PINK BOOK 1

Dimethiconol

CIR EXPERT PANEL MEETING

AUGUST 30-31, 2010

Cosmetic Ingredient Review
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30 August 2010

Memorandum

To: CIR Expert Panel

From: Wilbur Johnson, Jr.
Senior Scientific Analyst

Subject: Dimethiconol and its Esters and Reaction Products

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, Minutes from the June 28-29, 2010 Panel meeting, Literature search strategy, Comments from the Personal Care Products Council, and Data provided by Environmental, Health and Safety Council of North America/Dow Corning Corporation (mentioned below). Industry data are included in the current report. At the April 5-6, 2010 CIR Expert Panel meeting, the Panel issued an insufficient data announcement, and the data requested are included in the CIR Report History. The draft safety assessment was tabled at the June 28-29, 2010 Panel meeting pending receipt of data promised by the Silicones Environmental, Health and Safety Council of North America/Dow Corning Corporation, which included most of the data requested in the insufficient data announcement.

To date, the following data have been received, and will be made available as pdf files: (1) spreadsheet with data on physical properties, composition, impurities, and methods of manufacture for materials that are registered under the dimethiconol INCI name – Data 1; (2) spreadsheet with data on the composition of tested materials containing dimethyl siloxane, hydroxy-terminated (CAS No. 70131-67-8) - UV absorption data on 4 of these materials provided – Data 1 ; (3) justification for removal of certain studies from the safety assessment – Data 1; (4) definition of dimethiconol/silsesquioxane copolymer – Data 1; and (5) Complete Dow Corning reports for 9 study summaries previously submitted – Data 2 through 10. Composition data on the FD80/II polymer included in the safety assessment were not received. Prior to the Animal Toxicology section, data received from industry are identified by a vertical line in the right margin of the report text; industry data are also included in Tables 4 and 5. In the Animal Toxicology section, the vertical line identifies text associated with the 9 complete Dow Corning reports provided.

After reviewing the data provided, the Panel needs to determine whether these data are sufficient for arriving at a conclusion on the safety of dimethiconol and its esters and reaction products in personal care products. The Discussion section will be revised accordingly after this decision has been made. The Panel also needs to review item 3 above to determine whether the studies identified should be deleted from the safety assessment.

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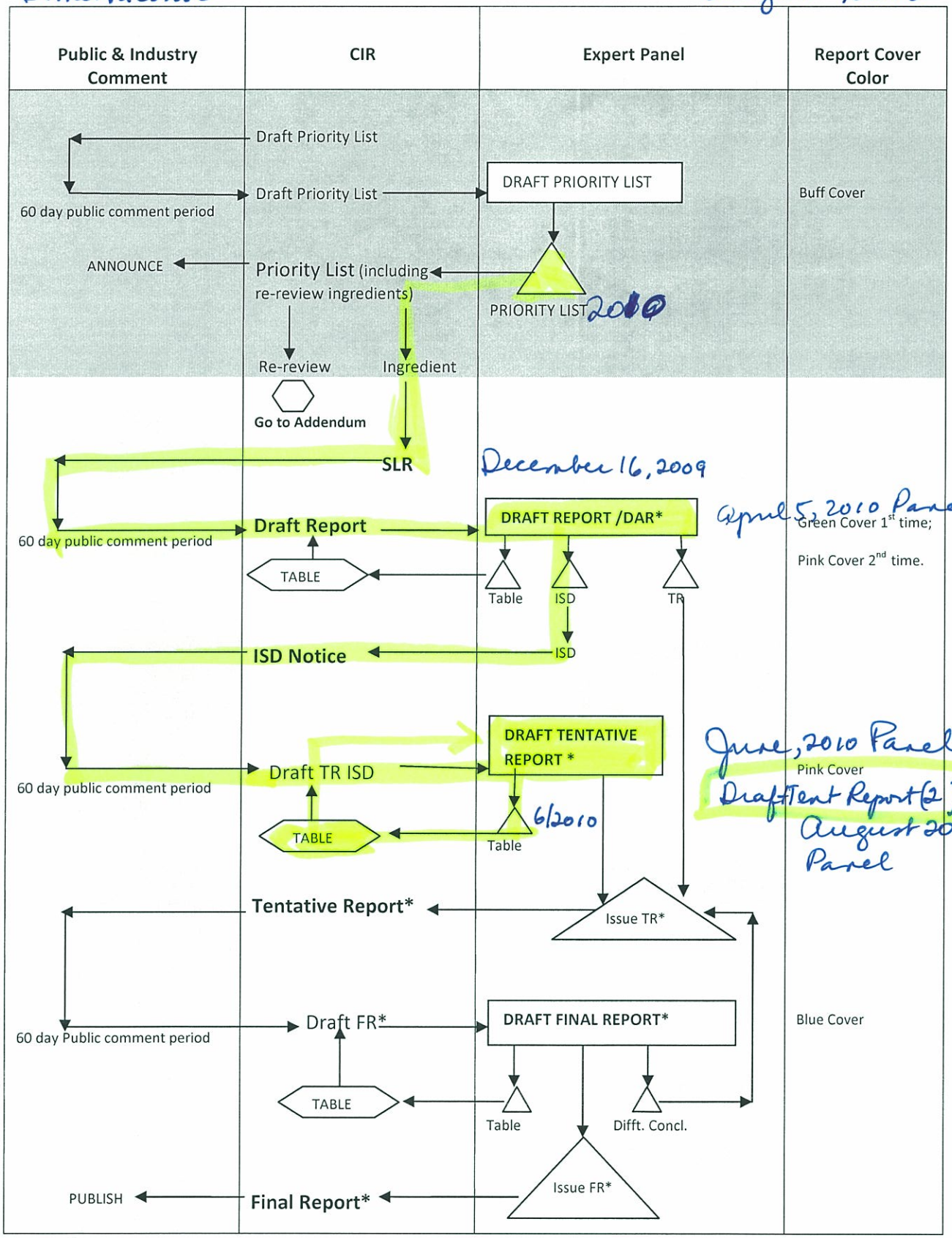
SAFETY ASSESSMENT FLOW CHART

Dimethiconol

August, 2010



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

△ Expert Panel Decision

▭ Document for Panel Review

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.

The draft safety assessment was tabled at the June 28-29, 2010 Panel meeting pending receipt of data promised by the Silicones Environmental, Health and Safety Council of North America/Dow Corning Corporation, which included most of the data requested in the insufficient data announcement.

3rd Review, Belsito and Marks Teams/Panel: August 30-31, 2010

To date, the following data have been received: (1) spreadsheet with data on physical properties, composition, impurities, and methods of manufacture for materials that are registered under the dimethiconol INCI name1; (2) spreadsheet with data on the composition of tested materials containing dimethyl siloxane, hydroxy-terminated (CAS No. 70131-67-8) - UV absorption data on 4 of these materials provided; (3) justification for removal of certain studies from the safety assessment; (4) definition of dimethiconol/silsesquioxane copolymer; and (5) Complete Dow Corning reports for 9 study summaries previously submitted. Composition data on the FD80/II polymer included in the safety assessment were not received. The safety assessment has been updated to include industry data.

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

Transcripts/ Minutes

Dimethiconol Group

5 DR. BELSITO: Dimethiconol. This is the
6 first time that we're looking at this ingredient.
7 We got quite a bit of data, but unfortunately not
8 all of the data that we needed to make a safety
9 assessment. We felt that we needed manufacturing
10 and impurities and UV absorption data, and, if UV
11 absorption, photosensitization and photoirritation
12 data may be needed.
13 Dermal absorption data are needed, and if
14 we have dermal absorption, then reproductive
15 toxicity data may be needed. We also received some
16 data on a polymer that was labeled FD80 and FD80/2
17 and we wanted clarification as to what exactly was
18 the composition of that polymer. It wasn't clear
19 to our group. Those were the data needs.
20 Then there were other compounds to
21 consider along with dimethiconol. Of that list,
22 some of them were plant-derived fatty acids and
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1 seed oils, and we look forward to Christina's
2 report to tell us exactly what the composition of
3 those were, things like the borageate and dhupa
4 butterate, et cetera. Some were amino acids and
5 we felt that those could stay in the report as
6 well as the fatty acids, pending a decision as to
7 the composition of those. There were a couple
8 though that we felt should come out of the report,
9 specifically, the isophorone diisocyanate
10 copolymer. It had no uses and I think it would be
11 an issue in terms of isocyanate, both IGE-mediated
12 sensitization respiratory-wise and also
13 delayed-type hypersensitivity skin-wise, so that
14 we would recommend that that dimethiconol IPDI
15 copolymer be removed.
16 Also there were two fluorinated
17 compounds that we felt should be removed from the
18 list, the dimethiconol fluoroalcohol dilinoleic
19 acid and the trifluoropropyl dimethiconol. One
20 compound that we didn't want to delete at this
21 point, but we did feel we needed more information
22 on the dimethiconol silsesquioxane copolymer. So
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1 moving ahead with an insufficient and deleting
2 three ingredients, the two fluoros and the
3 diisocyanate, and requesting if we're going to
4 keep the silsesquioxane copolymer in, more
5 information on exactly what that was.
6 DR. BERGFELD: So you're making a
7 motion?
8 DR. BELSITO: I'm making a motion.
9 DR. BERGFELD: And the motion is to go
10 insufficient?
11 DR. BELSITO: It is to go insufficient
12 and delete those three ingredients.
13 DR. BERGFELD: Is there a second?
14 DR. MARKS: Second.
15 DR. BERGFELD: Is there any further
16 discussion?
17 DR. MARKS: Yes. We had similar
18 concerns. We felt if we knew the molecular
19 weight, the dermal absorption data may not be
20 necessary. If it's a large enough molecule it
21 wouldn't be absorbed. The safety of these
22 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.

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: Okay. Dimethiconol.

DR. ANSELL: We have one comment on the table 1.

DR. BELSITO: Sure.

DR. ANSELL: It includes a lot of trade names, I think.

DR. BELSITO: Back on the --

DR. ANSELL: Table 1, page 34, chemical names, definitions, functions.

DR. BELSITO: Right.

DR. ANSELL: Does include trade names. We don't necessarily think that's particularly useful or appropriate within the document.

DR. BELSITO: Well, I guess -- so you want the trade names deleted from that table?

DR. ANSELL: Yeah.

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DR. BELSITO: We've traditionally included trade names, including when we looked at studies.

DR. ANSELL: I think to the extent that it's associated with a study, it may help inform structure -- when --

DR. BELSITO: But, I mean, all of our former documents for under synonyms have been the associated trade names. I don't have a problem eliminating them, but it's a -- you know, particularly when we report a study that would say, you know, whatever trade name and then in parentheses what the drug actually -- or what the

chemical actually was.

Why did you want them deleted?

DR. ANSELL: I -- when they're associated with identity, I think it's fine. When it's in a table that's talking about chemical structures, you know, the trade names come and go. And, you know, I don't know that I feel strongly about it as I did when we had formulation trade names, which are often, you know, gone within a year. But that was one of the comments that came through. So I will advance this argument no farther.

DR. BELSITO: I mean, I -- again, I'm totally neutral. Curt, Paul, Dan?

DR. KLAASSEN: I personally would like to have the trade names removed.

DR. BELSITO: One remove. Paul?

DR. SNYDER: I'm indifferent.

DR. BELSITO: Two indifferents, one remove. Dan?

DR. LIEBLER: Remove.

DR. BELSITO: Two removes, two indifferents. Madame Chair, what do you feel like?

DR. BERGFELD: (inaudible) I like the trade names in.

DR. BELSITO: Alan?

DR. ANDERSEN: I guess I'm in the indifferent category. It seems like it would be useful information for a reader in the off chance

that that reader is a formulator who is going to go rush out and now buy some of this stuff. But you don't buy it with the INCI name, you buy it with the trade name. And now I've got the trade names here, that's neat. Yes, I could go to the dictionary and get them, but it's nice that it's all here. This is an informative source.

So that -- it just seems like it -- you know, a very narrow window. Those pieces of information might be actually useful to somebody.

DR. SNYDER: I mean, historically --

DR. ANDERSEN: But I'm still indifferent.

DR. SNYDER: Historically, we look at studies that are with a trade name product that contains X percentage --

DR. ANDERSEN: No question. And those trade -- and they're often identified by the trade name. But in those circumstances, there's no reason we can't when we're talking about that study identify that this is a trade name for hexamethyl chicken fat. I mean, it's not difficult to do. And still be responsive to what Jay is saying here of having them out of this section of the report. We're not constrained to not say that it's a trade name. Just, there's a -- if there's a study that has a trade name, you say so. It's not hard.

I just -- it's just a -- sometimes it can be a huge amount of work to put them in. And if we didn't have to do that, to some small

degree, it's easier to write these things.

DR. BERGFELD: Looking at it from a different perspective and widening your reader base to the non- chemist, it's nice to have the trade names in because that's what we see.

DR. KLAASSEN: Well, there's -- to me, there's a number of problems with the trade names. One, it's a little bit of an advertisement. Number two, a trade name does -- I mean, you don't always have the same ingredient even though in the same trade name. For example, Tide soap is different in California than it is in Ohio. Another problem is, how many trade names are we going to put in? Is there only one trade name?

DR. ANSELL: Well, no, and I think that's it exactly. To the extent that it's associated with a study, it helps inform the material identity. To the extent where we're turning it upside down now, now the trade name is defining the chemistry as opposed to -- or the chemistry is defining the trade name as opposed to the other way around. So I think it's entirely appropriate in the study. I just don't think it's necessarily appropriate here where we're trying to tie a specific chemistry in. And the right place is in the supplier guides, where you can call them up and find out the details. But again, this was not intended to precipitate --

DR. BELSITO: Okay. Well, I mean, you got two to remove it and two who don't care, so that goes -- our panel will go with you to remove

it. We'll have the discussion with the other panel tomorrow.

Any other points on the pelargonic acid? If not --

DR. SNYDER: I just want to make one comment to Wilbur. I thought that the intro was very well written, and I liked the scope and extent section that you had in the use. Because I thought that put things in correct perspective of what we were viewing, what had been previously reviewed. And so, I thought that was very nicely done.

DR. BELSITO: Okay. Dimethiconol, Pink 1. What? And we've got handouts here. We got something from the silicone industry, and then we have responses -- who are these responses to the SEH -- SE from? It just says, "Responses to SEHSC comments on dimethiconol."

DR. ANDERSEN: Wilbur.

MR. JOHNSON: They're from the Silicones Environmental Health and Safety Council, SEHSC.

DR. BELSITO: No, this here.

MR. JOHNSON: Okay.

DR. BELSITO: Is titled, "Responses to SE --

MR. JOHNSON: Oh, yeah, that's my document. I produced that.

DR. BELSITO: Oh, this is what -- how we handle their comments.

MR. JOHNSON: Yes.

DR. BELSITO: Based upon our last meeting?

MR. JOHNSON: Yes.

DR. BELSITO: So this is our response -- the panel's responses to their comment?

DR. ANDERSEN: I don't know. I think it's the --

DR. BELSITO: More Wilbur's.

DR. ANSELL: Yeah. It's Wilbur's suggestions as to what the panel may say in response to the comments we did submit.

DR. BELSITO: Now, we reviewed those comments at our last meeting, no? We had the SEHSC's comments to look at at our last meeting.

MR. JOHNSON: Right, that's correct.

DR. BELSITO: And so I'm assuming this is a summary of our responses to their comments? Or, I mean, is this --

MR. JOHNSON: In red -- well, no. You have the -- basically, in response to SEHSC's comments, I developed a document, you know, addressing those.

DR. BELSITO: But based upon what, Wilbur, did you develop this? The comments that came from our team and the other team or?

MR. JOHNSON: No, no, I just purely, initially -- I had looked at the comments that were received from SEHSC, you know, based upon the recommendations that they were making and I had certain questions, you know, relating to those.

DR. BELSITO: Okay.

MR. JOHNSON: And they responded and the responses to those are included in this document.

DR. BELSITO: Okay. And then can you tell me what this document is supposed to be telling us?

DR. ANSELL: It was a -- one of the data requests went to manufacturing.

DR. BELSITO: So this is going to help us understand the manufacturing. So it's a hydrolysis reaction to polysiloxanes. Is that what I'm to understand?

MS. ANDROIT: Yes. So, you've got some different pieces of information that have come in. One is there's an Excel spreadsheet, which actually has molecular weight information and it has project names. It's the one that it was (inaudible) proprietary, but actually --

REPORTER: I'm sorry, (inaudible) can you turn on your microphone?

MS. ANDROIT: And so what this is is actually a (inaudible) that we collected on the number of companies. We sent out surveys, we gathered information based on the insufficient data request that you guys had put together. So we supplied molecular weight information, manufacturing information, and impurity information.

The other piece of information that I do have but unfortunately it's Dow Corning data right now and we have to get legal to sign off on it. In mid-June we did do some UV absorption work on

several -- four products. And based on that data there was no UV absorption seen with those materials. But I do have that data and I do have approval to give it to you once legal signs off on it. So I will be supplying those study reports, also.

And I did supply Wilbur with a CD today of -- we had supplied some robust summaries of additional information on dimethyconol, which is the CAS number -- they were all done on CAS Number 70131-678, and they were greater than 95 percent that CAS number, primary impurities being the starting products, the linears and the cyclics.

We only supply robust summaries, we were requested to provide the full study reports. And I just provided a CD with all of those full study reports to Wilbur today.

REPORTER: Ma'am, you are?

MS. ANDRIOT: Michelle Andriot, I actually -- I work for Dow Corning, but I'm here representing the silicone industry.

DR. LIEBLER: So I think our issue last time was that a lot of the toxicology that was described in our report draft was on this proprietary material. And we didn't know where this material fit in the chemical space that this class of compounds is supposed to represent. We didn't know how representative it is. And I'm still trying to figure that out from the spreadsheet.

DR. BELSITO: Well, what we had asked

for in April was, we came with an insufficient data announcement for method of manufacture and impurities. So, we now have method of manufacture and, I presume, impurities for the polysiloxanes. So, assuming you're comfortable with this document, it's page 21/22. And the -- what we're handed today, we have that.

We asked for UV absorption and if there was absorption, then photosensitization and photoirritation or phototoxicity. And we do not have that present in front of us, but we're told that it's available and will be given to us forthwith. And then the last was dermal absorption and if absorbed, yadda, yadda, yadda.

But if you look at the molecular weights of these compounds, I guess that would be your argument. There's no way in god's green earth that a compound of 530,000 is going to get across the stratum corneum. So that -- do we really need any more data other than the molecular weight to make us happy that there's no absorption?

MR. JOHNSON: Excuse me, Dr. Belsito. Michelle agreed to provide a data on the content of dimethiconol in each one of these materials. Because right now we don't even know, you know, what the content is of these materials and the table.

MS. ANDROIT: What the materials are is, they're basically dimethiconol at different percentages in things like D-5, hydrocarbon solvents. So they're basically emulsions of the

dimethiconol to get it to the right viscosity for whatever they're going to be used for.

So what I did is, I told Wilbur we could get some more detailed information so you could see that the different concentrations of the

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dimethiconol that are in there.

But the study reports that Wilbur has, those are actually on pretty much 95 percent pure dimethiconol. It's not in a solvent.

DR. BERGFELD: So you are promising to fulfill all these needs, then to come up with the information as Wilbur described?

MS. ANDROIT: Right. I mean --

DR. BERGFELD: So --

MS. ANDROIT: You know --

DR. BERGFELD: So things to come yet.

MR. JOHNSON: And in addition to that, Michelle agreed to provide data -- if you look at table 4 on page 18? A number of material are included in studies summarizing this report. And we don't know the composition of the materials that were actually tested. So those materials are included in table 4 on page 18. So, Michelle agreed to provide that information as well.

MS. ANDROIT: For the Dow Corning materials, which are the predominant amount of the materials on that table.

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DR. BERGFELD: And that could be provided by the -- before the next meeting?

MS. ANDROIT: Yes.

DR. LIEBLER: So the stuff on the

spreadsheet, the long page, is not an attempt to address that issue? Is that right?

DR. BELSITO: It is an attempt.

DR. LIEBLER: Then it's not -- I -- we just got it this morning and I haven't been able to compare this to the stuff in the tables and try and match every ingredient for ingredient. I'm trying to do that now. I'm not getting very far.

So you're saying that there's more information that could be provided to assist us in determining what is the chemical composition of materials that were tested?

MS. ANDROIT: Right. So what -- because what I provided -- what was provided in this table was, we did not provide the actual composition information. But what I can say is, on all the products -- except for the last two, they do all contain the CAS number -- you know, the

dimethiconol CAS number of 70131-678 at various percentages.

But what I agreed to do was to identify what those percentages are. So that you would have an understanding of what's in the materials -- and then I also agreed to look at the table 4. And for the materials that are Dow Corning, I can provide that information, which, again, is most of the materials in the table.

DR. BELSITO: Okay. And in my notes -- and I'm having trouble locating, going back to why I asked this -- I said we still need composition of FD80 and FD80/something that I cannot read now.

So, FD80/II.

DR. SNYDER: Two Roman numerals.

DR. BELSITO: Yeah. Roman numeral II, good. So, why did we need that?

DR. SNYDER: Because the study we got --

REPORTER: Microphone, please.

DR. SNYDER: The information we received parenthetically said composition not stated. So, you know, we didn't know what was comprised of.

DR. BELSITO: And are we getting that? We still don't' have that, right? And what study was that on?

DR. SNYDER: Page 5, on ocular irritation --

DR. BELSITO: Oh, right, okay.

DR. SNYDER: -- potential of the polymer FD80/II composition not stated.

MR. JOHNSON: No, we have not received that information.

DR. BELSITO: Okay. And then, I have a note that we need more information on the dimethiconol silsesquioxane mixture? And that came from -- where did we look at the mixture?

MR. JOHNSON: Is that -- what was it?

DR. BELSITO: It's just a note from the last meeting that for whatever reason we needed information on dimethiconol silsesquioxane.

MR. JOHNSON: Because what happened in looking at the data in table 1, you determined that certain ingredients should have been deleted from the safety assessment. And at that time you

said that if you received, you know, certain data on that particular chemical then, you know, possibly that ingredient could remain in the safety assessment.

DR. ANSELL: And we have -- through the INFRO database have a chemical description of the dimethiconol silsesquio --

DR. BELSITO: Ah, so it was whether it would stay in table 1 as one of the ingredients --

DR. ANSELL: Right --

DR. BELSITO: -- that we're reviewing, and we haven't received that yet.

MS. ANDROIT: What kind of information are you looking for on it?

DR. BELSITO: What the heck it is.

DR. ANSELL: It's a copolymer of siloxane consisting of the trimethyl -- trimethoxysilane and dimethylsiloxane terminated with hydroxyl groups.

MS. ANDROIT: Yeah, you're -- basically, your silsesquioxane starts to create a -- if you think of a straight chain siloxane polymer, your

silsesquioxane starts to create your 3-D structure to it. So you start to get branches and it's actually -- your silsesquioxanes are even bigger than your siloxane polymer. So it becomes even larger. And then when you start to have your dimethiconol, which has the OHN groups, you start to get -- you know, things can start attaching and it starts growing. So you get something very

large.

Your silsesquioxanes can actually start going more towards your resinous materials.

DR. BELSITO: Dan?

DR. ANDERSEN: Interesting.

DR. LIEBLER: So, I've lost track of what the question is here. (Laughter)

DR. BELSITO: Well, we wanted -- these are just notes that I have from the last meeting.

DR. LIEBLER: Right.

DR. BELSITO: It appears that we wanted information -- more information on dimethiconol silsesquioxane and as to whether it was appropriate to keep that grouped under the esters and reaction products in table 1 that we're reviewing.

DR. LIEBLER: Right.

DR. BELSITO: So having heard what you just heard, do you feel that it is appropriate to keep that in this group?

DR. LIEBLER: Yes. And if you're able to -- I appreciate the verbal description you gave, particularly with the hand motions. But if you could include that in your look-up list of things so that we can have a little bit more chemical composition information, that would be good.

I think you're going to research the things in table 4?

MS. ANDROIT: Mm-hmm.

DR. LIEBLER: And this item was not in

table 4. So, probably you should maybe include things that are in table 1 and table 4.

DR. BELSITO: Okay. So we're satisfied with the definition? We still don't have the composition of what we got information -- safety

information -- on FD80 and FD80/II so we need that.

Are we happy with basically the dimethiconol data and the molecular weight data supporting otherwise lack of absorption information for these materials?

DR. LIEBLER: Yes.

DR. SNYDER: Yes.

DR. BELSITO: Okay. So, we'll use the molecular weight argument in the dimethiconol data to support all of them.

It has some of the fatty acids are from plants, Wilbur, so we'll need the plant boilerplate. And there're hairspray uses, so we need the hairspray boilerplate added to the cosmetic use section, and the discussion.

It -- so, it looks like our prior reason for going insufficient on this group of chemicals is going to go away. But it's all based upon data that we don't have. So do we want to table this with the understanding that the -- either Dow Corning or the Silicon Council or whoever is going

to allow this data to come forward to us -- will be doing this by the September meeting, and it'll be back on the table and we'll dispense with it?

DR. ANDERSEN: Would probably be a good

idea to table it, because that's what Jim's going to move.

DR. BELSITO: Well, he must have read my mind. Okay.

DR. ANDERSEN: And we will pull together all of the new information -- knock on wood -- get it incorporated into the report for your review at the August meeting.

DR. BELSITO: So really it -- and I guess just to give industry a heads up, it looks like we have promises for everything we want, except we still don't know what FD80 and FD80/II are. And since we have safety information on those, it should be fairly easy for someone to tell us what those products are. And that would be the missing piece of information.

MS. ANDROIT: Yeah, I'll go back to the silicone industry on that, because those aren't Dow Corning materials. So I'll have to find out who they belong to and see if they'll provide that.

DR. BELSITO: Thank you.

MS. ANDROIT: They get worried because of CBI and they like to keep things -- but Dow Corning is kind of like, we need to get this out there so we can get this one done and finished. So, we'll go back.

DR. BELSITO: Good.

DR. LIEBLER: And I don't think we're going to need UV on these. I can't see any reason why they should absorb above.

DR. BELSITO: Well, we already have it now. We asked for it, so we're getting it.

(Laughter)

DR. LIEBLER: You've got a bunch of blank spectra, basically.

DR. ANSELL: That was our problem, since there is no chromophore, no absorption -- there weren't a lot of spectra available. But someone did promise to run a blank one for us.

DR. BELSITO: Okay. Anything else? We're going to table this with the understanding that hopefully we can squeeze out of whoever makes -- okay.

Dimethiconol Group

DR. MARKS: Okay. If there's no more

22 comments, we'll do the dimethiconol and its esters 31
1 and reaction products. And that's in the Pink 1
2 book.
3 MS. EISENMANN: Dr. Marks? Michelle
4 from Dow Corning. So if you have additional
5 questions, she should be able to help you.
6 DR. MARKS: Good. Thank you. So, after
7 my introduction, if, Michelle, you want to make
8 any comments to clarify some of the insufficient
9 data needs, that would be helpful.
10 So at the April 5th meeting of this
11 year, we issued an Insufficient Data Announcement,
12 with the following data request: Method of
13 manufacture and purity, UV absorption. And if
14 there's absorption, then photo irritation and
15 photosensitization. Molecular weights, for
16 information about the dermal absorption, that can
17 predict dermal absorption. And then if there were
18 absorption, obviously we need reproductive and
19 developmental toxicity.
20 And then the last -- although it's not
21 in the memo, the fourth really was additional
22 information on the composition on the dimethiconol 32
1 silsesquioxane, and also the Dow Corning mixtures
2 and the FD80, FD80/II.
3 And as of the antedated data, we hadn't
4 received anything. But it looks like we received
5 something this morning. So Michelle, maybe you

can talk to that.

MS. ANDRIOT: Yes, and actually this information -- I know it says "Dow Corning Proprietary" on it, but Tracy Guerrero from SEHSC actually liked my table that I sent her, and she forgot to take that indication off. Because that's actually SEHSC data, dimethiconol.

Granted, in Georgia, the products are primarily California materials. And so in that spreadsheet, what you'll see is the product name. There's molecular weight. There is information on manufacturing, and then also impurities.

Dimethiconol is primarily produced using our linears or our cyclics, the D4, the D5 and D6, with -- you use a hydroxide in there, and then that's stripped out.

Basically -- you're familiar with dimethicone, which is our polydimethylsioxane. And what this is, it's the same material with O-H end groups. So we end-block it with O-H. And it's a polymer. And if you look at the spreadsheets, you'll see for the most part these are fairly large polymers that are utilized.

And I should point out the tox data that was supplied -- and actually, I just gave Wilbur a disk, because it does take time to get tox reports actually released. And these were Dow Corning study reports. So we do have to go through a process. But I did provide him with all the tox study reports that I think we provided summaries of last time, and we were asked to actually

provide the full study reports. Those are now on a CD that Wilbur has. And that was actually on dimethiconol, itself. It's an approximate 95 percent purity -- with your impurities being some of your starting products, being the cyclics and the linears.

And then the other thing -- and this, I can't give to you today because we just got it

out. We did do some UV absorption data on four for the materials. And, basically, what the results say -- and I will, once I have approval from Legal to get the results -- this data was just done in June, mid-June. So the dimethiconol does not absorb within the UV spectrum. And the scans are roughly equivalent to the scan of a

(inaudible).

And then we've got the official approval to release, but Legal has to sign off. And I'll send those reports to Wilbur.

DR. MARKS: So that would appear -- we have two, we have the method of manufacture, and impurities. UV absorption sounds like that's going to be good -- report pending.

Molecular weights, or information about the dermal absorption, we had that. And we have the -- we have information on the composition.

So it sounds like we'll have all the information. It's just we're awaiting the UV absorption.

Does that sound correct, Rons and Tom?

And I guess the question is, do we, having a verbal that there's no UV absorption, do we move on in a tentative report with "safe," or do we table it and wait to see the hard data?

DR. SHANK: We probably should wait to see the data.

On the UV absorption, we didn't expect these compounds to absorb, anyway. And the question was were there impurities in there.

DR. MARKS: Okay. So, with that in mind --

DR. SHANK: (inaudible)

DR. MARKS: -- we could, could move forward. But I'll rely on -- do you want to table it, and await that?

DR. SHANK: I think we should.

DR. SLAGA: I move -- we went extensively through a discussion about it earlier. (inaudible) does not absorb (inaudible). But just to be on the safe side.

REPORTER: I can't -- I'm sorry, I cannot hear what you're saying.

DR. MARKS: Go ahead, Tom. Speak up.

DR. SLAGA: We had extensive discussion that it more likely does not absorb in the UV range, so therefore, you know, we could go forward. But to be safe, we need to have that data for inclusion (inaudible).

