 µl/plate); Dow Corning® 4-2797, dimethylsiloxane, hydroxy-terminated fluid (contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) (up to 5,000 µg/plate); and Dow Corning® 60,000CST NO Co-Solvent (contains ≥ 95% polysiloxanes, di-Me, hydroxy-terminated) (up to 5,000 µg/plate). In chronic implantation studies (38 pure-bred beagle dogs), 4 materials containing siloxanes and silicones, dimethyl, hydroxy-terminated at concentrations of 68%, 72%, 80%, and 96%, respectively, were tested. The materials were removed at various intervals up to 36 months post-implantation, and neither gross nor microscopic findings were indicative of polymer-induced toxicity or tumorigenesis.

In chronic implantation studies (38 pure-bred beagle dogs), 4 materials containing siloxanes and silicones, dimethyl, hydroxy-terminated at concentrations of 68%, 72%, 80%, and 96%, respectively, were tested. The materials were removed at various intervals up to 36 months post-implantation, and neither gross nor microscopic findings were indicative of polymer-induced toxicity or tumorigenesis. Neither mortalities nor test substance-related findings were reported for weanling rats fed a basal diet containing 0.05% Dow Corning special polymer (polymerized siloxane) for 1 year.

Neither skin irritation nor sensitization was observed in 200 subjects patch tested with 16% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning XET-40002. Negative results were also reported in the following RIPTs evaluating skin irritation and sensitization potential: body lotion containing 1.125% dimethiconol (104 subjects), lip product containing 0.5% dimethiconol behenate (50 subjects), and undiluted dimethiconol beeswax (102 subjects).

DISCUSSION

Section 1, paragraph (p) of the CIR Procedures states that "A lack of information about an ingredient shall not be enough to justify a determination of safety." In accordance with Section 30(j)(2)(A) of the Procedures, the Expert Panel informed the public of its decision that the data on dimethiconol and its esters and reaction products were insufficient to determine whether these ingredients, for purposes of cosmetic use, are either safe or unsafe. The Expert Panel issued a notice of insufficient data announcement on April 6, 2010, outlining the data needed to assess the safety of these ingredients. The types of data include:

(1) Method of manufacture and impurities;

(2) UV absorption; if there is absorption in the UVB/UVA band, then photoirritation and photosensitization data may be needed;
(3) Molecular weights or information about dermal absorption that can predict if dermal absorption can occur. If absorption occurs, then reproductive and developmental toxicity data may be needed.

The Panel also noted that composition data on the Dow Corning mixtures and FD80 and FD80/II polymers included in this safety assessment are needed.

The potential adverse effects of inhaled aerosols depend on the specific chemical species, the concentration and the duration of the exposure and their site of deposition within the respiratory system. In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 μm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 μm. Particles with an aerodynamic diameter of ≤ 10μm are respirable. In addition to the negative acute inhalation toxicity data considered in this safety assessment, the Expert Panel determined that dimethiconol cysteine, dimethiconol methionine, and dimethiconol panthenol can be used safely in hair sprays, because the product particle size is not respirable.

DRAFT CONCLUSION

The Expert Panel concludes that the available data are insufficient to support the safety of dimethiconol arginine, dimethiconol beeswax, dimethiconol behenate, dimethiconol borageate, dimethiconol candelillate, dimethiconol carnaubate, dimethiconol cysteine, dimethiconol dhupa butterate, dimethiconol, dimethiconol hydroxystearate, dimethiconol illipe butterate, dimethiconol isostearate, dimethiconol kokum butterate, dimethiconol lactate, dimethiconol meadowfoamate, dimethiconol methionine, dimethiconol mohwa butterate, dimethiconol panthenol, dimethiconol sal butterate, and dimethiconol stearate, hydrolyzed collagen PG-propyl dimethiconol, dimethiconol/methylsilanol/silicate crosspolymer, dimethiconol/silica crosspolymer, dimethiconol/silsesquioxane copolymer, dimethiconol/stearyl methicone/phenyl trimethicone copolymer, isopolyglyceryl-3 dimethiconol, trimethylsiloxysilicate/dimethiconol crosspolymer, and acrylates/dimethiconol acrylate copolymer in cosmetics products.

Table 1. Dimethiconol and its Esters and Reaction Products[2]

Chemical Names	Definition/Other Data	Functions in Cosmetics
Dimethiconol; dihydroxpolydimethylsiloxane; dimethylsilanediol homopolymer, silanol-terminated; poly[oxy(dimethylsilylene)], α-hydroxy-ω-hydroxy-; siloxanes and silicones, dimethyl, 14ydroxy-terminated; **CAS Nos. 31692-79-2 and 70131-67-8**	A dimethyl siloxane terminated with hydroxyl groups	Antifoaming agents; skin-conditioning agents – emollient
Dimethiconol arginine	Reaction product of dimethiconol and arginine	Hair conditioning agents
Diemthiconol beeswax**; CAS No. 227200-35-3***	Reaction product of dimethiconol and beeswax (reviewed by CIR – safe as used conclusion[35,36])	Skin-conditioning agents-occlusive
Diemthiconol behenate; **CAS No. 227200-34-2***	Ester of dimethiconol and behenic acid. Behenyl alcohol (reviewed by CIR – safe as used[37])	Skin-conditioning agents-occlusive
Dimethiconol borageate; **CAS No. 226994-45-2***	Reaction product of dimethiconol and fatty acids derived from Borago Officinalis seed oil	Skin-conditioning agents-emollient
Dimethiconol candelillate	Reaction product of dimethiconol and candelilla wax (reviewed by CIR – safe as used[35,36])	Skin-conditioning agents – occlusive
Dimethiconol carnaubate	Reaction product of dimethiconol and carnauba wax (reviewed by CIR – safe as used[35,36])	Skin-conditioning agents-occlusive
Dimethiconol cysteine	Reaction product of dimethiconol and cysteine	Hair conditioning agents
Dimethiconol dhupa butterate; **CAS No. 243981-39-7***	Reaction product of dimethiconol and fatty acids derived from dhupa butter	Skin conditioning agents-emollient
Dimethiconol hydroxystearate; siloxanes and silicones, dimethyl, [(12-hydroxy-1-oxooctadecyl)oxy-terminated; **CAS No. 133448-13-2**	Ester of dimethiconol and hydroxystearic acid (reviewed by CIR – safe as used[38])	Skin-conditioning agents-occulsive
Dimethiconol illipe butterate	Reaction product of dimethiconol and the fatty acids derived from illipe butter	Skin conditioning agents-emollient
Dimethiconol isostearate; siloxanes and silicones, dimethyl, [(oxoisooctadecyl)oxy]-terminated; **CAS No. 133448-14-3**	Ester of dimethiconol and isostearic acid (reviewed by CIR – safe as used[39,36])	Skin-conditioning agents-occlusive
Dimethiconol kokum butterate; **CAS No. 226994-48-5***	Reaction product of dimethiconol and the fatty acids derived from kokum butter	Skin-conditioning agents-emollient
Dimethiconol lactate; **CAS No. 227200-33-1***	Ester of dimethiconol and lactic acid (reviewed by CIR – safe with qualifications[40,41])	Hair conditioning agent; skin conditioning agents-emollient
Dimethiconol meadowfoamate	Reaction product of dimethiconol and the fatty acids derived from meadowfoam seed oil	Skin-conditioning agents-emollient
Dimethiconol methionine	Reaction product of dimethiconol and methionine	Hair conditioning agents
Dimethiconol/methylsilanol/silicate crosspolymer; **CAS No. 68956-02-6**	The cross polymer formed by the reaction of silica (reviewed by CIR – safe as used[42]), dimethylsilanol, and methylsilanol	Not reported

