
Safety Assessment of Polyurethanes as Used in Cosmetics

Status: Draft Final Report for Panel Review
Release Date: August 18, 2017
Panel Meeting Date: September 11-12, 2017

The 2017 Cosmetic Ingredient Review Expert Panel members are: Chair, 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 Interim Director is Bart Heldreth, Ph.D. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.



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MEMORANDUM

To: CIR Expert Panel and Liaisons

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

Date: August 18, 2017

Subject: Polyurethanes As Used In Cosmetics

Attached is the Draft Final Report of Polyurethanes as used in cosmetics. [*polyur092017rep*] The 66 polyurethane ingredients in this report are copolymers comprised, in part, of carbamate (i.e., urethane) linkages.

In April 2017, the Panel issued a tentative report with the conclusion that these ingredients are safe as used when formulated to be non-sensitizing.

The Council has reported that the definitions of Polyurethane-60 and -61 were erroneously stated in the *Web-Based Ingredient Dictionary* (wINCI), but that the monographs have since been updated. [*polyur092017PCPC_1*] A supplier, who is believed to be the only supplier of both polymers, reported that dimethyl aminopropylamine (DMAPA) was erroneously stated instead of dimethylolpropionic acid (DMPA). With these changes, there are now no ingredients in this report for which DMAPA was used as a monomer. Because of this change, references to DMAPA were removed from the report and the Discussion adjusted accordingly. Also, structures for the SMDI monomers in Polyurethane-2 and -29 were corrected and the names of the SMDI monomers were corrected in Polyurethane-11, -33, and -35. The correct monomers are present in other polyurethanes in the report and, therefore, do not create a new concern. The changes in Table 1 are marked by lines on the sides of the table.

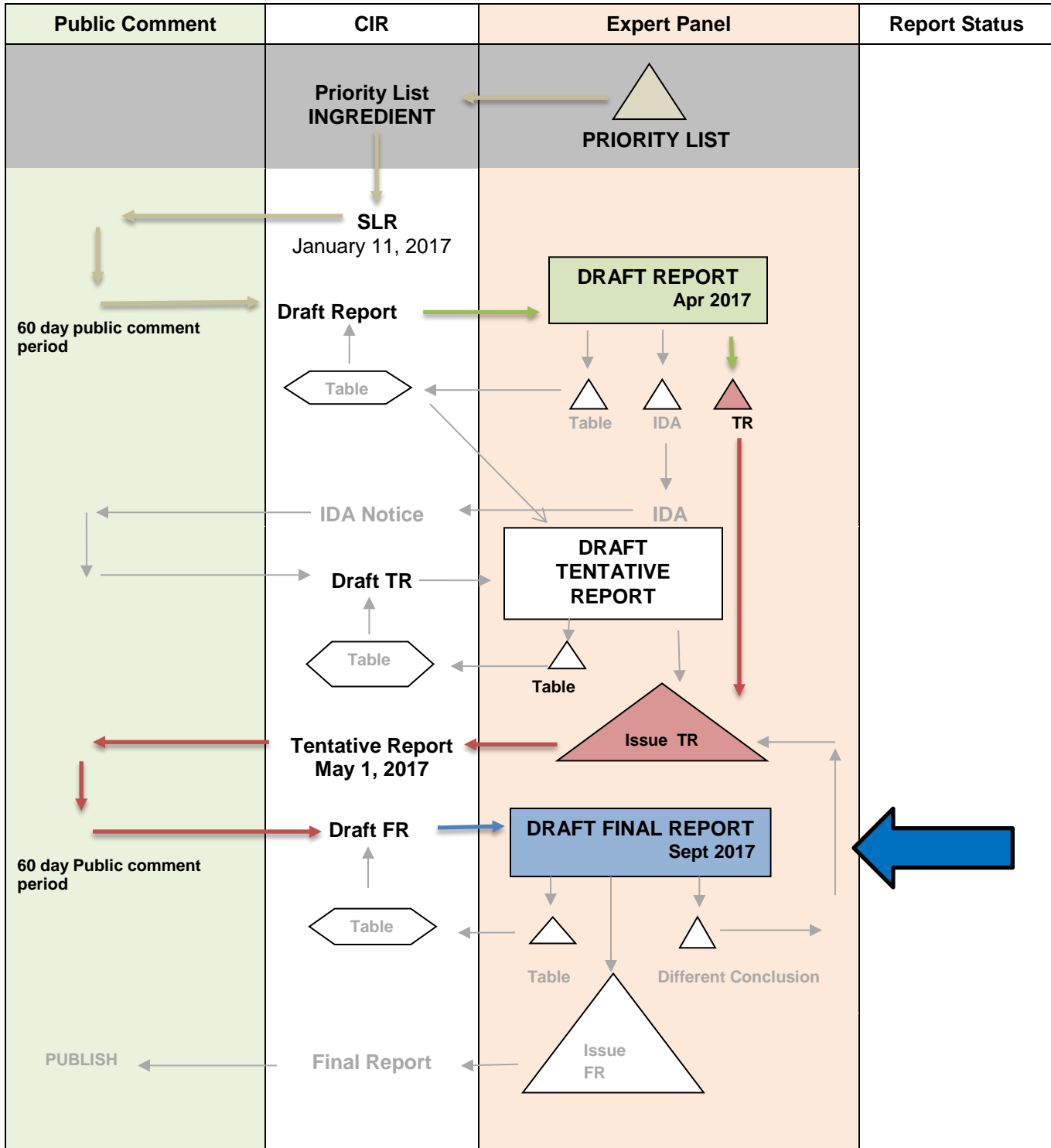
Council comments have been addressed. [*polyur092017PCPC_2* and *_3*] No new toxicity data were submitted.

Please review the Discussion to ensure that it captures the rationale for the report Conclusion. Please review the Abstract and Conclusion to ensure that they capture the Panel's thinking. The Panel should be prepared to issue a Final Report.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Polyurethanes

MEETING Sept 2017



History – Polyurethanes

June, 2016 – Polyurethanes added to Priority List due to reported VCRP usage of Polyurethane-11 (300 uses).

January, 2017 – SLR posted with a list of data needs:

- Chemical and physical properties, including molecular weight
- Method of manufacture
- Impurity data, especially on the monomers
- Dermal penetration
- Chronic dermal toxicity
- Inhalation toxicity
- Carcinogenicity
- Dermal irritation and sensitization

April, 2017 – Panel examined Draft Report and issued a Tentative report with the conclusion that these ingredients are safe as used when formulated to be non-sensitizing.

Residual monomers would be expected to be either consumed in reaction or washed away in manufacturing and purification processes. Producers and formulators should use cGMP to prevent conditions wherein monomers could be released from these polymeric ingredients.

Many of these polyurethanes are reported to be supplied as emulsions or solutions with multiple components, which may include sensitizers such as methylisothiazolinone (MI; e.g., Polyurethane-60 and -61). Suppliers and formulators should be aware of how these polymers ingredients are supplied, and should avoid reaching levels of components that may cause sensitization or other adverse health effects.

Because some of these polyurethanes are supplied as emulsions or in solution, there is some confusion about the concentrations of the polyurethanes in the safety evaluation data. While these ingredients are reported to be supplied in emulsions or solutions at concentrations ranging from 20% to 66%, it is not always clear from the submitted data whether the concentrations reported are the concentrations of the polyurethane ingredients or of the emulsions or solutions tested. The Panel asked for clarification of the concentrations reported in these studies.

September, 2017 – Panel examines the Draft Final Report.

	ADME		Acute toxicity			Repeated dose toxicity			Irritation					Sensitization							
	Dermal Penetration	Log K _{ow}	Use	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Animal	Ocular In Vitro	Dermal Animal	Dermal Human	Dermal In Vitro	Animal	Human	In Vitro	Repro/Devel	Genotoxicity	Carcinogenicity	Phototoxicity
Polyurethane-1			X	X		X			X		X	X			X	X			X		
Polyurethane-2			X																		
Polyurethane-4																					
Polyurethane-5																					
Polyurethane-6			X																		
Polyurethane-7			X																		
Polyurethane-8			X																		
Polyurethane-9			X																		
Polyurethane-10			X																		
Polyurethane-11			X																		
Polyurethane-12																					
Polyurethane-13																					
Polyurethane-14			X			X			X		X		X		X	X					
Polyurethane-15			X																		
Polyurethane-16			X																		
Polyurethane-17																					
Polyurethane-18			X																		
Polyurethane-19																					
Polyurethane-20																					
Polyurethane-21											X		X			X					
Polyurethane-23																					
Polyurethane-24			X																		
Polyurethane-25																					
Polyurethane-26																					
Polyurethane-27																					
Polyurethane-28																			X		
Polyurethane-29																					
Polyurethane-32																					
Polyurethane-33			X																		
Polyurethane-34			X																		
Polyurethane-35			X	X						X		X		X	X				X		
Polyurethane-36																					
Polyurethane-39			X	X								X			X						
Polyurethane-40			X																		
Polyurethane-41																					
Polyurethane-42											X								X		
Polyurethane-43																					
Polyurethane-44																					
Polyurethane-45																					
Polyurethane-46			X																		
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Polyurethane-59																					

[illegible]

[illegible]

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
Polyurethane-46		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-47		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-48		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-49		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-50		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-51		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-52		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-53		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-54		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-55		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-56	1342288-58-7	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-57	930592-39-5	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-58		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-59		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-60		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-61		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-62		Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N
Polyurethane-63		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-64		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-65		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-66		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-67	1334242-38-4	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-68	157420-46-7	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-69	1668562-30-8	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-70		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-71		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane-72	502761-95-7	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Polyurethane		N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N

ECHA Data Base – there is a Pre-Registration entry for “Polyurethane” with the CAS No. 9009-54-5 (which does not match any ingredient listed in the On-line DB) and Polyurethane-9.

Polyurethane Manufacturers Association (PMA) – no useful information.

Transcripts – Polyurethanes April 2017

Dr. Marks' Team

DR. MARKS: We're now on to polyurethanes. You know, it's interesting, I was just thinking about that. I was going to ask the team -- so, it's 10:20. Do you want to take a break till 10:30, approximately? Okay. I hear a yes. We won't take a vote on that. We're just going to take a break.

(Recess)

DR. MARKS: Are we ready, team?

DR. GILL: Yeah.

DR. MARKS: So on March 17th we received a memo from, -- or I should say dated March 17th memo from Lillian Becker. You notice I always now use the last name. So we have our Lillians straight here. We received a draft report on polyurethanes. The 66 polyurethane ingredients in this report are copolymers, and part of carbamate, that is, urethane. They are cause of occupational asthma, urine and salergic dermatitis, and --

DR. SLAGA: The monomers.

DR. MARKS: -- yes, the monomers. I'm sorry. This is the first review of these 66 ingredients. So Ron and -- Don, Ron, and Tom, as always, the first question is do you like all 66 ingredients, or do some of them are outliers and should not be included?

DR. SHANK: Well, I find the chemistry very confusing, and I need Dr. Hill's help. Can the chemists assure us that the polymers are stable, and they won't generate or release any monomer in the formulation? If that's true, then I feel pretty good about it. If that's not true, then I have a lot of questions. Sorry.

DR. MARKS: So we start with the chemistry and then a lot of questions. Beginning with the chemistry, I don't know if, Lillian Becker, you talk with Bart and can clear that up at all?

MS. BECKER: Is the impurity data on page 11. You need more, and I think there's some more --

DR. SHANK: It's not impurity data. It's --

DR. MARKS: Yes.

DR. SHANK: --if one puts the polymer in a formulation, is any monomer released? Because there are a great many monomers, and you have a whole table, Table 2 lists monomers used to make the polymers, but for which the panel has found insufficient data for the monomer. Table 3 has a long list of monomers used to make the polymers where there's no safety data.

So if these polymers are totally stable under conditions of use, that's okay. But if they're not, then I have a lot of problems.

DR. MARKS: Yes, I was thinking similarly, Ron. I wondered whether or not there should be some sort of limit in the diisocyanic monomers in the final ingredient. But then again, what limit do you place?

And, yes, Ron Hill's shaking his head saying I don't know is what I interpreted from your nonverbal communication. That it would be difficult to set limits.

DR. HILL: Yes, you know, that's the assertion I made a little bit ago in that other ingredient group was that you had data enough so that you've at least captured every one of the monomers and I'm not sure that's 100 percent sufficient. So, you know, the ideal world -- you started with the question of what about this ingredient group.

DR. MARKS: Yes.

DR. HILL: So let me just deal with that. I tried to come up with, well, if you were going to created subgroups, how would you do that. I couldn't come up with a good strategy for that.

If you were to exclude a small handful based on they're significantly different like the one that's created with the triglyceride epoxide as the reactive monomer, yeah, so then what happens if you pair that out of the report and there's limited number of uses then it languages without ever getting evaluated for who knows how long and that's probably not a good thing.

So then I thought, well, there is enough commonality for exactly the reason why the ingredient group was created that at least administratively keep them all there and keep them together. And then I still tried to figure out is there any reasonable strategy for subgroups and there's really not.

And then I thought should they all just be reviewed one at a time but then you lose some valuable read cross and you'll be looking at, what, 60 different reports or something like that. So that seems a little bit farfetched or not very reasonable from where I sit because I think there are valuable pieces of information that you get from being able to compare these five things that have this in common.

But that's the kind of question about the monomers I've been asking for a long time and there's really two different questions. One is can the chemistry that's used to cause them to react reverse so that you generate under conditions of use. I always think hitting something with a hot hair dryer can we have one of these carbamates revert back to generalize isocyanate. I haven't seen anything in the review that we did before with the HDMI and all that. I didn't see anything that suggested that we're seeing that happen and the chemistry suggested it doesn't.

But is that universally true for all of these monomers because every organic chemist knows you have this reaction with these two things and it works beautifully well, and then you come and you have these very close analogs and you try to do the same chemistry and it's not the same.

So at some level we say the industry knows they are dealing with reactive things, and they've done something to assure themselves that they're not going to have something that comes back later and bites them, and then we just have to believe that that's the case because otherwise for every one of these you need some information about what's the low molecular weight distribution because it's says, oh, 1,000, 10,000 we were just talking about.

If we say the polymer has an average molecular weight of 30,000, but then we have a piece of information to suggest, well, in this one there's 2 percent that are 700 to 1,400 then does that carry across to all of them. When I ask for impurities, I really like them for every single ingredient that's in use, and then if more than one manufacturer is making them how about that manufacturer and the lot variation versus that manufacturer and the variation between their lots.

And then the other question you asked which is the releasability if there's any very small amounts of residual monomers in there because some of these are quite reactive and they're entrained in the polymer, under what conditions might they get unentrained in a formulation or, again, hit with a hot hair dryer.

So I think expecting that answer for all how many ingredients, 66 ingredients that we have here is what I would like to see, but it's not realistic based on how we've been flying.

That's a long-winded answer, but I think that covered everything that I see relates to that none of which is in my notes.

MS. GILL: Yes. We're waiting on Bart. They're almost at priority [priorities], so he won't be able to join us immediately. But a number of these the panel has seen before, and I was trying to get online to pull up the HDI because that's the ingredient for which we had the longest discussion about the residual monomers.

And because some of them, as you say, there was data there, so I'll continue and try to get to that.

DR. EISENMANN: When I asked the priors [providers ?] about the diisocyanates, most of these are sold in water and they all kept saying --

DR. MARKS: It goes away.

DR. EISENMANN: -- when you add the water it goes away, and so that was not an issue for these.