DR. MARKS: So I would suggest then, with that in mind -- and we always err to be on the safe side -- that I would propose that we

table this, awaiting that data on UV absorption.

Does that sound like a reasonable --

DR. SHANK: Well, the data on UV absorption and molecular weight, and the three needs specified -- method of manufacture, impurities --

DR. MARKS: Is that -- right.

DR. SHANK: So, you can put that -- all of that is coming, so.

DR. MARKS: It's right here.

MS. ANDRIOT: The table has the molecular weight.

DR. SHANK: But it's not in the report.

DR. MARKS: No. I mean, we have the data, it's just not in the report.

At this point, I think the only data need is the UV absorption, which is coming.

MS. ANDRIOT: Which I have in my hands, and you guys can look at them. I just can't leave them. (Laughter)

DR. SHANK: Well, the UV absorption, you wouldn't expect these compounds to absorb.

DR. MARKS: No.

DR. SHANK: So if the only -- if there were impurities that will absorb.

So if that's the only thing outstanding, I would say let's just finish the report -- on the expectation that that's coming.

DR. MARKS: Alan.

MR. ANDERSEN: I think the caution,

though, is we have a disk full of all studies now, based on what were only summaries before. And on the usual circumstance is that the full study provides a lot more description for the document.

I think caution is still the right approach here. If it's tabled, that gives an opportunity to look through those data. It gives the opportunity for the new data to come in. And then, come August, which is not that far away, we could wrap this up with a much improved document.

DR. MARKS: Wilbur?

MR. JOHNSON: I just have a question. Dimethiconol and a number of its reaction products are being reviewed in this safety assessment. I guess my problem is associated with matching these data with a specific chemical name included in this table?

MS. ANDRIOT: Okay, all those products there actually contain the dimethiconol, not dimethiconol plus the reaction product. And I can provide you more specific information on the levels of dimethiconol. Because those would be products that we would -- so it's, for example, some of them are dimethiconol in D5, so that you can get the right viscosity. But the primary ingredient is dimethiconol, which is the CAS number -- I think it's 70131-67-8.

So they're not any of the other reaction products that are listed under this review. Those are for dimethiconol itself.

MR. JOHNSON: So we will receive that on

a percent composition of dimethiconol and each one of these materials.

MS. ANDRIOT: I can give you the general composition of those, yes.

MR. JOHNSON: And one other concern that I have relates to Table 4, on page 18.

Yes -- there are number of studies in which Dow Corning materials for which we do not have a description are included in the safety assessment. So we really don't know the composition of a number of those materials.

And is there any possibility that that information would be provided?

MS. ANDRIOT: Mm-hmm. So you're looking for additional information on the chemical composition in this table.

DR. MARKS: Yes, I think -- I'm not sure how helpful this would be, but in this document

that you gave us, some of the compounds -- like the 1870 HV, as you mention in here, are mixtures containing other ingredients which are known sensitizers, like methyl chloroxothiazolone, methyl isothiazalone. So one would have to interpret the study on those compounds rather cautiously, if we got a positive result, because sit may be due to the preservative in that mixture.

MS. ANDRIOT: (inaudible).

DR. MARKS: So I don't -- Wilbur, you can -- and then we're back to the IBT data issue here, which -- I forget how we handled that

before, but we had the issue before of IBT data not being valid.

And -- what did we do? Did we delete that from that report? I'm trying to remember.

MR. JOHNSON: Yes.

DR. MARKS: We did delete it. So I think we need to do that where we have concern about whether or not the actual data has been fabricated.

Okay. So --

DR. HILL: One more quick comment --

DR. MARKS: Sure.

DR. HILL: -- is that given that D4, D5 and D6 are listed as impurities, in aggregate could be up to 5 percent from what I think I heard her just say, we need to make sure that when those are noted in the report, that it references our previous review, where we looked at those specifically.

DR. MARKS: Good. Good point, Ron.

MR. JOHNSON: Dr. Marks, could I just ask one more question?

DR. MARKS: Sure. Of course.

MR. JOHNSON: I know that the IBT study is going to be deleted, but with respect to the other studies that SCSA should be deleted, should they be deleted?

MS. ANDRIOT: And I can talk a little bit about that.

Those are Dow Corning studies, and Dow Corning goes through -- before we actually use any

data in health and safety assessments, because some of our data is older data and we don't have all the raw material in our files, and we may not have all the information. And so Dow Corning does make a decision not to utilize that information, and we'll give it a (inaudible) code of "3" on some of them, or a "4" if it's insufficient data.

We have provided information like that before, but one of the things is that it needs to be -- some of these studies, I think, were actually feeding studies. So stability wasn't looked at. So we can't actually say what the dose was that was given to those animals. And that does raise a concern, because if you indicate, oh, these were the doses, they may have been dosed at something significantly less than that.

If you choose not to -- or if you choose to keep the information in there, we would highly recommend that you know that there are limitations on those studies and the interpretation of the data. And I think I've listed them in that document what Dow Corning said those limitations

are.

DR. HILL: Okay. We'll make sure that gets captured into wherever that's discussed in the report?

DR. MARKS: Yes. Thank you. Any other comments? So, since I'm the one who's going to be presenting this tomorrow, I'm going to move that we table this final conclusion -- or, I should

say, issuing a tentative report. But we expect there will be a tentative report with a "safe" conclusion. That the preliminary data we've received appear fine; that the full studies, with the caveats we discussed will be incorporated in the report, and we'll have time to be sure that the full studies support our preliminary data.

Does that capture it well? Ron, Ron, Tom?

Dimethiconol Group

DR. MARKS: In April of this year the CIR Expert Panel issued an insufficient data announcement for dimethiconol. There were four data requirements. We actually yesterday saw a summary of those data and they look like we will be able to issue a safe report. However, particularly data need number 2, the UV absorption, we had a verbal report that was okay but we didn't see anything in writing. We didn't see the full studies. So our team felt that we would prefer to table this, receive the full studies, confirm the preliminary reports that we have that all these four data needs, the method of manufacturing, impurities, UV absorption and molecular weights and the composition of the copolymer and also the Dow Corning mixtures that we have, the full studies and full information and then proceed with an expected safe. So I move that we table this report.

DR. BERGFELD: Is there a second?

DR. BELSITO: Second.

DR. BERGFELD: There is no discussion on the tabling. All those in favor of tabling please indicate by raising your hands. Thank you. Unanimous.

Report

Draft Tentative Report

Dimethiconol and its Esters and Reaction Products

August 30, 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.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Wilbur Johnson, Jr.., Scientific Analyst/Writer.

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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 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) 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 10 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, dimethiconol/silsesquioxane copolymer, 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. Because cyclotetrasiloxane (D_4) is listed as an impurity of dimethiconol and dimethiconol/silsesquioxane copolymer emulsions and D_4 and cyclopentasiloxane (D_5) are listed as impurities of materials containing dimethyl siloxane, hydroxy-terminated (CAS No. 70131-67-8) that were tested in studies included in this safety assessment, it should also be noted that the CIR Expert Panel has reviewed the safety of cyclomethicone, cyclotetrasiloxane, cyclopentasiloxane, cyclohexasiloxane, and cycloheptasiloxane in personal care products and concluded that these ingredients are safe in the present practices of use and concentration.[2]

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.[3] 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[4] 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[5] 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.[6]

In addition to definition of dimethiconol/silsesquioxane copolymer provided in Table 1, the Silicones Environmental, Health and Safety Council of North America (SEHSC) defines dimethiconol/silsesquioxane as the product of a condensation reaction between dimethiconol and methyl trimethoxysilane and defines silsesquioxanes as siloxane polymers that contain silicon atoms bonded to 3 other silicon atoms via siloxane bonds.[7] According to the SEHSC, the SiOH groups that terminate the siloxane polymer chains in dimethiconol are reactive under certain circumstances. One common reaction is a condensation reaction with alkoxy-terminated siloxanes and alkoxy silanes. In this reaction the SiOH groups react with the alkoxy groups to form a new siloxane bond (SiOSi) with the release of the corresponding alcohol. So, for dimethiconol/silsesquioxane, the dimethiconol polymer reacts with the methoxy groups on methyl trimethoxysilane, releasing methanol and forming new siloxane bonds. Since there are three methoxy groups on this silane, the reaction produces a three-dimensional siloxane polymer network in which dimethyl siloxane polymers link together silsesquioxane units.

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; octanol-water partition coefficients on these compounds are not included. Data on the remaining compounds reviewed in this safety assessment, including octanol-water partition coefficients, were not found**.** However, properties/composition data on Dow Corning materials and other materials that are considered by the silicones industry to represent dimethiconol are included in Table 4.[7] Table 5 contains data on the composition of materials that contain dimethyl siloxane, hydroxy-terminated (CAS No. 70131-67-8).[7] These data (Table 5) were provided by the SEHSC because the materials included are components of test materials evaluated in various toxicity tests included in this safety assessment.

ANALYTICAL METHODS

Dimethiconol has been analyzed via infrared spectroscopy.[8] The same method has been used to analyze dimethiconol (60%) in anionic surfactant emulsions[9] and dimethiconol/silsequioxane copolymer (5%) and dimethiconol (20%) in anionic surfactant emulsions.[10]

UV ABSORPTION

UV absorption data (spectra not provided) on the following Dow silicone products were provided by the Silicones Environmental Health and Safety Council of North America (SEHSC): Dow Corning® 9564 Silicone Elstomer Blend, Dow Corning® 1501 Fluid, Dow Corning® 1503 Fluid, and Dow Corning® Q1-3563.[7] Of these 4 materials, only Dow Corning® 9564 Silicone Elstomer Blend and Dow Corning® 1501 Fluid are registered under the INCI name Dimethiconol. Composition data on each of the 4 materials are included in Table 5. UV absorbance

was determined by spreading the silicone products onto a quartz plate and then testing each using a UV analyzer (LabSphere model UV 1000S). The samples were applied to the quartz plate to give an average of 2 mg of sample per square centimeter. The UV analyzer illuminated the sample on the quartz plate and measured absorbance after the UV radiation passed through the sample. A total of fourteen measurements were made for each product and the results were averaged. UV absorbance curves were produced and an attenuation factor (SPF) was calculated for the UVB portion of the UV radiation. An SPF of 1.0 was defined as no significant absorption of UVB radiation. Results are included below.

An SPF average of 1.07 was calculated for Dow Corning® 9564 Silicone Elstomer Blend, and this result indicated that between 6 and 7% of the UVB radiation was absorbed by this sample. However, based on the small amount of dimethiconol in this blend and the results obtained for the other samples, it was determined that there was no basis for concluding that dimethiconol was absorbing significant amounts of UVB or UVA radiation. A lower SPF average of 1.01 was calculated for Dow Corning® 1501 Fluid, indicating that ~ 1% of the UVB radiation was absorbed by the sample. Detector noise was thought to have contributed to this finding. Absorbance in the UVA region of the spectrum was very close to zero.

The SPF average of 0.99 reported for Dow Corning® 1503 Fluid was considered due to detector noise, and, similarly, absorbance in the UVA region was very close to zero. The lowest SPF average (0.98), also considered due to detector noise, was reported for Dow Corning® Q1-3563. This result indicated that the blank (quartz plate only) absorbed more UVB than the plate with the sample, which was not considered possible. It was concluded that Dow Corning® Q1-3563 was essentially transparent to UVB radiation. Absorbance in the UVB region was very close to zero.[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)[3].

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 2010,[11] 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 trimethylsiloxy-silicate/dimethiconol crosspolymer (2 products). These data are summarized in Table 6. 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 6.[12] 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 and acrylates/dimethiconol acrylate copolymer.

The use of amodimethiconol in personal care products is also being reported to the FDA;[13] however, amodimethiconol is not listed in the *International Cosmetic Ingredient Dictionary and Handbook* [3] 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.[14]

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).[15] *However, in the Chemical Abstract Service's Registry database,*[16] *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[17] 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 highest administered dose that did not cause death was 16 ml/kg.

The acute oral toxicity[17] 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 Dow Corning Corporation.[18] A single dose of the test substance (2 g/kg body weight) was administered to 10 fasted Sprague-Dawley rats (6 weeks old) 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[19].

Dimethiconol Stearate

The acute oral toxicity of dimethiconol stearate was evaluated using 10 fasted, Wistar-derived albino rats (5 males, 5 females).[20] 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[17] 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,[21] the acute dermal toxicity of siloxanes and silicones, dimethyl, hydroxy-terminated (22 wt. %) in Dow Corning ® 2-1845 microemulsion 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 Dow Corning Corporation.[22] 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.[23]

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,[24] 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 testis, 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.[24]

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)[25] 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[17] 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 Dow Corning Corporation.[26] The undiluted test substance was instilled (0.1 ml) into the right eye of each of 3 female New Zealand white rabbits (3 to 4 months old). 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[15] 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.[27]

Dimethiconol Stearate

The ocular irritation potential of dimethiconol stearate was evaluated using 6 healthy, young adult New Zealand albino rabbits.[28] 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® 60,000CST No Co-Solvent; and dimethiconol stearate.*

The skin irritation potential of a mixture[17] 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 study on Dow Corning® 60,000CST, No Co-Solvent was provided by Dow Corning Corporation.[29] 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 (3 to 4 months old). 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.[30] 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)[31] containing 82.1% siloxanes and silicones, dimethyl, hydroxy-terminated 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.[32]

A mucous membrane irritation study on Dow Corning® 4-2797 (X7-9192), dimethylsiloxane hydroxy-terminated fluid was provided by Dow Corning Corporation.[33] Following application of the test substance (0.5 g) to the vaginal mucosa of each of 6 New Zealand white rabbits (10 to 12 weeks old), 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 (non-irritant at concentrations up to100%); Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated (non-irritant at concnetrations up to 100%; non-sensitizer at 5%); Dow Corning® 60,000CSt, NO CO-SOLVENT in Dow Corning® 360 Medical Fluid (non-sensitizer at 5% w/v), and polymer FD 80 (non-irritant at concentrations up to 50%; non-sensitizer undiluted).

A primary irritation screen[34] on a microemulsion (Dow Corning® 2-1870 HV) containing 22 wt.% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning® 2-1845 microemulsion 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,[34] 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.[34]

A skin irritation and sensitization study on Dow Corning® X7-9192, dimethyl siloxane, hydroxy-terminated was provided by Dow Corning Corporation.[35] 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 young adult 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.[35]

Skin sensitization data on Dow Corning® 60,000CSt, NO CO-SOLVENT in Dow Corning® 360 Medical Fluid (5% w/v) were provided by Dow Corning Corporation.[36,36] The maximization test involved the following groups of male Hartley guinea pigs (4 weeks old): 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.[37] 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. [37]

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® Q4-2797, dimethylsiloxane, hydroxy-terminated fluid; and Dow Corning® 60,000CST NO Co-Solvent.

In the Ames spot plate test and overlay plate test, [38] 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,[39] 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 study on Dow Corning® Q4-2797, dimethylsiloxane, hydroxy-terminated fluid was provided by the Dow Corning Corporation.[40] 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.

A mutagenicity study on Dow Corning® 60,000CST NO Co-Solvent was also provided by Dow Corning Corporation.[41] 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.

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-terminate; 0.05% in diet) 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).[42] The 4 implanted materials (implant mass not stated) 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. Except for uncured Medical Adhesive Type A, the remaining compositions of materials tested (i.e., uncured DC 382 and DC 386) 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.[43] 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 was reported in patch tests or RIPTs involving the following ingredients/products: 16% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning XET-40002(no further information relating to test concentration); body lotion containing 1.125% dimethiconol; 0.5% dimethiconol behenate; and undiluted dimethiconol beeswax.

The skin irritation and sensitization potential of cotton treated with 16% siloxanes and silicones, dimethyl, hydroxy-terminated in Dow Corning XET-40002 was evaluated using 200 human subjects.[44] 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,[45] 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),[46] 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.[47] 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 beeswax 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 cyclomethicone) 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 10 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, dimethiconol/silsesquioxane copolymer ,and trimethylsiloxysilicate/dimethiconol crosspolymer. Based on the results of an industry use concentration survey, the following 2 additional ingredients are also being used: dimethiconol behenate 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 (only the instillation volume [0.1 ml] was stated).

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.

Because some of the dimethiconol reaction products reviewed in this safety assessment contain a plant-derived moiety, the Expert Panel expressed concern regarding pesticide residues and heavy metals that may be present in these cosmetic ingredients. They stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities in the ingredient before blending into cosmetic formulation.

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 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 cosmetic products.

Table 1. Dimethiconol and its Esters and Reaction Products[3]

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, 15ydroxy-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[48,49])	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[50])	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[48,49])	Skin-conditioning agents – occlusive
Dimethiconol carnaubate	Reaction product of dimethiconol and carnauba wax (reviewed by CIR – safe as used[48,49])	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[51])	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[52,49])	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[53,54])	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[55]), dimethylsilanol, and methylsilanol	Not reported

Table 1. Dimethiconol and its Esters and Reaction Products[3]

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[56,57])	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[55])	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[58,57]) – 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[59]), and phenyl trimethicone (reviewed by CIR – safe as used[60,57])	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[61,57]) 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[62]), or one of its simple esters	Film formers

* Source (CAS numbers): Siltech Personal Care[63]

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)[64]
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)[65]
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[66]
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[67]
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)[68]
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[69]
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 [70]

*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.[58]

Table 3. Properties of Dimethiconol and Dimethiconol Compounds

Property	Value	Reference
Dimethiconol		
Density	0.956g/cm^3	STN International[8]
Refractive index	1.3968	″
Dimethiconol (60%) in anionic surfactant emulsion		
Particle size	1μm max (for D50); 2μm max (for D90)	Anonymous[9]
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	″

Table 3. Properties of Dimethiconol and Dimethiconol Compounds

Property	Value	Reference
Dimethiconol Beeswax		
Form	Of white waxy solid	SafePharm Laboratories[71]
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 Products Council[72]
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	"
Dimethiconol/silsequioxane copolymer (5%) and dimethiconol (20%) in anionic surfactant emulsion		
Particle size	0.043µm max (for D50); 0.05µm max (for D90)	Anonymous[10]
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. Properties of Materials registered Under Dimethiconol INCI Name[7]

Material Name	Composition	Molecular Weight	Solubility	Production Method	Impurities
Dow Corning ®1401 Fluid	10-30% CAS 70131-67-8 (Dimethyl Siloxane, Hydroxy-terminated) - the rest is a mixture of cyclics (primarily D4 (CAS 556-67-2) and D5 (CAS 541-02-6))	530,000 to 570,000	Soluble in non-polar solvents	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6
Dow Corning® 1403 fluid	10-30% CAS 70131-67-8 - the rest is PDMS (CAS 63148-62-9)	720,000 to 760,000	″	″	″
Dow Corning® 1501 fluid	15-40% CAS 70131-67-8; >60% D5 (CAS 541-02-6)	530,000 to 570,000	″	″	″
Dow Corning® 7-3100 Gum Blend HIP Emulsion	10-30% CAS 70131-67-7; 10-30% Water; >60% D5 (CAS 541-02-6); Low level of preservatives and additives	530,000 to 570,000	″	″	″
Dow Corning® 1784 emulsion	40-70% CAS 70131-67-8; 10-30% Water; Low level of preservatives and additives	250,000 to 290,000	″	Linears are polym-erized in-situ to form polymer	D4, D5
Dow Corning® CB-1502 Fluid	15-40% CAS 70131-67-8; 15-70% Naptha (CAS 64742-48-9)	530,000 to 570,000	″	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6
Dow Corning® CB-1556 Fluid	10-30% CAS 70131-67-8; > 60% Phenyl siloxane (CAS 73559-47-4)	530,000 to 570,000	″	″	″
Dow Corning® CB-1596 Fluid	40-70% CAS 70131-67-8: 40-70% Trisiloxane (CAS 17955-88-3)	530,000 to 570,000	Soluble in non-polar solvents	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6
Dow Corning® 9546 Silicone Elastomer Blend	1% CAS 70131-67-8; >60% D5 (CAS 541-02-6)	300,000 cSt - viscosity	Not available	Cold blend of 1501 Fluid and D5 – dimethiconol only 1% of final formulation	D4, D5, D6 in the 1501 Fluid
Dow Corning® 1-1254 Fluid	>60% CAS 70131-67-8; 1-5% D5 (CAS 541-02-6); 1-5% D4 (CAS 556-67-2)	≥1000 (40 cSt - viscosity)	Low water solubility	Re-label of 4-2797. 4-2797 is produced by high pressure and high temperature equilibrium reaction of D4 cyclics with sodium hydroxide solution. Excess cyclics are stripped away.	D4, D5, D6

Table 4. Properties of Materials registered Under Dimethiconol INCI Name[7]

Material Name	Composition	Molecular Weight	Solubility	Production Method	Impurities
α,Ω- Dihydroxy-polydimethylsiloxane (i.e. Polydimethylsiloxanediol or Siloxanes and silicones, di-Me, OH-group terminated; Polymer FD 80; CAS 70131-67-8)	≥98% 70131-67-8; ≤ 2% dimethylcyclosiloxanes CAS 69430-24-6	70000 to 75000 (80000 mPa - viscosity)	virtually insoluble at 20 °C (68 °F)	Information on silicone synthesis is publicly available	Dimethylcyclosiloxanes (CAS No. 69430-24-6)
Material X (name CBI)	CBI	100,000 (20,000 to 24,000 mm2/s - viscosity)	Not available	Process (CBI)	D4, residual monomer, residual catalyst

Table 5. Composition Of Tested Materials Containing Dimethyl Siloxane, Hydroxy-Terminated[7]

Trade Name/Comments	Chemical Composition (%)
Dow Corning® 60,000CSt, NO CO-SOLVENT	≥ 95% Dimethyl Siloxane, Hydroxy-Terminated (CAS No. 70131-67-8) - the rest is a mixture of cyclics (primarily D4 (CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning® 7-9192	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning Q4-2797 (4-2797 INT and PA Fluid)	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning® 2-1870 HV Microemulsion (This material contains a mixture of triethanolamine dodecylbenzene sulfonate, triethanolamine sulfate, and Kathon, and this mixture have been shown to elicit an allergic skin response.)	15-40% CAS 70131-67-8; 10-30% Triethanolamine dodecylbenzene sulfonate (CAS 27323-41-7): 3-7% Polyethylene oxide lauryl ether (CAS 9002-92-0); 1-5% - Alkylbenzene sulfonic acid; 40-70% Water

Table 5. Composition Of Tested Materials Containing Dimethyl Siloxane, Hydroxy-Terminated[7]

Trade Name/Comments	Chemical Composition (%)
Silastic® Medical Adhesive Silicone, Type A	>60% CAS 70131-67-8; 10-30% Methylated Silica (CAS 68611-44-9); 3-7% Methyltriacetoxysilane; 3-7% Erhtyltriacetoxysilane (CAS 17689-77-9)
Dow Corning® 2-1845 Microemulsion	15-40% CAS 70131-67-8; 10-30% Triethanolamine dodecylbenzene sulfonate (CAS 27323-41-7): 3-7% Polyethylene oxide lauryl ether (CAS 9002-92-0); 40-70% Water
Dow Corning® 22 Emulsion	38% CAS 70131-67-8; >40% Water; 5% Toluene; 5% Perchloroethylene
Dow Corning® 35 Emulsion	13% CAS 70131-67-8; >50% Dimethyl siloxane, dimethylvinylsiloxy-terminated (CAS 68083-19-2); >20% treated silica (CAS 68909-20-6)
Dow Corning® PA Fluid	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning materials - TX-102A, TX-102B, and TX-102C	82.1% CAS 70131-67-8 - the rest is catalyst, curing agent, and vulcanizer
Dow Corning® 4-2797 INT	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning® X7-9192	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning® 360 Medical Fluid (This material does not contain dimethiconol - it is used as a solvent.)	PDMS (CAS 63148-62-9)
Dow Corning® X3-5040 Sealant	~75% CAS 70131-67-8 - the rest is a treated silica
Dow Corning® 386	~65% CAS 70131-67-8 with tetrapropyl orthosilicate and diatomaceous silica
Dow Corning® 5392	~95% CAS 70131-67-8 and ethyl polysilicate
Dow Corning® XET-40002	~16% CAS 70131-67-8; ~20% Methylhydrogen siloxane (CAS 63148-57-2) >40% Water; 5% Toluene; 5% Perchloroethylene
Dow Corning special polymer 5-26-64	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning special polymer	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))
Dow Corning® 9546 Silicone Elastomer Blend	1% CAS 70131-67-8; >60% D5 (CA 541-02-6)
Dow Corning® 1501 Fluid	15-40% CAS 70131-67-8; >60% D5 (CAS 541-02-6)
Dow Corning® 1503 Fluid	10-30% CAS 70131-67-8; >60% PDMS (CAS 63148-62-9)
Dow Corning® Q1-3563	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))

Table 6. Cosmetic Product uses[11] and Use Concentrations[12]

Product category	2010 uses (total number of products in category)	2010 concentrations (%)
Dimethiconol		
Baby products		
Lotions, oils, powders, and creams	4 (151)	-
Bath products		
Bubble baths	-	3
Eye makeup		
Eyebrow pencil	1 (153)	0.3
Eyeliner	3 (834)	1
Eye shadow	19 (1,343)	0.3 to 5
Eye lotion	11 (260)	0.3 to 0.6
Eye makeup remover	2 (133)	-
Mascara	37 (528)	0.3 to 1
Other	24 (412)	-
Fragrance products		
Perfumes	1 (742)	0.8
Powders	-	0.5
Other	9 (641)	0.3
Noncoloring hair care products		
Conditioners	114 (1,313)	0.2 to 13
Sprays/aerosol fixatives	5 (321)	0.004
Rinses	1 (34)	-
Shampoos	60 (1,487)	0.2 to 2
Tonics, dressings, etc.	112 (1,321)	0.4 to 12
Other	73 (838)	12
Hair coloring products		
Bleaches	1 (147)	-
Other	1 (168)	-

Table 6. Cosmetic Product uses[11] and Use Concentrations[12]

Product category	2010 uses (total number of products in category)	2010 concentrations (%)
Makeup		
Blushers	4 (471)	36
Face powders	8 (724)	0.3
Foundations	24 (624)	0.6 to 2
Leg and body paints	1 (29)	-
Lipstick	3 (2,045)	0.7 to 7
Makeup bases	2 (126)	0.2 to 0.6
Makeup fixatives	-	0.06
Other	3 (536)	-
Nail care products		
Basecoats and undercoats	1 (69)	0.2
Cuticle softeners	2 (30)	0.2
Nail extenders	-	0.5
Nail polish and enamel	4 (351)	-
Other	3 (137)	0.4
Personal hygiene products		
Deodorants (underarm)	3 (623)	0.2 to 11
Douches	-	0.2
Other	1 (925)	0.3 (in a body scrub)
Shaving products		
Aftershave lotion	14 (381)	0.3 to 4
Preshave lotions	2 (19)	2
Shaving cream	2 (128)	0.05
Shaving soap	-	3
Other	5 (126)	-
Skin care products		
Skin cleansing creams, lotions, liquids, and pads	13 (1,528)	2 to 6

Table 6. Cosmetic Product uses[11] and Use Concentrations[12]

Product category	2010 uses (total number of products in category)	2010 concentrations (%)
Depilatories	4 (56)	-
Face and neck creams, lotions, and powders	95 (1,652)	0.2 to 3
Body and hand creams, lotions, and powders	76(1,875)	0.05 to 5
Foot powders and sprays	1 (46)	-
Moisturizing creams, lotions, and powders	269 (2,750)	0.3
Night creams, lotions, and powders	40 (386)	0.6 to 0.8
Paste masks (mud packs)	3 (462)	0.6 to 2
Skin fresheners	2 (267)	1
Other	65 (1,446)	0.3 to 6
Suntan products		
Suntan gels, creams, and liquids	4 (106)	2
Indoor tanning preparations	32 (247)	0.2 to 0.5
Other	5 (61)	-
Total uses/ranges for dimethiconol	1169	0.004 to 36
Amodimethiconol		
Hair coloring products		
Dyes and colors	21 (2,382)	-
Total uses/ranges for amodimethiconol	21	
Dimethiconol arginine		
Noncoloring hair care products		
Conditioners	2 (1,313)	-
Sprays/aerosol fixatives	1 (321)	-
Shampoos	1 (1,487)	-
Total uses/ranges for dimethiconol arginine	4	
Dimethiconol beeswax		
Bath products		
Soaps and detergents	9 (1,781)	0.8

Table 6. Cosmetic Product uses[11] and Use Concentrations[12]

Product category	2010 uses (total number of products in category)	2010 concentrations (%)
Noncoloring hair care products		
Other	1 (838)	-
Personal hygiene products		
Other	4 (925)	-
Skin care products		
Body and hand creams, lotions, and powders	-	0.9
Moisturizers	1 (2,750)	-
Total uses/ranges for dimethiconol beeswax	15	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 (1,313)	0.07
Sprays/aerosol fixatives	1 (321)	-
Shampoos	1 (1,487)	-
Tonics, dressings, etc.	2 (1,321)	-
Total uses/ranges for dimethiconol cysteine	6	0.07
Dimethiconol meadowfoamate		
Eye makeup		
Other	1 (412)	-
Noncoloring hair care products		
Conditioners	6 (1,313)	0.5
Sprays/aerosol fixatives	-	1
Straighteners	1 (181)	-
Tonics, dressings, etc.	1 (1,321)	0.5

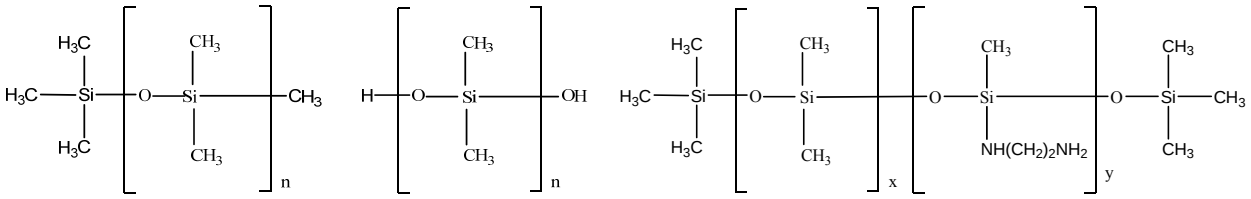
Table 6. Cosmetic Product uses[11] and Use Concentrations[12]