Table 1. Dimethiconol and its Esters and Reaction Products[2]

Chemical Names	Definition/Other Data	Functions in Cosmetics
Dimethiconol mohwa butterate; **CAS No. 225233-88-5***	Reaction product of dimethiconol and the fatty acids derived from mohwa butter	Skin-conditioning agents-emollient
Dimethiconol panthenol	Reaction product of dimethiconol and panthenol (reviewed by CIR – safe as used[43,44])	Hair conditioning agents
Dimethiconol sal butterate	Reaction product of dimethiconol and the fatty acids derived from sal butter	Skin-conditioning agents-emollient
Dimethiconol/silica cross polymer	Copolymer of dimethiconol and silica (reviewed by CIR – safe as used[42])	Film formers
Dimethiconol/silsesquioxane copolymer; **CAS No. 68554-67-6**	Siloxane polymer consisting of methyl trimethoxysilane and dimethyl siloxane	Antistatic agents; film formers; hair conditioning agents; hair fixatives; skin-conditioning agents-miscellaneous
Dimethiconol stearate; siloxanes and silicones, dimethyl, [(1-oxooctadecyl)oxy]-terminated; **CAS No. 130169-63-0**	Ester of dimethiconol and stearic acid (reviewed by CIR – safe as used[45,44]) – See figure 1B	Skin conditioning agents-occlusive
Dimethiconol/stearyl methicone/phenyl trimethicone copolymer	Polymer formed from dimethiconol, stearyl methicone (reviewed by CIR – safe as used[46]), and phenyl trimethicone (reviewed by CIR – safe as used[47,44])	Suspending agents-nonsurfactant
Hydrolyzed collagen PG-propyl dimethiconol	Silicone polymer that conforms generally to the structure, where R represents the hydrolyzed collagen (reviewed by CIR – safe as used[48,44]) moiety – See figure 1B	Emulsion stabilizers; hair conditioning agents; skin-conditioning agents-humectants; surfactants-suspending agents
Isopolyglyceryl-3 dimethiconol	Silicone polymer that conforms to the structure in figure 1B	Hair conditioning agents; skin conditioning agents-emollient; surfactants-cleansing agents; surfactants-emulsifying agents; surfactants-solubilizing agents; skin-conditioning agents-humectants; viscosity increasing agents-aqueous
Trimethylsiloxysilicate/dimethiconol crosspolymer; **CAS No. 68440-70-0**	Dimethiconol crosslinked with trimethylsiloxysilicate	Film formers; viscosity increasing agents-nonaqueous
Acrylates/dimethiconol acrylate copolymer	Copolymer of dimethiconol acrylate and one or more monomers consisting of acrylic acid, methacrylic acid (reviewed by CIR – safe with qualifications[49]), or one of its simple esters	Film formers

* Source (CAS numbers): Siltech Personal Care[50]

Table 2. Composition of Oil/Butter Sources of Dimethiconol FA Moieties*

Ingredient	Fatty Acid Composition of Oil/Butter Source
Dimethiconol borageate	*Borago officinalis* seed oil: 11.26% palmitic acid (C16:0), 4.52% stearic acid (18:0), 19.57% oleic acid (18:1), 36.12% linoleic acid (18:2), 18.46% gama-linolenic acid (γ 18:3), 4.22% arachidoleic acid (20:1), and 2.70% erucic acid (22:1)[51]
Dimethiconol dhupa butterate	Dhupa (*Vateria indica*) butter: 9% palmitic acid, 46.9% stearic acid, 41.4% oleic acid, 1.3% linoleic acid, and 1.4% eicosanoic acid (20:0)[52]
Dimethiconol illipe butterate	Illipe (*Shorea stenoptera*) butter: 15 to 19% palmitic acid, 42 to 48% stearic acid, 32 to 38% oleic acid, and 0 to 1.2% linoleic acid[53]
Dimethiconol kokum butterate	Kokum (*Garcinia indica*) butter: 15 to 19% palmitic acid, 42 to 48% stearic acid, 32 to 38% oleic acid, and 0 to 1.2% linoleic acid[54]
Dimethiconol meadowfoamate	Meadowfoam (*Limnanthes alba*) seed oil: 58 to 64% cis-11 eicosenoic acid (20:1, Δ5), 3 to 6% erucic acid (22:1, Δ5), 10 to 14% erucic acid (22:1, Δ13), and 15 to 21% docosadienoic acid (22:2, Δ5Δ13)[55]
Dimethiconol mohwa butterate	Mohwa (*Madhuca longifolia*) oil: 20 to 25% palmitic acid, 20 to 25% stearic acid, 41 to 51% oleic acid, 10 to 14% linoleic acid, and 0 to 3.3% eicosanoic acid[56]
Dimethiconol sal butterate	Sal (*Shorea robusta*) butter: 4 to 7% palmitic acid, 41 to 47% stearic acid, 37 to 43% oleic acid, and 0 to 4% linoleic acid [57]

*The Cosmetic Ingredient Review (CIR) Expert Panel has evaluated the safety of palmitic acid, stearic acid, and oleic acid and concluded that each is safe as used in personal care products.[45]