DR. MARKS: Sorry. Repeat that, Carol.

DR. EISENMANN: The diisocyanates when I would ask about water residual levels, they say there are not any because we're selling it in water and it reacts so it's gone.

DR. MARKS: Ha.

DR. HILL: So the big question there is --

DR. EISENMANN: So it's the other materials that I was trying to get him to hang onto.

DR. HILL: The big question there is, I agree. Unless they're a monomer entrained inside a polymer in such a way that it's not exposed to the water, but then somewhere along the lines in conditions of use it gets released. And, I mean, once a manufacturer parts ways with that ingredient, then it's the company's, the formulators, and it's on them.

So I think it's --

DR. EISENMANN: I don't know if you caught the other one, that poly -- the ingredient with the most uses, Polyurethane-11, it's only used as coating on glitter.

DR. HILL: Right.

DR. EISENMANN: That's it. I've got that confirmed by the supplier of the ingredient and the manufacturers of the glitter.

DR. MARKS: That has the most uses?

DR. EISENMANN: Yes.

DR. MARKS: Polyurethane 11?

DR. EISENMANN: Yes. And that it's only used --

DR. MARKS: How many?

DR. HILL: As a costing [coating?] on --

DR. EISENMANN: -- as a coating on glitter.

DR. HILL: -- glitter that's there in --

DR. MARKS: How many uses? I didn't have that? I didn't -- if it has the most uses, it must have more than 30 because so far I have a Polyurethane 14 with 33 uses.

DR. EISENMANN: I mean, it's all different uses of glitter, but, yes.

DR. MARKS: Okay. Correct? Those two things I think need [need] to be captured in the discussion if we say we're not concerned about the monomer.

DR. EISENMANN: That monomer.

DR. MARKS: But you had other monomers, and then as you're referring to, Lilian Gill, Table 2 has previous reports on precursors, monomers, morities [moieties], and related ingredients.

DR. SHANK: Table 2. Those are --

DR. MARKS: That's page 39. Oh.

MS. BECKER: Polyurethane 11 has 315 uses.

DR. MARKS: 315. Ron. Ron Shank, Page 39 it says, previous reports there's a lot of safe as used, safe when non irritating, safe non irritating, safe, safe, safe, safe, safe when I go down an look at these, and HDI polymers where 17 are safe as used, 2 insufficient data. That was from last year.

DR. HILL: And we worked very hard on that one to get to where that conclusion came, or at least I remember working very hard on it.

DR. MARKS: So, Ron Shank, that doesn't change your concerns?

DR. SHANK: No. Some of the, in Table 2, some of those are insufficient data. And in Table 3 there are no data.

DR. MARKS: Uh-huh.

DR. SHANK: Which if the monomer is of no concern, then it's okay. But I need somebody to assure me that the monomer is of no concern.

DR. MARKS: So it sounds like Carol did on the formula, or the supply. It isn't --

MS. EISENMANN: Excuse me. The only insufficient data on Table 2 is one that's currently under review but may change today.

DR. SHANK: So Table 2?

DR. EISENMANN: Yes.

DR. MARKS: (inaudible). One 14-B Diole [1,4-Butanediol]?

DR. HILL: One 14-B Diole [1,4-Butanediol]?

DR. EISENMANN: Right. Right. So I offered one 14-B Diole [1,4-Butanediol] will change from maybe the other two.

DR. SHANK: Okay. What about Table 3?

MS. BECKER: And just to address the stability issue, Polyurethane 21 in weight [wave ?] 2 does have data. It says it's stable. The ph range is 7 to 11, but not stable for lower ph settings.

DR. SHANK: Okay. Can you read across from that to all of the polymers?

DR. HILL: Uh-uh. No. This is a very diverse group. That's the issue here. Almost every single one is different from the next.

MS. BECKER: Right. I just want to make sure you knew what data we did have.

DR. SHANK: Oh, I do, but you're asking us to read across for 60-some-odd chemicals, and I can't do that at this time.

MS. BECKER: I'm not asking you move across. I'm just asking --

DR. SHANK: If you can convince --

MS. BECKER: I'm just asking --

DR. SHANK: -- if you can convince me.

VOICE: Oh, don't look at me.

DR. HILL: Go ahead, Carol.

MS. EISENMANN: The only issue is there are many of these means I have no suppliers. Many of them have no uses and have no suppliers so it's hard. And ones that have suppliers usually it's just one supplier.

DR. SHANK: Now, if we can say they're all so large that they don't pass through the epidermis --

MS. EISENMANN: But for no suppliers I can't tell you the size of them, so that's going to be an issue.

DR. SHANK: Okay. You see my dilemma? I just don't have anything to grab onto.

DR. EISENMANN: Oh, I agree. I think this is going to have to be a split, a split call.

DR. GILL: Can you divide them according to no use and use and the list gets shorter then for us to look at? No use we wouldn't look at unless it had data with it?

DR. SHANK: We've never done that before.

DR. GILL: But still --

DR. SHANK: I would like to, but --

DR. GILL: -- would reduce it.

DR. HILL: I guess for me what's the downside of all the ones where we don't have data, and there don't seem to be any uses and suppliers is to make those insufficient.

DR. GILL: Okay.

DR. HILL: I mean, I know we usually don't proceed that way, but the problem is we can explain why we would do that.

DR. MARKS: I mean, the other would be assuming we could say for the ones in the, I'm not sure we can do it in the conclusion, but in the discussion that we would assume that they have no little -- that's not a good way to put it, but the monomer level would not be of concern from a safety point of view.

I don't know if you can do that, Ron Shank. Wordsmith it that way because we're --

DR. SHANK: Well, someone has to tell me why. And then you have data, or the chemist to say that's a silly question. So far, I don't know what to do.

DR. HILL: And to me there's really two separate issues. Do we have things that are in the molecular rate [weight?] -- molecular weight range where we might have absorption in which case, even penetration well into the skin, those kinds of issues. And then in other cases, it's just under the conditions of use do we have any reason to believe that there would be something released that would be of concern.

DR. SHANK: Correct.

DR. MARKS: So I know you're in a quandary of how to proceed, but let's proceed.

DR. SHANK: Okay.

DR. MARKS: How can we -- what would you propose now? We'll hear from the Belsito Team tomorrow. I'm going to be, perhaps, seconding either a tentative report or an insufficient data announcement.

DR. SHANK: Yes, I would go insufficient.

DR. MARKS: Okay.

DR. SHANK: And we need a stability of each polymer under conditions of use in formulation and use, and then molecular weight ranges for each one.

DR. MARKS: Okay. Stability of ingredient, molecular weight ranges for each. And we're concerned about the -- this is because we're concerned about the diisocyanic monomers in the final product? Is that a good way to state that?

DR. HILL: The possibility for regenerating isocyanates if it's stability, then the other question is in a polymer because of the way some of these are made there's always potential for entrainment of low molecular weight things inside the matrices of the polymer. So then the question is is something like that releasable. We have rarely seen in the past data along those line, but that's not just something I made up in my sleep one night.

DR. GILL: Jim, we can also pull -- I'm looking at the report on HDI, and the panel did make a statement that manufacturers and formulators use current GNPs to insure that the polymers with low molecular weights or less than 1,000 daltons are minimize in product. And there was some data used for read across on the Steareth 100 page, and some of the others, and that the panel agreed that that data were appropriate, but one of them also had, was greater than 1,000, and there was no significant dermal absorption, and this was the rationale for saying that the ingredients in HDI except for the two were safe. So they did look at the size. They were concerned -- you were concerned about the low molecular weight.

And for those that they could read across, they did because of the structural formulas, and the others they didn't, so --

DR. HILL: I'd take care of these -- in terms of the monomers, the main concern there were a very second, there were only three in the whole group. Here we've got quite a bit more, and that --

DR. GILL: Right.

DR. SHANK: Sorry.

DR. MARKS: Oh, no. If you don't -- thank you, Lillian, for pointing that out. Is there anything that we can use from the HDI polymer report? They're making the conclusion there is that because these are so diverse it's really not helpful.

DR. SHANK: Perhaps you could use some, but you can't read across all 60-odd polymers. I can't.

DR. HILL: Me neither.

DR. SLAGA: It's so many monomers.

DR. MARKS: So many monomers.

DR. HILL: And I think the other thing for me is that we did get a good bit of information in Wave 2, and a limited time line to consolidate all of that in looking at this challenging read across scenario here. Matrix, I guess, would be the best way to put it.

So dealing with the one that, is it the 11 that we talked about that has, is coating for glitter, and we had that situation similarly come up where we were talking about a preliminarization [polymerization ?] in situ on those titanium dioxide particles not very long ago, so we know this is the use. This is the only use, and let me say under conditions of use that's what we're talking about. It's easy enough I think to deal with those kinds of ingredients and not be worried.

But you can't say --

DR. EISENMANN: I don't know it'd be nice if on your list your data needs that you're okay with that one use, and so I don't have to keep explaining it. I'm not sure what --

DR. HILL: And I think there are several others here in this group that it is the case, so we have data, and we have a comfort level of, that we can deal with that.

Then the question is are there any of these others that we can read across to, and I think there are. If they're not in use we can't get the information that we really need to read across and (inaudible) insufficient 'til somebody comes forward.

DR. MARKS: We have some -- the irritation sensitization data we have on the ingredients that are reported, they all looked okay. So it's Polyurethane, Polyurethane 13, Polyurethane 14, Polyurethane 21, but it's not being used that I see.

DR. HILL: That was interesting because we got data on it, but it doesn't show up in the use data.

DR. MARKS: Yes. I had that noted here. And then Polyurethane, let me see, that is Polyurethane 34. So those from an irritation sensitization, but I'm not sure we want to split things up right now. We're splitting an insufficient data announcement, and then let's see what we get in terms of stability and molecular range because I think the stability issue and molecular range at least from irritation sensitization presumably would be answerable these because they're safe from an irritation sensitization point.

And I agree. I had that noted in here. Another one is Polyurethane 62. We have data on that, but we have no use.

DR. SLAGA: And a good bit of data on (inaudible), but still the big issue is stability. If we understand, as Ron said, the stability, we could --

DR. MARKS: Now, Lillian, in was it the memo? Yeah. in your memo, you mention it causes occupational asthma, irritating contact, and allergic contact dermatitis and conjunctivitis. But was that in the actual draft report, and then how much more information do we have from that that might help us. To me, that's an alert, but I'm not sure which ingredient caused that, or which monomer.

MS. BECKER: That's the HDI, the isocyanates.

DR. MARKS: Oh. Okay. So that's what that's from.

MS. BECKER: Right.

DR. MARKS: Well, do you think it should be in the report so it refers back to it so we know when we mention that that we know where it's in the discussion, say?

MS. BECKER: Yes.

DR. MARKS: Or at least under -- usually, I think you have case reports or clinical reports after the studies, the irritation and sensitization studies. Did I miss it in the report?

MS. BECKER: I did the same thing I did with the HDI polymer report that I mentioned it there and gave a reference that talked about it.

DR. MARKS: So that's in here?

MS. BECKER: In the introduction.

DR. MARKS: Oh, in the introduction. Okay.

MS. BECKER: It's almost word-for-word what was in the HDI report.

DR. MARKS: Okay. Okay. So --

DR. SHANK: On page 11 under "Physical and Chemical Properties," the bottom of the second paragraph it says, "These ingredients potentially can range from liquid to solid, soluble to insoluble, and non penetrating to readily penetrating the skin." I don't find that reassuring.

DR. MARKS: Uh-Huh.

DR. EISENMANN: Well, I thought that the statement that it could be penetrating or non penetrating should be (inaudible) because you really don't have any data, and all the data you have so far are that they're very large.

DR. SHANK: So where did that come from?

DR. MARKS: Yes.

MS. BECKER: That was a statement I developed by (inaudible) [Bart?].

DR. SHANK: Okay. Thank you.

DR. EISENMANN: But, see, I think it's just speculation that, you don't know, and all the data you have so far is that they're large.

DR. HILL: Well, and again, when you say low molecular weight fraction is present at 4 percent at the end of that paragraph for one of the ingredients, that's Polyurethane 69, so if that ingredient is used in a formulation at 1 percent, then 4 percent of that's a small amount. If it's used in a formulation at 70 percent, then 4 percent of that is maybe nontrivial. So that's -- but then again, you know, then that raises the question is there any biological issue with that substance and what is that low molecular weight fraction which is why I keep asking for it.

DR. MARKS: So I think we keep coming back to an insufficient data announcement since this is the first time we reviewed it, and to, let me see here, get the molecular weight ranges for each of the polymers, and the stability of the ingredients and see where we go from there, and then, perhaps, the next time look at it, start separating out ones that we think could be safe, and which ones are unsafe, or not unsafe, insufficient.

Does that sound like a reasonable approach at this point?

DR. SHANK: Yes, it does.

DR. MARKS: Any other comments?

(No response.)

DR. MARKS: So, we'll see whether I second insufficient data announcement somewhere, and then we'll combine our needs of the two teams and come up with a conclusion for tomorrow.

DR. GILL: So, Dr. Marks, there were no other needs that the Marks Team thought they needed for this ingredient?

DR. MARKS: I don't think so. I think I --

DR. SHANK: That depends on what we get from our first request.

MS. BECKER: So if there's low molecular weights, do you want to say you want sensitization and dermal penetration?

DR. SHANK: We might.

DR. MARKS: It depends on the ingredient because if I look at some of these, we already have irritation sensitization data which would indicate it's safe no matter what the low molecular weight is.

DR. HILL: There was another goofy question that I came up with, and I'm just prefacing by saying "goofy," is there are quite a few of these that have low molecular weight amine monomers, and then I was entertaining the notion that we're going to need a nitrosamine boilerplate when, in fact, in the polymer they would not have that problem. So probably comes back to either entrained amines releasable under conditions of formulation or use -- no, formulation really. I don't know.

DR. BERGFELD: Does that have to do with stability though?

DR. SHANK: No. Well, it might. Theoretically, it might.

DR. MARKS: Ron, Ron, and Tom, you know, we mentioned specifically irritation and sensitization, but would you be concerned about other toxic effects because I could list four or five at this point where irritation sensitization is okay.

DR. SHANK: For some, yeah.

DR. MARKS: But --

DR. SHANKS: For ones that are given in the same way geno toxicity we have some data on some of them.

DR. MARKS: Okay. So, no. So we'll see how that sort of intersects, perhaps, at the next time when we, if we get more data on stability and molecular ranges.

DR. SHANK: That's right.

DR. HILL: Yeah.

DR. MARKS: Does that sound good?

DR. SHANK: Yes.

DR. MARKS: Okay. Well, that was fun.

DR. SHANK: Now you can relax.

Dr. Belsito's Team

DR. BELSITO: We've got (inaudible).

So this is the first time we're looking at 66 ingredients. (Inaudible) and artificial nail builders, binders, film formers, air fix additives, (inaudible), surface modifiers. And they're polyurethane, copolymers. And we originally only had information pretty much down to 14.

Now we have some information on polyurethane 1 from wave 2. It included ocular irritation and some mascara sensitization, irritation HRIPT. So we have some on the low molecular weight, but the question is does it really answer all of our questions about this.

DR. LIEBLER: I think here's where I interject something. These are really fundamentally different from the pegs and the PBG's where you got a name and a number. And the low number represents smaller molecules. These aren't like that at all. These are basically, polyurethanes are like submarine sandwiches. They might have some lettuce, they might have some meats, they might have some -- they have different meats, cheeses, pickles, olives. So these are all made from different monomers.