Product category	2010 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 (1,313)	-
Sprays/aerosol fixatives	1 (321)	-
Shampoos	1 (1,487)	-
Total uses/ranges for dimethiconol methionine	4	
Dimethiconol panthenol		
Noncoloring hair care products		
Conditioners	2 (1,313)	0.07
Sprays/aerosol fixatives	1 (321)	-
Shampoos	1 (1,487)	-
Tonics, dressings, etc.	2 (1,321)	-
Total uses/ranges for dimethiconol panthenol	6	0.07
Dimethiconol/silsesquioxane copolymer		
Noncoloring hair products		
Tonics, dressings, etc.	2 (1321)	-
Conditioners	-	0.3
Total uses/ranges for dimethiconol/silsesquioxane copolymer	2	0.3
Dimethiconol stearate		
Eye makeup		
Other	1 (412)	-
Noncoloring hair care products		
Conditioners	1 (1,313)	-
Shaving products		
Shaving cream (aerosol, brushless, and lather)	7 (128)	1

Table 6. Cosmetic Product uses[11] and Use Concentrations[12]

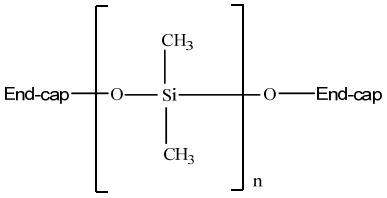
Product category	2010 uses (total number of products in category)	2010 concentrations (%)
Total uses/ranges for dimethiconol stearate	9	1
Trimethylsiloxysilicate/dimethiconol crosspolymer		
Eye makeup		
Mascara	4 (528)	-
Skin care products		
Body and hand creams, lotions, and powders	1 (1,875)	2
Moisturizers	1 (2,750)	-
Total uses/ranges for Trimethylsiloxysilicate/dimethiconol crosspolymer	6	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

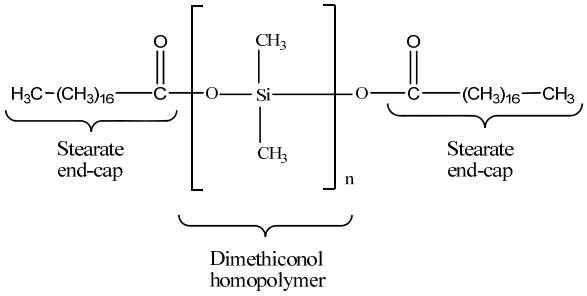


Dimethicone (CIR reviewed) Dimethiconol[4] Amodimethicone (CIR reviewed)

Reaction Product Type 1) End-capped homopolymers



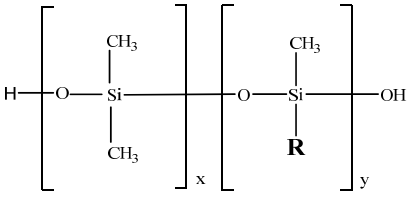
Examples



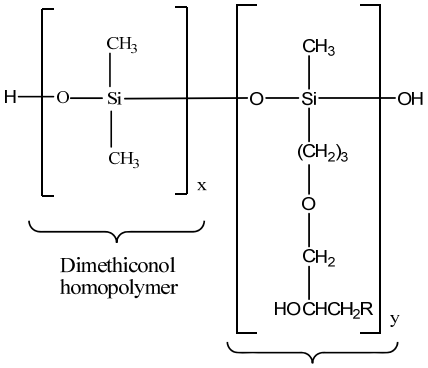
Dimethiconol Stearate

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



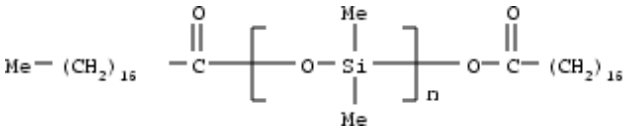
Examples



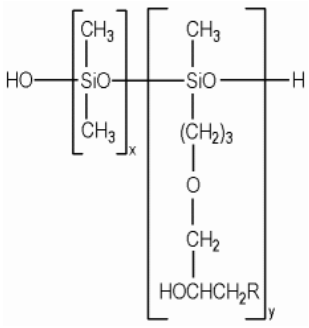
Hydrolyzed Collagen PG-Propyl Dimethiconol[3]

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

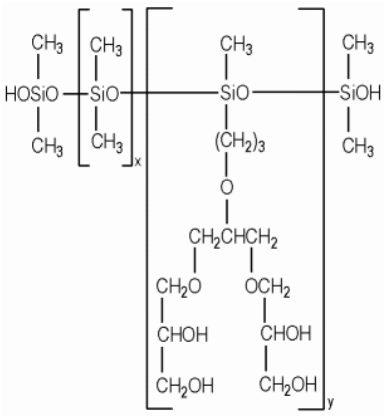
Figure 1B. Structures for Dimethiconol Polymers



Dimethiconol Stearate



Hydrolyzed Collagen PG-Propyl Dimethiconol



Isopolyglyceryl-3 Dimethiconol

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72. Personal Care Products Council. Unpublished data on Dimethiconol and Dimethiconol Behenate. Physical and chemical properties information on dimethiconol behenate. Unpublished data submitted by the Personal Care Products Council, January 21, 2010. 2010;1-1.

Data

SILICONES ENVIRONMENTAL, HEALTH AND SAFETY COUNCIL
NORTH AMERICA

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July 23, 2010

F. Alan Andersen, Ph.D.
Director
Cosmetic Ingredient Review (CIR)
1101 17th St. N.W., Suite 412
Washington D. C. 20036-4702

Dear Dr. Andersen:

On April 5-6, 2010, the Cosmetic Ingredient Review (CIR) Expert Panel met for their first review of the report on Dimethiconol and Dimethiconol containing ingredients. At this meeting, the CIR Expert Panel concluded that the data were insufficient to support the safety of Dimethiconol and the related ingredients. The following data were requested.

1. Method of manufacture and impurities
2. Physical/chemical properties, especially information to help determine if this material can penetrate the skin, such as molecular weight range and solubility, e.g., octanol/water partition coefficient
3. UV absorption, if it absorbs in the UV, dermal phototoxicity and photosensitization data may be needed
4. Dermal absorption data, if absorbed reproductive and developmental toxicity data
5. Identity of the trade name materials Polymer FD 80 and Polymer FD 80/II and composition data on the Dow Corning mixtures
6. More information about the properties and identity of Dimethiconol/Silsesquioxane Copolymer

The Silicones Environmental Health and Safety Council (SEHSC)[1] submitted, on behalf of its member companies, some of this information for review at the June 28-29 CIR Expert Panel Meeting. At the June meeting, the CIR Expert Panel voted to table the report so that the additional information provided at the meeting could be incorporated into the report. The CIR Expert Panel noted that data on the composition of Dimethiconol/Silsesquioxane Copolymer were still needed. If no information on this ingredient is received, it may be removed from the report. In addition, the CIR Expert Panel requested the composition of materials that are being used to assess the health and safety of Dimethiconol.

[1] SEHSC is a not-for-profit trade association whose mission is to promote the safe use of silicones through product stewardship and environmental, health, and safety research. The Council is comprised of North American silicone chemical producers and importers.

This letter and the included attachments provide responses to the different requests for data from the CIR Expert Panel. Below is a list and description of each Attachment:

- *Attachment 1*: Provides information that was requested following the April meeting. This table provides a list of materials that are registered under the INCI name – Dimethiconol (all the Dow Corning materials) and several other materials that are all considered to represent Dimethiconol by the silicone industry. The table contains the information that was requested by the CIR Expert Panel at the April 2010 meeting: manufacturing and impurities; molecular weight; solubility. It also contains the composition of the materials that was requested at the June 2010 meeting.

- *Attachment 2*: Provides the composition of the materials identified in Table 4 in the CIR Panel Book (Pink Book 1 – June 28-29, 2010). Additionally, it provides compositional information for the materials that were identified in the study reports provided to the CIR Expert Panel at the June meeting. [Note: During the June meeting, the CIR Expert Panel asked that compositional information be provided for the materials in the CIR that are being utilized to support the health and safety of Dimethiconol. This request was made so that the CIR Expert Panel could determine if the toxicity data on these materials are representative of Dimethiconol.]

- *Attachment 3*: Provides a summary of the UV data on Dimethiconol, as requested by the CIR Expert Panel during their April 2010 meeting.

- *Attachment 4:* Provides the compositional information on the materials that were tested for UV absorption.

- *Attachment 5*: Provides the identity of Dimethiconol/Silesquioxane Copolymer, as requested by the CIR Expert Panel at the April 2010 and the June 2010 meeting.

SEHSC would also like to re-iterate and expand on several key pieces of information that were provided to the CIR Expert Panel (via email) on February 19, 2010.

1. It should be noted that Dow Corning® 1870 does contain CAS 70131-67-8 but it also contains a combination of ingredients that can cause skin sensitization. These ingredients are: triethanolamine dodecylbenzene sulfonate, triethanolamine sulfate, and the active ingredients of Kathon (2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one). Although each of these components individually may not present a risk for skin sensitization at the levels in this material, the combination of all three has been shown to elicit an allergic skin response. So, the study data on skin sensitization for Dow Corning® 1870 should not be used to represent the health and safety of Dimethiconol. There are more representative data that were supplied on Dow Corning® 60,000 cSt NO COSOLVENT and Dow Corning® X7-9192, which contain ≥95% of CAS 70131-67-8. These materials do not contain the combination of ingredients that are known to cause skin sensitization.

   If the CIR Expert feels that these data should remain in the CIR, the report needs to clearly state that the sensitization is not from the Dimethiconol component but is due to the presence of preservatives.

2. The skin sensitization study on Dow Corning® XET-40002 (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) should not utilized

to assess the health and safety of Dimethiconol because the study was conducted at Industrial Bio-Test Laboratories (IBT). Audits of IBT found fabricated and falsified data. Because of the uncertainty in the data, all IBT studies are considered scientifically invalid.

3. There are several Dow Corning study reports in the CIR that have been reviewed by Dow Corning and they have been determined to scientifically invalid. Dow Corning recommends that these reports not be included in the CIR. Following is a list of the reports and the rational for not being 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.

     Rationale: No ability to determine the actual dose level that the rabbits received. No discussion on test article concentration, stability, homogeneity. We do not feel that this study should be used in health and safety assessments and do not want the general public using it because of the limitations.

   - 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.

     Rationale: No ability to determine the actual dose level that the rabbits received. No discussion on test article concentration, stability, homogeneity. We do not feel that this study should be used in health and safety assessments and do not want the general public using it because of the limitations.

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

     Rationale: There was no control eye for comparison. Both eyes were treated. Grading Scale not detailed. This Testing was screening level assessment for Industrial hazard potential. The method is not robust enough to satisfy current Health Safety testing standards.

   If the CIR Expert Panel feels that these reports need to be included, there must be a statement about the shortcomings and the lack of robustness of the reports clearly stated in the CIR.

We appreciate CIR's consideration of our comments. Please let me know if you have any questions or need additional information.

Sincerely,

Tracy Guerrero
Senior Scientific Programs Manager
SEHSC

Michelle D. Andriot, Ph.D., D.A.B.T
Global Technical Coordinator for Product Toxicology
Dow Corning Corporation

cc: Wilbur Johnson, C

Attachment 1

Information on Materials that are Registered Under Dimethiconol INCI name

		Method of Manufacture		Physical/Chemical Properties		UV Absorption Data	Dermal Phototoxicity Data	Dermal Absorption Data
Material Name	Composition	**Process**	**Impurities**	**Mw**	**Solubility**			
Dow Corning ® 1401 Fluid	10-30% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	530,000 - 570,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® 1403 fluid	10-30% CAS 70131-67-8 - the rest is PDMS (CAS 63148-62-9)	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	720,000 - 760,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® 1501 fluid	15-40% CAS 70131-67-8; >60% D5 (CAS 541-02-6)	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	530,000 - 570,000	soluble in non-polar solvents	Available	Not Available	Not Available
Dow Corning® 7-3100 Gum Blend HIP Emulsion	10-30% CAS 70131-67-7; 10-30% Water; >60% D5 (CAS 541-02-6); Low level of preservatives and additives	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	530,000 - 570,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® 1784 emulsion	40-70% CAS 70131-67-8; 10-30% Water; Low level of preservatives and additives	Linears are polymerized in-situ to form polymer	D4, D5	250,000 - 290,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® CB-1502 Fluid	15-40% CAS 70131-67-8; 15-70% Naptha (CAS 64742-48-9)	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	530,000 - 570,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® CB-1556 Fluid	10-30% CAS 70131-67-8; > 60% Phenyl siloxane (CAS 73559-47-4)	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	530,000 - 570,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® CB-1596 Fluid	40-70% CAS 70131-67-8: 40-70% Trisiloxane (CAS 17955-88-3)	Dimethyl cyclics are polymerized and then endblocked with -OH fluid. Catalyst is neutralized	D4, D5, D6	530,000 - 570,000	soluble in non-polar solvents	Not Available	Not Available	Not Available
Dow Corning® 9546 Silicone Elastomer Blend	1% CAS 70131-67-8; >60% D5 (CA 541-02-6)	Cold blend of 1501 Fluid and D5 - dimethiconol only 1% of final formulation	D4, D5, D6 in the 1501 Fluid	300,000 cSt - viscosity	Not Available	Available	Not Available	Not Available
Dow Corning® 1-1254 Fluid	>60% CAS 70131-67-8; 1-5% D5 (CAS 541-02-6); 1-5% D4 (CAS 556-67-2)	Re-label of 4-2797. 4-2797 is produced by high pressure and high temperature equilibrium reaction of D4 cyclics with sodium hydroxide solution. Excess cyclics are stripped away.	D4, D5, D6	≥1000(40 cSt - viscosity)	Low water solubility	Not Available	Not Available	Not Available
α,Ω- Dihydroxypolydimethylsiloxane (i.e. Polydimethylsiloxanediol or Siloxanes and Silicones, di-Me, OH-group terminated; Polymer FD 80; CAS 70131-67-8)	≥98% 70131-67-8; ≤ 2% dimethylcyclosiloxanes CAS 69430-24-6	see attached: publically available published information on silicone synthesis	dimethylcyclosiloxanes (CAS No. 69430-24-6)	70000 to 75000 (80000 mPa - viscosity)	virtually insoluble at 20 °C (68 °F)	Not Available	Not Available	Not Available
Material X (name CBI)	CBI	process (CBI)	D4, residual monomer, residual catalyst	100,000 (20,000 to 24,000mm2/s - viscosity)	Not Available	Member company in process of gathering; to be provided when available	Not Available	Not Available

Attachment 2

Composition of Materials that Contain CAS 70131-67-8 and Have Toxicity Data

Material	Composition	Source of Data	Comment
Dow Corning® 60,000 cSt NO CO-SOLVENT	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Toxicity data provided to CIR by SEHSC	
Dow Corning® 7-9192	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Toxicity data provided to CIR by SEHSC	
Dow Corning Q4-2797 (4-2797 INT and PA Fluid)	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Toxicity data provided to CIR by SEHSC	
Dow Corning® 2-1870 HV Microemulsion	15-40% CAS 70131-67-8; 10-30% Triethanolamine dodecylbenzene sulfonate (CAS 27323-41-7): 3-7% Polyethylene oxide lauryl ether (CAS 9002-92-0); 1-5% - Alkylbenzene sulfonic acid; 40-70% Water	CIR obtained study from EPA (from Table 4)	This material contains a mixture of triethanolamine dodecylbenzene sulfonate, triethanolamine sulfate, and Kathon and this mixture has been shown to elicit an allergic skin response.
Silastic® Medical Adhesive Silicone, Type A	>60% CAS 70131-67-8; 10-30% Methylated Silica (CAS 68611-44-9); 3-7% Methyltriacetoxysilane; 3-7% Erhtyltriacetoxysilane (CAS 17689-77-9)	CIR obtained study from EPA (from Table 4)	
Dow Corning® 2-1845 Microemulsion	15-40% CAS 70131-67-8; 10-30% Triethanolamine dodecylbenzene sulfonate (CAS 27323-41-7): 3-7% Polyethylene oxide lauryl ether (CAS 9002-92-0); 40-70% Water	CIR obtained study from EPA (from Table 4)	
Dow Corning® 22 Emulsion	38% CAS 70131-67-8; >40% Water; 5% Toluene; 5% Perchloroethylene	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning® 35 Emulsion	13% CAS 70131-67-8; >50% Dimethyl siloxane, dimethylvinylsiloxy-terminated (CAS 68083-19-2); >20% treated silica (CAS 68909-20-6)	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning® PA Fluid	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Toxicity data provided to CIR by SEHSC	
Dow Corning materials - TX-102A, TX-102B, and TX-102C	82.1% CAS 70131-67-8 - the rest is catalyst, curing agent, and vulcanizer	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning® 4-2797 INT	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Toxicity data provided to CIR by SEHSC	
Dow Corning® X7-9192	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	Toxicity data provided to CIR by SEHSC	
Dow Corning® 360 Medical Fluid	PDMS (CAS 63148-62-9)	CIR obtained study from EPA (from Table 4)	This material does not contain dimethiconol - it is used as a solvent
Dow Corning® X3-5040 Sealant	~75% CAS 70131-67-8 the rest is a treated silica	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning® 386	~65% CAS 70131-67-8 with tetrapropyl orthosilicate and diatomaceous silica	CIR obtained study from EPA (from Table 4) Not a commercial product	

Material	Composition	Source of Data	Comment
Dow Corning® 5392	~95% CAS 70131-67-8 and ethyl polysilicate	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning® XET-40002	~16% CAS 70131-67-8; ~20% Methylhydrogen siloxane (CAS 63148-57-2) >40% Water; 5% Toluene; 5% Perchloroethylene	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning special polymer 5-26-64	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	CIR obtained study from EPA (from Table 4) Not a commercial product	
Dow Corning special polymer	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))	CIR obtained study from EPA (from Table 4) Not a commercial product	

Attachment 3

UV Absorption Data for Dimethiconol

Several Dow Corning silicone products were tested for absorbance of ultraviolet radiation by spreading the products onto a quartz plate and testing them with a UV analyzer (LabSphere model UV 1000S). The samples we applied to the quartz plate to give an average of 2 mg of sample per square centimeter. The UV analyzer illuminates the sample on the quartz plate with UV radiation and measures absorbance of this radiation after it has passed through the sample. A total of fourteen measured measurements were made for each product and the results are averaged. The instrument provides UV absorbance curves for the fourteen measurements and also calculates an attenuation factor (SPF) for the UVB portion of the UV radiation. An SPF of one (1.0) indicates no significant absorption of UVB radiation.
Here is a description of the samples that were tested, the results, and my comments for each:

Q1-3563

SPF (average) = 0.98

This result indicates that the blank (quartz plate only) absorbed more UVB than the plate with the sample, which is not possible. I think this result is the result of detector "noise" and my conclusion is that Q1-3563 is essentially transparent to UVB radiation. The absorbance in the UVA region is also very close to zero.

1501 Fluid

SPF (average) = 1.01

This result indicates that about 1% of the UVB radiation was absorbed by the sample, but I think this is also due to detector noise. The absorbance in the UVA region of the spectrum is very close to zero.

1503 Fluid

SPF (average) = 0.99

This result is similar to that obtained for Q1-3563 and I believe this is also due to detector noise. The absorbance in the UVA region is also very close to zero.

9546

SPF (average) = 1.07

This result indicated that between 6 and 7% of the UVB radiation was absorbed by this sample but based on the small amount of Dimethiconol in this blend and the results obtained for the other samples, there is no basis for concluding that the Dimethiconol is absorbing significant amounts of UVB or UVA radiation.

Attachment 4

Composition of Materials that Have UV Absorption Data

Material	Composition
Dow Corning® 9546 Silicone Elastomer Blend	1% CAS 70131-67-8; >60% D5 (CA 541-02-6)
Dow Corning® 1501 Fluid	15-40% CAS 70131-67-8; >60% D5 (CAS 541-02-6)
Dow Corning® 1503 Fluid	10-30% CAS 70131-67-8; >60% PDMS (CAS 63148-62-9)
Dow Corning® Q1-3563	≥95% CAS 70131-67-8 - the rest is a mixture of cyclics (primarily D4(CAS 556-67-2) and D5 (CAS 541-02-6))

Attachment 5

Definition of Dimethiconol/Silsesquioxane Copolymer

Dimethiconol/Silsesquioxane is the product of a condensation reaction between Dimethiconol and methyl trimethoxysilane. The SiOH groups that terminate the siloxane polymer chains in Dimethiconol are reactive under certain circumstances. One common reaction is a condensation reaction with alkoxy-terminated siloxanes and alkoxy silanes. In this reaction the SiOH groups react with the alkoxy groups to form a new siloxane bond (SiOSi) with the release of the corresponding alcohol. So, for Dimethiconol/Silsesquioxane, the Dimethiconol polymer reacts with the methoxy groups on methyl trimethoxysilane, releasing methanol and forming new siloxane bonds. Since there are three methoxy groups on this silane, the reaction produces a three-dimensional siloxane polymer network in which dimethyl siloxane polymers link together silsesquioxane units. Silsesquioxanes are siloxane polymers in which contain silicon atoms bonded to three other silicon atoms via siloxane bonds.

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

Report No:	**1998-I0000-44385**
Title:	**ACUTE ORAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RATS (LIMIT TEST)**
Study No:	
External Testing Facility No:	
Test Substance:	**Dow Corning® 60,000CST, NO CO-SOLVENT**
Study Director:	
Author(s):	
Sponsor:	**Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686-0994**
Sponsor Representative:	
Testing Facility:	
Study Completion Date:	**February 18, 1998**
Security Statement:	

TABLE OF CONTENTS

ABSTRACT

The objective of this study was to evaluate the toxicity of Dow Corning® 60,000CST, NO CO-SOLVENT following administration of a single oral dose.

The study was performed using OECD Guidelines for Testing of Chemicals (Part 401, February, 1987), and according to U.S. Environmental Protection Agency (EPA) Good Laboratory Practice Standards set forth in Part 792 (TSCA) of Title 40 of the Code of Federal Regulations, Final Rule August 17, 1989 and OCDE/GD(92)32.

Dow Corning® 60,000CST, NO CO-SOLVENT was administered in corn oil at a dose of 2 g/kg of body weight by oral gavage to a group of five male and five female Sprague-Dawley rats. The rats were observed for 14 days after test substance administration. No overt signs of systemic toxicity were observed in any rat during the study. All of the rats gained weight during the study and no gross necropsy lesions were observed in any rat.

None of the animals died during the study. Therefore, under the specific conditions of testing, the acute oral median lethal dose (LD_{50}) of Dow Corning® 60,000CST, NO CO-SOLVENT in male and female rats was greater than 2 g/kg of body weight.

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the U.S. Environmental Protection Agency (EPA) Good Laboratory Practice (GLP) Standards as set forth in the *Code of Federal Regulations* (Part 792 of Title 40; TSCA) and OCDE/GD(92)32, except that no analyses pertaining to concentration, homogeneity and stability of the test substance/corn oil suspension were conducted. Records pertaining to the characterization and stability of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The study data have been reviewed by the Study Director, who certifies that the information contained in this report is consistent with and supported by the study raw data.

2/18/98

Date

Study Director

QUALITY ASSURANCE STATEMENT

Study Title: Acute Oral Toxicity Study of Dow Corning® 60,000CST, NO CO-SOLVENT in Rats (Limit Test)

Project Number:

Study No.:

Study Director:

This study has been subjected to inspections and the report has been audited by the Quality Assurance Unit in accordance with U.S. Environmental Protection Agency (EPA) TSCA, CFR Title 40 Section 792.35 "Good Laboratory Practice (GLP) Standards" and OCDE/GD(92)32. The report describes the methods and procedures used in the study and the reported results accurately reflect the study data.

The following are the inspection dates and the dates inspection findings were reported:

		Findings Reported To:	
Date of Inspection	Study Phase	Study Director	Management
July 11, 14, 16, 1997	Protocol	July 16, 1997	July 16, 1997
October 21, 1997	Protocol	October 21, 1997	October 21, 1997
October 29, 1997	Test Substance Administration	October 29, 1997	October 29, 1997
January 14, 1998	Raw Data/Report	January 14, 1998	January 14, 1998

2-17-98
Date

Manager, Quality Assurance

APPROVAL SIGNATURES

This report consists of Pages 1 through 19 including Tables 1 through 5 and Appendix 1.

2/18/98
Date

Research Toxicologist

2/18/98
Date

Manager, Regulatory Toxicology

2/10/98
Date

Associate Toxicology Scientist
Sponsor Representative

STUDY INFORMATION

Study Initiation Date:	October 29, 1997
Experimental Start Date:	October 29, 1997
Experimental Termination Date:	November 12, 1997
Study Completion Date:	February 18, 1998
Study Director:	
Sponsor:	Dow Corning Corporation
Sponsor Representative:	
Study Personnel:	
Report Preparation:	

I. INTRODUCTION

The purpose of this study was to determine the acute toxicity of Dow Corning® 60,000CST, NO CO-SOLVENT in rats following a single oral dose.

II. MATERIALS AND METHODS

A. Test Substance: Dow Corning® 60,000CST, NO CO-SOLVENT, Lot number was received October 3, 1997. The test substance was a colorless viscous liquid and was stored in the original container at room temperature (approximately 22°C) . The Material Safety Data Sheet (MSDS) indicated that the test substance was stable. Records pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The corn oil vehicle (Sigma Chemical Co., Lot No. was a purchased product and, as such was considered characterized by its labelling. All remaining test substance will be returned to the Sponsor after completion of all relevant studies.

B. Dosage Formulation: Suspension of the test substance was prepared in corn oil at a 20% (w/v) concentration for a dose of 2 g per kg of body weight. The test substance/corn oil suspension was prepared on the day of dosing.

C. Animals: Male and female Sprague-Dawley [Crl:CD®(CD)Br] rats, approximately 6 weeks of age, were received from for use in this study. The animals were received October 15, 1997 and a random sample (6 of 24 rats) weighed 130 to 144 g the next day. The rats were held in quarantine for approximately two weeks during which time they were observed for daily survival and at the end of the quarantine period examined carefully to ensure their health and suitability as test subjects. Rats selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number. This particular test system and the specific route by which the test substance was administered were chosen for the following reasons: 1) the rat is an animal model widely used and accepted for acute toxicity testing and against which its reaction to the test substance can be evaluated, and 2) oral dosing corresponds to a potential route by which humans may be exposed

to the test substance. The number of animals used for this study was based upon testing guideline requirements.

D. Food and Water: Certified Purina Lab Rodent Chow 5002 (PMI Feeds, Inc., was provided *ad libitum*, except for approximately 18.5 hours immediately prior to dosing and approximately 3.5 hours after dosing. water was provided *ad libitum* by means of an automatic watering system. No contaminants capable of adversely affecting the integrity or interpretation of the results from this study were known to be present in the basal diet or the drinking water during the conduct of this study.

E. Housing and Environment: The rats were housed individually in stainless steel cages (approximately 24 x 18 x 18 cm) suspended over absorbent animal cage boards. The animal room temperature and relative humidity during the treatment phase of the study ranged from 22.0 to 25.5°C and 13 to 46%, respectively. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness. This study was conducted in the The minimum number of air changes in the animal room was 10 changes per hour.

F. Methods:

1. Assignment to Groups: Rats for testing were selected from a larger pool of available candidates and assigned to a group of five males and five females using an in-house developed computerized randomization program (RANSD.EXE) constrained by body weight such that no animal's body weight differed from the group (sex) mean by more than two standard deviations. There was no control group.

2. Fasting: Approximately 18.5 hours prior to test substance administration, all food was removed from the cages and the test animals fasted until approximately 3.5 hours after dosing.

3. Dosing: The test substance was administered in corn oil at a dose of 2 g/kg by oral gavage using a constant dosing volume of 10 ml/kg. The test substance/corn oil dosing suspension was mixed using a magnetic stir plate

during dosing. A 3 cc syringe equipped with a stainless steel, ball-tipped intubation needle was used to dose the rats at approximately 11:00 am on October 29, 1997.

4. Clinical Observations: Study animals were observed at frequent intervals on the day of dosing (Day 1) and once per day on Days 2 through 14 for signs of toxicity.

5. Body Weights: All study animals were weighed prior to fasting (randomization weights) and immediately prior to dosing (fasted weights). Dosage calculations were based upon the fasted body weights. Rats were also weighed 7 and 14 days following test substance administration.

6. Necropsies: All surviving test rats were euthanized by carbon dioxide asphyxiation at the end of the 14-day observation period, November 12, 1997. A gross necropsy was performed on all animals.

G. Deviations: Deviations or circumstances known to have occurred during the conduct of this study and their effects, if any, on the quality or integrity of the data from this study are described in Appendix 1.

H. Archives: All original data and documents generated at and the signed original final report will be retained in the for five years from the date of this report. At that time, the Sponsor will be contacted in order to determine its final disposition.

III. RESULTS

A. Mortality: None of the rats died during the study. Mortality data is summarized in Table 1.

B. Clinical Observations: Clinical observations during the study are summarized in Table 2 and individual clinical observations are given in Table 3. No overt signs of systemic toxicity were observed in any rat during the study. On Day 10, two animals (one male and one female) exhibited scabs on either the right side of the neck (male) or the top of the head (female). This lesion persisted for the duration of the 14-day observation period, but cannot be directly attributed to the test substance. Irritability

was observed in one male rat on Day 13. No other clinical signs were observed in any of the other animals throughout the study.

C. Body Weights: Body weight data are summarized in Table 4. All of the rats gained weight during the study.

D. Gross Pathology: Gross necropsy findings were within normal limits in all rats and are presented in Table 5.

E. Statistics: Statistical procedures were limited to calculating the group mean and the standard deviation for body weight and cumulative body weight change.

IV. CONCLUSIONS

Based on the results of this study, and under the conditions of testing, the acute oral median lethal dose (LD_{50}) of Dow Corning® 60,000CST, NO CO-SOLVENT in male and female rats was greater than 2 g/kg.