Table 3. Properties of Dimethiconol and Dimethiconol Compounds

Property	Value	Reference
Dimethiconol		
Density	0.956g/cm^3	STN International[5]
Refractive index	1.3968	″
Dimethiconol (60%) in anionic surfactant emulsion		
Particle size	1µm max (for D50); 2µm max (for D90)	Anonymous[6]
Polymer viscosity	1.0 x 10^6 to 1.8 x 10^6 cps	″
pH	6 to 8	″
Nonvolatiles	58% to 62%	″
Silicones (as polydimethylsiloxane)	58% to 62%; target value = 60%	″
Cyclomethicone (as tetramer)	1% max	″
Dimethiconol Beeswax		
Form	Of white waxy solid	SafePharm Laboratories[58]
Density of liquids and solids	956 kg/m3 @ 19.7 ± 0.5°C	″
Water solubility	< 6.0 x 10^{-4} g/l of solution at 20.0 ± 0.5°C	″
Boiling point	> 673 ± 0.5°K @ 101.61 to 102.02 kPa	″
Melting point/melting range	301 to 349 ± 0.5°K	″
Dimethiconol Behenate		
Physical state	Soft paste	Personal Care [7]Products Council[59]
Appearance and odor	Off-white, bland odor	"
Specific gravity	~ 0.99 @ 25ºC	"
Water solubility	Insoluble	"
Freezing/melting point	63 ºC	"
% Volatile	Nil	"
Acid value	20.0 maximum	"

Table 3. Properties of Dimethiconol and Dimethiconol Compounds

Property	Value	Reference
Dimethiconol/silsequioxane copolymer (5%) and dimethiconol (20%) in anionic surfactant emulsion		
Particle size	0.043µm max (for D50); 0.05µm max (for D90)	Anonymous[7]
Polymer viscosity	1.0 x 10^6 to 3.5 x 10^6 cps; target value = 2.0 x 10^6 cps	″
pH	6.5 to 8; target value = 7	″
Nonvolatiles	38% to 43%	″
Silicones (as polydimethylsiloxane)	25% to 27%; target value = 26%	″
Cyclomethicone (as tetramer)	1.8% max	″

Table 4. Polymer Composition Data

Trade Name	**Chemical Composition (%)**
Dow Corning® 60,000CSt, NO CO-SOLVENT	≥ 95% polysiloxanes, di-Me, hydroxy-terminated
Dow Corning ® 2-1845 microemulsion	Not stated
Dow Corning special polymer 5-26-64	Not stated
Dow Corning® 35 emulsion	13% siloxanes and silicones, dimethyl, hydroxy-terminated
Dow Corning® 22 emulsion	38% siloxanes and silicones, dimethyl, hydroxy-terminated
Dow Corning® PA Fluid	Not stated
Dow Corning®, No Co-Solvent	Not stated
Dow Corning materials TX-102A, TX-102B, and TX-102C	82.1% siloxanes and silicones, dimethyl, hydroxy-terminated
Dow Corning® 4-2797 (X7-9192), dimethylsiloxane hydroxy-terminated fluid	Not stated
Dow Corning® 2-1870 HV microemulsion	22 wt.% siloxanes and silicones, dimethyl, hydroxy-terminated
Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated	Not stated
Dow Corning® 360 Medical Fluid	Not stated
Dow Corning® X3-5040 sealant	75% siloxanes and silicones, dimethyl, hydroxy-terminated
uncured DC 386 and uncured DC 5392	Not stated
Medical adhesive type A	Not stated
Dow Corning special polymer	Not stated
Dow Corning XET-40002	Not stated
Polymers FD 80 and FD 80/II	Not stated

Table 5. Current Cosmetic Product uses[8] and Use Concentrations[9]

Product category	2009 uses (total number of products in category)	2010 concentrations (%)
Dimethiconol		
Baby products		
Lotions, oils, powders, and creams	4 (137)	-
Bath products		
Bubble baths	-	3
Eye makeup		
Eyebrow pencil	1 (144)	0.3
Eyeliner	4 (754)	1
Eye shadow	15 (1,215)	0.3 to 5
Eye lotion	7 (254)	0.3 to 0.6
Eye makeup remover	2 (128)	-
Mascara	35 (499)	0.3 to 1
Other	20 (365)	-
Fragrance products		
Perfumes	1 (666)	0.8
Powders	-	0.5
Other	9 (566)	0.3
Noncoloring hair care products		
Conditioners	75 (1,226)	0.2 to 13
Sprays/aerosol fixatives	5 (312)	0.004
Rinses	1 (33)	-
Shampoos	33 (1,361)	0.2 to 2
Tonics, dressings, etc.	74 (1,205)	0.4 to 12
Other	54 (807)	12
Hair coloring products		
Bleaches	1 (149)	-

Table 5. Current Cosmetic Product uses[8] and Use Concentrations[9]

Product category	2009 uses (total number of products in category)	2010 concentrations (%)
Other	2 (168)	-
Makeup		
Blushers	6 (434)	36
Face powders	10 (661)	0.3
Foundations	28 (589)	0.6 to 2
Leg and body paints	2 (29)	-
Lipstick	7 (1,883)	0.7 to 7
Makeup bases	1 (117)	0.2 to 0.6
Makeup fixatives	-	0.06
Other	5 (485)	-
Nail care products		
Basecoats and undercoats	1 (79)	0.2
Cuticle softeners	1 (27)	0.2
Nail extenders	-	0.5
Other	-	0.4
Personal hygiene products		
Deodorants (underarm)	-	0.2 to 11
Douches	-	0.2
Other	-	0.3 (in a body scrub)
Shaving products		
Aftershave lotion	16 (367)	0.3 to 4
Preshave lotions	1 (22)	2
Shaving cream	-	0.05
Shaving soap	-	3
Skin care products		
Skin cleansing creams, lotions, liquids, and pads	8 (1,446)	2 to 6
Depilatories	4 (42)	-

Table 5. Current Cosmetic Product uses[8] and Use Concentrations[9]

Product category	2009 uses (total number of products in category)	2010 concentrations (%)
Face and neck creams, lotions, and powders	76 (1,583)	0.2 to 3
Body and hand creams, lotions, and powders	55(1,744)	0.05 to 5
Foot powders and sprays	1 (47)	-
Moisturizing creams, lotions, and powders	242 (2,508)	0.3
Night creams, lotions, and powders	32 (353)	0.6 to 0.8
Paste masks (mud packs)	3 (441)	0.6 to 2
Skin fresheners	2 (259)	1
Other	55 (1,308)	0.3 to 6
Suntan products		
Suntan gels, creams, and liquids	4 (107)	2
Indoor tanning preparations	26 (240)	0.2 to 0.5
Other	3 (62)	-
Total uses/ranges for dimethiconol	935	0.004 to 36
Amodimethiconol		
Hair coloring products		
Dyes and colors	21 (2,393)	-
Total uses/ranges for amodimethiconol	21	
Dimethiconol arginine		
Noncoloring hair care products		
Conditioners	2 (1,226)	-
Sprays/aerosol fixatives	1 (312)	-
Shampoos	1 (1,361)	-
Total uses/ranges for dimethiconol arginine	4	
Dimethiconol beeswax		
Bath products		
Soaps and detergents	7 (1,665)	0.8