They're all very large molecular weight, molecules, polymers. They all have as a group -- they have generically similar uses and properties. But polyurethane-1 for example is not a small molecule compared to polyurethane-10 or 24 or and so forth.

DR. BELSITO: Okay.

DR. LIEBLER: That was the thing I realized once I got into this report. These are all like the chef's special and there are so many ways that you could combine an isocyanate, polyol and an acrylic acid. And in different combinations you can get molecules that generically have these similar family of properties. But they're all big molecules, so they're not absorbed and we can treat the entire report like big molecule polymer kinds of reports.

DR. BELSITO: Okay. So we need to be more concerned about the impurities.

DR. LIEBLER: Impurities. Right. Although, I'll have a comment about the impurities when we get to talking about that.

DR. BELSITO: Okay. So there is a use for something that's called polyurethane, that doesn't have a definition. And we have no concentration abuse [of use]. But it's reported to VCRP as 17 uses what do we do with that?

MS. BECKER: We have no idea what it is cause it's not a name in the dictionary, as it stands.

DR. BELSITO: Right.

MS. BECKER: It's a technical name for an ingredient that's not on here. But it's not one of these, so you can know the existence and say we don't know what it is. But...

DR. BELSITO: Sloppy reporting to the FDA. Jay what do we do with that when we're told there's something that is not listed as a cosmetic. And the cosmetic ingredient were (inaudible)

DR. ANSELL: Has no applications and no concentrations and no structures.

DR. BELSITO: It's 17 reported uses to be VCRP that's all we know.

MS. BECKER: And all we know is they called polyurethane. And it could be any combination of the ones we're looking at.

DR. ANSELL: I mean, if we don't know what it is, I think we're pretty clear on that. We're insufficient based on, if nothing else...

DR. BELSITO: But it's not listed as a cosmetic ingredient we're even reviewing.

DR. ANSELL: You know, almost all of these have no cosmetic applications. So that is not the driver, the driver is whether the material. The safety assessment of the material can be reformed by the ingredients as a whole. The formation of the family whether one member of that family has an application or not. Has not been a problem in the past. But specific to something that we don't know what it is, then it's clearly insufficient for (inaudible).

DR. LIEBLER: Is it an ingredient?

MS. BECKER: No, it's not.

DR. BELSITO: It's not a cosmetic ingredient that's my problem. It's not even in the dictionary.

DR. LIEBLER: Should be out the report then.

MS. BECKER: Out the report or note that its existence is saying you're not going to address it.

DR. ANSELL: Well, it's not a cosmetic ingredient that's not in the family then...

MS. BECKER: It's listed in the VCRP as polyurethane no number afterward. Like all the others.

DR. BELSITO: I suspect it probably is a polyurethane with a number and very sloppy reporting by industry. But the question is what do we do with it. I mean, that's what I suspect. I don't know it for a fact, I mean, I would say that under the table where we discuss the ingredients and the concentration of use. There be

a star or a footnote and say there were 17 reported uses of "polyurethane." This is not a material that is in the Inky (phonetic) [INCI] Dictionary. We have no idea as to what that represents. That specific material may or may not be being reviewed here. Since we have no further information. But pending that, we're not considering the safety of that material that has been reported as polyurethane.

DR. ANSELL: Either drop it from the master list because it doesn't have any --

DR. BELSITO: It's not even on our master list. It's just in the table.

MS. BECKER: It's just noted that it exists. Because it was in the VCRP when you search polyurethane.

DR. LIEBLER: So we just add exactly what Don said, to the paragraph on uses. And it says, 17 reported uses to VCRP don't correspond to specifically any polyurethane in the Inky [INCI] Dictionary. You got that basically, right.

MS. BECKER: Yes.

DR. LIEBLER: And I think we're covered with that. Now, when you do have these reported uses, do you have the companies that report them. Is it possible to go back to the companies who reported those 17 and say, can you clarify? Did you mean polyurethane followed by a number?

MS. DEWA: Based on what I have it. Are you talking about the one which has maximum concentration of use 15 percent?

MS. BECKER: No, it has no use concentration. In the VCRP there was one polyurethane with no number after it, listed and has uses. But there's no -- we don't know what it is.

DR. ANSELL: I don't even know why we would carry this forward. I mean it's not on table, it's not on ingredients, it's not listed in the Inky [INCI] Dictionary.

DR. BELSITO: Right.

DR. ANSELL: It's just an error in the -- whether it's...

MS. DEWA: So they just state that's polyurethane (inaudible)

DR. ANSELL: We don't drive the families from the VCRP. We drive the families from the dictionary.

MS. DWA: That was my next question, you just took it out. Because usually this listing comes in how it is stated in Inky [INCI]? What's the function and so on. And what is reported in the VCRP, it is up to the establishment or the particle list and that's the way they do it.

We usually, do not go back and ask them. Because that's where they put it. But if there's a need we can check it but we haven't done that. So like I think I would go with it if there's no concentration or no use. Then the panel can decide if they want to drop it.

DR. BELSITO: Okay.

MS. BECKER: We have combined before with botanicals because they have names that were close. (Inaudible) technical name of that botanical. But this particular polyurethane no number, we have no idea what it's connected to.

DR. LIEBLER: You can't group it with anything it's not in the dictionary. Either solution is okay with me. Don so basically saying, there were some that were reported to VCRP that were not in the dictionary. It's not possible to group these with any of the other ingredients. We're not reviewing their safety period. Or you just strike this column out the table and be done with it. Either way I'm okay.

DR. ANSELL: It brings in -- then I noticed in reading the footnotes. Then they put in we don't know whether this is a powder, we don't know whether this is a spray. We don't know...

DR. KLAASSEN: We don't know nothing.

DR. SNYDER: I think based on (inaudible) I mean, I have a real problem with this report because it seems like we inappropriately grouped these like the pegs and other things, but there's so vastly different. Half of them you don't even have use or data on. I mean almost half of them. And they're all made up of these different constituents so need to know the impurities for each individual one. Because no two of them are the same, is that not correct?

DR. BELSITO: A lot of them are isocyanates, acrylates, methacrylate. I mean --

DR. ANSELL: The unifying is that they have one monomer in common and that they have at least four monomers in the (inaudible).

DR. LIEBLER: I'm not really worried about the impurities with these. I know that theoretically it's an issue. But the way that these are formulated and used any of the monomeric impurities are so highly reactive. That they will be (inaudible) with solvents before it even leaves the factory.

DR. SNYDER: Because you look at table one, I mean, the mere definition.

DR. BELSITO: So that will be a discussion?

DR. LIEBLER: Yeah.

DR. BELSITO: A la Dan Liebler.

DR. LIEBLER: We'll deal with it. I know it will come up tomorrow but we'll deal with it.

DR. BELSITO: I'll let you deal with it Dan.

MS. BECKER: So the monomers are so reactive.

DR. BELSITO: It'll be Dan versus Ron.

MR. LIEBLER: It's okay.

DR. BELSITO: Round 15. Abstain.

MR. LIEBLER: It's like the coyote -- Wiley Coyote.

DR. KLAASSEN: There is some information in the impurities that says, that it contains no detectable residual unreacted isophorone or isocyanate et cetera.

DR. BELSITO: Right.

DR. KLAASSEN: So for a few of the chemicals it even says that.

DR. BELSITO: Right. We know that.

DR. ANSELL: That is one of the unifying things that the monomers are highly reactive.

DR. KLAASSEN: Right.

DR. ANSELL: There's nothing less than a thousand bolt units.

DR. LIEBLER: These are big molecules. There's the slightest dispersions in water or alcohols.

DR. SNYDER: So we have molecular weight data on all of them?

DR. BELSITO: No, but Dan gave us the molecular weight data. I said we had no info on molecular weight et cetera. Molecular weight, manufacturing impurities were a lot, but all will be large and unreacted monomers readily consumed.

DR. LIEBLER: Right.

DR. BELSITO: That was Dan's comment.

DR. LIEBLER: I have a couple related things since we're on the chemistry stuff. Let me just get these up for (inaudible).

MS. BECKER: Okay.

DR. LIEBLER: So you have this figure one with just a urethane linkage. I don't think that helps much. What I would recommend is a three examples of structural motives. That contain the urethane link polymers with some of the other monomer components, in a final polymer structure or a portion of a structure. And you can pick any three that you can reasonably come up with structures for or talk to Bart and see what you can come up with.

But just to represent the diversity of these molecules. I've written a paragraph that goes at the end of the chemistry section right before this little figure 1. To explain the polyurethane, you know, copolymers or highly (inaudible). There's no systematic relationship between average molecular weight and numeric component of the ingredient named.

Representative structure of three different polyurethanes are depicted in a new figure 1. So you guys can see what you can come up with. Send to me I just like some illustration of the guts of these that shows these are the polyurethanes stuff. With other stuff attached to it.

MS. BECKER: Okay.

DR. LIEBLER: And then with, you know, little unresolved bonds hanging out to the edges just show these are parts of very large molecules.

DR. BELSITO: So Dan is going to work with Lillian for some structural representation.

MS. BECKER: I would work with Bart on that.

DR. LIEBLER: Take crack it at and e-mail it to me and I can give you my feedback. And...

DR. KLAASSEN: I wonder -- I don't know if we can change the title. It'd be better if this was polyurethane copolymers rather than polyurethanes or not.

DR. LIEBLER: I think it's reasonable, copolymer. I mean, they are all copolymers.

DR. KLAASSEN: Right. When you just say that, I mean, I don't what's legal or not legal.

DR. ANSELL: No, no, no. I'm just trying to think of whether co is the words opposed hetero. Because to be a polyurethane it has to have more than four or more monomers. Because if it's three or less than would be named like regular polymers.

DR. LIEBLER: They're certainly all polyurethanes.

DR. ANSELL: They certainly all polyurethanes.

DR. BELSITO: So the safety assessment of polyurethanes -- what Jay are you suggesting?

DR. ANSELL: You know, when we call something that has more than two monomers. It's not hetero, it's not a copolymer. I guess. Polymers of...

DR. LIEBLER: Let's cogitate on that and then may be bring (inaudible).

DR. BELSITO: Why can't we just say polymers?

DR. ANSELL: It is a good point to try to capture the fact that this is really quite unique. In comparison to other polymers we've worked with.

DR. LIEBLER: These are all called polyurethane dash something.

DR. BELSITO: Polyurethane macro polymers.

DR. ANSELL: Yeah, something like that.

DR. LIEBLER: Macro polymers is kind of redundant too. So...

DR. BELSITO: Safety assessment of a gamesha polyurethane polymer.

DR. KLAASSEN: That's more than just urethane (inaudible).

DR. LIEBLER: Urethane is the common structural feature that they all have.

DR. BELSITO: Right. And a whole bunch of other stuff.

DR. LIEBLER: And their polyurethanes. I take your point Curt. I think that coming up with something more specialized might not cover all of the ingredients.

DR. KLAASSEN: Fine.

DR. LIEBLER: I'll look through this and get back to you.

DR. SNYDER: So Dan polyurethane 11 has 315 formulations, 303 of them are leave ons. Is there anything in there in that what they define it as. Would be of concern as far as residual material or anything.

DR. LIEBLER: No not really. I mean no more than...

DR. SNYDER: Than the rest of them.

DR. LIEBLER: Any of the others.

DR. SNYDER: Okay.

DR. BELSITO: So let's get back to a question that we had earlier. Under use it says, "polyurethane-1 has the highest reported maximum concentration of use in the now product at 15 percent." Yet, in wave 2 we get two HRIPT's on mascara that's at 30 percent. So if it's only used at 15 percent, why are we getting information on a mascara at 30.

Now, I know that these aren't provided at a 100 percent. For instance, one of the issues I have is that we don't know the concentration of use. Polyurethane-60 and 61 which have methylisothiazolinone and benzothiazolinone thrown in as preservatives which then become an issue for sensitization. Which is why I ask the question earlier today, would that be labeled.

So the question is when we're given the data in the table as to use concentration. Is that the use concentration of the actual polyurethane? Let's say polyurethane-1 was provided as 10 percent and whatever. And the use concentration -- and they used it at one 1 percent. So the use concentration is 1 versus this report of 10 percent. I don't understand that, you know, why.

You don't do an HRIPT on a finished product. On never 200 patients unless that product exist at that concentration. Particularly, when it's negative results. I mean, I can see if the results were positive and the company, say oh, well we're not going to market this mascara.

MS. BECKER: I think part of the issue is a lot of these are provided in water or another solvent. And is the recorded concentration of the polyurethane as provided.

DR. BELSITO: That's my question.

MS. BECKER: And some of these I don't know either. Some of these I read them over and over again could not figure out which way they were vented. And I'd read again and change my mind. So it's not clear in a lot of these.

DR. LIEBLER: The technical data sheets that we got on some of these ingredients, indicated that there were like percent active. Or 20 percent in water.

DR. BELSITO: Right.

DR. ANSELL: 40 percent solvents.

DR. BELSITO: None of them seem to be pure.

DR. LIEBLER: No, not a 100 percent dry powder --

DR. BELSITO: Or not even close to pure. Right.

DR. LIEBLER: They're provided as suspensions.

DR. BELSITO: Right.

DR. LIEBLER: And so those are all necessarily less than 100 percent. So the problem is it's not clear if that HRIPT actually documents what the actual percentage of this is. Or whether it was -- they had 30 percent of the mix of this mascara was 20 percent in water.

DR. BELSITO: That's my point.

DR. LIEBLER: In that case you get 6 percent.

DR. BELSITO: Right. It's an issue with all of these that are provided. And I think that when Carol is going out -- I mean if she could verify for us that and point to facts. That the highest concentration of use in a mascara is X. Then we can infer that in that study they were saying 30 percent of the material as supplied. Which only constituted percent active, but you know, we can't. And since unfortunately the information this panel gets it's not always 100 percent accurate. It raises questions at least in mind as to whether the information we have on the use concentrations now. I know we state in our final conclusion, that it's based upon the concentrations that we were told exist in the table 3. It's just disconcerting to me. So I'm trying to get -- I have looked it up and I'm not seeing my note. What that reported use in the eye area was the highest one.

DR. SNYDER: So the wave 2 data there was a statement from a submission that said, "the active ingredient in this product," this polyurethane-39.

DR. BELSITO: Yeah. Because the outcome with other stuff.

DR. SNYDER: But active ingredient and how's that?

DR. LIEBLER: Active in the sense that --

DR. BELSITO: It meets the definition, it's the film former.

DR. SNYDER: And then it says, "the components of a preservative system are not covered in the toxicological summary."

DR. BELSITO: Right.

DR. SNYDER: I think solids would be a better description than active.

DR. LIEBLER: Right 30 percent solids.

DR. BELSITO: It says, "polyurethane-1 in the eye area of the highest is 4.6. And how is it supplied? Were we given that information? So 4.6 percent is the reported highest. So it's...

MS. BECKER: Table 7, don't know about number one whether it's a suspension or not. Checking the definition and the definition is not helpful.

DR. LIEBLER: So you've got table 7 probably illustrates the range of percentage solids here. For which we have data and their lowest is 20 percent and the highest looks like 60. Most of them or over around 40. And then the majority of these as Jay pointed out are not in use. Yeah, at least half.

DR. BELSITO: So basically, if you assumed that polyurethane-1 is provided as a 15 percent emulsion and it was tested at 30 percent of the product as provided. Then you would get down to the approximate 4 percent that is reported in the concentration of use.