V. TABLES

ACUTE ORAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RATS (LIMIT TEST)

TABLE I

Mortality Data
(5 rats/sex)

Dose level	Number Dead/Number Treated		Sexes Combined
	Males	Females	
2 g/kg	0/5	0/5	0/10

ACUTE ORAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RATS (LIMIT TEST)

TABLE 2

Summary of Clinical Observations
(5 rats/sex)

Observation	Incidence[a] M[b]	F[c]
Irritable	1	0
Lesion-Scab (right side of neck)	1	0
Lesion-Scab (top of head)	0	1
No signs observed[d]	3	4

[a] Number of animals for which the observation was recorded at least once during the study
[b] M = Male
[c] F = Female
[d] Number of animals that appeared normal for the duration of the study

ACUTE ORAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RATS (LIMIT TEST)

TABLE 3

Individual Clinical Observations

MALES

Day	ANIMAL NUMBER 881	882	883	884	885
1-9	No signs observed	No signs observed	No signs observed	No signs observed	No signs observed
10-12	No signs observed	No signs observed	No signs observed	Lesion-scab (right side of neck)	No signs observed
13	No signs observed	No signs observed	Irritable	Lesion-scab (right side of neck)	No signs observed
14	No signs observed	No signs observed	No signs observed	Lesion-scab (right side of neck)	No signs observed

FEMALES

Day	ANIMAL NUMBER 886	887	888	889	890
1-9	No signs observed	No signs observed	No signs observed	No signs observed	No signs observed
10-14	No signs observed	No signs observed	Lesion-scab (top of head)	No signs observed	No signs observed

ACUTE ORAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RATS (LIMIT TEST)

TABLE 4

Summary of Body Weights
(5 rats/sex)

MALES

Animal Number	Body Weight (g)				Cumulative Body Weight Change (g)
	Non-Fasted[a]	Day 1[b]	Day 8	Day 15	(Day 15 - Day 1)
881	263	234	317	370	136
882	249	222	303	334	112
883	240	206	304	366	160
884	256	226	307	358	132
885	259	225	311	369	144
Mean ± S.D.[c]	253 ± 9.1	223 ± 10.3	308 ± 5.7	359 ± 15.0	137 ± 17.5

FEMALES

Animal Number	Body Weight (g)				Cumulative Body Weight Change (g)
	Non-Fasted	Day 1	Day 8	Day 15	(Day 15 - Day 1)
886	203	185	223	245	60
887	195	178	210	225	47
888	211	195	234	248	53
889	185	171	203	227	56
890	195	174	228	237	63
Mean ± S.D.	198 ± 9.8	181 ± 9.6	220 ± 12.8	236 ± 10.3	56 ± 6.2

[a] Randomization weight
[b] Fasted body weight
[c] S.D. = Standard Deviation

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RATS (LIMIT TEST)

TABLE 5

Individual Gross Necropsy Observations

Animal Number	Sex	Observation
881	M	No gross lesions
882	M	No gross lesions
883	M	No gross lesions
884	M	No gross lesions
885	M	No gross lesions
886	F	No gross lesions
887	F	No gross lesions
888	F	No gross lesions
889	F	No gross lesions
890	F	No gross lesions

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

Report No:	**1998-I0000-44373**
Title:	**ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)**
Study No:	
External Testing Facility No:	
Test Substance:	**Dow Corning® 60,000CST, NO CO-SOLVENT**
Study Director:	
Author(s):	
Sponsor:	**Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686-0994**
Sponsor Representative:	
Testing Facility:	
Study Completion Date:	**April 1, 1998**
Security Statement:	

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ABSTRACT

The purpose of this study was to evaluate the toxicity of Dow Corning® 60,000CST, NO CO-SOLVENT in rabbits following dermal application of a single dose.

This study was performed using OECD Guidelines for Testing of Chemicals (Part 402, "Acute Dermal Toxicity", 1987) and according to U.S. EPA Good Laboratory Practice Standards set forth in Part 792 (TSCA) of Title 40 of the Code of Federal Regulations, Final Rule August 17, 1989 and OCDE/GD(92)32.

Dow Corning® 60,000CST, NO CO-SOLVENT was applied undiluted to the shaved backs of five male and five female adult New Zealand White rabbits at a dose of 2 g/kg of body weight. The test sites were wrapped and the test substance was left in contact with the skin for 24 hours. Residual test substance was removed with the aid of D.C.® 360 Medical Fluid-moistened gauze. All rabbits were observed frequently the day of treatment and at least once daily during the subsequent 14-day observation period. No overt signs of systemic toxicity were observed in any rabbit during the study. Signs of dermal irritation consisting of erythema at the application site were observed in all ten rabbits. All animals appeared normal by Day 7 and remained so for the rest of the observation period. All ten rabbits gained weight during the study and gross necropsy findings were within normal limits.

No rabbits died during the study. Therefore, under the specific conditions of testing, the acute dermal median lethal dose (LD_{50}) of Dow Corning® 60,000CST, NO CO-SOLVENT in adult male and female rabbits was greater than 2 g/kg of body weight.

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the following Good Laboratory Practice (GLP) Standards: U.S. Environmental Protection Agency (EPA) as set forth in the *Code of Federal Regulations* (Part 792 of Title 40; TSCA) and OCDE/GD(92)32. Records pertaining to the characterization and stability of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The study data have been reviewed by the Study Director, who certifies that the information contained in this report is consistent with and supported by the study raw data.

4/1/98

Date

Study Director

QUALITY ASSURANCE STATEMENT

Study Title: Acute Dermal Toxicity Study of Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits (Limit Test)

Project Number:

Study No.:

Study Director:

This study has been subjected to inspections and the report has been audited by the Quality Assurance Unit in accordance with U.S. Environmental Protection Agency (EPA) TSCA, CFR Title 40 Section 792.35 and OCDE/GD(92)32 "Good Laboratory Practice (GLP) Standards". The report describes the methods and procedures used in the study and the reported results accurately reflect the study data.

The following are the inspection dates and the dates inspection findings were reported:

		Findings Reported To:	
Date of Inspection	Study Phase	Study Director	Management
July 11, 1997	Draft Protocol Review	July 16, 1997	July 16, 1997
October 15, 1997	Revised Protocol Audit	October 15, 1997	October 15, 1997
November 4, 1997	Rabbits Skin Observation	November 4, 1997	November 4, 1997
January 2 & 5, 1998	Draft Report/Raw Data Audit	January 5, 1998	January 5, 1998

_____ 4-1-98
Date

Manager, Quality Assurance

APPROVAL SIGNATURES

This report consists of Pages 1 through 20 including Tables 1 through 5 and Appendix 1.

4/1/98
Date

Research Toxicologist

4/1/98
Date

Manager, Regulatory Toxicology

3/27/98
Date

Sponsor Representative

STUDY INFORMATION

Study Initiation Date:	October 27, 1997
Experimental Start Date:	November 3, 1997
Experimental Termination Date:	November 17, 1997
Study Completion Date:	April 1, 1998
Study Director:	
Sponsor:	Dow Corning Corporation
Sponsor Representative:	
Study Personnel:	
Report Preparation:	

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)

I. INTRODUCTION

The purpose of this study was to evaluate the toxicity of Dow Corning® 60,000CST, NO CO-SOLVENT in rabbits following dermal application of a single dose.

II. MATERIALS AND METHODS

A. Test Substance: Dow Corning® 60,000CST, NO CO-SOLVENT, Lot no. was received October 3, 1997. The test substance was a colorless viscous liquid and was stored in the original container at room temperature (approximately 22°C). The Material Safety Data Sheet (MSDS) indicated that the test substance was stable. All chemical analyses and attendant documentation pertaining to the characterization of the test substance were the responsibility of the Sponsor. All residual test substance will be returned to the Sponsor following completion of all relevant studies.

B. Dosage Formulation: Due to test substance viscosity, individual doses of 2 g/kg of body weight of undiluted test substance were dispensed into plastic weigh boats.

C. Animals: Male and female New Zealand White rabbits, approximately 3-4 months of age, were purchased from for use in this study. The animals were received on October 8, 1997 and a sample (11 of 46 rabbits received) weighed 2.49 to 2.68 kg (males) and 2.39 to 3.48 kg (females) the next day. The rabbits were held in quarantine approximately three weeks during which time they were observed daily for survival and at the end of the quarantine period examined carefully to ensure their health and suitability as test subjects. Rabbits selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number. This particular test system and the specific route by which the test substance was administered were chosen for the following reasons: 1) the rabbit is an animal model widely used and accepted for acute toxicity testing and against which its reaction to the test substance can be evaluated, and 2) dermal application corresponds to a potential route by which humans may be exposed to the test

substance. The number of animals used for this study was based upon testing guideline requirements.

D. Food and Water: Each rabbit was provided with approximately 150 g of Certified Purina Lab Rabbit Chow HF #5325 daily.

water was supplied *ad libitum* by means of an automatic watering system. No contaminants capable of adversely affecting the integrity or interpretation of the results from this study were known to be present in the basal diet or the drinking water during the conduct of this study.

E. Housing and Environment: The rabbits were housed individually in suspended stainless steel cages measuring approximately 61 x 46 x 41 cm. Absorbent cage liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the treatment phase of the study, the animal room temperature and relative humidity ranged from 20.0 to 22.0°C and 20 to 36%, respectively. Excursions of relative humidity outside the range specified in the protocol were not considered to have adversely affected the outcome of the study. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness. This study was conducted in the

The minimum number of air changes in the animal room was 10 changes per hour.

F. Methods:

1. Animals: Formal randomization of test subjects was not done. The first five male and five female rabbits from the available pool observed exhibiting healthy, intact skin and no other adverse clinical signs were selected for the study and assigned to a single test group of five males and five females. There was no control group.

2. Skin Preparation: Approximately 24 hours prior to dosing, fur was clipped from an area on the dorsum equaling approximately 10% (about 240 cm^2) of the dorsal skin surface of each rabbit. The skin was examined for abnormalities and care was taken to avoid abrading the animal's back.

3. Dosing: Undiluted test substance at a dose of 2 g/kg of body weight was applied with a spatula on November 3, 1997 to the shaved application site of each rabbit and the test site covered with a 12.8 x 11.5 cm surgical dressing The pad was covered with plastic film and then secured by lint-free cloth and an elastic adhesive bandage which prevented removal of the test substance without restricting the animal's mobility.

   The wrappings were removed after 24 hours and the application site wiped with Dow Corning 360® Medical Fluid-moistened gauze to remove residual test substance.

4. Clinical Observations: Animals were observed at least once daily on weekdays and weekends for mortality. All test rabbits were observed at frequent intervals on the day of dosing (Day 1) and once daily on Days 2 through 14 for signs of toxicity. Clinical observations following unwrapping included the examination of the application site skin for signs of dermal irritation.

5. Body Weights: All rabbits were weighed immediately prior to dosing on Day 1, on Day 8 and at the termination of the study (Day 15).

6. Necropsies: The day following the 14-day observation period (*i.e.*, November 17, 1997), all rabbits were euthanized using sodium pentobarbital and subjected to gross necropsy.

G. Deviations: Deviations or circumstances known to have occurred during the conduct of this study and their affect, if any, on the quality or integrity of the data from this study are described in Appendix 1.

H. Archives: All original data generated at and the signed original final report will be retained in the for five years from the date of this report. At that time, the Sponsor will be contacted in order to determine its final disposition.

III. RESULTS

A. Mortality: Mortality data are presented in Table 1. None of the rabbits died during the study.

B. Clinical Observations: Clinical observations are summarized in Table 2 and individual observations are presented in Table 3. No signs of systemic toxicity were observed in any rabbit during the study. Signs of dermal irritation (application site) consisting of erythema were observed in all ten rabbits beginning on Day 2 and persisted in only one rabbit through Day 6. All animals appeared normal by Day 7 and remained so for the rest of the observation period.

C. Body Weights: Body weight data are summarized in Table 4. All ten rabbits gained weight during the study.

D. Gross Necropsy: Gross necropsy findings were within normal limits in all rabbits and are summarized in Table 5.

E. Statistics: Statistical procedures were limited to calculating the group mean and the standard deviation for body weight and cumulative body weight change.

IV. CONCLUSIONS

Based on the results of this study, and under the conditions of testing, the acute dermal median lethal dose (LD_{50}) of Dow Corning® 60,000CST, NO CO-SOLVENT in male and female rabbits was greater than 2 g/kg.

V. TABLES

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)

TABLE 1

Mortality Data
(5 rabbits/sex)

Dose level (g/kg)	Number Dead/Number Treated		Sexes Combined
	Males	Females	
2	0/5	0/5	0/10

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)

TABLE 2

Summary of Clinical Observations
(5 rabbits/sex)

Observation	Incidence[a] Males	Females
No signs observed	5	5
Application site skin:		
Erythema	5	5

[a] Number of animals for which the observation was recorded at least once during the study

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)

TABLE 3

Individual Clinical Observations

Males

Animal Number	Observation	Days
701	No signs observed Erythema	1, 7-14 2-6
702	No signs observed Erythema	1, 4-14 2-3
703	No signs observed Erythema	1, 6-14 2-5
704	No signs observed Erythema	1, 6-14 2-5
705	No signs observed Erythema	1, 6-14 2-5

Females

Animal Number	Observation	Days
706	No signs observed Erythema	1, 4-14 2-3
707	No signs observed Erythema	1, 4-14 2-3
708	No signs observed Erythema	1, 4-14 2-3
709	No signs observed Erythema	1, 4-14 2-3
710	No signs observed Erythema	1, 6-14 2-5

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)

TABLE 4

Individual and Summary Body Weights
(5 rabbits/sex)

MALES

Animal Number	Body Weight (kg)			Cumulative Body Weight Change (kg)
	Day 1	Day 8	Day 15	(Day 15 - Day 1)
701	3.14	3.20	3.37	0.23
702	3.31	3.49	3.60	0.29
703	3.14	3.31	3.46	0.32
704	3.06	3.07	3.11	0.05
705	2.73	2.75	2.83	0.10
Mean	3.08	3.16	3.27	0.20
± S.D.[a]	0.21	0.28	0.31	0.12

FEMALES

Animal Number	Body Weight (kg)			Cumulative Body Weight Change (kg)
	Day 1	Day 8	Day 15	(Day 15 - Day 1)
706	3.53	3.61	3.65	0.12
707	3.46	3.59	3.71	0.25
708	3.44	3.44	3.57	0.13
709	3.21	3.26	3.40	0.19
710	4.03	4.10	4.12	0.09
Mean	3.53	3.60	3.69	0.16
± S.D.[a]	0.30	0.31	0.27	0.064

[a] S.D. = Standard Deviation

ACUTE DERMAL TOXICITY STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS (LIMIT TEST)

TABLE 5

Individual Gross Necropsy Observations

Animal Number	Sex	Observation
701	M	No signs observed
702	M	No signs observed
703	M	No signs observed
704	M	No signs observed
705	M	No signs observed
706	F	No signs observed
707	F	No signs observed
708	F	No signs observed
709	F	No signs observed
710	F	No signs observed

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

Report No:	**1998-I0000-44339**
Title	**ACUTE PRIMARY EYE IRRITATION/CORROSION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS**
Study No:	
External Testing Facility No:	
Test Substance:	**Dow Corning® 60,000CST, NO CO-SOLVENT**
Study Director:	
Author(s):	
Sponsor:	**Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686-0994**
Sponsor Representative:	
Testing Facility:	
Study Completion Date:	**February 5, 1998**
Security Statement:	

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

TABLE OF CONTENTS

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

ABSTRACT

The objective of this study was to evaluate the eye irritancy of Dow Corning® 60,000CST, NO CO-SOLVENT following a single application into the eye of rabbits.

This study was performed using OECD Guidelines for Testing of Chemicals (Part 405, February, 1987) and according to U.S. EPA Good Laboratory Practice Standards set forth in Part 792 (TSCA) of Title 40 of the Code of Federal Regulations, Final Rule, August 17, 1989 and the OCDE/GD (92) 32.

Dow Corning® 60,000CST, NO CO-SOLVENT was administered undiluted at a dose of 0.1 ml to the right eye of each of three female New Zealand White rabbits. The untreated left eye of each rabbit served as a control. The treated eye of each rabbit was rinsed with lukewarm water 24 hours after instillation of test substance. Rabbits were scored for irritation at 1, 24, 48 and 72 hours following test substance administration. No corneal or iridial irritation was observed in any rabbit during the study. Conjunctival erythema, chemosis and discharge were seen in all three rabbits at the 1-hour scoring interval. Conjunctival erythema and chemosis persisted in all three rabbits through the 48-hour scoring interval. Conjunctival discharge persisted in one rabbit through the 48-hour scoring interval while the other two rabbits were cleared of this sign by the 24-hour scoring interval. All animals had recovered from all signs of ocular irritation at the 72-hour scoring interval (study termination). A maximum primary eye irritation score of 9.3 (maximum possible Draize score = 110.0) was obtained at the 24-hour scoring interval.

Under the conditions of testing and according to the European Communities interpretive criteria (Official Journal of the European Communities, L 180/1, 1991), Dow Corning® 60,000CST, NO CO-SOLVENT was considered a nonirritant to the eye of the rabbit.

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with U.S. Environmental Protection Agency (EPA) Good Laboratory Practice (GLP) Standards as set forth in the *Code of Federal Regulations* (Part 792 of Title 40; TSCA) and OCDE/GD (92) 32. Records pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The raw data have been reviewed by the Study Director, who certifies that the information contained in this report is consistent with and supported by the study raw data.

2/5/98

Date

Study Director

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

QUALITY ASSURANCE STATEMENT

Study Title: Acute Primary Eye Irritation/Corrosion Study of Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

Project Number:

Study Director:

This study has been subjected to inspections and the report has been audited by the Quality Assurance Unit in accordance with U.S. Environmental Protection Agency (EPA) "Good Laboratory Practice (GLP) Standards" - "CFR Title 40 Section 792.35" and OCDE/GD (92) 32. The report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

The following are the inspection dates and the dates inspection findings were reported:

		Findings Reported To:	
Date of Inspection	Study Phase	Study Director	Management
July 11, 14, 16, 1997	Protocol Review	July 16, 1997	July 16, 1997
October 13, 14, 1997	Protocol Review	October 14, 1997	October 14, 1997
October 28, 1997	Test Substance Administration	October 28, 1997	October 28, 1997
November 24, 25, 1997	Report/Data Audit	November 25, 1997	November 25, 1997
February 4, 1998	Report/Data Correction Check	February 4, 1998	February 4, 1998

2/5/98
Date

Manager, Quality Assurance

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

APPROVAL SIGNATURES

This report consists of Pages 1 through 19 including Tables 1 and 2 and Appendices 1 through 3.

2/5/98
Date

2/5/98
Date

Manager, Regulatory Toxicology

1/28/98
Date

Associate Toxicology Scientist
Sponsor Representative

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

STUDY INFORMATION

Study Initiation Date:	October 27, 1997
Experimental Start Date:	October 28, 1997
Experimental Termination Date:	October 31, 1997
Study Completion Date:	February 5, 1997
Study Director:	
Sponsor:	Dow Corning Corporation
Sponsor Representative:	
Study Personnel:	
Report Preparation:	

Acute Primary Eye Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

I. INTRODUCTION

The purpose of this study was to determine the eye irritancy of Dow Corning® 60,000CST, NO CO-SOLVENT following a single application into the eye of rabbits.

II. MATERIALS AND METHODS

A. Test Substance: Dow Corning® 60,000CST, NO CO-SOLVENT, Lot No. was received October 3, 1997. The test substance was a colorless viscous liquid and was stored in the original container at room temperature. The Material Safety Data Sheet (MSDS) indicated that the test substance is stable. Records pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. All remaining test substance will be returned to the Sponsor after completion of all relevant studies.

B. Dosage Formulation: The test substance was administered undiluted. A dose of 0.1 ml was placed directly into the conjunctival sac of the right eye of each rabbit using a 1 cc syringe.

C. Animals: New Zealand White rabbits, approximately 3-4 months of age, were purchased from for use in this study. The rabbits were received on October 8, 1997 and a random sample (11 of 46 rabbits received) weighed 2.39 to 3.48 kg the next day. Upon arrival, the rabbits were held in quarantine for approximately three weeks during which time they were observed daily for survival and at the end of the quarantine period were examined carefully to ensure their health and suitability as test subjects. Rabbits selected for the study were identified by a unique numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number. This particular test system and the specific route by which the test substance was administered were chosen for the following reasons: 1) the rabbit is an animal model widely used and accepted for eye irritation testing and against which its reaction to the test substance can be evaluated; and, 2) ocular application corresponds to a potential route by which humans may be exposed to the test substance. The number of animals used for this study was based upon testing guideline requirements.

D. Food and Water: Each rabbit was provided with approximately 150 g of Purina Lab Rabbit Chow HF #5325 daily.

water was supplied *ad libitum* by means of an automatic watering system. No contaminants capable of adversely affecting the integrity or interpretation of the results from this study were known to be present in the basal diet or the drinking water during the conduct of this study.

E. Housing and Environment: The rabbits were housed individually in suspended stainless steel cages. Absorbent cage liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the treatment phase of the study, the animal room temperature ranged from 22.0°C to 24.0°C and relative humidity ranged from 26 to 43%. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness.

The minimum number of air changes in the animal room was 10 changes per hour.

F. Methods:

1. Animals: Formal randomization of test subjects was not done. The first three female rabbits exhibiting healthy eyes and no adverse clinical signs were selected and assigned to a single group.

2. Preparation: One day prior to treatment, the rabbits were examined for general health and for corneal lesions with and without the aid of 2% fluorescein (Aldrich Chemical, Milwaukee, WI) and ultraviolet light.

3. Dosing: On the day of treatment (October 28, 1997), 0.1 ml of undiluted test substance was placed in the everted lower lid of the right eye of each test rabbit. The lids of all treated eyes were held closed for approximately two seconds following test substance administration. The left eye of each rabbit served as an untreated control. The treated right eye of each rabbit was rinsed with lukewarm water 24 hours after instillation of the test substance.

4. Observations: All rabbits were observed daily for mortality and moribundity.

5. Ocular Examinations: The treated and control eyes of each test rabbit were examined at 1, 24, 48 and 72 hours after test substance administration using a slit

pen light. At each interval, ocular lesions were scored according to the criteria of the Organization for Economic Co-operation and Development (Appendix 1) and to the criteria of Draize (Appendix 2). The cornea was observed for presence and/or degree of opacity and area of opacity; the iris for deepened rugae (folds), congestion, swelling, circumcorneal hyperemia and reaction to light; and the conjunctiva for redness, chemosis and (Draize only) discharge. Fluorescein and ultraviolet light were used to aid in the examination for corneal lesions at the 24-hour scoring.

6. Animal Disposition: After the final observation (October 31, 1997) the rabbits were euthanized using sodium pentobarbital and discarded without necropsy.

G. Evaluation: For each animal, mean scores for corneal opacity, iris lesions, conjunctival erythema and conjunctival chemosis were calculated by adding the 24, 48 and 72 hour scores and dividing by three. The following criteria, based on the European Communities interpretive criteria (Official Journal of the European Communities, L 180/1, 1991), were used in assessing the irritation potential of the test substance:

1. The test substance will be considered a nonirritant if, in at least two animals, the corneal opacity mean score is less than 2.0, the iris lesion mean score is less than 1.0, the conjunctival erythema mean score is less than 2.5 *and* the chemosis mean score is less than 2.0.

2. The test substance will be considered a European Communities irritant if at least two of the three rabbits have a corneal opacity mean score greater than or equal to 2.0 but less than 3.0, an iris lesion mean score greater than or equal to 1.0 but less than 2.0, a conjunctival erythema mean score greater than or equal to 2.5 *or* a chemosis mean score greater than or equal to 2.0.

3. The test substance will be considered a European Communities severe irritant if either the corneal opacity mean score is greater than or equal to 3.0 *or* the iris lesion mean score is equal to 2.0 in at least two of the three rabbits tested.

H. Deviations: Deviations or circumstances known to have occurred during the conduct of this study and their effect, if any, on the quality or integrity of the data from this study are described in Appendix 3.

I. Archives: All original data generated at and the signed original final report will be retained in the for

five years from the date of this report. At that time, the Sponsor will be contacted in order to determine their final disposition.

III. RESULTS

A. Mortality: No deaths occurred during the study.

B. Ocular Lesions: Summation of OECD eye irritation scores for each of the test rabbits is presented in Table 1, and primary eye irritation scores are presented in Table 2. No corneal opacity or iris lesions were observed in any rabbit during the study. Conjunctival erythema, chemosis and discharge were seen in all three rabbits at the 1-hour scoring interval. Conjunctival erythema and chemosis persisted in all three rabbits through the 48-hour scoring interval. Conjunctival discharge persisted in one rabbit through the 48-hour scoring interval while the other two rabbits were cleared of this sign by the 24-hour scoring interval. All animals had recovered from all signs of ocular irritation at the 72-hour scoring interval (study termination). A maximum primary eye irritation score of 9.3 (maximum possible Draize score = 110.0) was obtained at the 24-hour scoring interval.

C. Statistics: Statistical procedures were limited to calculating the Primary Eye Irritation Score.

IV. CONCLUSIONS

The maximum primary irritation score was 9.3 (maximum possible Draize score = 110.0) at the 24-hour scoring interval. Under the conditions of testing and according to the European Communities interpretive criteria (Official Journal of the European Communities, L 180/1, 1991), Dow Corning® 60,000CST, NO CO-SOLVENT was considered a nonirritant to the eyes of rabbits.

V. TABLES

ACUTE PRIMARY EYE IRRITATION/CORROSION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE 1

Summation of OECD Eye Irritation Scores

Animal Number	Sex[a]	Cornea (Density of Opacity) Scoring Interval 1 hour	24 hours	48 hours	72 hours	Mean[b]
597	F	0	0	0	0	0.0
598	F	0	0	0	0	0.0
599	F	0	0	0	0	0.0

Animal Number	Sex	Iris Scoring Interval 1 hour	24 hours	48 hours	72 hours	Mean[b]
597	F	0	0	0	0	0.0
598	F	0	0	0	0	0.0
599	F	0	0	0	0	0.0

Animal Number	Sex	Conjunctiva Scoring Interval 1 hour A[c]	1 hour B[d]	24 hours A	24 hours B	48 hours A	48 hours B	72 hours A	72 hours B	Mean[b] A	Mean[b] B
597	F	1	1	2	2	1	1	0	0	1.0	1.0
598	F	1	1	2	2	1	1	0	0	1.0	1.0
599	F	1	1	2	2	2	2	0	0	1.3	1.3

[a] F = Female
[b] Mean = Sum of individual scores at 24, 48 and 72 hours divided by 3.
[c] A = Erythema
[d] B = Chemosis

ACUTE PRIMARY EYE IRRITATION/CORROSION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE 2

Summation of Draize Eye Irritation Scores

Cornea (A=Density of Opacity: B=Area of Opacity)

Animal		Scoring Interval							
		1 hour		24 hours		48 hours		72 hours	
Number	Sex[a]	A	B	A	B	A	B	A	B
597	F	0	0	0	0	0	0	0	0
598	F	0	0	0	0	0	0	0	0
599	F	0	0	0	0	0	0	0	0

Iris

Animal		Scoring Interval			
Number	Sex	1 hour	24 hours	48 hours	72 hours
597	F	0	0	0	0
598	F	0	0	0	0
599	F	0	0	0	0

Conjunctiva (A=Erythema, B=Chemosis, C=Discharge)

Animal		Scoring Interval											
		1 hour			24 hours			48 hours			72 hours		
Number	Sex	A	B	C	A	B	C	A	B	C	A	B	C
597	F	1	1	1	2	2	0	1	1	0	0	0	0
598	F	1	1	2	2	2	0	1	1	0	0	0	0
599	F	1	1	2	2	2	2	2	2	1	0	0	0

[a] F = Female

ACUTE PRIMARY EYE IRRITATION/CORROSION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE 2 (cont.)

Summation of Draize Eye Irritation Scores

SCORING INTERVAL	TOTAL IRRITATION SCORE[a] ANIMAL NUMBER 597	598	599	PRIMARY IRRITATION SCORE[b]
1 hour	6	8	8	7.3
24 hours	8	8	12	9.3
48 hours	4	4	10	6.0
72 hours	0	0	0	0.0

[a] Formula: Total Irritation Score = I + II + III, where,

I = Corneal Score = [Density (A) x Area (B)] x 5
II = Iris Score = Severity x 5
III = Conjunctival Score = [Erythema (A) + Chemosis (B) + Discharge (C)] x 2

[b] Primary Irritation Score = Sum of Total Irritation Scores ÷ 3

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

Report No:	**1998-I0000-44338**
Title:	**ACUTE DERMAL IRRITATION/CORROSION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS**
Study No:	
External Testing Facility No:	
Test Substance:	**Dow Corning® 60,000CST, NO CO-SOLVENT**
Study Director:	
Author(s):	
Sponsor:	**Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686-0994**
Sponsor Representative:	
Testing Facility:	
Study Completion Date:	**February 4, 1998**
Security Classification:	

Acute Dermal Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

TABLE OF CONTENTS

ABSTRACT

The purpose of this study was to evaluate the dermal irritancy and corrosivity of Dow Corning® 60,000CST, NO CO-SOLVENT following a single application to the intact skin of rabbits.

The study was performed using OECD Guidelines for Testing of Chemicals (Part 404, July, 1992) and according to U.S. EPA Good Laboratory Practice Standards set forth in Part 792 (TSCA) of Title 40 of the Code of Federal Regulations, Final Rule August 17, 1989 and OCDE/GD (92) 32.

Dow Corning® 60,000CST, NO CO-SOLVENT was applied undiluted at a dose of 0.5g for 4 hours to the shaved backs of three female New Zealand White rabbits. The residual test substance was removed with the aid of D.C.® 360 Medical Fluid-moistened gauze. All test sites were examined for signs of dermal irritation (*i.e.*, edema, erythema and/or eschar formation) and corrosivity (*i.e.*, ulceration and/or necrosis) 60 minutes, 24, 48 and 72 hours following removal of the wrappings. The Primary Dermal Irritation Score was calculated and the skin irritancy of the test substance was assessed using criteria provided by the Sponsor.

No signs of dermal irritation or corrosivity were observed in any rabbit during the study. The Primary Dermal Irritation Score for Dow Corning® 60,000CST, NO CO-SOLVENT was 0.0. Therefore, under the conditions of testing and according to the Dow Corning® skin irritancy rating scale, the test substance was non-irritating to the skin of rabbits.

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with U.S. Environmental Protection Agency (EPA) Good Laboratory Practice (GLP) Standards as set forth in the *Code of Federal Regulations* (Part 792 of Title 40; TSCA) and OCDE/GD (92)32. Records pertaining to the characterization and stability of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The raw data have been reviewed by the Study Director, who certifies that the results reported herein are consistent with and supported by the study raw data.

2/4/98
Date

Study Director

Acute Dermal Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

QUALITY ASSURANCE STATEMENT

Study Title: Acute Dermal Irritation/Corrosion Study of Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

Project Number:

Study Director:

This study has been subjected to inspections and the report has been audited by the Quality Assurance Unit in accordance with U.S. Environmental Protection Agency (EPA) TSCA "Good Laboratory Practice (GLP) Standards" CFR Title 40 Section 792.35 and OCDE/GD (92) 32. The report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

The following are the inspection dates and the dates inspection findings were reported:

		Findings Reported to:	
Date of Inspection	Phase	Study Director	Management
July 10, 1997	Protocol Review	July 10, 1997	July 10, 1997
October 15, 1997	Protocol Review	October 15, 1997	October 15, 1997
October 21, 1997	Test Substance Administration	October 21, 1997	October 21, 1997
November 24-25, 1997	Report/Raw Data Audit	November 25, 1997	November 25, 1997

2/4/98
Date

Manager, Quality Assurance

Acute Dermal Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

APPROVAL SIGNATURES

This report consists of Pages 1 through 18 including Tables 1 through 4 and Appendices 1 and 2.