Table 5. Current Cosmetic Product uses[8] and Use Concentrations[9]

Product category	2009 uses (total number of products in category)	2010 concentrations (%)
Noncoloring hair care products		
Other	1 (807)	-
Personal hygiene products		
Other	4 (792)	-
Skin care products		
Body and hand creams, lotions, and powders	-	0.9
Moisturizers	1 (2,508)	-
Total uses/ranges for dimethiconol beeswax	13	0.8 to 0.9
Dimethiconol behenate		
Makeup		
Lipstick	-	0.5
Total uses/ranges for dimethiconol behenate	-	0.5
Dimethiconol cysteine		
Noncoloring hair care products		
Conditioners	2 (1,226)	0.07
Sprays/aerosol fixatives	1 (312)	-
Shampoos	1 (1,361)	-
Tonics, dressings, etc.	2 (1,205)	-
Total uses/ranges for dimethiconol cysteine	6	0.07
Dimethiconol meadowfoamate		
Eye makeup		
Other	1 (365)	-
Noncoloring hair care products		
Conditioners	6 (1,226)	0.5
Sprays/aerosol fixatives	-	1
Straighteners	1 (178)	-
Tonics, dressings, etc.	1 (1,205)	0.5

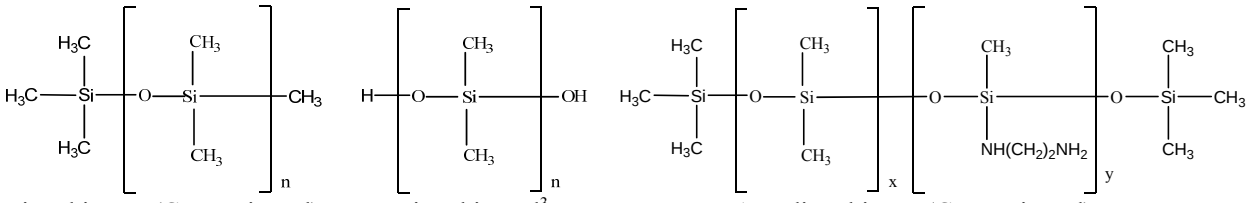
Table 5. Current Cosmetic Product uses[8] and Use Concentrations[9]

Product category	2009 uses (total number of products in category)	2010 concentrations (%)
Other	-	0.5
Total uses/ranges for dimethiconol meadowfoamate	9	0.5 to 1
Dimethiconol methionine		
Noncoloring hair care products		
Conditioners	2 (1,226)	-
Sprays/aerosol fixatives	1 (312)	-
Shampoos	1 (1,361)	-
Total uses/ranges for dimethiconol methionine	4	
Dimethiconol panthenol		
Noncoloring hair care products		
Conditioners	2 (1,226)	0.07
Sprays/aerosol fixatives	1 (312)	-
Shampoos	1 (1,361)	-
Tonics, dressings, etc.	2 (1,205)	-
Total uses/ranges for dimethiconol panthenol	6	0.07
Dimethiconol/silsesquioxane copolymer		
Noncoloring hair products		
Conditioners	-	0.3
Total uses/ranges for dimethiconol/silsesquioxane copolymer	-	0.3
Dimethiconol stearate		
Eye makeup		
Other	1 (365)	-
Noncoloring hair care products		
Conditioners	1 (1,226)	-
Shaving products		
Shaving cream (aerosol, brushless, and lather)	7 (122)	1
Total uses/ranges for dimethiconol stearate	9	1

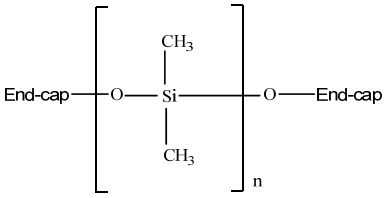
Table 5. Current Cosmetic Product uses[8] and Use Concentrations[9]

Product category	2009 uses (total number of products in category)	2010 concentrations (%)
Trimethylsiloxysilicate/dimethiconol crosspolymer		
Skin care products		
Body and hand creams, lotions, and powders	1 (1,744)	2
Moisturizers	1 (2,508)	-
Total uses/ranges for Trimethylsiloxysilicate/dimethiconol crosspolymer	2	2
Acrylates/dimethiconol acrylate copolymer		
Nail care products		
Basecoats and undercoats	-	0.5
Polish and enamel	-	0.5
Total uses/ranges for acrylates/dimethiconol acrylate copolymer	-	0.5

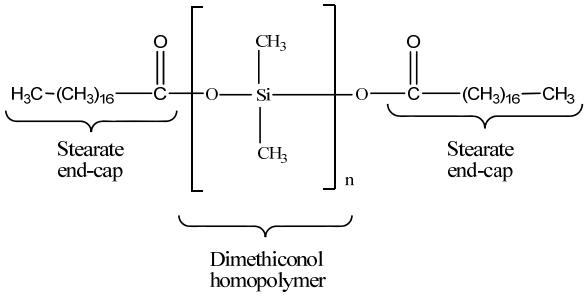
Figure 1A. Structures for Dimethiconol, examples of its reaction products and related, reviewed ingredients