MS. BECKER: Yes.

DR. BELSITO: So I'm guessing that when they're saying 30 percent they're talking about okay, here's the drama polyurethane-1 that we got. Take the material dilute it to 30 percent which gets you to 4.6 percent of actual polyurethane-1 and tested. We don't know that.

DR. LIEBLER: In the absence of having specific information on the percent solids of an ingredient in a product that was tested. Then perhaps we could assume that the maximum is the maximum reported to use. Or maybe it was just 60 percent or 66 percent. And use that as a type of approximation to say, that if it was 66 percent that were to keep the calculation easy 50 percent. But if it was 50 percent and that 30 percent in the mascara is actually 15 percent.

MS. BECKER: At most 15 percent assuming all those hold true.

DR. LIEBLER: Yeah, I don't...

MS. FIUME: So the VCRP data -- I guess my assumption would be it's being reported as provided not percent in solids. No.

DR. BELSITO: No, for the VCRP it's just a matter of used or not used. But the concentrations that we're getting for an HRIPT and from Carol. They're for tremendously for this mascara. Cause why do you do an HRIPT at 30 percent when the highest reported use in the eye area is 4.6 according to Carol. So my assumption is that it was --

MS. BECKER: 7 percent polyurethane and 35 on the mascara.

DR. BELSITO: Yes, I'm talking about polyurethane-1 which was done on HRIPT (inaudible) wave 2 at 30 percent. And is reported at 4.6 percent. So...

DR. LIEBLER: So I take one of our data needs is the percentages of solids in these.

DR. BELSITO: Then we at least try and determine that.

DR. LIEBLER: Right.

DR. BELSITO: And then we make sure that when Carol passes, she specifically says, when she knows that products particularly in this category are not being supplied at 100 percent. They're being supplied in other vehicles that she specifically asks for the concentration of use of the actual product, in finished

consumer goods.

DR. LIEBLER: Yeah.

DR. BELSITO: Not the concentration of what was supplied. But the actual material we're evaluating. I mean, because it's just very confusing. And so, I think that based upon what I'm seeing, that's my assumption of why they have a HRIPT a 30 percent. That it was probably 4 percent, 4.6 percent accurate.

DR. LIEBLER: I agree it's an agreeable assumption we can't prove with actual data. So I had a related sort of chemistry presentation idea Lillian. Table 1 has these structures that at first I thought, oh you're just showing the structures of the monomer components or the prepolymeric components. And not any constructual information about the polymer. But actually, I think it would probably hard to come up with a way to represent the polymer structure in a table like this.

They're huge, they may be known to some extent but in a way, they're largely theoretical. Just categorizing molecules of that size and at that level is probably pretty hard. So I was trying to think of another way to present this. But I think this is probably the best thing. However, you have the -- for example the polyurethane-50 I'm just looking it up. A copolymer of three or four things that you have listed. And then you have in brackets (inaudible) monomers colon and then you show these four structures.

And I guess I would simply -- I'm not sure what more you can do with this other than what you done. But I would do is change the title to definitions. And monomeric components or precursors definitions and components -- polymer components. Definitions comma polymer components and functions of the ingredients of the safety assessment.

MS. DEWA: My point is what you said, the calculation and the percentage of the ingredient tested in the product. Would apply across any of the study results and this particular study.

DR. BELSITO: Right. No, no, no.

MS. DEWA: Because that's like, I go back to my days at Dupont when we what we'll be testing. Then when we do the calculation then that would be a different concentration.

DR. BELSITO: Right.

MS. DEWA: So that point probably should be (inaudible) all the studies then.

DR. BELSITO: One would hope that usually when see them, but it's not clear to me from this polyurethane study data printed it out. But it's not clear even when you look at the hard data. Whether it was 30 percent poly-1 or 30 percent of a product that was a certain percentage of poly-1. Cause often times it'll be crossed out and it will, you know, contains x percent of this. And that exist in the materials that we received.

So then another issue that I've already touched upon, and that is that polyurethane-60 and 61 can have methyliso [methylisothiazolinone] in it as a preservative. And we have no concentration of use for polyurethane-60 or 61. We have reported uses but no concentration. So the highest leave on dermal exposure that we have reported as Lillian just mentioned is for polyurethane-33 at 7.5 percent. So when and if we were to sign off on this as safe as used. I would presumed that would mean that polyurethane-60 and 61 could be used in a leave on up to 60 -- or up to 7.5 percent.

In which case by back of the envelope calculations, MI could end up at 5.625 percent in a finished product. Which is enough in a deodorant in an intimate wipe to potentially cause sensitization. So if we do sign off on this we would have to make a note for this. And actually, since most of these and probably all of them are not supplied at 100 percent.

They're supplied in something else with a preservative or something else. That a note be made that since there are other materials added, manufacturers should be aware of limits on sensitization, irritation and other toxicity end points. That might be applicable to use of this material that potentially may contain those ingredients.

DR. ANSELL: The suppliers would -- the purchasers would know whether they were preserved. It was a question specific to labeling of --

DR. BELSITO: I understand --

DR. ANSELL: -- but you're right because it's the same issue --

DR. BELSITO: No, I'm ticked off about the labeling. Because when I as a dermatologist see someone who's severely allergic to methylisothiazolinone. I am not telling them, well oh you know what, polyurethane-61 and 60 may contain this. So you probably shouldn't use products with this polyurethane. Because it may not be on the label. I think that that's an issue. That's a separate issue that certainly doesn't apply to safety.

It applies to me and the consumer who's unable to read a label and know whether a material that they're allergic to is there. And I actually think those regulations should be changed. I think that if someone is

formulating -- even if they're not relying on the MI that's in that poly-1 to be their preservative it's there and should be labeled. As far as I'm concerned.

MS. BECKER: As I understand the rules when they get something that is a mixture as of these are, they have to list everything in that mixture. Including the MI on the label.

DR. BELSITO: Well, 1 percent if it's not a carcinogen, right. In their MSDS sheets so it's even possible that some of these could come in if they contain less than 1 percent. Without it even on the MSDS sheet to the blender.

DR. ANSELL: The definition and the trivial is there and it can't serve a technical function and has to be present to (inaudible) levels. And what one could easily argue in your case, that if it's carried through at a level where it could induce allergens. Then it would not meet the definition of trivial and would require labeling under those conditions. But you know, I'm not sure -- I think a note is very relevant because it's not clear that a formulator would have a sophisticated and understanding of the dermatologic implications as you...

DR. BELSITO: Right. I just think for these -- I mean ultimately, we'll get to say, I think based upon Dan's comment that the monomers are so reactive they're not going to persist. That the molecules are all large regardless of the number. That from the standpoint of the polyurethanes we're going go safe as used, I'm more concerned about what else is in there, when they're blending them and just looking at the example of MI in 60 and 61.

Because we don't know the concentration of use, safe as used. As used is up to 7.5 percent in a leave on from one of them. And if MI was present at the maximum range and 60, that it said it could be. Then it could be 5.625 in a finished product even if they don't add additional isothiazolinones. And that we know from QRA is sufficient to induce sensitization in intimate wipes and deos [deodorants ?]. So...

DR. ANSELL: We do with botanicals we put in notes - -

DR. BELSITO: Right.

DR. ANSELL: We put in notes that you should be aware that this ingredient may be present in more than one botanical.

DR. LIEBLER: So then we say when formulated to be non-sensitized. So for me I guess the issue is do we just put this in the discussion and point out that it could be an issue. Or could we actually incorporate it into the conclusion.

DR. BELSITO: We can put it in the conclusion too and say that, while we don't think a polyurethane are sensitizing. It is clear that they are not provided as pure materials and the materials provided are often times contain potentially sensitizing preservatives and other ingredients.

And therefore, manufacturer should be aware of this. And ensure that the final level of any materials ingredients of concern are below toxic thresholds including for sensitization, irritation etcetera.

And then in this case my concern is sensitization. We could actually create a boilerplate for that to be used for any material that's not provided as pure. And then in this one the concern is sensitization, so when formulated to be non-sensitized.

MS. BECKER: We're finding more -- especially as we are doing the polymers. They're provided in an emulsion something else.

DR. BELSITO: And I agree and I think, you know, that's why we need to probably create that boilerplate for the discussion. And why we need to make sure that Carol is specifically asking companies -- I mean, there's little we can do about the studies that have already been done, if it's not clear what was done. But she needs to be specific, as I don't want to know how your finished -- the concentration of your finished product.

I want to know the concentration of the actually ingredient in that finished product, what it is. Not, you know, the percent of polyurethane-1 that you put in from the manufacturer. What is the actual percentage of polyurethane-1.

DR. KLAASSEN: In regard to sensitization since we've talking about that. In the summary it says, "polyurethane-62 was predicted to be sensitizing and the DPRA." It actually was predicted not to be sensitizing in the DPRA.

DR. BELSITO: Right.

DR. KLAASSEN: A very important change.

MR. SNYDER: Also we have physical chemical properties. Listed for particle size for polyurethane-14. Which is 1.9 to 3.2 which is a (inaudible). So we can't just get away with a boiler and how many other ones are in that range. The (inaudible) so it kind of becomes the same question, right. We can't say they can all be used across the table.

DR. LIEBLER: It depends on how it's formulated. Because a droplet isn't -- I mean a droplet or particle size is

just the ingredient that's used in the product. It's the size of a particle that's from the product.

DR. SNYDER: So it's a particle size of polyurethane-14 was reported to be.

DR. LIEBLER: Right. But that's not the product. It's something that goes into the product.

DR. SNYDER: But then we're also saying but they're not metabolizing there's no...

DR. LIEBLER: Right. So that sets a basically a minimum size -- in other words, it might be that if you had some hairspray that had this, it could have a particle that is as small as the smallest particle size just mentioned. But there's other stuff in the spray that would be (inaudible) to the polyurethane and probably that might make for larger particle sizes.

I'm not sure that how much larger, but I think what you're describing for the ingredient in a product that's composed of multiple ingredients, it couldn't be any smaller than this single digit micron. But it probably could be a good bit larger. Does that make sense?

DR. BELSITO: I mean, we definitely need the respiratory boilerplate there. And these are such large molecules according Dan. I find that I wonder what they're measuring there in terms of particle size. I almost wonder if it's not monomer.

DR. LIEBLER: Well, it's not monomer but...

DR. BELSITO: Right. I'm teasing.

DR. LIEBLER: But -- I'm trying think how to respond to Paul's question. I'm not sure if you understand me (inaudible). Or you don't understand what I'm trying to say.

DR. BELSITO: (Inaudible) to a size that's not a concern. That's his discussion.

DR. LIEBLER: But we just addressed in the discussion that we didn't know that there's small particle size.

DR. BELSITO: Right.

DR. LIEBLER: But the panel is under the impression that there is (inaudible) that this will not be the (inaudible). But it's interesting cause it's unpublished dated submitted by the PCPC.

DR. BELSITO: Right. We have no developmental and breprotoc [reproductive?] studies? I assume we're okay with that because of lack of absorption. And the fact that the residual starting materials will be...

DR. LIEBLER: Washed away during the product preparation and consumed by reactions in product formulations.

DR. BELSITO: So washed away in what, Dan?

DR. LIEBLER: Ingredient preparation. In other words, at the factory where they're making this. They just did a polymer reaction they got this glob in the bottom of the vessel. And they're probably going to wash it with.

DR. BELSITO: End consumed and reactions in cosmetic formulas.

DR. LIEBLER: Yes.

MS. DEWA: (Inaudible) Can I ask a brief question.

DR. BELSITO: Sure.

MS. DEWA: So if an ingredient has -- say for example MIT or anything which we think can cause sensitization. Say in the end formulation, if it also has an MIT and the concentration that MIT may increase --

DR. BELSITO: Right.

MS. DEWA: -- as aversion to be because also part of another ingredient.

DR. BELSITO: Right.

MS. DEWA: And that could also cause sensitization correct?

DR. BELSITO: Right. That's the point that we're going to be putting in our discussion and then adding in this particular case. To the conclusion safe when formulated to be non-sensitizing.

DR. LIEBLER: It's the logic that we use with multiple botanicals.

MS. DEWA: Botanicals.

MALE SPEAKER: And probably relevant to anything sold as an emulsion.

MS. DEWA: Yes. Exactly, yes.

DR. BELSITO: Right.

DR. ANSELL: And I think copolymer would probably technically correct.

DR. LIEBLER: For this family.

DR. BELSITO: Yes.

MR. DEWA: Okay.

DR. BELSITO: Okay. Then in addition to the MI issue that I had (inaudible). The EU had an issue with trimethylamine and dimethylamine and dimethylethanolamine. That were present in poly-36 and 60. So how do want to handle that since they're not really sensitizers. I guess the issue are the amines and the toxicity of amine groups. Are these going to be rapidly consumed and washed away Dan.

DR. LIEBLER: Not by the same kind of reactions. I mean, they may be removed partially by washing of the ingredient as it's produced by the factory. But it's more of a residual, I mean, like ethylenediamine for

example or triethylamine. These are in some of these products.

DR. BELSITO: They're neutralizing agents.

DR. ANSELL: Probably the same way as DMI putting out that there are restrictions for triethylamines.

DR. BELSITO: But in this case the EU was very specific, right. Remember they I haven't write their percentages probably is in the --

MS. BECKER: 2.5.

DR. BELSITO: 2.5 percent. So do we want to be very specific in the absence of knowing why they chose 2.5. I mean this is just from -- you have those from an eco-document or --

DR. ANSELL: It's annexed, right?

MS. BECKER: Yes.

DR. BELSITO: Is the annex codex?

DR. ANSELL: Annex 2, annex 3.

MS. BECKER: European Commission Regulation numbers and a coating [CosIng] database.

DR. BELSITO: Okay. But we don't know why or how they reached their conclusion.

MS. BECKER: No.

DR. BELSITO: But those were the limits that she used.

MS. BECKER: Don't have the source.

DR. SNYDER: Do we have that in this study?

DR. BELSITO: We have it at the cosmetic use --

MS. BECKER: At the end of the use section.

DR. BELSITO: -- don't we?

MS. BECKER: End of the use section. So 12.

DR. BELSITO: Then under sensitization --

DR. SNYDER: (Inaudible) non-cosmetic use.

MS. BECKER: Right above non-cosmetic use. Page 12.

DR. BELSITO: And then on page 17 of the PDF we're told that polymer 36 is approximately 1 to 1.5 percent. Trimethylamine and that polyurethane-60 and 61 I have approximately 1.3 and 1.5 percent by weight dimethylethanolamine.

MS. BECKER: What page please?

DR. BELSITO: 17 of the PDF the summary.

MS. BECKER: Oh.

DR. BELSITO: I just picked it up there so it obviously comes from some prior page number.

DR. LIEBLER: It must be under impurities

DR. BELSITO: Yeah, I'm sure.

DR. LIEBLER: Well, these aren't sensitizer.

DR. BELSITO: The amines can be sensitizers but I don't think that's the major issue why we be concerned. I don't think it's the weak link in the safety chain here. I think the weak link is the presence of amines.

MS. BECKER: That information is from page 11 and table 7.

DR. LIEBLER: You can't see any mention of amines on page 11. So where are we stuck here, is this just -- or we're just hung up on the fact that they're --

DR. BELSITO: I mean, safe as used and then discussions.