Research Toxicologist — Date: 2/4/98

Manager, Regulatory Toxicology — Date: 2/4/98

Associate Toxicology Scientist — Date: 1/28/98

Acute Dermal Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

STUDY INFORMATION

Study Initiation Date:	October 21, 1997
Experimental Start Date:	October 21, 1997
Experimental Termination Date:	October 24, 1997
Study Completion Date:	February 4, 1998
Study Director:	
Sponsor:	Dow Corning Corporation
Sponsor Representative:	
Study Personnel:	
Report Preparation:	

Acute Dermal Irritation/Corrosion Study of
Dow Corning® 60,000CST, NO CO-SOLVENT in Rabbits

I. INTRODUCTION

The purpose of this study was to determine the dermal irritancy and corrosivity of Dow Corning® 60,000CST, NO CO-SOLVENT when applied once to the intact skin of rabbits.

II. MATERIALS AND METHODS

A. Test Substance: Dow Corning® 60,000CST, NO CO-SOLVENT was received October 3, 1997. The test substance was a colorless viscous liquid and was stored at room temperature in the original container. The Material Safety Data Sheet indicated that the test substance was stable. Records pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. All remaining test substance will be returned to the Sponsor after completion of all relevant studies.

B. Dosage Formulation: Individual doses of 0.5 g of undiluted test substance were dispensed into plastic weight boats and subsequently applied directly to the skin of the rabbits.

C. Animals: New Zealand White rabbits, approximately 3-4 months of age from were used in this study. The rabbits were received on October 8, 1997 and a sample (11 of 46 rabbits received) weighed 2.39 to 3.48 kg the next day. The rabbits were held in quarantine for approximately two weeks during which time they were observed daily for survival and at the end of the quarantine period, were examined carefully to ensure their health and suitability as test subjects. Rabbits selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number. This particular test system and the specific route by which the test substance was administered were chosen for the following reasons: 1) the rabbit is an animal model widely used and accepted for acute toxicity testing and against which its reaction to the test substance can be evaluated, and 2) dermal application corresponds to a potential route by which humans may be exposed to the test substance. The number of animals used for this study was based upon testing guideline requirements.

D. Food and Water: Each rabbit was provided with approximately 150 g of Certified Purina Lab Rabbit Chow HF #5325 (PMI Feeds, Inc., St. Louis, MO) daily. water was supplied *ad libitum* by means of an automatic watering system. No contaminants capable of adversely affecting the integrity or interpretation of the results from this study were known to be present in the basal diet or the drinking water during the conduct of this study.

E. Housing and Environment: The rabbits were housed individually in suspended stainless steel cages measuring approximately 46 x 41 x 61 cm. Absorbent liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the

experimental phase of the study, the animal room temperature and relative humidity were 22.0 to 23.5°C and 30 to 50%, respectively. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness.

The minimum number of air changes in the animal room was 10 changes per hour.

F. Methods:

1. Animals: Formal randomization of test subjects was not done. The first three female rabbits exhibiting healthy intact skin were selected and assigned to a single group.
2. Skin Preparation: Fur was clipped from an area of approximately 240 cm^2 on the back of each rabbit and the skin examined for abnormalities approximately 23 hours prior to test substance administration. Rabbits found at the time of shaving to have significant skin abnormalities were excluded from the study.
3. Dosing: A 0.5 g quantity of undiluted test substance was applied to the shaved backs of three female rabbits on October 21, 1997. Upon test substance application, each test site was covered with a 2.5 x 2.5 cm 12-ply cotton gauze patch secured with porous tape

   The mid-section of each rabbit was wrapped in lint-free cloth secured by an elastic adhesive bandage

   which prevented removal of the test substance while allowing the rabbit free movement.
4. Observations: All rabbits were observed at least once daily for mortality and moribundity.
5. Body Weights: The rabbits were weighed prior to dosing and at the conclusion of the study.
6. Skin Examinations: All wrapping materials and adhesive dressings were removed 4 hours after application of the test substance and the application site wiped with D.C.® 360 Medical Fluid-moistened gauze to remove residual test substance. The application site was examined for dermal irritation [*i.e.*, edema, erythema and/or eschar (superficial crust/scab) formation] and corrosivity (*i.e.*, ulceration and/or necrosis) 60 minutes, 24, 48 and 72 hours following removal of the wrappings. The descriptive criteria and scores of Draize (Appendix 1) were used. A skin irritancy rating scale provided by the Sponsor is presented in Appendix 2.

7. Animal Disposition: Following the final skin examination (October 24, 1997), the rabbits were euthanized by sodium pentobarbital overdose and discarded without necropsy.

G. Evaluation: The edema and erythema/eschar formation scores obtained at the 60 minute and 24-, 48- and 72-hour observation intervals following removal of the wrappings were averaged. An irritation score for each of these intervals was calculated by adding the averaged scores, and the irritation scores of the 24-, 48- and 72-hour intervals were then averaged to yield the Primary Dermal Irritation Score (Table 3).

Generally, a test substance is considered "corrosive" if both of the following criteria are satisfied:

1) The test substance has a Primary Dermal Irritation score of 5.0 or higher based on a maximum score of 8.0;

2) Full-thickness skin necrosis and/or ulceration are (is) evident.

H. Deviations: There were no deviations or circumstances known to have occurred during the conduct of this study that would affect the quality or integrity of the data from this study.

I. Archives: All original data generated at and the signed original final report will be retained in the for five years from the date of this report. At that time, the Sponsor will be contacted in order to determine its final disposition.

III. RESULTS

A. Mortality: No deaths occurred during the study.

B. Body Weights: The weight range for the three rabbits used in this study was 3.20 to 3.59 kg at experiment initiation and 3.33 to 3.61 kg at the conclusion. All rabbits gained weight during the study (Table 4).

C. Skin Effects: A description of individual application site skin reactions is presented in Table 1, and a summary of dermal irritation scores is presented in Table 2. No signs of dermal irritation were observed in any animal during the study. The Primary Dermal Irritation Score for Dow Corning® 60,000CST, NO CO-SOLVENT was 0.0 (Table 3).

D. Statistics: Statistical procedures were limited to calculating the Primary Dermal Irritation Score.

IV. CONCLUSIONS

The Primary Dermal Irritation Score for Dow Corning® 60,000CST, NO CO-SOLVENT was 0.0. Therefore, under the conditions of testing and according to the Dow Corning® skin irritancy rating scale (Appendix 2), Dow Corning® 60,000CST, NO CO-SOLVENT was considered non-irritating to the skin of rabbits.

V. TABLES

ACUTE DERMAL Irritation/Corrosion STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE I

Description of Individual Skin Reactions

Animal Number	Sex[a]	Scoring Interval			
		60 minutes	24 hours	48 hours	72 hours
766	F	ED - 0[b] ER - 0[c]	ED - 0 ER - 0	ED - 0 ER - 0	ED - 0 ER - 0
767	F	ED - 0 ER - 0	ED - 0 ER - 0	ED - 0 ER - 0	ED - 0 ER - 0
768	F	ED - 0 ER - 0	ED - 0 ER - 0	ED - 0 ER - 0	ED - 0 ER - 0

[a] F = Female
[b] ED (Edema): 0 = none, 1 = very slight, 2 = slight, 3 = moderate, 4 = severe
[c] ER (Erythema): 0 = none, 1 = very slight, 2 = well-defined, 3 = moderate to severe, 4 = severe erythema to slight eschar formation

ACUTE DERMAL Irritation/Corrosion STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE 2

Summary of Dermal Irritation Scores

	Scoring Interval			
Edema Score	60 minutes	24 hours	48 hours	72 hours
0	3/3[a]	3/3	3/3	3/3
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
Mean	**0.0**	**0.0**	**0.0**	**0.0**
Erythema and/or Eschar Formation Score	60 minutes	24 hours	48 hours	72 hours
0	3/3	3/3	3/3	3/3
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
Mean	**0.0**	**0.0**	**0.0**	**0.0**
Irritation Score[b]	**0.0**	**0.0**	**0.0**	**0.0**

[a] Number of animals with score/number of animals dosed
[b] Irritation Score = Mean Edema Score + Mean Erythema Score

ACUTE DERMAL Irritation/Corrosion STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE 3

Primary Dermal Irritation Score

Skin Reaction:	Erythema and/or Eschar Formation	Edema
24 Hours Following Removal of wrapping	0.0	0.0
		Subtotal A: 0.0
48 Hours Following Removal of wrapping	0.0	0.0
		Subtotal B: 0.0
72 Hours Following Removal of wrapping	0.0	0.0
		Subtotal C: 0.0

Subtotal A + Subtotal B + Subtotal C = Total Score

0.0 + 0.0 + 0.0 = 0.0

Total Score ÷ 3 = Primary Dermal Irritation Score

0.0 ÷ 3 = 0.0

ACUTE DERMAL Irritation/Corrosion STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN RABBITS

TABLE 4

Summary of Body Weights

Animal Number	Sex	Body Weight (kg) 1 Day	Body Weight (kg) 4 Day	Cumulative Body Weight Change (kg) (Day 4 - Day 1)
766	F	3.20	3.40	0.20
767	F	3.59	3.61	0.02
768	F	3.31	3.33	0.02

DOW CORNING CORPORATION
Health and Environmental Sciences

PRIMARY VAGINAL IRRITATION STUDY OF DOW CORNING® 4-2797 INT (X7-9192) IN THE RABBIT

File No.:

Reference No.:

Lot No.:

Document I.D.: 1991-I0000-36045

Authors:

Submitted By:

Reported By:
Checked By:

Date: February 6, 1991

This summary of data and conclusions is based upon the samples received. Additional studies may be required as specific uses and formulations are developed or if process changes occur.

ABSTRACT

DOW CORNING® 4-2797 INT (X7-9192) was evaluated for its potential to produce primary irritation in albino rabbits following a single topical application. The test material was introduced (0.5g) into the vaginal cavity by syringe in six animals. Two animals designated as control were similarly dosed with 0.5 ml USP 0.9% sodium chloride solution. Tissues were evaluated for signs of irritation at 24, 48, and 72 hours post-treatment with the aid of an otoscope. Observations were scored according to a standard Draize Scale. Neither the test or control material produced any sign of irritation, weight loss or clinical signs of toxicity during the 72 hour observation period. The primary vaginal irritation index for both the control and test material was 0.0. 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.

Distribution

*Abstract and Title Page Only

1.0 SUMMARY

Based on the standards set forth in the study protocol, the test article, Dow Corning® 4-2797INT(X7-9192), Lot #: is not considered an irritant to the vaginal tissues of albino rabbits. Primary Vaginal Irritation Index for the test and control articles are 0.00.

2.0 PURPOSE

The purpose of the test was to evaluate the potential of the test article to produce primary vaginal irritation after a single topical dose application to the vaginal tissues of albino rabbits.

3.0 REFERENCE

The test was conducted based on the Federal Hazardous Substance Act-Consumer Product Safety Commission, 16 CFR, Part 1500, Chapter II, Subpart C, Section 1500.41, 1990.

4.0 MANAGEMENT OF THE STUDY

4.1 Sponsor Dow Corning Corp.

Project Officer:

4.2 Testing Laboratory

Study Director:
Study Supervisor:
Quality Assurance:

5.0 COMPLIANCE

The study conformed to all applicable laws and regulations. Specific regulatory requirements included the current FDA 21 CFR, Part 58 - Good Laboratory Practice for Non-Clinical Laboratory Studies; AAALAC, "Guide for the Care and Use of Laboratory Animals", DHHS Pub. No. (NIH) 85-23, Revised 1985; NIH (OPRR), "Public Health Service Policy on Humane Care and Use of Laboratory Animals", Health Research Extension Act of 1985 (Public Law 99-158), Revised 1986; USDA, Department of Agriculture, Animal and Plant Health Inspection Service, 9 CFR, Parts 1, 2, and 3, Animal Welfare, Final Rules 1989.

6.0 TEST ARTICLE

The following information was supplied by the Sponsor. The Sponsor was responsible for all test article characterization data as specified in the GLP regulations.

TEST ARTICLE
Test Article Name: Dow Corning ^{R} 4-2797INT (X7-9192)
Chemical/Common/Trade Name: Not Supplied by Sponsor (N/S)
Molecular Formula: N/S
Composition/Purity: N/S
Physical State: Liquid
Color: Clear
Density: N/S
pH: N/S
Specific Gravity: 25/15.6°C, at 77°F/25°C:0.9
Stability: Stable
Solubility: Less than 0.1% in water
Hygroscopic Properties: N/S
Boiling Point: N/S
Flash Point: N/S
Lot/Batch #:
CAS/Code #: 70131-67-8
Quantity: 1 litre
Source:
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

CONTROL ARTICLE (Supplied)
Control Article Name: USP 0.9% Sodium Chloride for Injection
Lot/Batch #: QC Inventory #:CSC 90-10-004VIV
Physical State: Liquid
Color: Colorless
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

6.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE
Rabbits were used in this study because they have historically been used in vaginal safety evaluation studies. Vaginal exposure corresponds to a likely route of human exposure.

7.0 IDENTIFICATION OF THE TEST SYSTEM
7.1 Eight healthy young adult, female, New Zealand White rabbits (Oryctolagus cuniculus) were used in the study. Animals were purchased from a registered commercial breeding laboratory . At the start of the study, animals were in the weight range between 2.0 and 3.0 kilogram (10 to 12 weeks old).

7.2 Animals were individually housed in suspended stainless steel cages. Hardwood Sani-Chips were used as non-contact bedding under the cages. Animal rooms were maintained at 68±3°F, with a relative humidity of 30-70%, a minimum of 10 to 13 complete air exchanges per hour, and a 12 hour light/dark cycle using full spectrum fluorescent lights. The laboratory and animal rooms were maintained as limited access facilities.

Animals were supplied with a controlled diet of a commercial rabbit ration and municipal tap water *ad libitum*. There were no known contaminants present in the feed, bedding, or water expected to interfere with the test data. Feed and bedding analysis will not be performed for acute testing purposes.

8.0 EXPERIMENTAL DESIGN

8.1 Quarantine
Upon receipt, animals were placed in quarantine for 7 days, under the same conditions as for the actual test.

8.2 Pretreatment Screening Procedure and Selection of Animals
Animals selected for the test were not subjected to any previous experimental procedures. The animals were nulliparous and non-pregnant. Animals selected for the study were chosen from a larger pool of animals and were examined to insure that the vaginas are free of abnormality, damage and disease.

8.3 The animals were weighed to the nearest 10 grams and individually identified by ear tattoo.

8.4 Six animals were subjected to the test article and two animals to the control article. USP 0.9% Sodium Chloride Solution served as the control article. Following the 24 hour reading, the vaginal area was not washed.

8.5 After the test or control article application, the animal was returned to its cage. Each cage was labeled with a card describing the toxicology number, Study Director, room number, animal number, date of study initiation and completion, sex, and species.

8.6 Post Treatment Procedures
Animals were observed for signs of erythema and edema at 24 48, and 72 hours after application of the test article. Readings were facilitated by the use of an otoscope.

Observations were scored according to the "Draize Scale for Scoring Skin Reactions" described in this protocol. Dermal irritation is scored according to the method of Draize (Draize, J.H., "Dermal Toxicity". Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity, Pp. 46-59, Association of Food and Drug Officials of the U.S., Topeka, Kansas, 1965) as described in Appendix A.

8.7 Observations were conducted daily for all clinical, toxicologic, and pharmacologic signs. Observations include nature, onset, severity, and duration of abnormal or unusual cardiovascular, respiratory, excretory, behavioral and other activities; as well as signs indicating adverse effect on the central nervous system (paralysis, lethargy, lack of coordination, staggering).

8.8 Moribund and Dead Animals
Any animal found dead were necropsied as soon as possible but in no case later than 12 hours.

8.9 No therapeutic agents were used in any phase of the study.

8.10 Animals were weighed at the end of the study and sacrificed with an improved euthanasia solution

9.0 ROUTE OF ADMINISTRATION
Animals were treated by gently inserting a lightly lubricated syringe, without the needle, into the vagina and dispensing the test or control article.

10.0 DOSAGE
A dose volume of 0.5 g of the test article or 0.5 ml of the control article was applied into the vagina.

11.0 INTERPRETATION OF RESULTS
11.1 General Requirements
For a valid vaginal irritation test, all animals must survive the test.

11.2 Evaluation of Animal Data
Observation values were calculated by averaging the individual animals scores found for each of the different categories of observation values, namely, erythema formation in intact tissue a 24, 48 and 72 hours and edema formation in intact tissue at 24, 48, 72 hours. These values were averaged to produce a Primary Vaginal Irritation Index for the test.

The same procedure was used to obtain a Primary Irritation Index for the control.

11.3 Evaluation of Test Results
A test article with a Primary Irritation Index of 0 will be considered a non-irritant. A test article with an index of 2 or less will be considered a mild irritant. Test articles with indices greater than 2 and less than 5 will be moderate irritants. Any test articles with an index of 5 or more will be considered vaginal irritants. Those test articles that destroy the structure of the intact tissue or change it irreversibly will be considered corrosive.

12.0 RESULTS
12.1 Body Weight (Table I)
None of the treated and control animals lost weight during the observation period.

12.2 Clinical Observations (Table I)
None of the test or control animals exhibited any clinical signs of toxicity during the observation period.

12.3 Irritation (Table II)
No reactions were observed for any of the animals at any of the observation points.

12.4 Primary Vaginal Irritation Index (PVII)
PVII (Test) = 0.00
PVII (Control) = 0.00

13.0 DISCUSSION AND CONCLUSION
Based on the standards set forth in the study protocol, the test article, Dow Corning® 4-2797INT(X7-9192), Lot #: is not considered an irritant to the vaginal tissues of albino rabbits. Primary Vaginal Irritation Index for the test and control articles are 0.00.

14.0 STORAGE LOCATION OF RECORDS
Original Data:
Final Report:
Test Article: All unused test article shall be destroyed per Sponsor request.

15.0 VERIFICATION DATA

Date of Signed Protocol: 11/15/90
Date of Sample Receipt: 12/27/90
Date of Study Initiation: 01/07/91
Date of Study Completion: 01/10/91
Date of Study Report: 01/23/91

16.0 CONFIDENTIALITY
Statements of confidentiality were as agreed upon prior to study contract initiation.

15.0 SIGNATURE OF AUTHORIZED PERSONNEL

_____ 01/23/91
Study Director Date

TABLE I

Body Weights and Clinical Observations

Test Article: Dow Corning^{R} 4-2797INT (X7-9192) Technical Initiation: 01/07/91

Control Article: USP 0.9% Sodium Chloride Injection Technical Completion: 01/10/91

Dose/Animal: 0.5 g (Test Article)
0.5 ml (Control Article)

			Body Weight (Kg)			
Group	Animal #	Sex	01/07/91 Day 0	01/10/91 Day 3	Weight Change	Signs of Toxicity*
Test Article	1087	Female	2.31	2.32	0.01	None
	1088	Female	2.44	2.45	0.01	None
	1089	Female	2.50	2.53	0.03	None
	1090	Female	2.39	2.41	0.02	None
	1091	Female	2.60	2.60	0.00	None
	1092	Female	2.29	2.30	0.01	None
		Mean	2.42	2.44		
		STD	0.12	0.12		
Control Article	1093	Female	2.55	2.56	0.01	None
	1094	Female	2.39	2.42	0.03	None

* Summary of Animal Observations Day 0 through Day 3 exclusive of skin irritation each day of observation (24, 48 and 72 h)

TABLE II

Draize Scores

Test Article: Dow Corning[R] 4-2797INT (X7-9192) Technical Initiation: 01/07/91

Control Article: USP 0.9% Sodium Chloride Injection Technical Completion: 01/10/91

Dose/Animal: 0.5 g (Test Article)
0.5 ml (Control Article)

		Erythema/Edema		
Group	Animal #	01/08/91 24 hr	01/09/91 48 hr	01/10/91 72 hr
Test Article	1087	0/0	0/0	0/0
	1088	0/0	0/0	0/0
	1089	0/0	0/0	0/0
	1090	0/0	0/0	0/0
	1091	0/0	0/0	0/0
	1092	0/0	0/0	0/0
Control Article	1093	0/0	0/0	0/0
	1094	0/0	0/0	0/0

Note: Primary Vaginal Irritation Index (PVII) = 0.00 Test Article
0.00 Control Article

QUALITY ASSURANCE STATEMENT

Client:

Testing Laboratory:

Test Article: Dow Corning^{R} 4-2797INT (X7-9192)
Lot #:

The study listed above conformed to the best of my knowledge to the current FDA GLP regulations, 21 CFR, Part 58.

Signature of Authorized Personnel:

_____ 01/23/91
Quality Assurance Date

QUALITY ASSURANCE INSPECTIONS	REPORTS TO MANAGEMENT	REPORTS TO STUDY DIRECTOR
01/07/91	01/07/91	01/07/91
01/23/91	01/23/91	01/23/91

DOW CORNING CORPORATION
Health and Environmental Sciences

REPORT NO.: 1991-I0000-36155

FILE NO.:

AUTHORS:

SUBMITTED BY:

DEPARTMENT: Health and Environmental Sciences

SUPERVISOR:

LOCATION:

DATE: April 4, 1991

TITLE: Guinea Pig SKin Sensitization Study of DOW CORNING® X7-9192

Distribution

Full Report

Title Page and Abstract

Toxicology File

REPORT NO.: 1991-I0000-36155
FILE NO.:
REFERENCE NO.:
LOT NO.:
AUTHORS:
SUBMITTED BY:
REPORTED BY:
CHECKED BY:
DEPARTMENT: Health and Environmental Sciences
SUPERVISOR:
LOCATION:
DATE: April 4, 1991
TITLE: Guinea Pig Skin Sensitization Study of Dow Corning® X7-9192*

ABSTRACT

DOW CORNING® X7-9192 was evaluated for its potential to cause primary skin irritation and/or skin sensitization in the quinea pig maximization test (Magnusson and Kligman, 1969, 1970). Prior to intradermal application, 0.1 ml aliquots representing 100, 75, 50, and 25 percent concentrations (dilutions prepared in U.S.P. Water for Injection) of the test material were applied to the skin of four guinea pigs. Irritation was scored at 0, 24, 48 and 72 hours by the Method of Draize. No irritation was noted at any of the concentrations employed.

The sensitization assay was conducted using ten animals (5 male and 5 female) for each of the treatments (100% Test material; USP 0.9 sodium chlorides as negative control; and 0.1% DNCB in 95% ethanol as positive control). Each treatment was administered both with and without Freunds Complete Adjuvant. On day 0, each material was introduced as a series of six 0.1 ml intradermal injections along the dorsal surface of the test animal. On day 7 of the induction phase, test and control materials were applied topically for 48 hrs. Animals were challanged on day 21 by topical application (24 hr) to the hind quarters and reactions read on days 23 and 24. Dow Corning® X7-9192 produced 0% sensitization. The positive control material (DNCB) produced 100% sensitization. It should be noted that the scoring system of Kligman classifies a 0-8% reaction as a grade I; weak allergenic potential even though the test material produced no sensitization in this assay.

* PA Fluid (Dow Corning® 4-2797 Int)

1.0 SUMMARY

Based on the standards set by the study protocol, Dow Corning® 4-2797INT (X7-9192), exhibited no reaction to the challenge (0% sensitization). Therefore, as defined by the scoring system of Kligman, this is a Grade I reaction and the test article is classified as having weak allergenic potential. A Grade I sensitization rate is not considered significant according to Magnusson and Kligman (1969, 1970).

2.0 PURPOSE

The test was designed to evaluate the allergenic potential or sensitizing capacity of a test article. The test is used as a procedure for screening of contact allergens in guinea pigs and extrapolating the results to humans, but it does not establish the actual risk of sensitization.

3.0 MANAGEMENT OF STUDY

3.1 Sponsor: Dow Corning Corp.

Project Officer:

3.2 Testing Laboratory:

Study Director:
Study Supervisor:
Quality Assurance:

4.0 REFERENCE

4.1 This study was based upon the procedures described in Dermatoxicology, I.N. Marzulli and H.I. Maibach, editors, 3rd edition, 1987, Hemisphere Publishing Corporation, New York. Extraction procedures were based upon the standards set by USP XXII, National Formulary XVI, 1990, pp. 1497-1499.

4.2 Magnusson, B. and Kligman, A.M. 1969. The identification of contact allergens by animal assay. The guinea pig maximization test. J. Invest. Dermatol. 52:268-276.

4.3 Magnusson, B. and Kligman, A.M. 1970. Allergic contact dermatitis in the guinea pig. Identification of contact allergens. Springfield. Ill.: Thomas.

5.0 COMPLIANCE

The study conformed to all applicable laws and regulations. Specific regulatory requirements included the current FDA, 21 CFR, Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies; AAALAC, "Guide for the Care and Use of Laboratory Animals", DHHS Pub. No. (NIH) 85-23, Revised 1985; NIH (OPRR), "Public Health Service Policy on Humane Care and Use

of Laboratory Animals", Health Research Extension Act of 1985 (Public Law 99-158), Revised 1986; USDA, Department of Agriculture, Animal and Plant Health Inspection Service, 9 CFR, Parts 1, 2, and 3, Animal Welfare, Final Rules 1989.

6.0 TEST ARTICLE
The following information was supplied by the Sponsor wherever applicable; it did not apply to confidential information. The Sponsor was responsible for all test article characterization data as specified in the GLP regulations.

6.1 Test Article
Test Article Name: Dow Corning^{R} 4-2797INT (X7-9192)
Chemical/Common/Trade Name: Not Supplied by Sponsor (N/S)
Molecular Formula: N/S
Composition/Purity: N/S
Physical State: Liquid
Color: Clear
Density: 0.9
pH: N/S
Specific Gravity: 0.9
Stability: Stable
Solubility: In water less than 1%
Hygroscopic Properties: N/S
Boiling Point: N/S
Flash Point: N/S
Lot/Batch #:
CAS/Code #: 70131-67-8
Quantity: 1 liter
Storage Conditions: Room temperature
Safety Precautions: Standard Laboratory Safety Precautions

6.2 Negative Control Substance (Supplied)
Control Article Name: USP 0.9% Sodium Chloride
QC Inventory #:
Physical State: liquid
Color: clear
Storage Conditions: Room Temperature
Safety Precautions: Standard laboratory safety precautions apply

6.3 Positive Control Article (Supplied)
Control Article Name: Dichloronitrobenzene (DNCB)
QC Inventory #:
Physical State: Solid
Color: Yellow
Storage Conditions: Room temperature
Safety Precautions: Standard laboratory safety precautions apply

7.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE
Guinea pigs were used in this study because they historically have been used and are generally regarded as the species of choice for laboratory identification of skin allergies. Dermal application corresponds to the likely route of human exposure.

8.0 IDENTIFICATION OF TEST SYSTEM

8.1 Animals Used in the Test

Thirty-four young adult, Hartley Guinea Pigs (Cavia porcellus), 17 male and 17 female, were used in the study. Animals were purchased from a registered commercial breeder At the start of the study animals weighed between 300-500 grams (26-67 days old).

8.2 Animal Care and Maintenance

Animals were group housed using polycarbonate cages. Hardwood chips were used as contact bedding within the cages. Animal rooms were maintained at 68±3°F, with a relative humidity at 30-70%, a minimum of 10 to 13 complete air exchanges per hour, and a 12-hour light/dark cycle using full spectrum fluorescent lights. The laboratory and animal rooms are maintained as limited-access facilities.

Animals were supplied with a commercial guinea pig ration and municipal tap water, ad libitum. There were no known contaminants present in the feed, water, or bedding expected to have interfered with the test data. Feed and bedding analyses are not performed for acute testing purposes.

9.0 PREPARATION OF THE TEST ARTICLE

Induction/Intradermal Application: A 5% emulsion was made with USP Water for Injection (WFI), by adding 1 ml of test article to 19 ml WFI.

Topical Application: The test article was applied at the highest non-irritating concentration.

Challenge Application: The test article was applied at the highest non-irritating concentration.

10.0 EXPERIMENTAL DESIGN

10.1 Quarantine

Upon receipt, animals were placed in quarantine for 2 days (Primary Irritation Group) and 5 days (Test and Control Groups) under the same conditions as for the actual test.

10.2 Pretreatment Screening Procedures and Selection of Animals

Animals selected for the study were not subjected to any previous experimental procedures. Animals were selected from a larger pool of animals and were examined to insure their skin was free from irritation, trauma and disease.

10.3 Identification and Body Weight

Selected animals were weighed to the nearest 0.1 gram and identified by ear-punch bearing the individual animal number.

10.4 Distribution of Animals
Test animals were distributed into the following groups:

(1)	Experimental	(5 males/ 5 females)
(2)	Negative Controls	(5 male / 5 female)
(3)	Positive Controls	(5 male / 5 female)
(4)	Primary Irritations	(2 male / 2 female)

10.5 Preparation of the Test Animals
The application sites were prepared by clipping the skin of the test site free of hair. On day 0 and on day 7, an approximately 5 x 7 cm area over the shoulder region was prepared. On day 21, an approximately 4 x 4 cm area of the flanks was prepared.

10.6 Primary Irritation Phase
Prior to the intradermal application, a primary irritation was conducted with four animals. One intact skin site on each animal was treated with 0.1 ml of the test article extract at concentrations of 100% (neat) and 75% or 50% and 25% diluted with WFI and applied under Finn chambers. The primary irritation study indicates whether the test article is or is not a skin irritant.

Skin observations for the primary irritancy test were scored according to the method of Draize (Draize, J.H., "Dermal Toxicity". Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity, pp. 46-59, Association of Food and Drug Officials of the U.S., , as shown in Table 1.

10.7 Induction/Intradermal Application (Day 0)
Three pairs of id injections were made simultaneously, so that on each side of the midline there was one row of three injections each. Injections 1 and 2 were given in close proximity to each other cranially, injection 3 was located caudally. The injection sites (6) were just within the boundaries of a 2 x 4 cm patch, which was applied 1 week following the injections. The dosing solutions were as follows:

Experimental Group:
(1) 0.1 ml FCA 1:1 with NaCl
(2) 0.1 ml test article
(3) 0.1 ml test article 1:1 with FCA

Negative Control Group:
(1) 0.1 ml FCA 1:1 NaCl
(2) 0.1 ml NaCL
(3) 0.1 ml NaCl 1:1 with FCA

Positive Control Group:
(1) 0.1 ml FCA 1:1 NaCl
(2) 0.1 ml 0.1% DNCB in 95% EtOH
(3) 0.1 ml 0.1% DNCB in 95% EtOH 1:1 with FCA*

* DNCB (Dinitrochlorobenzene) dissolved in 95% Ethanol and suspended in FCA to a final concentration of 0.1%

10.8 Topical Application (Day 7)
The test article was not an irritant, therefore, the area was pretreated with 10% sodium lauryl sulfate in petrolatum 24 hours before the topical induction application.