Reaction Product Type 1) End-capped homopolymers



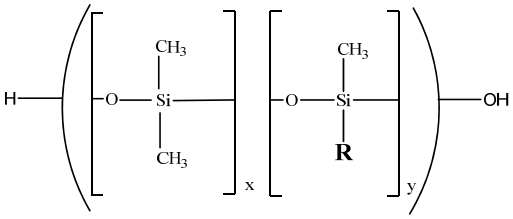
Examples



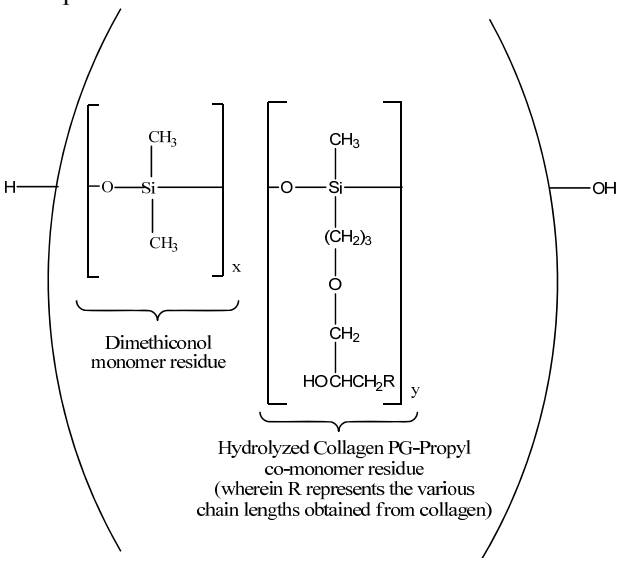
Dimethiconol Stearate

Dimethiconol Arginine, Dimethiconol Beeswax, Dimethiconol Behenate, Dimethiconol Borageate, Dimethiconol Candelillate, Dimethiconol Carnaubate, Dimethiconol Cysteine, Dimethiconol Dhupa Butterate, Dimethiconol Hydroxystearate, Dimethiconol Illipe Butterate, Dimethiconol Isostearate, Dimethiconol Kokum Butterate, Dimethiconol Lactate, Dimethiconol Meadowfoamate, Dimethiconol Methionine, Dimethiconol Mohwa Butterate, Dimethiconol Panthenol, and Dimethiconol Sal Butterate

Reaction Product Type 2) Copolymers



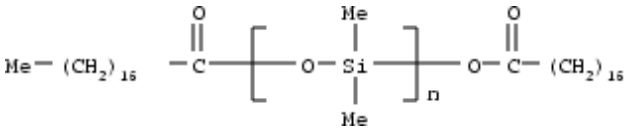
Examples



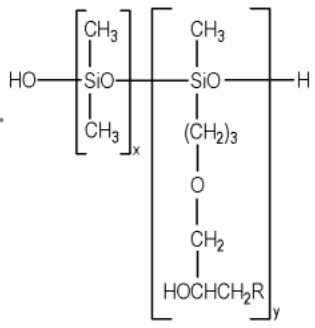
Hydrolyzed Collagen PG-Propyl Dimethiconol[2]

Dimethiconol/ Methylsilanol/Silicate Crosspolymer, Dimethiconol/ Silica Crosspolymer, Dimethiconol/Silsesquioxane Copolymer, Dimethiconol/Stearyl Methicone/Phenyl Trimethicone Copolymer, Isopolyglyceryl-3 Dimethiconol, Trimethylsiloxysilicate/Dimethiconol Crosspolymer, and Acrylates/Dimethiconol Acrylate Copolymer

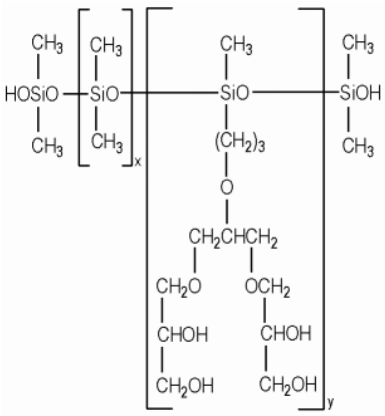
Figure 1B. Structures for Dimethiconol Polymers



Dimethiconol Stearate



Hydrolyzed Collagen PG-Propyl Dimethiconol



Isopolyglyceryl-3 Dimethiconol

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SEHSC Comments on Scientific Literature Review for Dimethiconol and its Esters and Reaction Products (dated December 8, 2009)

Page 2; Paragraph 5; Line 2 – should read "conditioning agent or as a hair conditioning agent…"

Page 3; Paragraph 3 (under Noncosmetic Use) – this is a very general statement and should be more specific and contain additional information. Suggest something like…Insecticidal activity was noted for mosquito larva, mourning cloak, caterpillars, and asparagus beetle larvae.

Page 4; Paragraph 3; Line 2 and 3 - should read "…was evaluated using 10 (5 males, 5 females) New Zealand…."

Page 4; Paragraph 4; entire paragraph - Reference 8 has been reviewed for scientific validity by Dow Corning and this study it was determine this study was not scientifically valid and should be removed from the CIR review.

Page 5; Skin Irritation and Sensitization Section – remove reference 10

> This study was conducted on an emulsions which contained 22% of the siloxanes and silicones, dimethyl, hydroxy-terminated. This material also contains preservatives that are known sensitizers and it is believed that these preservatives are the cause of the skin sensitization not the siloxanes and silicones, dimethyl, hydroxy-terminated. Because the other chemicals in the composition of this material can have an impact on the study results, we recommend that this study not be used to evaluate the skin sensitization potential of the siloxanes and silicones, dimethyl, hydroxy-terminated.
>
> This study can be replaced with the skin sensitization studies that Dow Corning has located on CAS 70131-67-8.

Page 6; Last paragraph – Mucous Membrane Irritation – Line 4 - should read " ….using an aluminum mold"

Page 7; First paragraph – last sentence – change to….Microscopic examinations were considered normal for all samples.

Page 7; Second paragraph; Genotoxicity - replace paragraph with….

> In the Ames spot plate test and overlay plate test,11 the mutagenicity of uncured and cured Dow Corning® X3-5040 sealant containing approximately 75% siloxanes and silicones, dimethyl, hydroxy-terminated was evaluated using the following *Salmonella typhimurium* strains with and without metabolic activation: TA98, TA100, TA1535, TA1537, and TA1538. The test substance was extracted with dimethylsulfoxide. and doses up to 500 µl/plate were tested. The positive control for activation assays was 2-anthramine, and the nonactivation assay positive controls were sodium azide, 9-amino acridine, and 2-nitrofluorene. Dimethylsulfoxide was used as the

solvent control. In both the spot and overlay plate tests, results for the test substance and solvent control were negative in all strains, both with and without metabolic activation, and the positive controls were mutagenic. The test material was considered nonmutagenic.

Page 8 and 9; References 14, 15, and 16 have been reviewed by Dow Corning for scientific validity by Dow Corning and it was determined that these studies were not scientifically valid and should be removed from the CIR review.

Summary:

The summary section needs to be updated with the changes in the summary paragraphs; removal of invalid studies; and addition of new data.

References:

Remove references 8, 10, 14, 15, and 16.