DR. LIEBLER: I mean, I think it just minimize the quantities of -- I mean even though we can point to the monomer -- the reactive monomers. Would be consumed by some of the chemistry. We can still put some, you know, fairly generic language that says, you know, our efforts should be taken to reduce the concentrations of any residual monomers or low molecular weight amines.

DR. SNYDER: Be just like the botanicals where we say (inaudible) of concern should be minimized because you may accumulate over formulations.

DR. LIEBLER: I don't think we have a particular hazard if we're stuck with these (inaudible) what may be amines.

DR. SNYDER: So why no 3, 22, 30, 31, 37, 38. Why are there six missing?

MS. BECKER: I have no idea.

DR. LIEBLER: They weren't popular.

DR. ANSELL: Apparently, the numbering is just the order in which applications are received.

DR. LIEBLER: That's what I wonder, yeah.

DR. ANSELL: So yeah, it just never caught on.

DR. KLAASSEN: The other just beat them to the market. They had no added advantage.

DR. LIEBLER: It's like the island of loss of boys -- the island of unpopular polyurethane formulas.

DR. BELSITO: Okay. So in the discussion inhalation, boilerplate which in this case would include the fact that it was poly-14 you said, Paul.

DR. SNYDER: Yes.

DR. BELSITO: That had this.

DR. SNYDER: (Inaudible) given.

DR. BELSITO: That we don't have a method of manufacture and molecular weight, but for all of these impurities residuals but these will all be large.

DR. SNYDER: You start with you don't ADME.

DR. BELSITO: Right.

DR. SNYDER: So they're large.

DR. BELSITO: Large. Not absorbs.

DR. SNYDER: Yeah.

DR. BELSITO: And the starting materials will be consumed.

DR. LIEBLER: The reactive monomers.

DR. BELSITO: Washed or consumed away. Okay. That other materials of concern to the panel include triethanolamine. That are added to as part of the finished product. Such as amines and

DR. LIEBLER: Ethylenediamine. I think -- just say low molecular weight amines that are used in the manufacture.

DR. ANSELL: Are they monomers or are they actually.

DR. LIEBLER: The low molecular amines and things like ethylenediamine. They're actually part of the polymerization process.

DR. BELSITO: Right.

DR. LIEBLER: Where they use to control steps in the polymerization process.

DR. BELSITO: So residual low molecular weight amines, how we saying they should be handled.

DR. SNYDER: I think you just need to be aware of them.

DR. BELSITO: Dan had the comment.

DR. LIEBLER: They should be (inaudible) is that what mean?

DR. BELSITO: Did you just say minimize or do you want to go with the --

DR. SNYDER: What potential sensitizing amines.

DR. BELSITO: No, it's not sensitization that we're concerned about with the amines.

DR. LIEBLER: These aren't really toxicants, I mean, at the levels that we're talking about, these are small contaminants. Of big molecules that are going to rinsed and washed and then put into formulations, where there's at least alcohols and probably water. That consume the reactive monomers and then the amines, you know, they put in enough to neutralize the acidic components during the manufacturer essentially.

DR. SNYDER: So we have a whole paragraph on that under the cosmetic use where Europe puts a restriction on (inaudible)

DR. BELSITO: Yeah, I know, that's what we're discussing before. Whether, you know, we don't have a basis as to why they chose that number. So do we just go along with them or do we have a way of crafting this.

DR. KLAASSEN: I think we craft it.

DR. BELSITO: What.

DR. KLAASSEN: I like the crafting it. Not saying a number but just minimizing it.

DR. BELSITO: Minimizing it below what?

DR. KLAASSEN: I wouldn't say below what.

DR. LIEBLER: You don't have any basis to choose a number.

DR. BELSITO: And our concern is nitrosation?

DR. ANSELL: Right. I mean, we have boilerplate about lead, we have boilerplate about...

DR. BELSITO: So residual low molecular weight amines should be minimized. And products containing this should not be...

DR. LIEBLER: Should be minimized to reduce the risk of nitrosating reactions.

DR. KLAASSEN: Don't they already have boilerplate for that?

MS. BECKER: Somewhat, yeah.

DR. BELSITO: So we'll use the nitrosation boilerplate?

DR. KLAASSEN: Sure.

DR. BELSITO: Okay. And then manufacturers need to be aware that sensitizing materials such as MI could be added.

- DR. SNYDER: Yeah. I think we just bringing that into the discussion and then we know that the polyurethane-60, contain low levels of MI therefore formula (inaudible) concerned about the cumulative blah, blah, blah, blah, blah.
- DR. LIEBLER: And that explains our non-sensitizing conclusion.
- DR. BELSITO: Right.
- DR. SNYDER: This is your report.
- DR. BELSITO: Okay. So let me go through what we have so far. So discussion, inhalation boilerplate with some discussion of the size that was given for poly-14. But our -- not impression, our experiences that these molecules won't be aggregated in formulation. And would not be (inaudible) and use of the (inaudible) boilerplate.
- DR. LIEBLER: Yeah. I would simply say that the size of the particle of an ingredient in a product does not predict what the size of the particles from the product (inaudible).
- DR. BELSITO: So the size the of a particle added to the product is not predictive of the size of the (inaudible) particle end product.
- DR. LIEBLER: Right.
- DR. BELSITO: Okay. So you got that Lillian? And then the usual respiratory boilerplate. They're all are large and not absorb, so we're concerned about the lack of reproductive or geneo toxicity or systemic effects.
- DR. LIEBLER: Right.
- DR. BELSITO: That the reactive monomers would either be washed away in the manufacturing of the product itself or consumed quickly in the final product.
- DR. LIEBLER: Right.
- DR. BELSITO: Other materials of concern added to the panel, include the amines which should be minimized to reduce the risk of nitrosation with a nitrosation boilerplate. And manufactures need to be aware that some of these products have sensitizers added, such as methylisothiazolinone. And finished products should be formulated to be non-sensitizing. And then our conclusion is safe as used when formulated to be non-sensitizing.
- DR. SNYDER: Good luck.
- MS. BECKER: Thank you.
- DR. BELSITO: And then this could go out as a tentative final. And we get to see the discussion. Which will be the really most critical part of this whole thing. A discussion has to be really very well crafted. Okay. Capisce.

Day Two

- DR. BERGFELD: Polyurethanes.
- DR. BELSITO: So, this is the first time we're looking at this report of 66 ingredients that function as artificial nail builders, finders, film formers, hair fixatives, plasticizers and surface modifiers. We previously reviewed other types of monomers [monomers], polyurethane types and non- polyurethane ingredients that have included many of the monomers [monomers] used here, such as the isocyanates. And, we've got a whole bunch of data and weight too. Particularly, on polyurethane 1, which initially, I think at least I was thinking that the numbers referred to molecular weight. But it was pointed out by my esteemed colleague Dan that the numbers have nothing to do with molecular weight. They're all very high molecular weight compounds. That also the residual monomers [monomers] that are there, are so reactive, that they'd either be washed out in ingredient preparation. Or very rapidly consumed in a cosmetic formulation that they were put into. We did notice that there were some limits for the trimethylamines in the EU. In specifically 1-5 trimethylamine and dimethyl ethanolamine that are used as neutralizing agents. But they're used at very low concentrations. And we didn't think that was an issue, although we did feel that an amine boilerplate may be needed. Overall, we felt that we could go with a safe as used when formulated to be non-sensitizing. And I'll explain that non-sensitization in a moment, with a discussion dealing with the inhalation of boilerplate, that they are large and wouldn't be absorbed. That the reactive monomers [monomers] would disappear. And the residual low molecular amines would be minimized to reduce the risk of nitro setting reactions with the use of the nitrosation boilerplate. The issue with sensitization came about, and I'd like to have a little bit of further discussion unrelated to this chemical. But related with the fact that polyurethane 60 and 61 can contain significant amounts of methylisothiazolinone or methylisothiaz. Or benzisothiazolinone. None of these appear to be provided as pure materials. They're provided as 20 percent. 30 percent. And something else with preservatives. So

doing an off the cuff calculation, assuming that, since we have no concentration of poly quarternium [polyurethane ?] 60 or 61, these could be used at levels as high as whatever level we're passing off on. It turns out that methylisothiazolinone could be present in a product as low -- as high a concentration of close to six --. Let me look to make sure. Well, levels -- yeah, it could be present at 5.625 percent. 5.625 parts per million. Which is an extremely low amount. But if put into the QRA, probably would clear a lot of products. I'm not sure it would clear baby wipes. I'm not sure that it would clear underarm deodorants. So, that was the issue. And also, to point out to manufacturers in discussion, that it's clear that some of these have sensitizing preservatives or other materials added. And, therefore, they should be aware of what those materials are. And be careful when formulating with the same material that also could be a sensitizer. And they could exceed the concentration.

DR. BERGFELD: So, an additive effect.

DR. BELSITO: Yes. So, safe when formulated to be non-sensitizing based upon the fact that many of these are supplied with preservatives and other materials.

DR. BERGFELD: And so that would appear in the discussion?

DR. BELSITO: The discussion as to why we put sensitization. Yes.

DR. BERGFELD: And would you be bringing forth the 60 and 61 polyurethane?

DR. BELSITO: We just --

DR. BERGFELD: Are they --?

DR. BELSITO: -- we can point that out --

DR. BERGFELD: Yeah.

DR. BELSITO: -- as an example.

DR. BERGFELD: Okay.

DR. MARKS: Yeah.

DR. BERGFELD: Okay. Any other discussion on the Marks side? Oh Bart. You have a question?

DR. LIEBLER: Dr. Shank (inaudible).

DR. BERGFELD: Dr. Shank, go ahead.

DR. SHANK: We have in Table 3, a long list of monomers [monomers] that are used to make the polymers. But we have no Safety Assessment on any of them. Table 2 lists some of the polymers, where we say they are insufficient data. Can the chemists assure us that there is no release of the monomer [monomers] in formulation and use?

DR. LIEBLER: No release of the monomer [monomers] from the finished polyurethane --

DR. SHANK: Yeah.

DR. LIEBLER: -- once it's being mixed into a cosmetic product?

DR. SHANK: Yes.

DR. LIEBLER: No. I mean, I can't. I mean, I don't know. These -- my inference would be that these polyurethanes would be selected for this use because of their stability. It wouldn't make any sense to use something that was shaky chemically speaking, that would degrade and release monomers [monomers]. But I can't tell you that we've seen any data. And I certainly don't have any. So, you know, it basically is a question of stability under, let's say solvent PH conditions relevant to formulations. And I don't think we have anything like that. So I -- my instinct is not to be concerned about that. But I couldn't show you data.

DR. SHANK: Okay. It's something I think we should handle in the discussion at least. Because we have this fair amount of data that, on monomers [monomers], where we're not -- we don't have data.

DR. LIEBLER: Yeah. And I think it's absolutely a fair point and it belongs in the discussion. And along with the issue kind of on the front end of the residual monomer [monomers] from production, which I think is largely taken care of by the chemical realities of the reactivities --

DR. SHANK: Okay.

DR. LIEBLER: -- as the individual precursors. But, that's a good point.

DR. SHANK: That's the only comment I have.

DR. BERGFELD: Ron Hill.

DR. HILL: And so they -- they're formulated to be non-sensitizing is interesting, because it's not for the ingredients themselves that that restriction is being placed. It's for other things in there. And, I mean, a lot of cosmetic products have preservatives. I don't know how many as ingredient classes do, but I'm guessing it's not just restricted to this. And I, at least in my, what are we now, seven years on this panel. We haven't seen anything like that. So I, I mean, I guess it's okay. I didn't explain, because we talked about it and it was captured in the transcripts earlier, when I voted against those other polymers. But it's

my contention that, if we at least have sensitization data on a range of materials so that all the monomers [monomers] are covered. Because I agree, and when we have communication, that if these things are sold as solutions where there are other compounds in there that would take out any of the isocyanates that might be residually retained when they're made, that that's an assurance. And other than hitting these things with a hot hairdryer, my instinct is the same with Dan's. That we wouldn't have something reverting to an -- and even if we -- isocyanate, I have a bad habit of cutting off my words. And then in the transcript it's miserable. And so, I tend to agree with that. But, when you say formulate to be non-sensitizing, I wonder, because it's not based on these ingredients. Except if we consider them as a mixture. And then those preservatives might be different. Depending on the vendor, it might change when they -- if they completely, in the future, ban the thiazolinone, for example. So I -- that's seems to be a philosophical departure. I don't totally object with it. But, on the flip side, the use of the sensitization for me is a good sentinel. Because if there's any reactives, excuse me, in any of these substances, and then you test for sensitization, and you have data, at least covering the range of monomers [monomers], then I feel assured. So if you're putting formulated to be non-sensitizing, then that would catch anything. And I think the sentinel would be sound in terms of use. I don't know how to think about this.

DR. LIEBLER: The way I think about it Ron, is with botanicals, we have sensitizer's, in many cases, in mother- nature.

DR. HILL: Mm-hmm.

DR. LIEBLER: But the ingredient is a collection of stuff.

DR. HILL: Mm-hmm.

DR. LIEBLER: In this case, the ingredient is also a collection of stuff that the manufacturers --

DR. HILL: Could you turn your microphone.

DR. LIEBLER: -- (inaudible) some purpose.

DR. BELSITO: Dan, Mike.

DR. BERGFELD: It's on now.

DR. LIEBLER: I had it on and then it went off. Sorry. Yeah. The manufacturer puts the sensitizers in now.

DR. HILL: Right.

DR. LIEBLER: A potential sensitizer.

DR. HILL: Exactly.

DR. BERGFELD: Bart has something to say.

DR. HELDRETH: Okay. So my question is closely related to this. I think we're talking about two different issues here. We're talking about an ingredient.

DR. LIEBLER: We are.

DR. HELDRETH: And we're talking about a pre- formulation. And these polyurethane 60 and 61 that you're talking about as ingredients, do not contain any MI or MCI. Now it may be provided to the finishing house as a pre- formulation, and they may have added MI or MCI or some other preservative. But if the supplier and the finishing house are putting these into the product, then that should end up on the label. And the safety of those preservatives is a separate issue. It's not necessary that MI and MCI are part of these ingredients. These ingredients per se, are not mixtures without MI and MCI. The pre-formulation may be, and we commonly look at pre-formulations in other instances, surely because it's very hard to get a polymer into solution. And so that the raw material supplier will provide that material already pre-dissolved. And in this case, they pre-added a preservative. But that's a separate ingredient. That's something else that the finishing house should make sure ends up on the label, if it's a kind of percentage to meet the bar.

DR. MARKS: I hear you Bart.

DR. BERGFELD: Jim.

DR. MARKS: First of all, our team seconds the Belsito team's motion. And I really like that in the discussion Don. I like your reasoning. And that ought to be very clear, the concern about MI and potentially other sensitizing preservatives, as supplied to the end product manufacture. It's interesting, because our team was concerned about the stability of ingredients in molecular range for each of these. Ron Shank addressed that stability. And can we be assured? But I think with non-sensitizing, now we are less concerned about perhaps very small diisocyanate monomers [monomers]. In the HDI polymer report, we had, in the conclusion, minimized low molecular weight monomers [monomers]. So for that reason, I think our team can second the motion, safe when formulated to be non-sensitizing. And a lot of this be in the discussion. Which was really, I thought, robust and good.

DR. BERGFELD: I want to ask Don a question before you respond Don. So, it would be important for you to list

the things that you believe should be in the discussion at this point in time.

DR. BELSITO: Well, I mean, again, I'm just -- first of all --

DR. BERGFELD: Just categories.