Experimental Group: The test article was spread over a 2 x 4 cm piece of filter paper to saturation. The patch was covered by an impermeable sheet and secured with a non-adhesive bandage, (Vetrap, 3M, which was wound around the torso of the animal. The dressing was left in place for 48 hours.

Negative Control Group: The animals were exposed to the NaCl without the test article in the same way as the experimental group.

Positive Control Group: The animals were exposed to 0.1% DNCB solution in 95% Ethanol in the same way as the experimental group.

10.9 Challenge Application (Day 21)
Pieces of filter paper measuring 2 x 2 cm were secured to the flanks for 24 hours with the same occlusive bandage as for topical induction: (1) on the left side, a patch was saturated with the test article and (2) on the right side, a patch with the NaCl. In the positive control animals, the patch on the left side was saturated with 0.1% DNCB in ethanol instead of the test article extract.

10.10 Skin Readings (Day 23 and 24)
At 21 hours after removing the patches the flank skin was cleaned and shaved, and 3 hours later the first reading of the reactions was performed (24 hour readings on Day 23). The second reading was made the next day (Day 24). For evaluation of skin reactions a four point scale was used:

0 = No reaction
1 = Scattered reaction
2 = Moderate and diffuse reaction
3 = Intense reddening and swelling

10.11 Daily clinical observations were made for toxicological and pharmacological signs.

10.12 Animals were weighed at the end of the observation period and sacrificed by exposure to carbon dioxide.

11.0 EVALUATION
Using the Scoring System of Kligman, the allergic potential of a test article is classified as follows:

Sensitization Rate (%)	Grade	Class
0-8	I	Weak
9-28	II	Mild
29-64	III	Moderate
65-80	IV	Strong
81-100	V	Extreme

The test results were interpreted based upon the percentage sensitization observed.

12.0 RESULTS

12.1 Body Weights: All animals gained in body weight.

12.2 Clinical Observations: No overt signs of toxicity were exhibited in treated or control animals

12.3 Sensitization: None of the treated or negative control animals exhibited any reaction to the challenge (0% sensitized).

The positive control animals exhibited skin reactions of 2 or 3 at each observation point (100% sensitized).

13.0 CONCLUSIONS
Based on the standards set by the study protocol, Dow Corning^{R} 4-2797INT (X7-9192), exhibited no reaction to the challenge (0% sensitization). Therefore, as defined by the scoring system of Kligman, this is a Grade I reaction and the test article is classified as having weak allergenic potential. A Grade I sensitization rate is not considered significant according to Magnusson and Kligman (1969, 1970).

14.0 RECORDS

Original Data:	Archives
Final Report:	Archives
Test Article:	All unused test article will be returned to the Sponsor.

15.0 CONFIDENTIALITY
Statements of confidentiality were as agreed upon prior to study initiation.

16.0 VERIFICATION DATA

Protocol Signature:	11/15/90	
Test Article Receipt:	12/27/90	
Technical Initiation	01/09/91	
Primary Irritation:	01/06/91	to 01/09/91
Intradermal Application:	01/09/91	
Topical Application:	01/16/91	
Challenge Application:	01/30/91	
Technical Completion:	02/02/91	
Final Report:	03/13/91	

17.0 APPROVAL SIGNATURES

_____ 03/13/91
Study Director Date

TABLE I

Primary Irritation
Animal Weights and Skin Reactions (Erythema/Edema)

Primary Initiated: 01/06/91 Primary Completed: 01/09/91

Test Article: Dow Corning® 4-2797INT (X7-9192) Lot #:

An.# Sex	Dose*	Wt (g) Day 0	Day 0 01/06/91	24 h 01/07/91	48 h 01/08/91	72 h 01/09/91	Wt(g) 72 h	Weight Change
31/M	100 %	301.7	0/0	0/0	0/0	0/0	316.7	15.0
	75 %		0/0	0/0	0/0	0/0		
	50 %		0/0	0/0	0/0	0/0		
	25 %		0/0	0/0	0/0	0/0		
32/M	100 %	323.2	0/0	0/0	0/0	0/0	334.3	11.1
	75 %		0/0	0/0	0/0	0/0		
	50 %		0/0	0/0	0/0	0/0		
	25 %		0/0	0/0	0/0	0/0		
33/F	100 %	315.7	0/0	0/0	0/0	0/0	326.8	11.1
	75 %		0/0	0/0	0/0	0/0		
	50 %		0/0	0/0	0/0	0/0		
	25 %		0/0	0/0	0/0	0/0		
34/F	100 %	330.1	0/0	0/0	0/0	0/0	341.1	11.0
	75 %		0/0	0/0	0/0	0/0		
	50 %		0/0	0/0	0/0	0/0		
	25 %		0/0	0/0	0/0	0/0		

* Extract diluted with WFI

TABLE II

Animal Weight and Clinical Observations

Study Initiated: 01/09/91 Study Completed: 02/02/91

Test Article: Dow Corning^{R} 4-2797INT (X7-9192) Lot #:

Group	An. #	Sex	Body Weight (g) Day 0 01/09/91	Body Weight (g) Day 24 02/02/91	Weight Change	Signs of Toxicity*
Test	1	Male	332.3	429.7	97.4	None
	2	Male	338.6	441.2	102.6	None
	3	Male	336.5	436.3	99.8	None
	4	Male	332.1	449.4	117.3	None
	5	Male	346.2	438.2	92.0	None
		Mean	337.1	439.0		
		±SD	5.8	7.2		
Test	6	Female	313.4	397.4	84.0	None
	7	Female	301.1	389.6	88.5	None
	8	Female	327.1	395.2	68.1	None
	9	Female	330.6	429.7	99.1	None
	10	Female	316.1	425.1	109.0	None
		Mean	317.7	407.4		
		±SD	11.7	18.5		

* Summary of Clinical Observations - Day 0 through Day 24

TABLE II (Cont.)

Animal Weight and Clinical Observations

Study Initiated: 01/09/91 Study Completed: 02/02/91

Test Article: Dow Corning^{R} 4-2797INT (X7-9192) Lot #:

Group	An. #	Sex	Body Weight (g) Day 0 01/09/91	Day 24 02/02/91	Change	Signs of Toxicity*
Negative Control	11	Male	319.5	437.2	117.7	None
	12	Male	317.1	429.6	112.5	None
	13	Male	318.8	423.2	104.4	None
	14	Male	320.5	435.6	115.1	None
	15	Male	333.3	457.2	123.9	None
		Mean ±SD	321.8 6.5	436.6 12.8		
Negative Control	16	Female	309.9	398.7	88.8	None
	17	Female	311.1	395.2	84.1	None
	18	Female	320.5	415.7	95.2	None
	19	Female	325.5	420.8	95.3	None
	20	Female	322.1	413.6	91.5	None
		Mean ±SD	317.8 6.9	408.8 11.2		

* Summary of Clinical Observations - Day 0 through Day 24

TABLE II (Cont.)

Animal Weight and Clinical Observations

Study Initiated: 01/09/91 Study Completed: 02/02/91

Test Article: Dow Corning^{R} 4-2797INT (X7-9192) Lot #:

Group	An. #	Sex	Body Weight (g) Day 0 01/09/91	Day 24 02/02/91	Change	Signs of Toxicity*
Positive Control	21	Male	330.0	425.7	95.7	None
	22	Male	325.1	431.2	106.1	None
	23	Male	323.3	429.6	106.3	None
	24	Male	318.8	427.3	108.5	None
	25	Male	316.6	435.6	119.0	None
		Mean	322.8	429.9		
		±SD	5.5	4.0		
Positive Control	26	Female	329.9	397.2	67.3	None
	27	Female	339.8	421.6	81.8	None
	28	Female	340.0	456.1	116.1	None
	29	Female	339.0	433.2	94.2	None
	30	Female	329.8	426.6	96.8	None
		Mean	335.7	426.9		
		±SD	5.5	21.9		

* Summary of Clinical Observations - Day 0 through Day 24

TABLE III

Skin Examination Data

Study Initiated: 01/09/91 Study Completed: 02/02/91

Test Article: Dow Corning^{R} 4-2797INT (X7-9192) Lot #:

Group	An. #	Sex	Observations/Scores Day 23 02/01/91	Day 24 02/02/91	Percent Animals Sensitized	Allergenic Potential
Test Article	1	Male	0	0	0	Weak
	2	Male	0	0		
	3	Male	0	0		
	4	Male	0	0		
	5	Male	0	0		
	6	Female	0	0		
	7	Female	0	0		
	8	Female	0	0		
	9	Female	0	0		
	10	Female	0	0		
Control Article	11	Male	0	0	0	Weak
	12	Male	0	0		
	13	Male	0	0		
	14	Male	0	0		
	15	Male	0	0		
	16	Female	0	0		
	17	Female	0	0		
	18	Female	0	0		
	19	Female	0	0		
	20	Female	0	0		
Positive Control	21	Male	3	3	100	Extreme
	22	Male	2	2		
	23	Male	2	2		
	24	Male	3	2		
	25	Male	2	2		
	26	Female	3	3		
	27	Female	2	2		
	28	Female	3	3		
	29	Female	3	2		
	30	Female	2	2		

QUALITY ASSURANCE STATEMENT

Client: Dow Corning Corp.

Testing Laboratory:

Test Article and Lot Number:
Test Article: Dow Corning® 4-2797INT (X7-9192)
Lot #:

The study listed above conformed to the best of my knowledge to the current FDA GLP regulations, 21 CFR, Part 58.

Signature of Authorized Personnel

_____ 03/13/91
Quality Assurance Date

QUALITY ASSURANCE INSPECTIONS	MANAGEMENT REPORTS	STUDY DIRECTOR REPORTS
01/09/91	01/09/91	01/09/91
03/13/91	03/13/91	03/13/91

Report No:	**1998-I0000-44651**
Title:	**SKIN SENSITIZATION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)**
Study No:	
External Testing Facility No:	
Test Substance:	**Dow Corning® 60,000CST, NO CO-SOLVENT**
Study Director:	**Research Toxicologist**
Author(s):	**Research Toxicologist** **Technical Editor**
Sponsor:	**Dow Corning Corporation**
Sponsor Representative:	**Associate Toxicology Scientist**
Testing Facility:	
Study Completion Date:	**April 28, 1998**
Security Classification:	

TABLE OF CONTENTS

ABSTRACT

The purpose of this study was to determine the dermal sensitizing potential of Dow Corning® 60,000CST, NO CO-SOLVENT using the Guinea Pig Maximization Test (GPMT).

This study was performed using OECD Guidelines for Testing of Chemicals (Part 406, July, 1992) and according to U.S. EPA Good Laboratory Practice Standards set forth in Part 792 (TSCA) of Title 40 of the Code of Federal Regulations, Final Rule, August 17, 1989 and the OCDE/GD (92)32.

Dow Corning® 60,000CST, NO CO-SOLVENT was administered in Dow Corning® 360 Medical Fluid (5% w/v) by intradermal (i.d.) injection to the shaved shoulder region of twenty male guinea pigs. Another group of ten male vehicle control guinea pigs was handled in a similar manner, but was treated (i.d.) with Dow Corning® 360 Medical Fluid only. A third group of ten male guinea pigs was treated (i.d.) with DNCB in propylene glycol (0.1% w/v) and served as a positive control. On Day 7 of the study, the area over the intradermal injection sites of the test and vehicle control groups was treated with 10% sodium lauryl sulfate in petrolatum. One week following injection of the first induction dose (Day 8), a second induction dose of undiluted test substance was applied topically to the test group for 48 hours. Animals in the vehicle control and positive control groups were dosed (topical application) on the same day with Dow Corning® 360 Medical Fluid and DNCB, respectively. Three weeks following the first induction dose (Day 22), test and vehicle control guinea pigs received a topical challenge dose of undiluted test substance for 24 hours. Positive control guinea pigs were similarly dosed with DNCB in propylene glycol. All guinea pigs were scored for erythema and edema according to the Draize scale 24 and 48 hours following the challenge dose. The results of the challenge were expressed in terms of the incidence and severity of the skin response, with an erythema and/or edema score of 1 or greater being considered a positive response.

All ten positive control animals (100%) exhibited a positive reaction at the DNCB challenge site. None of the twenty (0%) test substance-treated nor the ten vehicle control (0%) animals exhibited a positive reaction at either the 24- or 48-hour scoring interval. Therefore, under the conditions of testing and according to the modified scoring rating of Magnusson, B. and Kligman, A.M., *J. Invest. Dermatology*, 1969, Dow Corning® 60,000CST, NO CO-SOLVENT was not considered a skin sensitizer in guinea pigs.

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with U.S. Environmental Protection Agency (EPA) Good Laboratory Practice (GLP) Standards as set forth in the *Code of Federal Regulations* (Part 792 of Title 40; TSCA) and OCDE/GD (92)32 with the following exceptions: (1) No analyses were performed to determine the concentration, homogeneity (as appropriate) and stability of the test and positive control dosing formulations and (2) Reserve samples of FCA, DNCB and propylene glycol will not be retained. Records pertaining to the characterization of the bulk test substance and Dow Corning® 360 Medical Fluid were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The various vehicle and control substances used in the study were purchased materials and, as such, were considered characterized by their labelling and/or by vendor provided documentation. The study data have been reviewed by the Study Director, who certifies that the information contained in this report is consistent with and supported by the study raw data.

4/28/98

Date

Study Director
Life Sciences Operation

QUALITY ASSURANCE STATEMENT

Study Title: Skin Sensitization Study of Dow Corning® 60,000CST, NO CO-SOLVENT Using the Guinea Pig Maximization Test (GPMT)

Project Number:

Study Number: 22

Study Director:

This study has been subjected to inspections and the report has been audited by the Quality Assurance Unit in accordance with the U.S. Environmental Protection Agency (EPA) Good Laboratory Practice (GLP) Standards "CFR Title 40 Section 792.35" and OCDE/GD (92)32. The report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

The following are the inspection dates and the dates inspection findings were reported:

		Findings Reported To:	
Date of Inspection	Study Phase	Study Director	Management
July 11, 14, 16, 1997	Draft protocol review	July 16, 1997	July 16, 1997
November 11, 1997	Revised draft protocol review	November 11, 1997	November 11, 1997
November 25, 1997	Test/control substance i.d. administration	November 25, 1997	November 25, 1997
December 2, 1997	Test substance preparation	December 2, 1997	December 2, 1997
December 10, 1997	Protocol amendment #1 review	December 10, 1997	December 10, 1997
December 16, 1997	First challenge dose	December 16, 1997	December 16, 1997
December 18, 1997	24 hour scoring	December 18, 1997	December 18, 1997
January 27-29, 1998	Draft report/raw data audit	January 29, 1998	January 29, 1998

4/28/98
Date

Manager, Quality Assurance

APPROVAL SIGNATURES

This report consists of Pages 1 through 24 including Tables 1 and 2 and Appendices 1 through 5.

4/28/98
Date

Research Toxicologist
Life Sciences Operation
Study Director

4/28/98
Date

Manager, Regulatory Toxicology
Life Sciences Operation

4/20/98
Date

Associate Toxicology Scientist
Sponsor Representative

STUDY INFORMATION

Study Initiation Date:	November 21, 1997
Experimental Start Date:	November 17, 1997
Experimental Termination Date:	December 19, 1997
Study Completion Date:	April 28, 1998
Study Director:	
Sponsor:	Dow Corning Corporation
Sponsor Representative:	
Study Personnel:	
Report Preparation:	

SKIN SENSITIZATION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

I. INTRODUCTION

The purpose of this study was to determine the dermal sensitization potential of DOW CORNING® 60,000CST, NO CO-SOLVENT in guinea pigs by use of the Guinea Pig Maximization Test (GPMT).

II. MATERIALS AND METHODS

A. Test and Control Substances: Dow Corning® 60,000CST, NO CO-SOLVENT, Lot No. was received October 3, 1997. The test substance was a colorless, viscous liquid and was stored at room temperature in the original container. The Material Safety Data Sheet (MSDS) indicated that the test substance is stable. Records pertaining to the characterization of the bulk test substance and vehicle (Dow Corning® 360 Medical Fluid) were the responsibility of the Sponsor, and are maintained at the address indicated for the Sponsor. The test substance vehicle was chosen because it was completely soluble in the test substance and it was non-irritating to the skin of guinea pigs. All remaining test substance will be returned to the Sponsor after completion of all relevant studies. Characterization of the 0.9% Sodium Chloride Injection, USP (0.9% saline), positive control substance (1-chloro-2,4-dinitrobenzene; DNCB), Freund's Complete Adjuvant (FCA), petrolatum, sodium lauryl sulfate (SLS) and propylene glycol was provided by the vendors.

B. Dosage Formulations: The following were used to prepare the dosing formulations used in this study: (1) the test substance (TS); (2) Dow Corning® 360 Medical Fluid, Lot No. (3) FCA (4) DNCB ; (5) 0.9% sodium chloride injection (saline) ; and (6) propylene glycol (PG) In this study, Dow Corning® 360 Medical Fluid was used as the vehicle and 0.9% saline was used as the diluent for FCA. The animals were dosed with one or more of the following formulations: 5% (w/v) test substance in Dow Corning® 360 Medical Fluid; undiluted test substance; 5% (w/v) test substance in 0.9% saline and FCA (1:1); 0.9% saline in FCA (1:1); undiluted Dow Corning® 360 Medical Fluid; 5% (w/v) Dow Corning® 360 Medical Fluid in FCA and 0.9% saline; 0.1% DNCB in propylene glycol; 0.1% DNCB in FCA

and 0.9% saline (1:1); undiluted propylene glycol. Dosing formulations were prepared at four separate times: (1) for preliminary range-finding studies; (2) for the first (intradermal) induction; (3) for the second (topical) induction; and, (4) for the challenge dose.

In a range-finding intradermal toxicity test, 0.1 ml i.d. injections of 2% and 5% test substance in Dow Corning® 360 Medical Fluid were tolerated both locally and systemically by two guinea pigs. Based on these findings, 5% was considered to be the appropriate test substance concentration for the i.d. induction (Appendix 3). For the range-finding topical toxicity test, 0.3 ml of various concentrations (*i.e.*, 25%,50%, 75% and 100%) of test substance in Dow Corning® 360 Medical Fluid applied under Hill Top Chambers to shaved skin sites for 48 hours produced no erythema and/or edema among four guinea pigs used (Appendix 3). Based on these results, 100% concentration (undiluted) was considered to be appropriate for both the topical induction and challenge applications. Various formulations were vortexed during preparation to ensure thorough mixing. Formulations of DNCB in both propylene glycol and FCA were sonicated to dissolve material.

C. Animals: Male Hartley guinea pigs, approximately 4 weeks of age were received from on November 12, 1997. A sample (9 of 88 guinea pigs received) weighed between 257 and 289 g the following day. Upon arrival, the animals were held in quarantine for approximately two weeks during which time they were observed daily for survival and at the end of the quarantine period examined carefully to ensure their health and suitability as test subjects. Guinea pigs selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number. This particular test system and the specific route by which the test substance was administered were chosen for the following reasons: 1) the guinea pig is typically the animal model of choice for evaluating the dermal sensitization potential of a test substance; and 2) dermal application corresponds to a potential route by which humans may be exposed to the test substance. The number of animals used for this study was based upon guideline requirements.

D. Food and Water: Certified Purina Guinea Pig Chow #5026 and City of Chicago water, supplied by means of an automatic watering system, were available *ad libitum*. No contaminants capable of adversely affecting the integrity

or interpretation of the results from this study were known to be present in the basal diet or the drinking water during the conduct of the study.

E. Housing and Environment: The guinea pigs were housed individually in stainless steel wire cages measuring approximately 24 x 18 x 40 cm and suspended over excrement pans. Absorbent liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the treatment phase of the study, the animal room was maintained at a temperature range of 20.5 to 22.5°C and a relative humidity range of 41.5 to 71.0%. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness. This study was conducted in the Toxicology Facility (animal room #24) of the Life Sciences Research Building (LSR). The minimum number of air changes in the animal room was 10 changes per hour.

F. Methods:

1. Animals: Guinea pigs selected for testing were assigned to three groups: a test group of 20 males, a vehicle control group of 10 males, and a positive control group of 10 males. Group assignments were made using an in-house developed computerized randomization procedure constrained by body weight (RANSD.EXE).

2. Skin Preparation: The guinea pigs were clipped free of hair prior to each induction and before the challenge dose. The animals were also depilated with Neet® Hair Remover approximately 3 hours before the 24-hour scoring of the challenge.

3. Dosing:

   a. First Induction: On November 25, 1997 (Day 1), the fur over the scapula of each animal in an area of approximately 4 x 6 cm was shaved and six intradermal injections (three pairs) of 0.1 ml of the dosing formulations were made flanking the dorsal midline according to the following scheme:

	Test Substance (N = 20)			Vehicle Control (N = 10)			Positive Control (N = 10)	
	(Left)	(Right)		(Left)	(Right)		(Left)	(Right)
1[a]	TS/V[b]	TS/V	1	V	V	1	DNCB/PG	DNCB/PG
2	saline[c]/FCA	saline/FCA	2	saline/FCA	saline/FCA	2	saline/FCA	saline/FCA
3	TS/saline/FCA	TS/saline/FCA	3	V/FCA/saline	V/FCA/saline	3	DNCB/FCA/saline	DNCB/FCA/saline

[a] = site
[b] V = Vehicle (Dow Corning® 360 Medical Fluid)
[c] saline = 0.9% saline

b. Second Induction: Due to the absence of erythema and/or edema in the topical range-finding studies, animals in the test and vehicle control group were treated with 0.5 ml of 10% sodium lauryl sulfate (SLS)

in petrolatum

on Day 7 (December 1, 1997), one day prior to the second induction. The SLS was massaged into the skin of the animals with a glass rod. On Day 8 (December 2, 1997), the same region of each animal was again shaved and a 2 x 4 cm Webril® Appli-Pad was saturated (1.5 ml) with undiluted test substance and applied topically over the six i.d. injection sites of each test substance-treated animal. Vehicle control animals were similarly dosed with undiluted vehicle (Dow Corning® 360 Medical Fluid), while positive control animals were similarly dosed with 0.1% DNCB in PG. The animals were then wrapped with an elastic adhesive bandage

All wrapping materials were removed approximately 48 hours after application.

c. Challenge: On Day 22 (December 16, 1997), two weeks following application of the last induction dose, 0.3 ml of undiluted test substance was applied to the shaved upper left flank and 0.3 ml of undiluted Dow Corning® 360 Medical Fluid was applied to the shaved upper right flank of each of the twenty test substance-treated guinea pigs. Vehicle control guinea pigs also received a challenge dose of 0.3 ml of undiluted test substance applied to the upper left flank and 0.3 ml of undiluted Dow Corning® 360 Medical Fluid applied to the upper right flank. Positive control animals received 0.3 ml of 0.1% DNCB/PG applied to the upper left flank and undiluted PG applied to the upper right flank. The dosing material for the challenge doses were applied using Hilltop

Chambers® and the animals were wrapped with an adhesive bandage (Elastoplast®). All wrapping materials were removed approximately 24 hours after the challenge dose. The application sites of the test and vehicle control groups were wiped with Dow Corning® 360 Medical Fluid-moistened gauze to remove excess test substance. The application sites of the positive control group were wiped with propylene glycol-moistened gauze to remove excess DNCB.

4. Skin Examination: Twenty-four (24) and 48 hours following removal of the wrappings after the challenge dose (Days 24 and 25), the test sites were scored for erythema and edema according to the Draize scale (Appendix 1). To facilitate scoring, all animals were depilated with Neet® Hair Remover approximately 3 hours prior to the 24-hour scoring.

5. Observations: All guinea pigs were observed at least once daily for mortality and moribundity during the treatment period of the study.

6. Body Weights: Animals were weighed weekly.

7. Animal Disposition: After the final skin scoring (December 19, 1997), all guinea pigs were euthanized by carbon dioxide asphyxiation and discarded without necropsy.

G. Evaluation: Results obtained from each of the test substance-exposed animals were compared within the test substance group and between the test substance and vehicle control groups. The results of the challenge were expressed in terms of the incidence and severity of the skin response (*i.e.*, erythema and/or edema scores). An incidence index (%) was calculated by dividing the number of animals with responses of a score of 1 or greater at 24 and 48 hours by the number of animals tested and multiplying by 100. The severity index is the sum of the skin scores divided by the number of animals tested. A comparison of the reactions elicited in terms of incidence, severity, and duration between the vehicle control and treated groups was made to determine whether the test substance induced sensitization. The test substance was then classified according to its allergic potential using the modified scoring rating of Magnusson, B. and Kligman, A.M. (Appendix 1).

H. Deviations: Deviations or circumstances known to have occurred during the conduct of this study and their effect, if any, on the quality or integrity of the data from this study are described in Appendix 5.

I. Archives: All original data generated at and the signed original final report will be retained in the for five years from the date of this report. At that time, the Sponsor will be contacted in order to determine final disposition of the raw data.

III. RESULTS

A. Mortality: No deaths occurred during the study.

B. Skin Effects: A summary of the observations after intradermal administration and erythema scores after topical application for preliminary testing of the test substance is presented in Appendix 3. Individual erythema and edema scores after challenge are presented in Appendix 2. Erythema scores are summarized as incidence and severity indices in Table 1. All of the DNCB-treated animals (positive control) exhibited a positive response at the DNCB challenge site, resulting in a 24- and 48-hour incidence index of 100% and a severity index of 3.60. None of the test substance-treated nor vehicle control animals exhibited a positive response at any time during the study and, therefore, the incidence and severity indices for these groups were equal to zero.

C. Body Weights: Individual body weights are presented in Appendix 4 and a summary of mean body weights is presented in Table 2. All animals gained weight during the study.

D. Statistics: Statistical analyses were limited to the calculation of group mean body weights and standard deviations and cumulative body weight change.

IV. CONCLUSIONS

All 10 positive control animals exhibited a positive response (*i.e.*, erythema scores of 1 or more) during the study; therefore, the test system was considered valid. Since no positive responses were observed with the test substance during the study, Dow Corning® 60,000CST, NO CO-SOLVENT, under the conditions of testing, was not considered a skin sensitizer in guinea pigs.

V. TABLES

SKIN SENSITIZATION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

TABLE 1

Summary of Incidence and Severity Indices After Challenge

	Treated Group	
	24 hours	48 hours
Incidence[a] index		
Left side	0/20 (0%)	0/20 (0%)
Right side	0/20 (0%)	0/20 (0%)
Severity[b] index		
Left side	0/20 (0)	0/20 (0)
Right side	0/20 (0)	0/20 (0)

	Vehicle Control Group	
	24 hours	48 hours
Incidence index		
Left side	0/10 (0%)	0/10 (0%)
Right side	0/10 (0%)	0/10 (0%)
Severity index		
Left side	0/10 (0)	0/10 (0)
Right side	0/10 (0)	0/10 (0)

	Positive Control Group	
	24 hours	48 hours
Incidence index		
Left side	10/10 (100%)	10/10 (100%)
Right side	0/10 (0%)	0/10 (0%)
Severity index		
Left side	36/10 (3.60)	36/10 (3.60)
Right side	0/10 (0)	0/10 (0)

[a] Number of animals showing a positive score (erythema and/or edema response of 1 or greater) at that site ÷ total number of animals in the group x 100

[b] Sum of the erythema scores for the site ÷ total number of animals in the group

SKIN SENSITIZATION STUDY OF DOW CORNING® 60,000CST, NO CO-SOLVENT USING THE GUINEA PIG MAXIMIZATION TEST (GPMT)

TABLE 2

Summary of Mean Body Weights (g)

		Week 0	Week 1	Week 2	Week 3	Gain[a]
Test Substance-Treated	Mean	375	418	439	496	121
	Std. Dev.	18.3	24.8	29.4	38.1	24.9
	N[b]	20	20	20	20	20
Vehicle Control	Mean	357	391	415	469	112
	Std. Dev.	12.2	22.5	21.8	31.1	21.9
	N	10	10	10	10	10
Positive Control	Mean	354	394	411	466	112
	Std. Dev.	17.1	24.6	27.3	38.2	29.8
	N	10	10	10	10	10

[a] Total Gain = Week 3 - Week 0
[b] N = number of animals

DOW CORNING CORPORATION
Toxicology Department

GENETIC EVALUATION OF DOW CORNING® Q4-2797* IN BACTERIAL REVERSE MUTATION ASSAYS

Reference No.:

File No.:

Reference No.: TX-85-0130-65

Series No.: I-0005-1345

Authors:

GLP/QAU:

Submitted By:

Reported By:

Checked By:

Date: April 24, 1985

This summary of data and conclusions is based upon the sample received. Additional studies may be required as specific uses and formulations are developed or if process changes occur.

ABSTRACT

The test material was evaluated for genetic activity in the Salmonella typhimurium and Escherichia coli Reverse Mutation assays as outlined in "O.E.C.D. Guidelines for Testing of Chemicals" - Draft Protocol Nos. 419 and 420. No evidence of genetic activity was observed.

Distribution

TABLE OF CONTENTS

OBJECTIVE

The objective of this study was to evaluate the test material for genetic activity in the Salmonella typhimurium and Escherichia coli Reverse Mutation Assays as outlined in O.E.C.D. GUIDELINES FOR TESTING OF CHEMICALS (CRF 46 (162)/8-21-81) as part of the Minimum Premarket Data Set for new chemicals.

MATERIALS

A. Test Material

TX-85-0130-65

B. Indicator Microorganisms

Salmonella typhimurium, str.	TA-1535	TA-98
	TA-97	TA-100
Escherichia coli, str.	WP2	

C. Activation System

Bacteria were exposed to the test substance both in the presence and absence of a mammalian activation mixture (S-9 mix) prepared in accordance with published protocols (Ames, et al., 1975; Matsushima, et al., 1976).

1. Component

Component	Final Concentration/ml
$MgCl_2$	8 µ moles
KCl	33 µ moles
NADP	4 µ moles
Glucose-6-phosphate	5 µ moles
Sodium phosphate, pH 7.4	100 µ moles
Homogenate fraction equivalent to 25 mg of wet tissue	

2. S-9 Homogenate

A 9000 x g supernatant prepared from Sprague-Dawley adult male rat liver induced by AROCLOR 1254 five days prior to kill. Purchased from Litton-Bionetics, Inc., Kensington, Maryland. Stored until use at $-76^{o}C$.