Add report numbers to the following references and remove NTIS report no. and with cover letter from the citation:

5 – Dow Corning report number 1975-I0030-4380
7 – Dow Corning report number 1995-I0000-40945
9 – Dow Corning report number 1965-I0065-1019-01
11 – Dow Corning report number 1981-I0005-833
13 – Dow Corning report number 1968-I0039-11

Additional Data Identified for inclusion in the CIR review

Dow Corning has identified 10 additional studies on materials that contain greater than 90% of CAS 70131-67-8: vaginal irritation study; acute dermal irritation/corrosion study; 2 skin sensitization studies; acute dermal toxicity study; 2 Ames studies; eye irritation study; and an acute oral study. Summaries of these studies have been prepared and included with the comments.

The following summaries are on materials that contain 95% or greater of CAS 70131-67-8.

ACUTE ORAL TOXICITY

The acute oral toxicity of a suspension containing Dow Corning® 60,000CSt, NO CO-SOLVENT in corn oil (20% w/v) was evaluated using a single group of ten Sprague-Dawley rats (5 males, 5 females) (**REFERENCE**). The test substance was administered via a single oral gavage dose of 2 g/kg body weight. Animals were observed for a 14-day interval following dosing. All animals survived with no overt signs of systemic toxicity or gross necropsy lesions. The acute oral LD_{50} was >2 g/kg body weight.

Reference: Dow Corning Corporation, Acute Oral Toxicity Study of Dow Corning® 60,000CSt, NO COSOLVENT in Rats (Limit Test), 1998, TIS Report Number: 1998-I0000-44385

OCULAR IRRITATION

The ocular irritation potential of Dow Corning® 60,000CSt, NO CO-SOLVENT was evaluated using three female New Zealand White rabbits (**REFERENCE**). The right eye of each animal was administered a 0.1ml dose of undiluted test substance and rinsed with water 24 hours following administration. The eyes were observed for conjunctival and corneal response for up to 72 h. No corneal or iris lesions were observed. Conjunctival erythema, chemosis and discharge were seen in all three animals up to 48-h following administration with full recovery by 72 h. A maximum primary eye irritation score of 9.3 was obtained at 24 h. Under the conditions of testing, Dow Corning® 60,000CSt, NO CO-SOLVENT was considered a non-irritant to the eyes of rabbits.

Reference: Dow Corning Corporation, Acute Primary Eye Irritation/Corrosion Study of Dow Corning® 60,000CSt, NO COSOLVENT in Rabbits, 1998, TIS Report Number: 1998-I0000-44339.

ACUTE DERMAL TOXICITY

The acute dermal toxicity of Dow Corning® 60,000CSt, NO CO-SOLVENT was evaluated following a single application to New Zealand White rabbits (5 males, 5 females)(**REFERENCE**). The test substance was left in contact with the skin for 24 h post application. Animals were observed for a 14-day post application period. No rabbits died during the study and there were no overt signs of systemic toxicity. Signs of dermal irritation consisted of erythema at the application site 2 – 6 days following application with all ten animals returning to normal by day 7. The acute dermal LD50 was >2 g/kg body weight.

Reference: Dow Corning Corporation, Acute Dermal Toxicity Study of Dow Corning® 60,000CSt, NO COSOLVENT in Rabbits (Limit Test), 1998, TIS Report Number: 1998-I0000-44373.

SKIN SENSITZATION

Skin sensitization potential **(REFERENCE)** of Dow Corning® 60,000CSt, NO COSOLVENT in Dow Corning® 360 Medical Fluid (5% w/v) was evaluated using the following groups of Hartley guinea pigs: 1 test group (20 males), 1 vehicle control group (10 males, Dow Corning® 360 Medical Fluid), and 1 positive control group (10 males, DNCB in propylene glycol (PG) 0.1% (w/v). The first induction included 0.1 ml intradermal injections of the Dow Corning® 60,000CSt, NO COSOLVENT in Dow Corning® 360 Medical Fluid (5% w/v), Dow Corning® 360 Medical Fluid, and DNCB in PG (1% w/v) for the treated, vehicle control and positive control respectively. One day prior to the second induction (day 7), animals in the test and vehicle control group were treated with sodium lauryl sulfate (SLS).

During the second induction, a 2 x 4 pad saturated with either undiluted test substance, undiluted vehicle, or 1% DNCB in PG was topically applied to the treated, vehicle control and positive control groups respectively. Patches remained for a period of 48 h and the sites followed by a 2-week non treatment period. On day 22 (two weeks after last induction), treated and vehicle control animals were challenged with 0.3 ml of undiluted test substance and 0.3 ml of vehicle. Positive control animals

received 0.3 ml of 1% DNCB in PG. All challenge doses were applied using Hilltop Chambers® wrapped with bandages which were removed 24 h later.

There were no positive responses observed at any time for either the test substance or vehicle control treated animals. Under the conditions tested, Dow Corning® 60,000CSt, NO COSOLVENT was not considered a skin sensitizer in guinea pigs.

Reference: Dow Corning Corporation, Skin Sensitization Study of Dow Corning® 60,000CSt, NO COSOLVENT Using the Guinea Pig Maximization Test, 1998, TIS Report Number: 1998-I0000-44651

Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated, was evaluated for its potential to cause primary skin irritation and skin sensitization (maximization test procedure of Magnusson and Kligman) in Hartley guinea pigs. The primary skin irritation study used 2 male and 2 female guinea pigs where 0.1 mL of 25, 50, 75, and 100% hydroxy terminated dimethylsiloxane (prepared in U.S.P. water for injection) was applied to the skin under Finn chambers. Skin sites were examined at 0, 24, 48, and 72 hours for signs of irritation. Irritation was scored by the method of Draize and no irritation was noted at any of the concentrations applied.

In the skin sensitization assay 5 male and 5 female animals were used in each of the following treatments; 100% test material as a 5% in water emulsion, USP 0.9% sodium chloride as negative control and 0.1% dichloronitrobenzene in 95% ethanol as a positive control. The test material, negative control and positive control were also administered both with and without Freund's Complete Adjuvant. On Day 0, each treatment was introduced as 0.1 mL intradermal injections in the clipped area of the shoulder region. On Day 7 of the induction phase, test and control materials are applied topically and occluded for 48 hours. Animals were challenged on Day 21 by topical application to the clipped area of the hind quarters and occluded for 24 hours (challenge phase). All animals were evaluated on Days 23 and 24 for evidence of sensitization. Dow Corning® X7-9192 produced 0% sensitization and the positive control produced 100% sensitization. Dow Corning® X7-9192 is not a sensitizer in guinea pigs.