DR. BELSITO: -- to address Bart's question, I mean, it says here, polyurethane is a complex polymer, da-da-da-da. And what it's supplied with to the manufacturer, followed by dispersion in water with dimethyl ethanolamine and subsequent chain extension with (inaudible) diamine. And then it talks about the things that are put in there. So it's actually being, at least from Table 1, and the information we're getting in this material is, it is not supplied as a pure material. It actually ends up in the final --

DR. BERGFELD: Product.

DR. BERGFELD: -- consumer product company that's going to manufacture the ingredient with these materials already added. Very much like in the Oil and Cooling industry, when you buy cutting oils, many times they already have a bio side [biocide?] added. The second part, and this is an issue that I wanted to bring up for discussion that is related to this and other materials is, the labeling. I specifically asked Jay yesterday whether, if this product contained methylisothiazilinone, that would end up on the label. Jay, I hope I don't misquote you, the answer I got was, that if the company was using the methylisothiazolinone in the product that was provided, in this case a polyurethane as a preservative, it would. If it was not, it would not be. So, that would not necessarily end up on the label. The other issue is, material safety data sheets, if the MI was present in less than one percent, may not reflect the fact that MI was present, since it's not a carcinogen. And it's not required to be labeled below one percent. The third issue, and Jim can comment on this, is we've been looking at issues with oils, massage oils, with allergic reactions. And there have been assays by people such as Magnus Bruce in Sweden that identify a number of other components in these oils, like antioxidants that don't appear on the label. So, my concern is that the labels may not reflect what's truly in the finished cosmetic product. And there's data to support that from MALMO, in other laboratories.

DR. MARKS: Yeah. No, I agree Don. And the only other comment I'd have is, Lillian mentions in the memo that these ingredients have been reported to cause occupational asthma, irritant contact dermatitis, allergic contact and conjunctivitis.

MS. BECKER: And I think (inaudible) one of the monomers [monomers].

DR. BELSITO: Pardon?

DR. BERGFELD: One of the monomers [monomers].

DR. MARKS: Monomers [monomers]. Yeah. The diisocyanate Don.

DR. BERGFELD: So Don, are you making a proposal regarding the labeling or the lack of labeling?

DR. BELSITO: I would just like --

DR. BERGFELD: Or in the discussion?

DR. BELSITO: -- to point that out. I think it's an issue that the cosmetic industry needs to look at.

DR. BERGFELD: Okay.

DR. BELSITO: Because many of the sensitizers are present at less than one percent. They have to, you know, the bio sides [biocides?]. They're not carcinogens and they theoretically could appear in product supply to consumer good companies who will be blending them into a finished material. And that the consumer goods company may not even be aware of the presence of that material, if it doesn't appear in the material safety data sheet.

DR. BERGFELD: So for the context of this discussion, what would --?

DR. BELSITO: The context of this discussion, it's clear that these materials are not supplied pure. They're supplied as emulsions, with additional materials put in, that may contain potential sensitizers. So, for instance, polyurethane 61 has DMAPA in it. We set limits on DMAPA based upon a QRA. There are a number, I don't even think, you know, we can just point out that some of them have MI, some of them have DMAPA and some of them have known sensitizers.

DR. BERGFELD: So, we'll put those examples into the discussion.

DR. BELSITO: Just examples. And, therefore, that, you know, individual companies using these materials should be aware of other components of the emulsion that's supplied to them. And take care not to formulate with the same potential sensitizers that they could exceed in induction threshold.

DR. BERGFELD: Excellent. Bart.

DR. HELDRETH: And so if our understanding is that these, as ingredients, do include those types of things, should we be petitioning the INCI Committee to make sure that those are included in the definition? So that it's something that all formulators will be aware of?

DR. BELSITO: I think that would be a great idea. I mean, I don't -- I'm trying to figure out. So, if Table 1

definition --

DR. BERGFELD: Okay. Carol wants to speak.

DR. BELSITO: -- idealized structures functions of ingredients and Safety Assessment, where is that table coming from?

DR. EISENMANN: I'm not sure of the table, but many of these ingredients were named as mixtures. So, if some of them have that as, I don't know if all of them do, but some of them were named as mixtures and have the preservative listed as part of the mixture. But, not all, I mean, I don't know if all of them.

DR. BELSITO: Right. I mean, that's the difference between this material --.

DR. EISENMANN: So, in other words, it doesn't need to be in the definition of the material, because they're named as mixtures.

UNIDENTIFIED: It's the same as (inaudible) botanicals.

DR. EISENMANN: Right. But botanicals too. There is the extract and then there is the solvent diol, so it's usually the solvent first. But.

DR. SNYDER: I think we talked about this yesterday. I think Dan brought up the analogy that these are Subway sandwiches, where you can get all these different combinations of things. And, so I think that we're going to have an addition of the introduction, to exactly what these are. That these are not -- these are very complicated mixtures as Carol is indicating. And then, I think, capturing in the discussion, that in the definition as in Table 2, that some of them are known to contain sensitizers. And there should be an awareness of that. And I think that's the best we can do. I mean, it's what we're driven by the data that we have. We're told that these are not simple chemicals. That there is mixture as chemicals that define them to be in that. Because I was struck by that too. I didn't realize that until Dan brought that up yesterday.

DR. BERGFELD: So, Ron Hill.

DR. HILL: Yeah. I just wanted to make sure that we're not making a false assumption about the molecular weights on these as well. Because we don't have the molecular weight information. In particular, we are missing information as to potential amounts of low molecular weight fractions. And so, circumstances where a polymer is being formed, and then converted to a finished product without isolation and purification steps. I mean, I was focused earlier what I said about reactives. But, if you've got a dermally penetrable small molecular weight, something that can be converted into a reactant, that's --. If we're going with a non-sensitizing, then that would be a sentinel and presumably anything like that would be caught. But, I don't understand with these polymer products, why we don't have a molecular weight distribution for every single one we want to read-across to and declare we're comfortable with the safety. I mean, that's -- I realize that's analytical chemistry, which is costly. But, I don't really know why we don't have it.

DR. BERGFELD: All right. Any other discussion before we move on Don?

DR. BELSITO: Yeah. My chair is broken. But so the second part of the issue that I wanted to bring up when we're dealing with a material, but is not supplied as 100 percent pure, is to try and clarify the information that we're getting regarding maximum concentration of use.

DR. MARKS: Mm-hmm.

DR. BERGFELD: And also, sensitization, irritation, other toxicity data. In case in point, in wave 2, we got data on a mascara that was said to have 30 percent polyurethane 1. When you look at a frequency in concentration of use in Table 8, polyurethane 1 is, in fact, used in an eye area. But the max is 4.6 percent. So, I'm presuming that the polyurethane 1 that was supplied to them, and that they claimed they did an HRIPT at 30 percent, was actually only probably 4.6 percent active polyurethane 1. It just creates a great deal of confusion in my mind, when I'm looking at the data that I specifically need to concentrate on, as to what exactly was studied. So I think it's very critical, and I know Carol tries to do that when she goes out to industry, to ask them, what concentration active do you use? Not concentration of the material that supplied to you. And when we get reports from industry that claim that they used a mascara at 30 percent, are they saying that it's a 30 percent of this mascara in which the poly quaternium 1 that they added, was not truly 30 percent. But was only 4.6 percent. Because, otherwise, the data is always going to be questionable.

DR. MARKS: I had the -- tagging onto that Don, and if you look at polyurethane 62, the question is it even used? It's not in Table 8 or 9. However, we have data on it.

DR. BELSITO: Yes.

DR. MARKS: So, why do we get data on something that isn't being used?

DR. BELSITO: I have the same question.

DR. MARKS: Yeah.

DR. BERGFELD: All right.

DR. SHANK: Used for something else?

DR. BERGFELD: Are we through discussing this ingredient?

DR. BELSITO: Yeah. I think so.

DR. BERGFELD: Oh thank you. Would you restate the motion Dr. Belsito?

DR. BELSITO: The motion was safe as used when formulated to be non-irritating and --

DR. BERGFELD: Sensitizing?

DR. BELSITO: -- sensitizing rather. And point out that there were a number of ingredients in the emulsions as supplied, such as dimethylaminopropylamine and methylisothiazolinone, that are known sensitizers. That have been restricted and in those two cases, I believe we used QRA. The Cosmetics Europe has used specific numbers. But, regardless, worldwide they have been restricted because of sensitization.

DR. BERGFELD: So those are discussion points?

DR. BELSITO: Yes.

DR. BERGFELD: Rather than the conclusion. And we've had a second.

DR. MARKS: Second.

DR. BERGFELD: So I'm going to call the question. All those in favor of approval of this ingredient. Unanimous. Thank you. A very robust discussion. Go ahead Jim.

DR. MARKS: Yeah. Besides that in the discussion, we talked about the stability of ingredients and molecular weight ranges. I think that should be addressed briefly --

DR. BERGFELD: Okay.

DR. MARKS: -- in the discussion also.

DR. BERGFELD: Anything else to go on the discussion before we leave this ingredient? No. Okay. Moving onto the next ingredient, which is lard. Dr. Marks.

Safety Assessment of Polyurethanes as Used in Cosmetics

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ABSTRACT

This report is a safety assessment of 66 polyurethane ingredients as used in cosmetics. The functions of these ingredients include artificial nail builders, binders, and surface modifiers. The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed available data related to these ingredients and determined that there would be no detectable residual isocyanate or other monomers in these ingredients. The Panel concluded that these polyurethanes are safe in the practices of use and concentration of this safety assessment when formulated to be non-sensitizing.

INTRODUCTION

This is a safety assessment of polyurethane ingredients as used in cosmetics. According to the *Web-Based Ingredient Dictionary* (wINCI), the functions of these 66 ingredients include artificial nail builders, binders, film formers, hair fixatives, plasticizers, and surface modifiers ([Table 1](#)).^{1,2} The ingredients in this group are:

Polyurethane-1	Polyurethane-25	Polyurethane-51
Polyurethane-2	Polyurethane-26	Polyurethane-52
Polyurethane-4	Polyurethane-27	Polyurethane-53
Polyurethane-5	Polyurethane-28	Polyurethane-54
Polyurethane-6	Polyurethane-29	Polyurethane-55
Polyurethane-7	Polyurethane-32	Polyurethane-56
Polyurethane-8	Polyurethane-33	Polyurethane-57
Polyurethane-9	Polyurethane-34	Polyurethane-58
Polyurethane-10	Polyurethane-35	Polyurethane-59
Polyurethane-11	Polyurethane-36	Polyurethane-60
Polyurethane-12	Polyurethane-39	Polyurethane-61
Polyurethane-13	Polyurethane-40	Polyurethane-62
Polyurethane-14	Polyurethane-41	Polyurethane-63
Polyurethane-15	Polyurethane-42	Polyurethane-64
Polyurethane-16	Polyurethane-43	Polyurethane-65
Polyurethane-17	Polyurethane-44	Polyurethane-66
Polyurethane-18	Polyurethane-45	Polyurethane-67
Polyurethane-19	Polyurethane-46	Polyurethane-68
Polyurethane-20	Polyurethane-47	Polyurethane-69
Polyurethane-21	Polyurethane-48	Polyurethane-70
Polyurethane-23	Polyurethane-49	Polyurethane-71
Polyurethane-24	Polyurethane-50	Polyurethane-72

These ingredients are copolymers containing carbamate (i.e., urethane) linkages. Some of these polyurethane ingredients, as defined, are dispersed in water (e.g., Polyurethane-17, -35, -36, -58, -60, -61, -70, -71, and -72).^{1,2} Many of these polyurethanes are reported to be supplied to formulators in an emulsion or solution that may consist of several chemicals creating complicated mixtures.

Polyurethane-type ingredients with 4 or more monomers, such as the ingredients in this report, are named "Polyurethane-x".^{1,2}

Several precursors and moieties of these polymers have been reviewed by the CIR Panel.³⁻²⁸ [Table 2](#) lists the previously reviewed ingredients and connects them to the relevant polyurethanes in this report. Chemicals, including cosmetic ingredients, which have not been reviewed by the Panel, but are precursors or moieties of the polyurethanes in this safety assessment, except diisocyanate monomers, are listed in [Table 3](#). Diisocyanate monomers in the cosmetic ingredients addressed in this report are listed in [Table 4](#). These ingredients are copolymers, each of which is synthesized, in part, from isocyanate analogs.^{29,30} Exposure to diisocyanates in the work place is one of the leading causes of occupational asthma and related issues; diisocyanates have also been associated with irritant and allergic contact dermatitis, as well as skin and conjunctival irritation. The Panel has reviewed hexamethylene diisocyanate (HDI) polymers, which are polymers (polyurethanes) also derived from isocyanates, and found that 17 of these ingredients are safe in cosmetics in the present practices of use and concentration, and that the available data are insufficient to make a determination that 2 of these ingredients are safe ([Table 2](#); the full reports on these and all ingredients are available on the CIR website: <http://www.cir-safety.org/ingredients>).³¹

Data on polyurethanes that are not listed in the wINCI as cosmetic ingredients have been included for potential supporting information (e.g., cosmetic use and inflammatory response).

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (<http://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and->

websites; <http://www.cir-safety.org/supplementaldoc/cir-report-format-outline>). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition and Structure

The structures, definitions, and functions of the polyurethane ingredients in this safety assessment are provided in Table 1. Some of the definitions may give insight into the method of manufacture. Several of these polyurethane ingredients, as defined, are the polymers dispersed in water (e.g., Polyurethane-17, -35, -36, -58, -60, -61, -70, -71, and -72).^{1,2} Other polyurethanes may be supplied as dispersions (in water or other solvents), as indicated in ingredient specifications (e.g. Polyurethane-1, 14, -21, -28, -39 -42, and -69).³²⁻³⁶

The polyurethane ingredients in this report are copolymers containing carbamate (i.e., urethane) linkages. Polyurethanes are formed by reacting a polyol (e.g., a glycol) with a diisocyanate or a polyisocyanate. These polyurethane copolymers are a highly heterogeneous group of structures created from diverse diisocyanate, glycol, and carboxylic acid monomers. Representative structure motifs of three different urethane copolymers are depicted in Figure 1.