D. Positive Control Chemicals

Chemicals used for positive controls in the non-activation and activation assays.

Assay	Chemical*	Solvent**
Non-activation	Sodium Azide (AZ)	Water or Saline
	4-Nitroquinoline-N-oxide (NQNO)	Dimethylsulfoxide
	Daunomycin (D)	Water
	N-Methyl-N-nitro-N-nitrosoquanidine (MNNG)	Water
Activation	2-Anthramine (ANTH)	Dimethylsulfoxide
	2-Aminofluorene (AF)	Dimethylsulfoxide

*Concentrations given in Results section.
**Previously shown to be non-mutagenic.

E. Solvent

Dimethylsulfoxide (DMSO) was used to prepare dilutions of the test material. The solvent employed and concentrations of chemicals are recorded in the Results section.

EXPERIMENTAL DESIGN

A. Principle of the Test Method

Bacteria are exposed to test chemical with and without metabolic activation and plated on minimal medium. After a suitable period of incubation, revertant colonies are counted and compared to the number of spontaneous revertants in an untreated (solvent) control culture. Positive and negative (solvent) controls are included in each experiment.

B. Description of the Test Method

Five different amounts of test chemical separated by half-log intervals were tested (de Serres and Shelby, 1979). Substances were tested up to the limit of solubility or toxicity. Toxicity may be evidenced by a reduction in the number of spontaneous revertants, a clearing of the background lawn or by degree of survival of treated cultures. Nontoxic chemicals are tested to 5 mg/plate before considering the test substance negative.

Plates were incubated for 72 hours at 37°C.

1. Direct Plate Incorporation Method

Nonactivation Assay

To a sterile 13 x 100 mm test tube placed in a 43°C water bath, the following is added in order:

. 2.00 ml of 0.6% agar containing:

0.05 mM histidine and 0.05 mM biotin (Salmonella Assay)
0.05 mM tryptophan (Escherichia coli Assay)

. 0.05 ml of a solution of the test chemical to give the appropriate dose.

. 0.01 ml - 0.2 ml of indicator organism/s.

. 0.50 ml of 0.2M phosphate buffer, pH 7.4.

This mixture is swirled gently and then poured over the surface of minimal agar plates. After the top agar has set, the plates are incubated at 37°C for 72 hours. The number of revertant colonies growing in the plates is counted and recorded.

Activation Assay

The activation assay is run concurrently with the nonactivation assay. The only difference is the addition of 0.5 ml of S-9 mix to the tubes in place of 0.5 ml of phosphate buffer which is added in nonactivation assays. All other details are similar to the procedure for nonactivation assays.

All plating was done in triplicate.

RESULTS

A. Spot Plate Test

The test material was negative against all testor strains, with and without metabolic activation.

B. Overlay Plate Test

See attached Tables I-V for results. Solvent of choice and concentrations of material tested are given in the tables. No evidence of mutagenic potential was observed.

DATA

A. Data Presentation

The data are presented as the number of revertant colonies per plate. The number of revertant colonies on both negative (solvent) and positive control plates are also presented.

Individual plate counts, the mean number of revertant colonies per plate and standard deviation are presented for test chemical and positive and negative (solvent) controls.

B. Statistical Evaluation

Data was evaluated using appropriate statistical methods.

C. Results

Because the test article and the cells are incubated in the overlay for approximately two days and a few cell divisions occur during the incubation period, the test is semiquantitative in nature. Although these features of the assay reduce the quantitation of results, they provide certain advantages not contained in a quantitative suspension test:

- The small number of cell divisions permits potential mutagens to act on replicating DNA, which is often more sensitive than nonreplicating DNA.
- The combined incubation of the test article and the cells in the overlay permits constant exposure of the indicator cells for approximately two days.

1. Surviving Populations

Plate test procedures do not permit exact quantitation of the number of cells surviving chemical treatment. At low concentrations of the test article, the surviving population on the treatment plates is essentially the same as that on the negative control plate. At high concentrations, the surviving population is usually reduced by some fraction. Our protocol employs several doses ranging over two or three log concentrations.

2. Dose-Response Phenomena

The demonstration of dose-related increases in mutant counts is an important criterion in establishing mutagenicity. A factor that might modify dose-response results for a mutagen would be the selection of doses that are too low (usually mutagenicity and toxicity are related). If the highest dose is far lower than a toxic concentration, no increases may be observed over the dose range selected. Conversely, if the lowest dose employed is highly cytotoxic, the test article may kill any mutants that are induced, and the test article will not appear to be mutagenic.

3. Control Tests

Positive and negative control assays are conducted with each experiment and consist of direct-acting mutagens for nonactivation assays and mutagens that require metabolic biotransformation in activation assays. Negative controls consist of the test article solvent in the overlay agar together with the other essential components. The negative control plate for each strain gives a reference point to which the test data is compared. The positive control assay will be conducted to demonstrate that the test systems are functional with known mutagens.

4. Evaluation Criteria for Toxicity

Complete Toxicity

When there are no revertants observed on the plate(s) treated with the test compound, the test compound will be defined as toxic to all or any of the indicator strains at that (those) particular dose(s).

Slight Toxicity

When there are fifty percent or less number of revertants on the plate(s) treated with the test compound as compared to the solvent plate(s), the test compound will be defined as slightly toxic to all or any of the indicator strains at that (those) particular dose(s).

5. Evaluation Criteria for Ames Assay

Because the procedures to be used to evaluate the mutagenicity of the test article are semiquantitative, the criteria to be used to determine positive effects are inherently subjective and are based primarily on a historical data base. Most data sets are evaluated using the criteria established by K. C. Chu, et al., (1981), Mutation Res., 119-132.

If the solvent control value is within the normal range, a chemical that produces a positive dose response over three concentrations with the lowest increase equal to twice the solvent control value is considered to be mutagenic.

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This report constituted of pages 1-10, and Tables I-V, signed this 8th day of April, 1985.

Authors: [signature]

Principal Investigator/Study Director

[signature]

Genetic Toxicologist

Approved By: [signature]

Toxicology Department

Typed By:

[signature]

QUALITY ASSURANCE STATEMENT

This report represents data generated by the Toxicology Department, Dow Corning Corporation, This study was conducted according to EPA Toxic Substances Control; Good Laboratory Practices Regulations; 40 CFR, Part 797, Vol. 48, No. 230. The results reported accurately reflect the data generated. All raw data is located at

Study Started:	February 1, 1985
Study Completed:	February 4, 1985
Date Audited:	February 1, 1985 and February 4, 1985
Report Issued:	April 24, 1985

Quality Assurance
Health & Environmental Sciences

April 8, 1985
Date:

TABLE I

TEST MATERIAL : TX-85-0130-65 PREPARED BY:
INITIATION DATE: 2-1-85

NONACTIVATION TEST--TA-1535

REVERTANTS PER PLATE	SOLV CON	POS* CON	CONC.OF TEST COMPOUND (UG/PLATE) 312.5	625.0	1250	2500	5000
PLATE 1	16	352	21	22	21	27	22
PLATE 2	20	317	19	20	19	17	20
PLATE 3	19	412	17	18	21	19	20
MEAN	18	360	19	20	20	21	20
S.D.	2	48	2	2	1	5	1

ACTIVATION TEST--TA-1535

PLATE 1	22	378	23	16	22	23	27
PLATE 2	20	291	19	20	18	24	20
PLATE 3	20	312	20	17	20	16	19
MEAN	20	327	20	17	20	21	22
S.D.	1	45	2	2	2	4	4

****

* NONACTIVATION AZ 10 UG/PLATE
ACTIVATION ANTH 10 UG/PLATE
SOLVENT DMSO 50 UL/PLATE

***

TABLE II

TEST MATERIAL : TX-85-0130-65 PREPARED BY:
INITIATION DATE: 2-1-85

NONACTIVATION TEST--TA-97

REVERTANTS PER PLATE	SOLV CON	POS* CON	CONC.OF TEST COMPOUND (UG/PLATE) 312.5	625.0	1250	2500	5000
PLATE 1	115	436	122	117	128	124	114
PLATE 2	111	452	120	124	130	119	112
PLATE 3	98	461	118	136	122	117	122
MEAN	108	449	120	125	126	120	116
S.D.	8	12	2	9	4	3	5

ACTIVATION TEST--TA-97

PLATE 1	122	697	128	128	124	119	120
PLATE 2	119	714	124	130	119	124	119
PLATE 3	126	732	119	133	122	120	116
MEAN	122	714	123	130	121	121	119
S.D.	3	17	4	2	2	2	1

****

* NONACTIVATION	NQNO	10	UG/PLATE
ACTIVATION	AF	10	UG/PLATE
SOLVENT	DMSO	50	UL/PLATE

***

TABLE III

TEST MATERIAL : TX-85-0130-85 PREPARED BY:
INITIATION DATE: 2-1-85

NONACTIVATION TEST--TA-98

REVERTANTS PER PLATE	SOLV CON	POS* CON	CONC.OF TEST COMPOUND (UG/PLATE) 312.5	625.0	1250	2500	5000
PLATE 1	33	368	36	31	30	29	32
PLATE 2	34	412	34	27	32	34	27
PLATE 3	30	352	34	36	28	30	24
MEAN	32	377	34	31	30	31	27
S.D.	2	31	1	4	2	2	4

ACTIVATION TEST--TA-98

PLATE 1	41	819	46	48	50	44	43
PLATE 2	44	836	48	44	37	40	38
PLATE 3	50	853	39	46	41	42	36
MEAN	45	836	44	46	42	42	39
S.D.	4	17	4	2	6	2	3

********** **********

* NONACTIVATION D 10 UG/PLATE
ACTIVATION AF 10 UG/PLATE
SOLVENT DMSO 50 UL/PLATE

***

TABLE IV

TEST MATERIAL : TX-85-0130-65 PREPARED BY:
INITIATION DATE: 2-1-85

NONACTIVATION TEST--TA-100

REVERTANTS PER PLATE	SOLV CON	POS* CON	CONC.OF TEST COMPOUND (UG/PLATE) 312.5	625.0	1250	2500	5000
PLATE 1	125	516	133	124	128	117	120
PLATE 2	131	548	137	135	121	129	117
PLATE 3	142	612	129	130	147	133	122
MEAN	132	558	133	129	132	126	119
S.D.	8	48	4	5	13	8	2

ACTIVATION TEST--TA-100

PLATE 1	163	796	137	141	123	165	171
PLATE 2	153	772	157	138	142	174	155
PLATE 3	147	812	158	151	147	158	161
MEAN	154	793	150	143	137	165	162
S.D.	8	20	11	6	12	8	8

****

* NONACTIVATION AZ 10 UG/PLATE
ACTIVATION AF 10 UG/PLATE
SOLVENT DMSO 50 UL/PLATE

***

TABLE V

TEST MATERIAL : TX-85-0130-65 PREPARED BY:
INITIATION DATE: 2-1-85

NONACTIVATION TEST--WP2

REVERTANTS PER PLATE	SOLV CON	POS* CON	CONC.OF TEST COMPOUND (UG/PLATE) 312.5	625.0	1250	2500	5000
PLATE 1	24	236	30	35	26	26	28
PLATE 2	24	242	34	30	34	30	30
PLATE 3	28	222	31	28	29	30	24
MEAN	25	233	31	31	29	28	27
S.D.	2	10	2	3	4	2	3

ACTIVATION TEST--WP2

PLATE 1	47	501	57	37	34	40	45
PLATE 2	51	478	43	42	30	36	42
PLATE 3	43	484	46	38	29	33	40
MEAN	47	487	48	39	31	36	42
S.D.	4	11	7	2	2	3	2

****

* NONACTIVATION	MNNG	10	UG/PLATE
ACTIVATION	ANTH	10	UG/PLATE
SOLVENT	DMSO	50	UL/PLATE

***

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

Final Report

Report No.: **1998-I0000-44378**

Title: **Genetic Evaluation of Dow Corning® 60,000CST, NO CO-SOLVENT in a Bacterial Reverse Mutation Assay**

Study No.:

External Testing Facility No.:

Test Article: **Dow Corning® 60,000CST, No Co-Solvent, Lot No.**

Study Director:

Authors:

Sponsor: **Dow Corning Corporation**
2200 W. Salzburg Road
Auburn, MI 48611

Study Monitor:

Testing Facility:

Study Completion Date: **May 6, 1998**

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

TABLE OF CONTENTS

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

ABSTRACT

The test article, Dow Corning® 60,000CST, No Co-Solvent, Lot No. was tested in the bacterial reverse mutation assay using *S. typhimurium* tester strains TA98, TA100, TA1535 and TA1537 and *E. coli* tester strains WP2 *uvr*A and WP2 *uvr*A (pKM101) in the presence and absence of Aroclor-induced rat liver S9. The assay was performed in two phases, using the preincubation method. The first phase, the preliminary toxicity assay, was used to establish the dose range for the mutagenicity assay. The second phase, the mutagenicity assay (initial and independent repeat assays), was used to evaluate the mutagenic potential of the test article.

Dow Corning® OS-10, (hexamethyldisiloxane), supplied by the Sponsor, was selected as the solvent of choice based on solubility (performed by the Sponsor) of the test article and compatibility with the target cells. Since the solvents listed on page 10 did not yield a soluble or workable concentration the Sponsor provided solubility information as noted.

In the preliminary toxicity assay, the maximum dose tested was 5000 μg per plate; this dose was achieved using a concentration of 200 mg/mL and a 25 μL plating aliquot. The test article was soluble in Dow Corning® OS-10 at 200 mg/mL, the maximum concentration tested. Precipitate was observed at ≥333 or at ≥667 μg per plate but no appreciable toxicity was observed. Based on the findings of the toxicity assay, the maximum dose plated in the mutagenicity assay was 5000 μg per plate.

In the mutagenicity assay no positive response was observed. Precipitate was observed at ≥500 or at ≥1500 μg per plate but no appreciable toxicity was observed. The overall evaluation and dose ranges tested are as follows:

S9 Activation	Overall Evaluation* and Dose Range Tested (μg/plate)											
	TA98		TA100		TA1535		TA1537		WP2 *uvr*A		WP2 *uvr*A (pKM101)	
	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High
None	-		-		-		-		-		-	
	50	5000	50	5000	50	5000	50	5000	50	5000	50	5000
Rat	-	-	-		-		-		-		-	
	50	5000	50	5000	50	5000	50	5000	50	5000	50	5000

*-=negative, + =positive (maximum fold increase)

Under the conditions of this study, **Dow Corning® 60,000CST, No Co-Solvent, Lot** was considered nonmutagenic in this Bacterial Reverse Mutation Assay.

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

STATEMENT OF COMPLIANCE

Study No. was conducted in compliance with the U.S. EPA GLP Standards 40 CFR 792 in all material aspects with the following exceptions:

> The identity, strength, purity and composition or other characteristics to define the test or control article have not been determined by the testing facility.
>
> Analyses to determine the uniformity, concentration, or stability of the test or control mixtures were not performed by the testing facility.
>
> The stability of the test or control article under the test conditions has not been determined by the testing facility.

Confirmatory analyses of the test article were conducted by the Sponsor and the records for these analyses are located at the address indicated for the Sponsor.

_____ 6-May-1998
Date

Study Director

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

QUALITY ASSURANCE STATEMENT

Study Title: GENETIC EVALUATION OF DOW CORNING® 60,000CST, NO CO-SOLVENT IN A BACTERIAL REVERSE MUTATION ASSAY

Study Number:

Study Director:

This study has been divided into a series of in-process phases. Using a random sampling approach, Quality Assurance monitors each of these phases over a series of studies. Procedures, documentation, equipment records, etc. are examined in order to assure that the study is performed in accordance with the the U.S. EPA GLPs (40 CFR 792) and to assure that the study is conducted according to the protocol.

The following are the inspection date, phases inspected, and report dates of QA inspections of this study.

INSPECT ON 31 OCT 97, TO STUDY DIR 31 OCT 97, TO MGMT 04 NOV 97
PHASES: PROTOCOL REVIEW

INSPECT ON 14 NOV 97, TO STUDY DIR 14 NOV 97, TO MGMT 14 NOV 97
PHASES: STRAIN CHARACTERIZATION

INSPECT ON 20 NOV 97, TO STUDY DIR 20 NOV 97, TO MGMT 20 NOV 97
PHASES: PREPARATION OF S9 MIXTURE

INSPECT ON 27 DEC 97, TO STUDY DIR 29 DEC 97, TO MGMT 09 JAN 98
PHASES: DATA AND DRAFT REPORT AUDIT

INSPECT ON 23 APR 98, TO STUDY DIR 23 APR 98, TO MGMT 23 APR 98
PHASES: DRAFT TO FINAL REPORT

This report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

5-6-98
Date

Quality Assurance Unit

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

APPROVAL SIGNATURES

This report consists of pages 1 through 45, including Tables 1 through 28 and Appendix I.

_____ 6-May-1998
Study Director Date

_____ 5/4/98
Associate Toxicology Scientist Date
Study Monitor

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

STUDY INFORMATION

Study Initiation Date: **October 29, 1997**

Experimental In-Life Start Date: **November 14, 1997**

Experimental In-Life Termination Date: **December 9, 1997**

Study Completion Date: **May 6, 1998**

Study Director:

Sponsor: **Dow Corning Corporation**

Study Monitor:

Study Personnel:

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

PURPOSE

The purpose of this study was to evaluate the mutagenic potential of the test article (or its metabolites) by measuring its ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* tester strains WP2 *uvr*A (pKM101) and WP2 (pKM101) in the presence and absence of S9 activation.

CHARACTERIZATION OF TEST AND CONTROL ARTICLES

The test article, Dow Corning® 60,000CST, No Co-Solvent, Lot No. was received by on October 03, 1997 and was assigned the code number The test article was described by the Sponsor as a colorless, viscous liquid that should be stored in a closed container at room temperature. An expiration date of 01/24/2000 was provided. Records pertaining to the characterization of the test article and vehicle (Dow Corning® OS-10) were the responsibility of the Sponsor and are maintained at the address indicated for the Sponsor. Upon receipt, the test article was described as a clear, colorless, viscous liquid and was stored at room temperature, protected from exposure to light. At the Sponsor's request, all residual test article will be returned to the Sponsor following finalization of the report.

The vehicle used to deliver Dow Corning® 60,000CST, No Co-Solvent to the test system was Dow Corning® OS-10, (hexamethyldisiloxane, Lot No.), supplied by the Sponsor. The vehicle was received by on November 13, 1997 and was assigned the code number The vehicle was described by the Sponsor as a colorless liquid that should be stored at room temperature. An expiration date of 02/28/1999 was provided. Upon receipt, the vehicle was described as a clear, colorless liquid and was stored at room temperature.

Positive controls plated concurrently with the mutagenicity assay are listed below:

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Strain	S9 Activation	Positive Control	Concentration (μg/plate)
All *Salmonella* Strains	rat liver	2-aminoanthracene (Sigma Chemical Co.)	1.0
Both *E. coli* Strains			10
TA98	none	2-nitrofluorene (Aldrich Chemical Co., Inc.)	1.0
TA100, TA1535		sodium azide (Sigma Chemical Co.)	1.0
TA1537		9-aminoacridine (Sigma Chemical Co.)	75
Both *E. coli* Strains		methyl methanesulfonate (Aldrich Chemical Co., Inc.)	1,000

To determine the sterility of the test article, the highest test article dose level used in the mutagenicity assay was plated on selective agar with an aliquot volume equal to that used in the assay.

MATERIALS AND METHODS

Test System

The tester strains used were the *Salmonella typhimurium* histidine auxotrophs TA98, TA100, TA1535 and TA1537 as described by Ames *et al.* (1975) and *Escherichia coli* tester strains WP2 *uvr*A and WP2 *uvr*A (pKM101). *Salmonella* tester strains were received on 11/10/92 directly from
E. coli was received on 07/01/87 from the National Collection of Industrial and Marine Bacteria, Aberdeen, Scotland.

Tester strains TA98 and TA1537 are reverted from histidine dependence (auxotrophy) to histidine independence (prototrophy) by frameshift mutagens. Tester strain TA1535 is reverted by mutagens that cause basepair substitutions. Tester strain TA100 is reverted by mutagens that cause both frameshift and basepair substitution mutations. Specificity of the reversion mechanism in *E. coli* is sensitive to base-pair substitution mutations, rather than frameshift mutations (Green and Muriel, 1976).

Overnight cultures were prepared by inoculating from the appropriate master plate or from the appropriate frozen permanent stock into vessels containing ~50 mL

of culture medium. Both inoculation methods were used during the course of the study. Following inoculation, each flask was placed in a resting shaker/incubator at room temperature. The shaker/incubator was programmed to begin shaking at approximately 125 rpm at 37±2°C approximately 12 hours before the anticipated time of harvest. Each culture was monitored spectrophotometrically for turbidity and was harvested at a percent transmittance yielding a titer of approximately $1X10^9$ cells per milliliter. The actual titers were determined by viable count assays on nutrient agar plates.

Metabolic Activation System

Aroclor 1254-induced rat liver S9 was used as the metabolic activation system. The S9 was prepared from male Sprague-Dawley rats induced with a single intraperitoneal injection of Aroclor 1254, 500 mg/kg, five days prior to sacrifice. The S9 was batch prepared on 06/30/97 and 08/06/97 and stored at ≤-70°C until used. Each bulk preparation of S9 was assayed for its ability to metabolize 2-aminoanthracene and 7,12-dimethylbenz(a)anthracene to products mutagenic to *Salmonella typhimurium* TA100.

The S9 mix was prepared immediately before its use and contained 10% S9, 5 mM glucose-6-phosphate, 4 mM β-nicotinamide-adenine dinucleotide phosphate, 8 mM $MgCl_2$ and 33 mM KCl in a 100 mM phosphate buffer at pH 7.4. The Sham S9 mixture (Sham mix), containing 100 mM phosphate buffer at pH 7.4, was prepared immediately before its use. To confirm the sterility of the S9 and Sham mixes, a 0.5 mL aliquot of each was plated on selective agar.

Solubility Test

A solubility test was conducted to select the vehicle. The test was conducted using one or more of the following solvents in the order of preference as listed: purified water, dimethyl sulfoxide, ethanol, acetone, dimethylformamide, methanol. The test article was tested to determine the vehicle, selected in order of preference, that permitted preparation of the highest soluble or workable stock concentration, up to 500 mg/mL.

Preliminary Toxicity Assay

The preliminary toxicity assay was used to establish the dose-range over which the test article would be assayed. Untreated controls, vehicle controls and ten dose levels of the test article were plated, one plate per dose, with overnight cultures of TA100 and WP2 *uvr*A (pKM101) on selective minimal agar in both the presence and absence of rat liver S9 activation.

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Mutagenicity Assay

The mutagenicity assay (initial and independent repeat assays) was used to evaluate the mutagenic potential of the test article. Five dose levels of test article (5000, 1500, 500, 150 and 50 μg per plate) along with appropriate untreated, vehicle and positive controls were plated with tester strains TA98, TA100, TA1535, TA1537, WP2 *uvr*A and WP2 *uvr*A (pKM101) in the presence and absence of rat liver S9 activation. All dose levels of test article, untreated controls, vehicle controls and positive controls were plated in triplicate.

Plating and Scoring Procedures

The test system was exposed to the test article via the preincubation methodology described by Yahagi *et al.* (1977). This methodology has been shown to detect a wide range of classes of chemical mutagens (McCann *et al.*, 1975; McCann and Ames, 1976).

On the day of its use, minimal top agar, containing 0.8 % agar (W/V) and 0.5 % NaCl (W/V), was melted and supplemented with L-histidine, D-biotin and L-tryptophan solution to a final concentration of 50 μM each. Top agar not used with S9 or Sham mix was supplemented with 25 mL of water for each 100 mL of minimal top agar. For the preparation of media and reagents, all references to water imply sterile, deionized water produced by the Milli-Q Reagent Water System. Bottom agar was Vogel-Bonner minimal medium E (Vogel and Bonner, 1956) containing 1.5 % (W/V) agar. Nutrient bottom agar was Vogel-Bonner minimal medium E containing 1.5 % (W/V) agar and supplemented with 2.5 % (W/V) Oxoid Nutrient Broth No. 2 (dry powder). Nutrient Broth was Vogel-Bonner salt solution supplemented with 2.5 % (W/V) Oxoid Nutrient Broth No. 2 (dry powder).

Each plate was labeled with a code system that identified the test article, test phase, dose level, tester strain, and activation, as described in detail in Standard Operating Procedures.

Test article dilutions were prepared immediately before use. One-half (0.5) milliliter of S9 or sham mix, 100 μL of tester strain and 25 μL of vehicle or test article were added to 13 X 100 mm glass culture tubes pre-heated to 37$\pm$2°C. After vortexing, these mixtures were incubated without shaking for 60$\pm$2 minutes at 37$\pm$2°C. Following the preincubation, 2.0 mL of selective top agar was added to each tube and the mixture was vortexed and overlaid onto the surface of 25 mL of minimal bottom agar. Untreated controls were plated as above without the addition of vehicle or test article dilution. When plating the positive controls, the test article aliquot was replaced by a 50 μL aliquot of appropriate positive control. After the

overlay had solidified, the plates were inverted and incubated for approximately 48 to 72 hours at 37±2°C. Plates that were not counted immediately following the incubation period were stored at 2-8°C until colony counting could be conducted.

The condition of the bacterial background lawn was evaluated for evidence of test article toxicity by using a dissecting microscope. Precipitate was evaluated by visual examination without magnification. Toxicity and degree of precipitation were scored relative to the vehicle control plate using the codes shown below.

Code	Description	Characteristics
1	Normal	Distinguished by a healthy microcolony lawn.
2	Slightly Reduced	Distinguished by a noticeable thinning of the microcolony lawn and possibly a slight increase in the size of the microcolonies compared to the vehicle control plate.
3	Moderately Reduced	Distinguished by a marked thinning of the microcolony lawn resulting in a pronounced increase in the size of the microcolonies compared to the vehicle control plate.
4	Severely Reduced	Distinguished by an extreme thinning of the microcolony lawn resulting in an increase in the size of the microcolonies compared to the vehicle control plate such that the microcolony lawn is visible to the unaided eye as isolated colonies.
5	Absent	Distinguished by a complete lack of any microcolony lawn over ≥90% of the plate.
6	Obscured by Precipitate	The background bacterial lawn cannot be accurately evaluated due to microscopic test article precipitate.
NP	Non-Interfering Precipitate	Distinguished by precipitate on the plate that is visible to the naked eye but any precipitate particles detected by the automated colony counter total less than 10% of the revertant colony count (e.g., ≤3 particles on a plate with 30 revertants.)
IP	Interfering Precipitate	Distinguished by precipitate on the plate that is visible to the naked eye and any precipitate particles detected by the automated colony counter exceed 10% of the revertant colony count (e.g., >3 particles on a plate with 30 revertants.)

Revertant colonies for a given tester strain and activation condition were counted either entirely by automated colony counter or entirely by hand unless the assay was the preliminary toxicity assay. Plates with sufficient test article precipitate to interfere with automated colony counting were counted manually.

Evaluation of Results

For each replicate plating, the mean and standard deviation of the number of revertants per plate (Sokal and Rohlf, 1981) were calculated and are reported.

For the test article to be evaluated positive, it must cause a dose-related increase in the mean revertants per plate of at least one tester strain with a minimum of two increasing concentrations of test article. Data sets for strains TA1535 and TA1537 were judged positive if the increase in mean revertants at the peak of the dose response is equal to or greater than three times the mean vehicle control value. Data sets for strains TA98, TA100 and WP2 *uvr*A and WP2 *uvr*A (pKM101) were judged positive if the increase in mean revertants at the peak of the dose response is equal to or greater than two times the mean vehicle control value.

Criteria for a Valid Test

The following criteria must be met for the mutagenicity assay to be considered valid. All *Salmonella* tester strain cultures must demonstrate the presence of the deep rough mutation (*rfa*) and the deletion in the *uvr*B gene. Cultures of tester strains TA98, TA100, and WP2 *uvr*A (pKM101) must demonstrate the presence of the pKM101 plasmid R-factor. All WP2 *uvr*A (pKM101) cultures must demonstrate the deletion in the *uvr*A gene. All cultures must demonstrate the characteristic mean number of spontaneous revertants in the vehicle controls as follows (inclusive): TA98, 10 - 50; TA100, 80 - 240; TA1535, 5 - 45; TA1537, 3 - 21; WP2 *uvr*A, 10 - 60; WP2 *uvr*A (pKM101), 150 - 380. To ensure that appropriate numbers of bacteria are plated, tester strain culture titers must be greater than or equal to $0.3x10^9$ cells/ml. The mean of each positive control must exhibit at least a three-fold increase in the number of revertants over the mean value of the respective vehicle control. A sterility check on the most concentrated dosing solution, the Sham mix and S9 mix at the conclusion of the mutagenicity assay must yield less than two viable colonies per plate. A minimum of three non-toxic dose levels are required to evaluate assay data. A dose level is considered toxic if one or both of the following criteria are met: (1) A >50 % reduction in the mean number of revertants per plate as compared to the mean vehicle control value. This reduction must be accompanied by an abrupt dose-dependent drop in the revertant count. (2) A reduction in the background lawn.

Deviations

There were no deviations or circumstances known to have occurred during the conduct of this study that would affect the quality or integrity of the data from this study.

Archives

Upon completion of the final report, all raw data, the original protocol and the original final report will be maintained by the Quality Assurance Unit of in accordance with the relevant Good Laboratory Practices Regulations.

RESULTS AND DISCUSSION

Solubility Test

Dow Corning® OS-10, (hexamethyldisiloxane), supplied by the Sponsor, was selected as the solvent of choice based on solubility (performed by the Sponsor) of the test article and compatibility with the target cells. Since the solvents listed on page 10 did not yield a soluble or workable concentration the Sponsor provided solubility information as noted.

Preliminary Toxicity Assay

The results of the preliminary toxicity assay are presented in Tables 1 and 2. In the preliminary toxicity assay, the maximum dose tested was 5000 μg per plate; this dose was achieved using a concentration of 200 mg/mL and a 25 μL plating aliquot. The subsequent dose levels were 3333, 1000, 667, 333, 100, 67, 33 and 10 μg per plate, delivered with a 25 μL aliquot. The test article was soluble in Dow Corning® OS-10 at 200 mg/mL, the maximum concentration tested. Precipitate was observed at $\geq$333 or at $\geq$667 μg per plate but no appreciable toxicity was observed. Based on the findings of the toxicity assay, the maximum dose plated in the mutagenicity assay was 5000 μg per plate.