Reference: Dow Corning Corporation, Guinea Pig Skin Sensitization Study of Dow Corning® X7-9192, DCC Report No. 1991-I0000-36155

AMES ASSAY

Dow Corning® Q4-2797, dimethylsiloxane, hydroxy-terminated fluid, was evaluated for genetic activity in *Salmonella typhimurium* and *Escherichia coli* reverse mutation assays as outlined in OECD testing guidelines **(REFERENCE)**. Concentrations of the test article tested in *Salmonella typhimurium strains*, TA 97, TA 98, TA 100, TA 1535 and *Escherichia coli* strain, WP2, were 312.5, 625.0, 1250, 2500 and 5000 µg/plate with and without the use of an Arochlor-induced liver S9 metabolic activation system. Solvent controls were dimethylsulfoxide at 50 µl/plate and this solvent was used to prepare dilutions of the test material. Chemicals used as positive controls in the assay that require metabolic biotransformation were sodium azide, 4-nitroquinoline-N-oxide, daunomycin, and N-methyl-N-nitro-N-nitrosoguanidine at 10 µg/plate. Positive controls used without a metabolic activation system were 2-anthramine and 2-aminofluorene, all at 10 µg per plate. The positive controls with and without metabolic activation demonstrated a marked increase in the number of revertants/plate over solvent or negative control plates. The test article at all concentrations tested with and without metabolic activation and in all strains did not demonstrate genetic activity.

Reference: Dow Corning Corporation, Genetic Evaluation of Dow Corning® Q4-2797 in Bacterial Reverse Mutation Assays, DCC Report No. 1985-I0005-1345.

Dow Corning® 60,000CST. No Co-Solvent was tested in a bacterial reverse mutation assay suing *S. typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 and *E. Coli* tester strains WP2*uvr*A and WP2*uvr*A (pKM101) in the presence and absence of Aroclor-induced rat liver S9 **(REFERENCE)**.

Concentrations of the test article tested were 0, 50, 150, 500, 1500 and 5000 µg/plate using Dow Corning OS-10 as a solvent with and without the use of an induced liver S9 metabolic activation system. 25 µL/plate. A non-interfering precipitate was observed at concentrations greater than or equal to 500 or at greater than or equal to 1500 µg/plate. Chemicals used as positive controls in the assay without S9 activation were sodium azide (1 µg/plate), 2-nitrofluorene (1 µg/plate), 9-aminoacridine (75 µg/plate) and methyl methanesulfonate (10 µg/plate). The positive control used with a metabolic activation system was 2-aminoanthracene (1 or 10 µg/plate). The positive controls with and without metabolic activation demonstrated a marked increase in the number of revertants/plate over vehicle control plates. The test article at all concentrations tested with and without metabolic activation and in all strains did not demonstrate genetic activity.

Reference: Dow Corning Corporation, Genetic Evaluation of Dow Corning 60,000CST, No Co-Solvent in a Bacterial Reverse Mutation Assay, DCC Report No. 1998-I0000-44378

PRIMARY EYE IRRITATION

Direct contact with DOW CORNING® PA Fluid with the eyes of a laboratory rabbit produced very slight redness in the unwashed eye through 48 hours while the washed eye was clear when examined 24 hours after exposure **(REFERENCE)**.

Reference: Dow Corning Corporation, Primary Eye Irritation Test with Dow Corning® PA fluid, DCC Report No. 1981-I0005-0842

DERMAL IRRITATION

Dow Corning® 60,000CST, No Co-Solvent was applied undiluted at a dose of 0.5 g for 4 hours to the clipped/shaved backs of three female New Zealand White rabbits **(REFERENCE)**. The study was performed using OECD guidelines for testing (Part 404). The application site was covered with a cotton gauze patch secured with porous tape. The residual test substance was removed with the aid of DC® 360 Medical Fluid-moistened gauze. All test sites were examined for signs of dermal irritation (edema, erythema and/or eschar formation) and corrosivity (ulceration and/or necrosis) at 60 minutes, 24, 48, and 72 hours following removal of the wrappings. No signs of dermal irritation or corrosivity were observed in any of the rabbits during the study. The primary dermal irritation score was 0.0. The test substance was non-irritating to the skin of rabbits.

Reference: Dow Corning Corporation, Acute Dermal Irritation/Corrosion study of Dow Corning® 60,000CST, No Co-Solvent in Rabbits, DCC Report No. 1998-I0000-44338

VAGINAL IRRITATION

Dow Corning® 4-2797 INT (X7-9192), dimethylsiloxane hydroxy-terminated fluid, was evaluated for its potential to produce primary irritation in six New Zealand white rabbits following a single topical application of 0.5 g into the vaginal cavity **(REFERENCE)**. Two control animals were similarly dosed with 0.5 mL of USP 0.9% sodium chloride solution. Tissues were evaluated with an otoscope for signs of irritation, erythema and edema, at 24, 48, and 72 hours post-treatment. There were no signs of irritation, weight loss or clinical sings of toxicity during the 72 hour observation period. The primary vaginal irritation index, base on a standard Draize Scale was 0.0. No changes in body weight or signs of toxicity were reported. Under the conditions of this assay Dow Corning® 4-2797 INT (X7-9192) is not considered to be an irritant to the vaginal tissues of albino rabbits.

Reference: Dow Corning Corporation, Primary Vaginal Irritation Study of Dow Corning® 4-2797 INT (X7-9192) in the Rabbit, DCC Report No. 1991-I0000-36045

RESPONSES TO SEHSC COMMENTS ON DIMETHICONOL SLR

[Page numbers, etc. relate to SLR]

Page 3; Paragraph 3 (under Noncosmetic Use) – The statement included will remain until SEHSC provides a reference for the specific insecticidal activities.

Page 4; Paragraph 4; entire paragraph – The following reference (# 16 in draft report, ocular irritation studies on Dow Corning 35 emulsion and Dow Corning 22 emulsion) should be deleted from the Draft Report at SEHSC's request because Dow Corning says that the study is not scientifically valid.

Dow Corning Corporation. Eye irritation potential of several Dow Corning emulsions with cover letter dated 4/20/94. *NTIS Report No.OTS0556579*. 1968.

The request to delete has been placed on hold. It would be helpful for thePanel to know why this study is not considered scientifically valid.