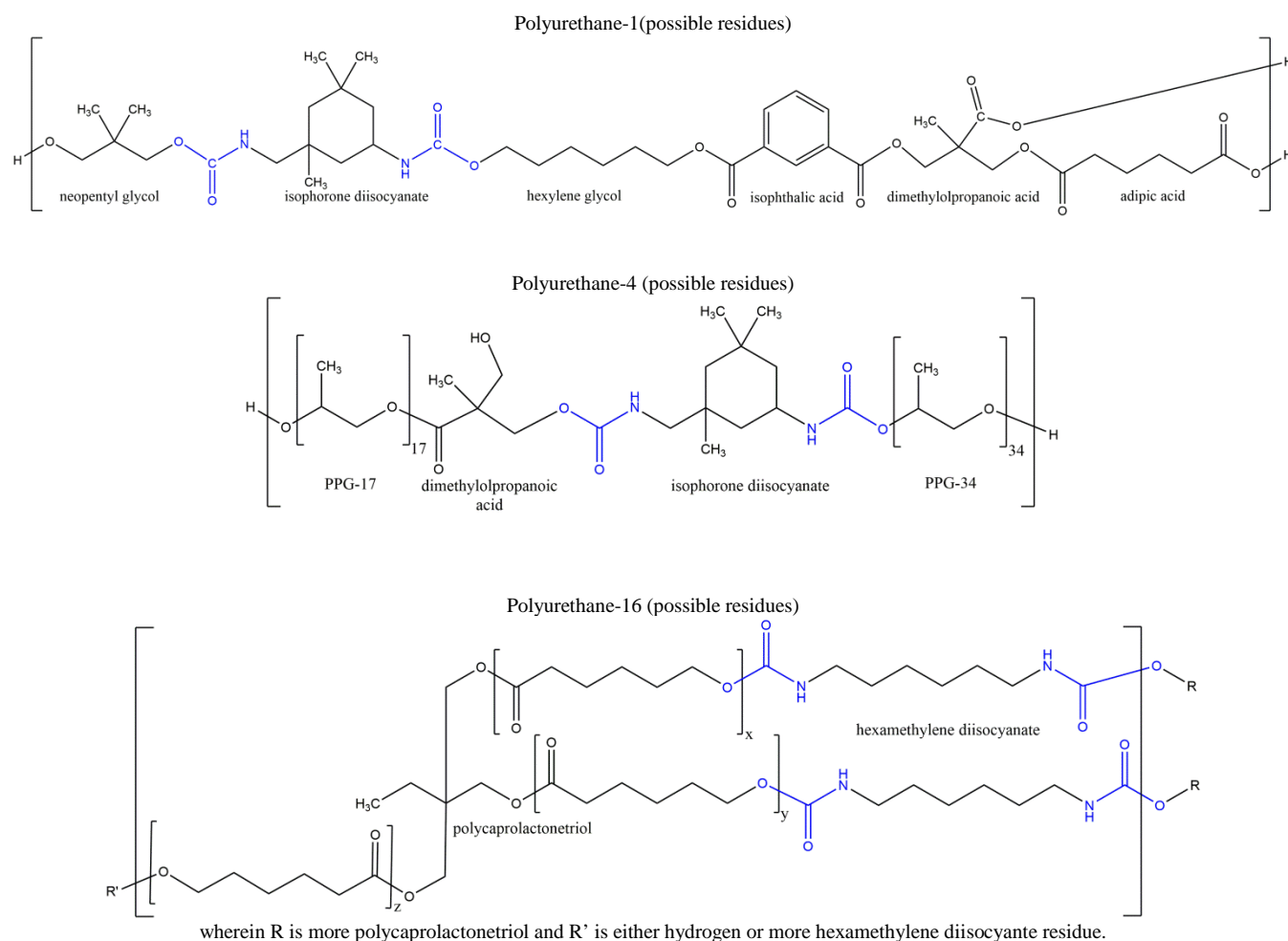


Figure 1. Examples of monomeric linkages in these urethane copolymers

Physical and Chemical Properties

Chemical and physical properties are provided in Table 5.

Some of the polyurethanes are linear polymers, but when multi-functional monomers (e.g., glycerin) are used as reactants, branched or cross-linked structures are probable. The degree of polymerization of these ingredients can be controlled to obtain a product having a desired functionality, such as rheology modifier. Accordingly, the molecular weights and molecular volumes of these ingredients could vary widely, unless otherwise noted in specifications. These polymers, by virtue of their monomers, contain both hydrophilic and hydrophobic groups. The ratio of hydrophilic and hydrophobic groups may vary within one ingredient name. Estimating some of the chemical and physical properties of these ingredients is challenging in the absence of ingredient-explicit specifications. These ingredients potentially can range from liquid to solid

and soluble to insoluble. Aside from the potential presence of a diisocyanate or end-capping agent residue, these ingredients are likely to be similar to unmodified polyurethane-type polymers.

Polyurethane-11

Polyurethane-11 is reported to have a mean molecular weight > 100,000 daltons (Da), with no fractions < 1000 Da.³⁷

Polyurethane-14

Based on the monomer composition and general hydrophobic properties of Polyurethane-14, it is not expected to be significantly soluble in water.³⁵ It is not expected to undergo significant hydrolysis within a pH range of 4 to 9. Polyurethane-14 partitions primarily in the organic phase in octanol-water separation systems.

Polyurethane-21

Polyurethane-21 is stable at a pH range of 7 to 11, but is not stable below pH 7.³⁴

Polyurethane-28

Polyurethane-28 is reported to have a mean molecular weight > 30,000 Da with no molecules < 1000 Da.³⁶ This ingredient is reported to be stable at 5 to 50°C for 3 years under storage conditions.

Polyurethane-35

Based on the high mean molecular weight (> 1000 Da) and predominantly hydrophobic structure, Polyurethane-35 is expected to have low solubility in water.³⁸ This polymer is stable under normal environmental conditions and will not degrade in cosmetic products at 5% to 15%.

Polyurethane-42

Polyurethane-42 is reported to have a mean molecular weight of > 36,000 with no molecules < 1000 Da.³⁶ This ingredient is reported to be stable at 5 to 50°C for 3 years under storage conditions.

Polyurethane-60

A supplier reported that Polyurethane-60 is supplied as an aqueous, low viscosity, anionic dispersion polycarbonate-polyurethane.³⁹ The mean molecular weight of Polyurethane-60 is > 50,000 Da.

Polyurethane-61

A supplier reported that Polyurethane-61 is supplied as an aqueous, low viscosity dispersion of an aliphatic polyester-polyurethane.⁴⁰ The mean molecular weight of Polyurethane-61 is > 50,000 Da.

Polyurethane-62

A supplier reported that the particle size of Polyurethane-62 was 50 to 1000 µm and the mean molecular weight is > 70,000 Da.⁴¹ Polyurethane-62 is stable under normal environmental conditions and yields no degradation products under normal conditions of use. Another supplier reports that the average molecular weight of Polyurethane-62 is approximately 100,000 Da.⁴²

Polyurethane-69

The average total molecular weight of Polyurethane-69 is > 3400 Da.³⁶ Low molecular weight fractions (< 1000 Da) were detected at 4%. Polyurethane-69 is stable for 16 weeks at 5, 25, and 50°C in normal storage conditions; there is no formation of high molecular weight crosslinked fractions and no depolymerization is detected.

Method of Manufacture

In general, polyurethanes are formed by reacting a polyol (e.g., a glycol) with a diisocyanate or polyisocyanate.

[Table 6](#) cites the methods of manufacture of individual polyurethanes.

Infrared spectroscopy is typically used to make sure the reaction is complete and that no diisocyanates are present.³⁷

Impurities/Constituents

[Table 7](#) cites the polyurethanes that are reported to commonly be supplied, in tradename mixtures, as suspensions or solutions. Such suspensions typically include water and cyclopentasiloxane. However, preservatives, such as methylisothiazolinone (MI), and neutralizing agents may also be included in the suspension.^{35,36,38-40,43} The non-polyurethane components of these tradename mixtures are not impurities or constituents of the ingredients in this report. Thus, their safety is assessed elsewhere. The CIR Panel concluded that MI is safe for use in rinse-off cosmetic products at concentrations up to 100 ppm and safe in leave-on cosmetic products when they are formulated to be non-sensitizing, which may be determined based on a quantitative risk assessment (QRA).⁴⁴

A supplier reports that Polyurethane-36, -60, and -61, which are supplied as dispersions in water, are reported to be free from other solvents and isocyanate groups; residual isocyanates are expected to react with water in the dispersion and

form polyureas.^{39,40,43}

Polyurethane-11

Polyurethane-11 is reported to contain no residual isocyanates since free isocyanates react with water.³⁷

Polyurethane-28, -42, and -69

Polyurethane-28, -42, and -69 are reported to contain no detectable residual isophorone diisocyanate (IPDI; a monomer used in their synthesis), as determined by high-performance liquid chromatography-mass spectrometry (HPLC-MS; detection limit 5 ppm).³⁶

Polyurethane-59

Polyurethane-59 is reported to contain no detectable residual ethylene oxide (detection limit < 1 ppm), dioxane (< 10 ppm), formaldehyde (< 1 ppm), and HDI (< 20 ppm).⁴⁵

Polyurethane-62

Polyurethane-62 is reported to contain no detectable residual unreacted isocyanate (HDI; a monomer used in their synthesis).⁴²

Polyurethane-2, -17, -29, -33, -40, -60, and -61

4,4'-Diaminodiphenylmethane (MDA) is classified as a carcinogen and is used in the production of methylene diphenyldiisocyanate (MDI).⁴⁶ MDI, or an analog thereof, is a monomer component of some of the polyurethanes in this safety assessment (e.g., Polyurethane-2, -17, -29, -33, -40, -60, and -61).^{1,2} In a study to determine the safety profile of MDI in consumer products, no residual MDA was detected in the resultant production of MDI.⁴⁶ Furthermore, any remaining MDA would be expected to be further reduced when MDI is polymerized in the manufacture of polyurethanes.

USE

Cosmetic

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

According to VCRP survey data received in 2017, Polyurethane-11 was reported to be used in 315 formulations, with 303 uses reported in leave-on formulations and 12 uses in rinse-off formulations ([Table 8](#)).⁴⁷ The additional ingredients with reported uses in the VCRP were reported to have uses in 33 or fewer formulations.

The VCRP has an entry for "polyurethane" with 17 uses in a pattern similar to the polyurethanes in this safety assessment. It is unknown to what extent, if any, "polyurethane" is the same as or similar to, one or more of the polyurethane ingredients in this safety assessment. Since the composition of this ingredient is unknown, this ingredient will not be further addressed in this safety assessment.

The results of the concentration of use survey conducted by the Council in 2016 indicate that Polyurethane-1 has the highest reported maximum concentration of use; it is used at up to 15% in nail products.⁴⁸ The highest maximum concentration of use reported for products resulting in leave-on dermal exposure is 7.5% Polyurethane-33 in the category of other skin care preparations.

In some cases, uses were reported to the VCRP, but concentrations of use data were not provided. For example, Polyurethane-7 was reported to be used in 14 cosmetic formulations, but no use concentration data were reported. In other cases, no uses were reported to the VCRP, but concentration of use data were received from industry; for example, Polyurethane-10 had no reported uses in the VCRP, but use concentrations in the categories of mascara; tonics, dressings, and other hair grooming aids; and foundations were provided in the industry survey. Therefore, it should be presumed there is at least one use in every category for which a concentration is reported.

The ingredients not in use according to the VCRP and industry survey are listed in [Table 9](#).

Polyurethane-1, -2, -10, -11, -14, -33, -34, -35, and -40 were reported to be used in products that are applied around the eye; the highest reported concentration of use was 7%, which was for Polyurethane-35 in mascara. Polyurethane-11, -15, and -34 were reported to be used in products that may be ingested and come in contact with mucous membranes; the highest reported concentration of use was 2.9%, which was for Polyurethane-34 in lipsticks.

Several of the polyurethanes are used in cosmetic sprays and could possibly be inhaled. Polyurethane-1, -6, -11, -14, -18, -24, -33, and -34 were reported to be used in spray products; the maximum reported concentration for a spray product was 6% Polyurethane-6 in pump hair sprays. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 μm .⁴⁹⁻⁵² Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.^{49,51} Polyurethane-2, -7, -11, and -15 were reported to be used in

powders; the highest maximum reported concentration was at up to 3.2% Polyurethane-11. Conservative estimates of inhalation exposures to respirable particles during the use of loose-powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.⁵³⁻⁵⁵

In Europe the amount of residual trialkylamines is limited to 2.5% in ready-for-use preparations in the category of leave-on products (which may be residuals in Polyurethane-17 and -21).^{56,57} Also, trialkylamines are further limited in that they are not to be used with nitrosating systems, have a maximum secondary amine content of 0.5%, have a maximum nitrosamine content of 50 µg/kg, have a minimum purity of 99%, and must be kept in nitrite-free containers.

The National Industrial Chemical Notification and Assessment Scheme (NICNAS) of Australia determined that there is negligible concern to public health when Polyurethane-14 is used as a hair fixative agent in hair care products such as pump sprays and hair gel formulations at concentrations up to 6%.³⁵ NICNAS also determined that Polyurethane-35 and -62 were not considered to pose an unreasonable risk to the health of workers and the public.^{38,41}

Polyurethane-11 is reported to be used to coat cosmetic glitter.³⁷

Non-Cosmetic

In the United States, polyurethanes may come in contact with food as direct and indirect food additives, and in single use and repeated use food containers. [21 CFR 174.5; 21 CFR 175.105; 21 CFR 176.170; 21 CFR 177.1210; 21 CFR 177.1390; 21 CFR 177.1395; 21 CFR 177.1680; 21 CFR 177.2600] Polyurethanes used in food packaging adhesives and polyurethane resins may not contain 4,4'-methylenebis (2-chloroaniline). [21 CFR 189.280]

Polyurethanes may be used in ear, nose and throat medical devices, and in general and plastic surgery devices (e.g., silicone gel-filled breast prosthesis and occlusive wound dressing). [21 CFR 874.3695; 21 CFR 878.3540; 21 CFR 878.4020]

A supplier states that Polyurethane-36, -60, and -61 are not in compliance for use in food contact adhesives according to FDA regulations.^{39,40,43}

The FDA stipulates that polyurethane resins that are used in adhesives that may come in contact with food must be produced by one of four methods. 1) Reacting diisocyanates with one or more of the listed polyols or polyesters (this is a large list and is not provided here; an abbreviated list of monomers and precursors are provided in [Table 10](#)). 2) Reacting the chloroformate derivatives of one or more of the listed polyols or polyesters with one or more of the polyamines listed in [Table 10](#). 3) Reacting toluene diisocyanate or 4,4'-methylenebis(cyclohexylisocyanate) with either one or more of the listed polyols or polyesters listed in [Table 10](#) and with either *N*-methyldiethanolamine and dimethyl sulfate or dimethylolpropionic acid and triethylamine, or a fumaric acid-modified polypropylene glycol or fumaric acid-modified tripropylene glycol, triethylamine, and ethylenediamine. 4) Reacting *meta*-tetramethylxylene diisocyanate with one or more of the listed polyols and polyesters (not listed here; [Table 10](#)) and with dimethylolpropionic acid and triethylamine, *N*-methyldiethanolamine, 2-dimethylaminoethanol, 2-dimethylamino-2-methyl-1-propanol, and/or 2-amino-2-methyl-1-propanol. [21 CFR 175.105]

Polyurethane-36 is exempt from the Toxic Substances Control Act (TSCA) Inventory listing requirements under the provisions of the TSCA Polymer Exemption.³⁵ [40 CFR 723.250] The CFR citation is the exemption for polymers, so it is likely that many of the polymers in this report are exempt from TSCA.

Polyurethane foam or porous polyurethane films are used to make wound dressings.⁵⁸⁻⁶⁰ Polyurethane prostheses are being developed for soft tissue scaffolds of blood vessels and tissues of the cardiovascular system; some of these are impregnated with drugs to control smooth muscle cell proliferation.⁶¹ Polyurethanes are used to coat medical implants, including percutaneous leads, catheters, tubing, and intra-aortic balloons.^{62,63} Polyurethane has been used as a coating on breast implants.⁶⁴

Sprayed polyurethane foam is used for roofing material and other protective applications such as truck bed liners.⁶⁵

TOXICOKINETIC STUDIES

Toxicokinetic studies were not found in the published literature and no unpublished data were submitted.

TOXICOLOGICAL STUDIES

Acute Dose Toxicity

Acute dermal toxicological studies were not found in the published literature and no unpublished data were submitted.