Mutagenicity Assay

The results of the mutagenicity assay are presented in Tables 3 through 26 and summarized in Tables 27 and 28. These data were generated in Experiments B1 and B2. Precipitate was observed at $\geq$500 or at $\geq$1500 μg per plate but no appreciable toxicity was observed. Historical vehicle and positive control data are provided in Appendix I.

In Experiment B1, the initial mutagenicity assay, no positive responses were observed with any of the tester strains in the presence and absence of S9 activation.

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

In Experiment B2, the independent repeat assay, no positive responses were observed with any of the tester strains in the presence and absence of S9 activation.

CONCLUSION

All criteria for a valid study were met as described in the protocol. The results of the Genetic Evaluation of Dow Corning® 60,000CST, No Co-Solvent in a Bacterial Reverse Mutation Assay indicate that, under the conditions of this study, **Dow Corning® 60,000CST, No Co-Solvent** did not cause a positive response with any of the tester strains in the presence and absence of Aroclor-induced rat liver S9.

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Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Preliminary Toxicity Assay

Table 1

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No. : A1
Date Plated : 11/14/97
Counted by : machine
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL

Test Article Concentration µg per plate	TA100 With S9 Activation Revertants per plate	With S9 Activation Background Code[a]	TA100 Without Activation Revertants per plate	Without Activation Background Code[a]
Untreated Control	132	1	114	1
Vehicle	145	1	101	1
10	133	1	131	1
33	121	1	109	1
67	147	1	119	1
100	142	1	135	1
333	162	1NP	109	1NP
667	155	1NP	136	1NP
1000	145	1NP	125	1NP
3333	166	1NP	142	1NP
5000	138	1NP	108	1NP

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Preliminary Toxicity Assay

Table 2

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No. : A1
Date Plated : 11/14/97
Counted by : machine
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL

Test Article Concentration µg per plate	WP2 *uvrA* (pKM101) With S9 Activation Revertants per plate	With S9 Activation Background Code[a]	Without Activation Revertants per plate	Without Activation Background Code[a]
Untreated Control	247	1	192	1
Vehicle	217	1	189	1
10	230	1	192	1
33	231	1	181	1
67	228	1	152	1
100	221	1	190	1
333	233	1NP	196	1
667	197	1NP	192	1NP
1000	220	1NP	173	1NP
3333	207	1NP	189	1NP
5000	252	1NP	220	1NP

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 3

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B1
Strain : TA98
Cells Seeded : 2.1 X 10^8
Liver Microsomes : None
Date Plated : 11/20/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	NC			
Control	02	15	1		
	03	19	1	17	3
Vehicle	01	16	1		
	02	15	1		
	03	15	1	15	1
50	01	21	1		
	02	17	1		
	03	15	1	18	3
150	01	14	1		
	02	16	1		
	03	17	1	16	2
500	01	15	1		
	02	15	1		
	03	19	1	16	2
1500	01	17	1NP		
	02	15	1NP		
	03	20	1NP	17	3
5000	01	12	1NP		
	02	NC			
	03	20	1NP	16	6
Positive Control 2-nitrofluorene 1.0 µg per plate[b]					
	01	575	1		
	02	630	1		
	03	680	1	628	53

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

[b]Positive control plates were machine counted

NC=No count due to procedural error in which plate did not receive an aliquot of tester strain

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 4

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B1
Strain : TA98
Cells Seeded : 2.1 X 10^8
Liver Microsomes : Rat liver S9
Date Plated : 11/20/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	14	1		
Control	02	11	1		
	03	21	1	15	5
Vehicle	01	19	1		
	02	26	1		
	03	15	1	20	6
50	01	17	1		
	02	16	1		
	03	13	1	15	2
150	01	16	1		
	02	20	1		
	03	14	1	17	3
500	01	18	1		
	02	13	1		
	03	17	1	16	3
1500	01	11	1NP		
	02	20	1NP		
	03	10	1NP	14	6
5000	01	19	1NP		
	02	20	1NP		
	03	24	1NP	21	3
Positive Control 2-aminoanthracene 1.0 µg per plate[b]					
	01	890	1		
	02	640	1		
	03	980	1	837	176

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 5

Test Article Id	: Dow Corning® 60,000CST, No Co-Solvent		
Study Number	: ----------	Experiment No	: B1
Strain	: TA100	Cells Seeded	: 1.1 X 10^8
Liver Microsomes	: None	Date Plated	: 11/20/97
Vehicle	: sponsor vehicle		
Plating Aliquot	: 25 µL	Counted by	: machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	140	1		
Control	02	120	1		
	03	135	1	132	10
Vehicle	01	112	1		
	02	128	1		
	03	134	1	125	11
50	01	146	1		
	02	140	1		
	03	145	1	144	3
150	01	115	1		
	02	135	1		
	03	119	1	123	11
500	01	118	1		
	02	126	1		
	03	129	1	124	6
1500	01	115	1NP		
	02	146	1NP		
	03	110	1NP	124	20
5000	01	134	1NP		
	02	135	1NP		
	03	115	1NP	128	11
Positive Control sodium azide 1.0 µg per plate					
	01	875	1		
	02	740	1		
	03	695	1	770	94

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 6

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number : Experiment No : B1
Strain : TA100 Cells Seeded : 1.1 X 10^8
Liver Microsomes : Rat liver S9 Date Plated : 11/20/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL Counted by : machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	118	1		
Control	02	160	1		
	03	129	1	136	22
Vehicle	01	155	1		
	02	130	1		
	03	146	1	144	13
50	01	147	1		
	02	128	1		
	03	138	1	138	10
150	01	132	1		
	02	148	1		
	03	131	1	137	10
500	01	126	1		
	02	135	1		
	03	NC		131	6
1500	01	148	1NP		
	02	134	1NP		
	03	132	1NP	138	9
5000	01	131	1NP		
	02	115	1NP		
	03	138	1NP	128	12
Positive Control 2-aminoanthracene 1.0 µg per plate					
	01	625	1		
	02	285	1		
	03	686	1	532	216

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
NC=No count due to procedural error in which plate did not receive an aliquot of tester strain

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 7

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B1
Strain : TA1535
Cells Seeded : 1.8 X 10^8
Liver Microsomes : None
Date Plated : 11/20/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	11	1		
Control	02	2	1		
	03	7	1	7	5
Vehicle	01	7	1		
	02	12	1		
	03	11	1	10	3
50	01	4	1		
	02	8	1		
	03	6	1	6	2
150	01	11	1		
	02	7	1		
	03	5	1	8	3
500	01	8	1NP		
	02	12	1NP		
	03	5	1NP	8	4
1500	01	7	1NP		
	02	10	1NP		
	03	6	1NP	8	2
5000	01	10	1NP		
	02	6	1NP		
	03	6	1NP	7	2
Positive Control sodium azide 1.0 µg per plate[b]					
	01	502	1		
	02	550	1		
	03	506	1	519	27

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 8

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B1
Strain : TA1535
Cells Seeded : 1.8 X 10^8
Liver Microsomes : Rat liver S9
Date Plated : 11/20/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	12	1		
Control	02	11	1		
	03	10	1	11	1
Vehicle	01	8	1		
	02	10	1		
	03	9	1	9	1
50	01	13	1		
	02	7	1		
	03	10	1	10	3
150	01	8	1		
	02	8	1		
	03	9	1	8	1
500	01	14	1		
	02	10	1		
	03	7	1	10	4
1500	01	15	1NP		
	02	9	1NP		
	03	4	1NP	9	6
5000	01	14	1NP		
	02	10	1NP		
	03	9	1NP	11	3
Positive Control 2-aminoanthracene 1.0 µg per plate[b]					
	01	108	1		
	02	126	1		
	03	89	1	108	19

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 9

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Strain : TA1537
Liver Microsomes : None
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Experiment No : B1
Cells Seeded : 0.8×10^8
Date Plated : 11/20/97
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	6	1		
Control	02	7	1		
	03	7	1	7	1
Vehicle	01	7	1		
	02	9	1		
	03	5	1	7	2
50	01	5	1		
	02	4	1		
	03	5	1	5	1
150	01	6	1		
	02	3	1		
	03	5	1	5	2
500	01	4	1NP		
	02	5	1NP		
	03	3	1NP	4	1
1500	01	6	1NP		
	02	5	1NP		
	03	3	1NP	5	2
5000	01	4	1NP		
	02	4	1NP		
	03	3	1NP	4	1
Positive Control 9-aminoacridine 75 µg per plate[b]					
	01	1158	1		
	02	970	1		
	03	674	1	934	244

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 10

Test Article Id	: Dow Corning® 60,000CST, No Co-Solvent		
Study Number	:	Experiment No	: B1
Strain	: TA1537	Cells Seeded	: 0.8 X 10^8
Liver Microsomes	: Rat liver S9	Date Plated	: 11/20/97
Vehicle	: sponsor vehicle		
Plating Aliquot	: 25 µL	Counted by	: hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	3	1		
Control	02	6	1		
	03	11	1	7	4
Vehicle	01	3	1		
	02	7	1		
	03	12	1	7	5
50	01	3	1		
	02	8	1		
	03	4	1	5	3
150	01	5	1		
	02	5	1		
	03	4	1	5	1
500	01	5	1		
	02	3	1		
	03	6	1	5	2
1500	01	6	1NP		
	02	1	1NP		
	03	2	1NP	3	3
5000	01	1	1NP		
	02	7	1NP		
	03	7	1NP	5	3
Positive Control 2-aminoanthracene 1.0 µg per plate[b]					
	01	105	1		
	02	96	1		
	03	60	1	87	24

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 11

Test Article Id	: Dow Corning® 60,000CST, No Co-Solvent		
Study Number	:	Experiment No	: B1
Strain	: WP2 *uvrA*	Cells Seeded	: 14.2 X 10^8
Liver Microsomes	: None	Date Plated	: 11/20/97
Vehicle	: sponsor vehicle		
Plating Aliquot	: 25 µL	Counted by	: hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	8	1		
Control	02	16	1		
	03	13	1	12	4
Vehicle	01	8	1		
	02	11	1		
	03	12	1	10	2
50	01	7	1		
	02	6	1		
	03	14	1	9	4
150	01	5	1		
	02	9	1		
	03	12	1	9	4
500	01	11	1NP		
	02	16	1NP		
	03	16	1NP	14	3
1500	01	12	1NP		
	02	14	1NP		
	03	9	1NP	12	3
5000	01	14	1NP		
	02	9	1NP		
	03	6	1NP	10	4
Positive Control methyl methanesulfonate 1000 µg per plate[b]					
	01	545	1		
	02	380	1		
	03	340	1	422	109

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 12

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B1
Strain : WP2 uvrA
Cells Seeded : 14.2 X 10^8
Liver Microsomes : Rat liver S9
Date Plated : 11/20/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	10	1		
Control	02	10	1		
	03	15	1	12	3
Vehicle	01	12	1		
	02	8	1		
	03	12	1	11	2
50	01	15	1		
	02	11	1		
	03	10	1	12	3
150	01	13	1		
	02	8	1		
	03	17	1	13	5
500	01	7	1		
	02	15	1		
	03	13	1	12	4
1500	01	17	1NP		
	02	15	1NP		
	03	16	1NP	16	1
5000	01	7	1NP		
	02	6	1NP		
	03	8	1NP	7	1
Positive Control 2-aminoanthracene 10 µg per plate[b]					
	01	600	1		
	02	355	1		
	03	240	1	398	184

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 13

Test Article Id	: Dow Corning® 60,000CST, No Co-Solvent		
Study Number	:	Experiment No	: B1
Strain	: WP2 *uvrA* (pKM101)	Cells Seeded	: 27.3 X 10^8
Liver Microsomes	: None	Date Plated	: 11/20/97
Vehicle	: sponsor vehicle		
Plating Aliquot	: 25 µL	Counted by	: machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	232	1		
Control	02	257	1		
	03	271	1	253	20
Vehicle	01	181	1		
	02	258	1		
	03	304	1	248	62
50	01	223	1		
	02	199	1		
	03	214	1	212	12
150	01	191	1		
	02	225	1		
	03	253	1	223	31
500	01	262	1		
	02	209	1		
	03	203	1	225	32
1500	01	254	1NP		
	02	228	1NP		
	03	262	1NP	248	18
5000	01	268	1NP		
	02	184	1NP		
	03	256	1NP	236	45
Positive Control methyl methanesulfonate 1000 µg per plate					
	01	1820	1		
	02	1680	1		
	03	1798	1	1766	75

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 14

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Strain : WP2 *uvrA* (pKM101)
Liver Microsomes : Rat liver S9
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Experiment No : B1
Cells Seeded : 27.3×10^8
Date Plated : 11/20/97
Counted by : machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	218	1		
Control	02	286	1		
	03	265	1	256	35
Vehicle	01	250	1		
	02	208	1		
	03	290	1	249	41
50	01	214	1		
	02	195	1		
	03	255	1	221	31
150	01	260	1		
	02	220	1		
	03	189	1	223	36
500	01	154	1NP		
	02	200	1NP		
	03	160	1NP	171	25
1500	01	220	1NP		
	02	245	1NP		
	03	134	1NP	200	58
5000	01	210	1NP		
	02	230	1NP		
	03	180	1NP	207	25
Positive Control 2-aminoanthracene 10 µg per plate					
	01	1999	1		
	02	1482	1		
	03	1950	1	1810	285

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 15

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Strain : TA98
Liver Microsomes : None
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Experiment No : B2
Cells Seeded : 2.7 X 10^8
Date Plated : 12/05/97
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	12	1		
Control	02	20	1		
	03	16	1	16	4
Vehicle	01	18	1		
	02	19	1		
	03	19	1	19	1
50	01	16	1		
	02	16	1		
	03	22	1	18	3
150	01	24	1		
	02	22	1		
	03	25	1	24	2
500	01	18	1		
	02	18	1		
	03	20	1	19	1
1500	01	14	1NP		
	02	20	1NP		
	03	12	1NP	15	4
5000	01	25	1NP		
	02	21	1NP		
	03	14	1NP	20	6
Positive Control 2-nitrofluorene 1.0 µg per plate[b]					
	01	457	1		
	02	408	1		
	03	483	1	449	38

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 16

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B2
Strain : TA98
Cells Seeded : 2.7 X 10^8
Liver Microsomes : Rat liver S9
Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	25	1		
Control	02	19	1		
	03	18	1	21	4
Vehicle	01	19	1		
	02	18	1		
	03	26	1	21	4
50	01	23	1		
	02	20	1		
	03	15	1	19	4
150	01	19	1		
	02	15	1		
	03	28	1	21	7
500	01	22	1		
	02	22	1		
	03	22	1	22	0
1500	01	18	1NP		
	02	17	1NP		
	03	20	1NP	18	2
5000	01	21	1NP		
	02	23	1NP		
	03	16	1NP	20	4
Positive Control 2-aminoanthracene 1.0 µg per plate[b]					
	01	1054	1		
	02	786	1		
	03	989	1	943	140

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 17

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B2
Strain : TA100
Cells Seeded : 4.0 X 10^8
Liver Microsomes : None
Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	128	1		
Control	02	122	1		
	03	143	1	131	11
Vehicle	01	140	1		
	02	141	1		
	03	139	1	140	1
50	01	118	1		
	02	117	1		
	03	135	1	123	10
150	01	107	1		
	02	115	1		
	03	128	1	117	11
500	01	112	1		
	02	116	1		
	03	118	1	115	3
1500	01	126	1NP		
	02	132	1NP		
	03	111	1NP	123	11
5000	01	136	1NP		
	02	120	1NP		
	03	138	1NP	131	10
Positive Control sodium azide 1.0 µg per plate					
	01	932	1		
	02	1094	1		
	03	789	1	938	153

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 18

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B2
Strain : TA100
Cells Seeded : 4.0 X 10^8
Liver Microsomes : Rat liver S9
Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	145	1		
Control	02	186	1		
	03	147	1	159	23
Vehicle	01	158	1		
	02	149	1		
	03	141	1	149	9
50	01	139	1		
	02	163	1		
	03	154	1	152	12
150	01	193	1		
	02	181	1		
	03	168	1	181	13
500	01	128	1		
	02	136	1		
	03	NC		132	6
1500	01	125	1NP		
	02	127	1NP		
	03	136	1NP	129	6
5000	01	128	1NP		
	02	105	1NP		
	03	119	1NP	117	12
Positive Control 2-aminoanthracene 1.0 µg per plate					
	01	754	1		
	02	1123	1		
	03	1004	1	960	188

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
NC=No count due to procedural error in which plate did not receive an aliquot of tester strain

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 19

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B2
Strain : TA1535
Cells Seeded : 4.9 X 10^8
Liver Microsomes : None
Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	11	1		
Control	02	11	1		
	03	6	1	9	3
Vehicle	01	11	1		
	02	16	1		
	03	12	1	13	3
50	01	13	1		
	02	13	1		
	03	10	1	12	2
150	01	9	1		
	02	14	1		
	03	11	1	11	3
500	01	7	1		
	02	17	1		
	03	11	1	12	5
1500	01	12	1NP		
	02	11	1NP		
	03	15	1NP	13	2
5000	01	18	1NP		
	02	17	1NP		
	03	12	1NP	16	3
Positive Control sodium azide 1.0 µg per plate[b]					
	01	421	1		
	02	557	1		
	03	989	1	656	297

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 20

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number : Experiment No : B2
Strain : TA1535 Cells Seeded : 4.9 X 10^8
Liver Microsomes : Rat liver S9 Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	9	1		
Control	02	14	1		
	03	11	1	11	3
Vehicle	01	5	1		
	02	11	1		
	03	15	1	10	5
50	01	14	1		
	02	14	1		
	03	18	1	15	2
150	01	19	1		
	02	14	1		
	03	20	1	18	3
500	01	15	1		
	02	15	1		
	03	16	1	15	1
1500	01	16	1NP		
	02	17	1NP		
	03	20	1NP	18	2
5000	01	17	1NP		
	02	12	1NP		
	03	17	1NP	15	3
Positive Control 2-aminoanthracene 1.0 µg per plate[b]					
	01	192	1		
	02	161	1		
	03	156	1	170	20

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 21

Test Article Id	: Dow Corning® 60,000CST, No Co-Solvent		
Study Number	:	Experiment No	: B2
Strain	: TA1537	Cells Seeded	: 2.2 X 10^8
Liver Microsomes	: None	Date Plated	: 12/05/97
Vehicle	: sponsor vehicle		
Plating Aliquot	: 25 µL	Counted by	: hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	6	1		
Control	02	6	1		
	03	7	1	6	1
Vehicle	01	3	1		
	02	12	1		
	03	16	1	10	7
50	01	9	1		
	02	9	1		
	03	11	1	10	1
150	01	10	1		
	02	9	1		
	03	8	1	9	1
500	01	9	1NP		
	02	8	1		
	03	7	1	8	1
1500	01	8	1NP		
	02	8	1NP		
	03	9	1NP	8	1
5000	01	6	1NP		
	02	6	1NP		
	03	9	1NP	7	2
Positive Control 9-aminoacridine 75 µg per plate[b]					
	01	851	1		
	02	1091	1		
	03	485	1	809	305

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella Mutagenicity Assay

Table 22

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number : Experiment No : B2
Strain : TA1537 Cells Seeded : 2.2 X 10^8
Liver Microsomes : Rat liver S9 Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	11	1		
Control	02	13	1		
	03	10	1	11	2
Vehicle	01	9	1		
	02	10	1		
	03	11	1	10	1
50	01	12	1		
	02	7	1		
	03	12	1	10	3
150	01	6	1		
	02	11	1		
	03	8	1	8	3
500	01	10	1		
	02	19	1		
	03	10	1	13	5
1500	01	13	1NP		
	02	10	1NP		
	03	15	1NP	13	3
5000	01	16	1NP		
	02	11	1NP		
	03	14	1NP	14	3
Positive Control 2-aminoanthracene 1.0 µg per plate[b]					
	01	127	1		
	02	75	1		
	03	107	1	103	26

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 23

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Strain : WP2 uvrA
Liver Microsomes : None
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Experiment No : B2
Cells Seeded : 5.5 X 10^8
Date Plated : 12/05/97
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	16	1		
Control	02	24	1		
	03	15	1	18	5
Vehicle	01	16	1		
	02	18	1		
	03	17	1	17	1
50	01	15	1		
	02	13	1		
	03	15	1	14	1
150	01	12	1		
	02	10	1		
	03	16	1	13	3
500	01	16	1		
	02	21	1		
	03	14	1	17	4
1500	01	12	1NP		
	02	12	1NP		
	03	16	1NP	13	2
5000	01	12	1NP		
	02	17	1NP		
	03	20	1NP	16	4
Positive Control methyl methanesulfonate 1000 µg per plate[b]					
	01	720	1		
	02	604	1		
	03	553	1	626	86

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 24

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Experiment No : B2
Strain : WP2 uvrA
Cells Seeded : 5.5 X 10^8
Liver Microsomes : Rat liver S9
Date Plated : 12/05/97
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Counted by : hand

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated Control	01	13	1		
	02	22	1		
	03	14	1	16	5
Vehicle	01	18	1		
	02	18	1		
	03	18	1	18	0
50	01	22	1		
	02	18	1		
	03	24	1	21	3
150	01	21	1		
	02	18	1		
	03	23	1	21	3
500	01	15	1		
	02	14	1		
	03	18	1	16	2
1500	01	19	1NP		
	02	14	1NP		
	03	13	1NP	15	3
5000	01	17	1NP		
	02	24	1NP		
	03	17	1NP	19	4
Positive Control 2-aminoanthracene 10 µg per plate[b]					
	01	229	1		
	02	278	1		
	03	275	1	261	27

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate
[b]Positive control plates were machine counted

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 25

Test Article Id	: Dow Corning® 60,000CST, No Co-Solvent		
Study Number	:	Experiment No	: B2
Strain	: WP2 uvrA (pKM101)	Cells Seeded	: 6.7 X 10^8
Liver Microsomes	: None	Date Plated	: 12/05/97
Vehicle	: sponsor vehicle		
Plating Aliquot	: 25 µL	Counted by	: machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated	01	287	1		
Control	02	276	1		
	03	263	1	275	12
Vehicle	01	298	1		
	02	285	1		
	03	264	1	282	17
50	01	305	1		
	02	269	1		
	03	274	1	283	20
150	01	325	1		
	02	283	1		
	03	255	1	288	35
500	01	322	1		
	02	282	1		
	03	294	1	299	21
1500	01	300	1NP		
	02	330	1NP		
	03	242	1NP	291	45
5000	01	243	1NP		
	02	223	1NP		
	03	260	1NP	242	19
Positive Control methyl methanesulfonate 1000 µg per plate					
	01	1283	1		
	02	1760	1		
	03	1683	1	1575	256

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

E. coli Mutagenicity Assay

Table 26

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number :
Strain : WP2 *uvrA* (pKM101)
Liver Microsomes : Rat liver S9
Vehicle : sponsor vehicle
Plating Aliquot : 25 µL
Experiment No : B2
Cells Seeded : 6.7 X 10^8
Date Plated : 12/05/97
Counted by : machine

Concentration µg per plate	Plate Number	Revertants per plate	Background Code[a]	Average Revertants	Standard Deviation
Untreated Control	01	251	1		
	02	249	1		
	03	231	1	244	11
Vehicle	01	235	1		
	02	253	1		
	03	280	1	256	23
50	01	280	1		
	02	293	1		
	03	288	1	287	7
150	01	320	1		
	02	264	1		
	03	291	1	292	28
500	01	302	1NP		
	02	274	1NP		
	03	294	1	290	14
1500	01	282	1NP		
	02	221	1NP		
	03	317	1NP	273	49
5000	01	272	1NP		
	02	285	1NP		
	03	269	1NP	275	9
Positive Control 2-aminoanthracene 10 µg per plate					
	01	1694	1		
	02	1087	1		
	03	1345	1	1375	305

[a]Background bacterial evaluation code
1=Normal 2=Slightly reduced 3=Moderately reduced
4=Extremely reduced 5=Absent 6=Obscured by precipitate
NP=Non-Interfering Precipitate IP=Interfering Precipitate

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella/E. coli Mutagenicity Assay
Summary of Results

Table 27

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number : Experiment No : B1

Average Revertants Per Plate ± Standard Deviation

Liver Microsomes: None

Dose (μg)	TA98	TA100	TA1535	TA1537	WP2 uvrA	WP2 uvrA (pKM101)
Untreated	17 ± 3	132 ± 10	7 ± 5	7 ± 1	12 ± 4	253 ± 20
0.0	15 ± 1	125 ± 11	10 ± 3	7 ± 2	10 ± 2	248 ± 62
50	18 ± 3	144 ± 3	6 ± 2	5 ± 1	9 ± 4	212 ± 12
150	16 ± 2	123 ± 11	8 ± 3	5 ± 2	9 ± 4	223 ± 31
500	16 ± 2	124 ± 6	8 ± 4	4 ± 1	14 ± 3	225 ± 32
1500	17 ± 3	124 ± 20	8 ± 2	5 ± 2	12 ± 3	248 ± 18
5000	16 ± 6	128 ± 11	7 ± 2	4 ± 1	10 ± 4	236 ± 45
Pos	628 ± 53	770 ± 94	519 ± 27	934 ± 244	422 ± 109	1766 ± 75

Liver Microsomes: Rat liver S9

Dose (μg)	TA98	TA100	TA1535	TA1537	WP2 uvrA	WP2 uvrA (pKM101)
Untreated	15 ± 5	136 ± 22	11 ± 1	7 ± 4	12 ± 3	256 ± 35
0.0	20 ± 6	144 ± 13	9 ± 1	7 ± 5	11 ± 2	249 ± 41
50	15 ± 2	138 ± 10	10 ± 3	5 ± 3	12 ± 3	221 ± 31
150	17 ± 3	137 ± 10	8 ± 1	5 ± 1	13 ± 5	223 ± 36
500	16 ± 3	131 ± 6	10 ± 4	5 ± 2	12 ± 4	171 ± 25
1500	14 ± 6	138 ± 9	9 ± 6	3 ± 3	16 ± 1	200 ± 58
5000	21 ± 3	128 ± 12	11 ± 3	5 ± 3	7 ± 1	207 ± 25
Pos	837 ± 176	532 ± 216	108 ± 19	87 ± 24	398 ± 184	1810 ± 285

0.0 = Vehicle plating aliquot of 25 μL
Pos = Positive Control concentrations as specified in Materials and Methods section.

Bacterial Reverse Mutation Assay of Dow Corning® 60,000CST, NO CO-SOLVENT

Salmonella/E. coli Mutagenicity Assay
Summary of Results

Table 28

Test Article Id : Dow Corning® 60,000CST, No Co-Solvent
Study Number : Experiment No : B2

Average Revertants Per Plate ± Standard Deviation

Liver Microsomes: None

Dose (μg)	TA98	TA100	TA1535	TA1537	WP2 uvrA	WP2 uvrA (pKM101)
Untreated	16 ± 4	131 ± 11	9 ± 3	6 ± 1	18 ± 5	275 ± 12
0.0	19 ± 1	140 ± 1	13 ± 3	10 ± 7	17 ± 1	282 ± 17
50	18 ± 3	123 ± 10	12 ± 2	10 ± 1	14 ± 1	283 ± 20
150	24 ± 2	117 ± 11	11 ± 3	9 ± 1	13 ± 3	288 ± 35
500	19 ± 1	115 ± 3	12 ± 5	8 ± 1	17 ± 4	299 ± 21
1500	15 ± 4	123 ± 11	13 ± 2	8 ± 1	13 ± 2	291 ± 45
5000	20 ± 6	131 ± 10	16 ± 3	7 ± 2	16 ± 4	242 ± 19
Pos	449 ± 38	938 ± 153	656 ± 297	809 ± 305	626 ± 86	1575 ± 256

Liver Microsomes: Rat liver S9

Dose (μg)	TA98	TA100	TA1535	TA1537	WP2 uvrA	WP2 uvrA (pKM101)
Untreated	21 ± 4	159 ± 23	11 ± 3	11 ± 2	16 ± 5	244 ± 11
0.0	21 ± 4	149 ± 9	10 ± 5	10 ± 1	18 ± 0	256 ± 23
50	19 ± 4	152 ± 12	15 ± 2	10 ± 3	21 ± 3	287 ± 7
150	21 ± 7	181 ± 13	18 ± 3	8 ± 3	21 ± 3	292 ± 28
500	22 ± 0	132 ± 6	15 ± 1	13 ± 5	16 ± 2	290 ± 14
1500	18 ± 2	129 ± 6	18 ± 2	13 ± 3	15 ± 3	273 ± 49
5000	20 ± 4	117 ± 12	15 ± 3	14 ± 3	19 ± 4	275 ± 9
Pos	943 ± 140	960 ± 188	170 ± 20	103 ± 26	261 ± 27	1375 ± 305

0.0 = Vehicle plating aliquot of 25 μL
Pos = Positive Control concentrations as specified in Materials and Methods section.

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.
Industry Liaison to the CIR Expert Panel

DATE: June 21, 2010

SUBJECT: Comments on the Draft Report on Dimethiconol and its Esters and Reaction Products
CIR Expert Panel Meeting June 28-29, 2010

Memo - In the future, it would be helpful if memos were dated with the date they were written.
p.2 - Please provide a reference for the information in the first paragraph under the heading Chemical and Physical Properties.
p.3 - In the summary of the Acute Oral Exposure section, please provide the highest dose that did not result in deaths.
p.6 - At what concentrations were the Dimethiconol ingredients found not irritating or sensitizing?
p.8 - In the summary of the Chronic Exposure/Tumorigenicity section, please include the dose and species used in the 1-year oral feeding study.
p.9 - If available, please provide the mass of the implants used in the chronic implantation studies.
p.9 - In the summary of the Skin Irritation and Sensitization section, please provide the concentrations that did not result in skin irritation or sensitization.
p.10 - In the last sentence under the Dimethiconol Beeswax heading, the word "Beeswax" is missing after Dimethiconol.
p.10 - In the summary of the Dimethicone report, please include the concentrations of Dimethicone that were classified as mild to minimal irritants. Please provide the vehicle in which Dimethicone was tested at 5% in a clinical RIPT (or indicate if it was a formulation).
p.11 - In the Summary, please include the concentration of Dimethiconol Stearate that was not irritating to the skin of rabbits.
p.13 - This report should not yet include a conclusion. The conclusion should be the conclusion of the CIR Expert Panel.
p.17, Table 3 - Why are two references presented with Personal Care[7] Products Council[59]? Reference 7 (about Dimethiconol/Silsesquioxane Copolymer) does not appear to be an appropriate reference for the information about Dimethiconol Behenate.
p.19-24 - Please delete the word "Current" from the title of the table, as the information will not be "Current" by the time the report is published (or when someone reads the report 10 years from now).