Page 5; Skin irritation and sensitization section – The following reference [# 20 in draft report, skin irritation and sensitization study on microemulsion (Dow Corning® 2-1870 HV) containing 22 wt.% siloxanes and silicones, dimethyl, hydroxy-terminated (remaining composition not stated) in Dow Corning® 2-1845 microemulsion (composition not stated)] should be deleted from the Draft Report at SEHSC's request because SEHSC says that Dow Corning 2-1870 V contains preservatives that are known sensitizers and it is believed that these preservatives were responsible for the sensitization reactions observed.

International Research and Development Corporation. Skin sensitization study (maximization test) of Dow Corning 2-1870 HV microemulsion in the albino guinea pig. 1995. Report No. NTIS Report No.OTS0558304.

The request to delete has been placed on hold. It is important to note that the composition of Dow Corning® 2-1870 HV (preservative and other component concentrations) remains unknown. The Panel would need this information in order to determine whether it is likely that the sensitization reactions were due to preservatives, dimethiconol (CAS No. 70131-67-8), dimethiconol-like components, or some combination.

SEHSC's recommendation that this study can be **replaced** with the skin sensitization study summaries on CAS No. 70131-67-9 (located by Dow Corning; each summary included in draft report) deserves consideration. However, the Panel would need to know the composition of the test materials (all under CAS No. 70131-67-9) in these studies in order to determine whether data on these test materials can be used to evaluate the sensitization potential of dimethiconol and its reaction products.

Pages 8 and 9 – According to the SEHSC, Dow Corning concluded that the following studies were not scientifically valid and should be removed from this safety assessment.

Subchronic Oral Toxicity

The request to delete has been placed on hold. In that this is the only subchronic toxicity study that was identified, it would be helpful for the Panel to know why this study is not considered scientifically valid.

Food and Drug Research Laboratories, Inc. Chronic (8-month) feeding studies with DC special siloxane polymer in rabbits with cover letter dated 04/20/94. *NTIS Report No.OTS0556539*. 1966.

Chronic Feeding Study

The request to delete has been placed on hold. In that this is one of 2 chronic studies (i.e., limited data) identified, it would be helpful for the Panel to know why this study is not considered scientifically valid.

Food and Drug Research Laboratories, Inc. Chronic (1-year) feeding studies with Dow Corning special polysiloxane in rats with cover letter dated 04/20/94. *NTIS Report No.OTS0556494*. 1966.

Clinical Skin Irritation and Sensitization

The request to delete has been placed on hold. In that this is one of 2 skin irritation and sensitization studies (i.e., limited data) identified, it would be helpful for the Panel to know why this study is not considered scientifically valid.

Dow Corning Corporation. Results of human skin irritation and skin sensitization tests of XET-40002 set 2 treated and untreated cotton with cover letter dated 4/20/94. *NTIS Report No.OTS0556494*. 1958.

Reference List - Add report numbers to the following references and remove NTIS report no. with cover letter from the citation.

With the exception of adding the Dow Corning report number to each reference, there would be **resistance to modifying** these bibliographic entries. "With cover letter" and NTIS report numbers appear in the following references because each was ordered from NTIS and "with cover letter" appears in the NTIS docment name. The inclusion of NTIS order numbers indicates that interested parties may order these documents from NTIS (i.e., they are readily accessible).

Dow Corning Corporation. Acaricidal and insecticidal activity of various silicone fluids with cover letter dated 4/20/94. *NTIS Report No.OTS0572228*. 1975.

To be added: Dow Corning report number 1975-10030-4380

International Research and Development Corporation. An acute dermal toxicity study of Dow Corning 2-1845 microemulsion in rabbits, with cover letter dated 11/14/95. *NTIS Report No.OTS0558305*. 1995.

To be added: Dow Corning report number 1995-10000-40945

Hill Top Research, Inc. Primary irritation study on TX-102A, TA-102B, and TX-102C in dogs with cover letter dated 4/20/94. *NTIS Report No.OTS0556512*. 1965.

To be added: Dow Corning report number 1965-10065-1019-01

Dow Corning Corporation. Mutagenicity evaluation of Dow Corning X3-5040 in the Ames bacterial assay, with cover letter dated 4/20/94. *NTIS Report No.OTS0558117*. 1981.

To be added: Dow Corning report number 1981-10005-833

Food and Drug Research Laboratories, Inc. Chronic implantation studies of polysiloxanes in dogs with cover letter dated 4/20/94. *NTIS Report No.OTS0556574*. 1968.

To be added: Dow Corning report number 1968-10039-11

Additional Data Identified for Inclusion in the CIR Review

The study summaries included with SEHC's comments have been incorporated. However, the complete report for each of the10 additional studies needs to be provided.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: John Bailey, Ph.D. 3/29/10
Industry Liaison to the CIR Expert Panel

DATE: March 29, 2010

SUBJECT: Comments on the Draft Report on Dimethiconol and its Esters and Reaction Products
CIR Expert Panel Meeting April 5-6, 2010

General comment - In many places in the report the "h" in "hydroxy" is replaced with the page number, e.g, on p. 8 it says "8ydroxy".

p.1 - As there are a few human studies on products containing some of the other ingredients, it is not correct to say the data "exclusively" relate to Dimethiconol.

p.2 - Please revise the cosmetic use section as the use concentration data have been provided.

p.4 - In the summary of the Ocular Irritation section, it would be helpful to state the compound tested and the highest concentration that did not result in irritation.

p.5-8 - In the summaries of the Skin Irritation, Mucous Membrane Irritation, Skin Irritation and Sensitization, Genotoxicity, Chronic Exposure/Tumorigenicity and Clinical Skin Irritation and Sensitization sections, please state the ingredients tested, e.g., several Dimethiconol preparations, Dimethiconol, Dimethiconol Behenate and Dimethiconol Beeswax.

p.9 - The Council concentration of use information still needs to be added to the Summary.

p.10 - In the summary, please add that the Dimethiconol Beeswax tested in the HRIPT was undiluted.

p.11, Table 1 - The monograph for Dimethiconol Behenate is now available on the On-Line (and wINCI), so both the definition and functions of this ingredient can be added to Table 1.

p.12, Table 1 - As Hydrolyzed Collagen PG-Propyl Dimethiconol, Isopolyglyceryl-3 Dimethiconol and Isopolyglyceryl-3 Dimethiconol are defined by their structures, the structures of these compounds need to be included somewhere in this report.

p.20, Figure 1 - Please provide additional references for these structures.

p.22-24 - It is not clear why "Date Accessed" is needed for unpublished references provided by industry. It would be more appropriate to include "Date Accessed" for websites such as reference 5 and 29.