Oral

Polyurethane-1

The oral LD₅₀ of Polyurethane-1 in rats was reported to be > 2000 mg/kg.³² The test was conducted in accordance with the Organisation for Economic Co-operation and Development test guideline (OECD TG) 423 (Acute Oral toxicity).

Polyurethane-35

The oral LD₅₀ of Polyurethane-35 in rats was reported to be 4890 mg/kg.³⁸ The test was conducted in accordance with the OECD TG 423. No further details were provided.

Polyurethane-39

The oral LD₅₀ for Polyurethane-39 was reported to be > 2000 mg/kg for female Sprague-Dawley rats (n = 6).³³ The test substance was administered by gavage and the rats were observed for 14 days after dosing.

InhalationPolyurethane-1

The inhalation no-observed-adverse-effects-concentration (NOAEC) for Polyurethane-1 (tested at 0, 3, 10, 30, and 100 mg/m³) was 3 mg/m³ when administered to rats (n = 8) for 6 h/day for 5 days.³²

Polyurethane-14

Sprague Dawley rats (n = 5/sex) were exposed to Polyurethane-14 (9.6% in 55% ethanol) for 4 h in a whole body inhalation chamber at 110 mg/m³ Polyurethane-14 and 964,000 mg/m³ ethanol as a liquid droplet aerosol.⁶⁶ The mean aerodynamic diameter of the particles was 1.9 ± 3.21 μ m. There were no mortalities during the experiment or during the 14-day observation period. Clear nasal discharge was observed in one male following exposure. No toxicologically significant clinical findings were observed. There were no remarkable body weight changes or observations at necropsy. The LC₅₀ of Polyurethane-14 was reported to be > 110 mg/m³.

Short-Term Toxicity Studies

Short-term dermal and oral toxicity studies were not found in the published literature and no unpublished data were submitted.

InhalationPolyurethane-14

Sprague Dawley rats (n = 5/sex) were exposed to Polyurethane-14 (9.6% in 55% ethanol) 6 h/day for 14 days in a whole body inhalation chamber at 10, 30, and 100 mg/m³ Polyurethane-14 and 964 ppm ethanol as a liquid droplet aerosol.⁶⁷ There were no mortalities during the exposure period. At necropsy, pallor was observed in the lungs of one male and one female in the 30 mg/m³ group; this finding was consistent with histopathologic observations of alveolar histiocytosis and was considered an effect of exposure to the test material. The mean absolute lung weights were increased in both sexes of the 100 mg/m³ group and the females of the 30 mg/m³ group; mean relative lung weights were increased in both sexes in the 30 and 100 mg/m³ groups. The increased lung weights were considered an effect of exposure to the test material and correlated with the increased incidence and severity of alveolar histiocytosis. The diffuse alveolar histiocytosis, observed in the lungs of the rats in the 30 and 100 mg/m³ groups, increased in severity with increased exposure. Multifocal, minimal alveolar histiocytosis was observed in the lungs of some of the rats in the control and 10 mg/m³ groups and was not considered to be an effect of exposure to the test material.

Subchronic Toxicity Studies

Subchronic oral and dermal toxicity studies were not found in the published literature and no unpublished data were submitted.

InhalationPolyurethane-1

The inhalation NOAEC for Polyurethane-1 (tested at 0, 1, 3, and 10 mg/m³) was 1 mg/m³ when administered to rats (n = 20) for 6 h/day for 65 exposures over 90 days.³² The experiment was conducted in a head/nose apparatus and the recovery period was 3 months.

Polyurethane-14

Sprague Dawley rats (n = 15/sex) were exposed to Polyurethane-14 (9.6% in 54.9% ethanol neutralized with adenosine monophosphate) 6 h/day, 5 days/week, for 90 days (66 doses) in a nose-only inhalation chamber at 1.17 ± 0.3 , 5.3 ± 1.1 , and 40.6 ± 4.8 mg/m³ (50, 147, 320 ppm, respectively) Polyurethane-14 and 964 ppm ethanol as a liquid droplet aerosol.⁶⁸ The particle aerodynamic diameters were 1.5 ± 2.7 , 1.4 ± 2.1 , and 1.9 ± 2.2 μ m (\pm geometric standard deviation), which resulted in a respirable percentage of 97.2%, 99.6%, and 98.3%, respectively. After exposure, 5 rats/sex were allowed to recover for 13 weeks.

There were no test material-related deaths or clinical observations. There were no toxicologically significant effects on mean body weights, body weight gains, feed consumption, microscopic organ evaluations (except the lung and lymph nodes), or on hematology or serum chemistry parameters. In the air and ethanol controls and the low dose group, a background syndrome was present, which was described as concurrent mild perivascular inflammatory cell infiltrate and/or subacute inflammation (mixed cell type) with interstitial pneumonia. This pattern was distinguishable from test-article induced responses. Exposure to Polyurethane-14 in the 5.3 and 40.6 mg/m³ groups resulted in a low incidence of macroscopic findings, such as white areas in the lungs and enlarged lymph nodes, a dose-dependent increase in lung weights, accumulation of foamy alveolar macrophages, interstitial pneumonia, and acute inflammation (alveolar neutrophils) in the

lung. The incidence and severity of the above findings generally decreased in the recovery animals, indicating partial recovery. A few 1.2 mg/m³ and greater numbers of 5.3 and 40.6 mg/m³ exposed rats had foamy macrophage accumulations in the mediastinal and/or tracheobronchial lymph nodes. Accumulation of foamy macrophages in the lung or lymph node is considered a normal physiological response necessary to remove particles from the lung, and was not considered to be an adverse health effect. Based on the results of this study, the no observed adverse effect level (NOAEL) was 1.2 mg solids/m³. The lack of primary parenchymal toxicity and progressive lesions demonstrated that Polyurethane-14 is a polymer of low toxicity.⁶⁸

Chronic Toxicity Studies

Chronic toxicity studies were not found in the published literature and no unpublished data were submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

DART studies were not found in the published literature and no unpublished data were submitted.

GENOTOXICITY STUDIES

In Vitro

Genotoxicity studies are summarized in [Table 11](#).

Polyurethane-1 (30%) was not mutagenic in an Ames test; Polyurethane-1 was tested up to 16,000 µg/plate in Ames assays, both with and without metabolic activation. Polyurethane-28 (concentration not specified) was not mutagenic in a bacterial reverse mutation assay conducted in accordance with OECD TG 471 (Bacterial Reverse Mutation Test) using *Salmonella typhimurium* and *Escherichia coli*.³⁶ Polyurethane-35 (concentration not specified) was not mutagenic in a bacterial reverse mutation assay conducted in accordance with OECD TG 471.³⁸ Polyurethane-42 (concentration not specified) was not mutagenic in a bacterial reverse mutation assay conducted in accordance with OECD TG 471 using *S. typhimurium* and *E. coli*.³⁶ In an Ames mutagenicity test of Polyurethane-62 (up to 5000 µg/plate) using *S. typhimurium* and *E. coli*, no cytotoxicity or precipitation was observed with or without metabolic activation and there were no significant increases in the frequency of revertant colonies.⁶⁹

In Vivo

In vivo genotoxicity studies were not found in the published literature and no unpublished data were submitted.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not found in the published literature and no unpublished data were submitted.

OTHER RELEVANT STUDIES

Inflammatory Response

Male Swiss albino mice (n = 6) received a polyurethane nanoparticle solution (0, 2, 5, or 10 mg/kg in saline) by gavage daily for 10 days.⁷⁰ The polyurethane tested was manufactured with a natural triol, diisocyanate, and olive oil that were added to a solution of Polysorbate 80 while stirring at room temperature. The polyurethane particles had a diameter of 249 ± 5.7 nm and a polydispersity index (PDI) of 0.3 ± 0.04. All mice survived the study and there were no behavioral changes observed. At necropsy, there were no differences in body weights or organ weights among the groups. There was increased visceral fat accumulation in the mice in all treatment groups compared to controls. The lungs of mice in the 5 and 10 mg/kg/day groups (4 and 6 mice, respectively) showed inflammation, and inflammatory infiltrate was observed in all treatment groups. The kidneys of mice in the 5 and 10 mg/kg/day groups (5 and 6 mice, respectively) showed glomerular necrosis and glomerular atrophy. Histological examination of the adipose tissue did not reveal any alterations in morphology in any group. Oral polyurethane administration induced an increase in alanine aminotransferase (ALT) levels (58 ± 7.7, 69 ± 15, and 78 ± 4.5 IU/L in the 2, 5, and 10 mg/kg groups, respectively, versus control mice 34 ± 3.5 IU/L). Mice in the 5 and 10 mg/kg groups also showed an increase in alkaline phosphatase activities (ALP; 20 ± 4 and 24 ± 2 IU/L, respectively, versus controls, 8.5 ± 1.7 IU/L). Hematological evaluation revealed no changes in any parameter. There was an increase in TNF-α level (approximately 80-fold) in mice in the 10 mg/kg group. The authors concluded that oral administration of polyurethane nanoparticles generates an inflammatory response in mice.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

In Vitro

Polyurethane-35

In an in vitro dermal corrosion assay conducted in accordance with OECD TG 431 (In Vitro Skin Corrosion: Human Skin Model Test), Polyurethane-35 was not corrosive.³⁸ No further information was provided.

Polyurethane-62

An EpiSkin assay using the reconstructed human epidermis (RhE) model conducted in accordance with OECD TG 439 (In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method) was conducted on Polyurethane-62 (tested without trideceth-6 solvent; not specified if tested in water or other neutral solvent).⁶⁹ Polyurethane-62-treated cells had a 95% survival rate. Survival greater than 50% is considered negative for dermal irritation. The control had the expected result.

AnimalPolyurethane-1

Polyurethane-1 (30% in water and ethanol; 0.5 mL) was not a dermal irritant in rabbits when exposed for 4 h under semi-occlusion.³²

Polyurethane-35

In a skin irritation study conducted in accordance with OECD TG 404 (Acute Dermal Irritation/Corrosion), Polyurethane-35 (40% in water) was slightly irritating to the skin of rabbits (n = 3).³⁸ The author noted that the removal of the patch was not possible without altering the response or the integrity of the epidermis in one rabbit. All irritation effects were reversible within 7 days. The irritant effects were not sufficient to warrant classification as a skin irritant. No further information was provided.

Polyurethane-39

Polyurethane-39 was not irritating to rabbits (n = 2 males, 1 female) when applied under semi-occlusion.³³ The experiment was conducted in accordance with OECD TG 404.

HumanPolyurethane-14

In a cumulative irritation assay, subjects (n = 29) were topically exposed to Polyurethane-14 (9.6% in 55% ethanol; 0.2 mL), 55% ethanol, distilled water, or sodium lauryl sulfate (0.075%) for 21 days.⁷¹ Exposure was under semi-occlusive conditions for days 1 through 9; exposure was changed to semi-open due to irritation observed in the polyurethane and ethanol control groups. Scoring for cumulative irritation was performed every 24 h immediately prior to reapplication or until excessive irritation was noted. Polyurethane-14 produced erythema and papules in three subjects by the fourth application. After changing to semi-open patches, an additional subject was observed with erythema and papules on day 19. Under identical conditions, the ethanol control produced erythema and papules in three subjects by the third application. No to very slight erythema was observed at the majority of sites treated with Polyurethane-14 or ethanol. Sites treated with distilled water elicited a very low response. Distilled water and 0.1% sodium lauryl sulfate produced the expected results. The cumulative scores were 232 (Polyurethane-14 solution), 208 (ethanol solution), 13 (water), and 338 (sodium lauryl sulfate) out of a possible 1575. Under the conditions of the study, both 9.6% Polyurethane-14 and the ethanol control produced mild to moderate irritation in a few subjects, with no differences in the responses to these two test articles.

Polyurethane-21

In a human dermal irritation study (n = 10), Polyurethane-21 was applied twice to scarified skin for 24 h using a chamber device with a 12 mm well.⁷² Saline was used as the control. The test substance had an average irritation score of 0.50 (out of 4); the saline control had an average score of 0.55. The irritation potential of Polyurethane-21 was low.

Sensitization***In Vitro***Polyurethane-62

A Direct Peptide Reactivity Assay (DPRA) measuring reactivity (percent depletion) of cysteine and lysine peptides by liquid chromatography with a UV detector (LC-UV) was conducted on Polyurethane-62 (tested without trideceth-6 solvent; not specified if tested in water or other neutral solvent).⁶⁹ This assay was conducted in accordance with the OECD Draft Proposal for Guideline, *In Chemico* Skin Sensitization (Direct Peptide Reactivity Assay). The mean depletion rates were 0.02% for Polyurethane-62 and 78.04% for the positive control. Depletion less than 6.38% is considered to have no, or minimal, reactivity and is predicted to be negative for dermal sensitization. The control had the expected result.

AnimalPolyurethane-1

Polyurethane-1 30% (in water and ethanol) was not sensitizing to guinea pigs (n = 20; control = 10) in a Buehler assay.³² The induction was conducted at 10% (approximately 3% Polyurethane-1 in distilled water) and the challenge at 5% (1.5%). The induction and challenge applications were in contact with the skin for 6 h.

Polyurethane-14

A guinea pig maximization test was conducted in accordance with OECD TG 406 (Skin Sensitization) on Polyurethane-14 (23.4% solids in 27% ethanol).⁷³ The guinea pigs (n = 10/sex; control = 5/sex) were injected with 0.1 mL of a 1% solution of Polyurethane-14 with and without Freund's Complete Adjuvant. After pretreatment with 10% sodium lauryl sulfate, an 8 cm²-patch of filter paper saturated with the test article was applied topically for 48 h. The challenge was applied to virgin sites. A 4-cm² patch of filter paper saturated with the test material was applied topically for 24 h. The application sites were evaluated for erythema 48 and 72 h after application. Moderate to intense redness was observed after the intradermal injection, which was reduced to scabbing for the remainder of the induction period. No erythema was observed after challenge with the test material or the control. Under the described test conditions, the test material did not cause a sensitization reaction in guinea pigs.

Polyurethane-35

In Buehler and maximization tests conducted in accordance with OECD TG 406, Polyurethane-35 showed no evidence of causing sensitization.³⁸ No further information was provided.

Polyurethane-39

Polyurethane-39 (0, 3%, 10%, and 30% in 70% ethanol in water) was not sensitizing to mice (n = 5) in a local lymph node assay (LLNA).³³

Human

Human repeated insult patch tests (HRIPT) of polyurethanes are summarized in [Table 12](#).

Mascaras containing Polyurethane-1 (28.5% and 30%) were not sensitizing in HRIPTs.^{74,75} Polyurethane-14 (9.61% solids) caused mild erythema in a few subjects but did not demonstrate a hypersensitivity response.⁷⁶ Polyurethane-21 (tested at 21% and 35% solids) was not a sensitizer.^{77,78}

OCULAR IRRITATION STUDIES***In Vitro***

In vitro ocular irritation assays are summarized in [Table 13](#).

A mascara containing Polyurethane-1 (30%) was not predicted to be an ocular irritant in a neutral red release assay (NRR), chorioallantoic membrane of the embryonic hen's egg assay (HET-CAM), and reconstituted human epithelial culture (REC) assays.⁷⁹ Considering the 3 assays above, the estimated Draize classification of the test material is a slight irritant with a score of 0 to 15. Another mascara containing Polyurethane-1 (30%) was tested for ocular irritation in a HET-CAM assay (tested at 50%; final concentration 15%), BCOP, and EpiOcular™ assay (tested at 20%; final concentration 6%), and was predicted to not be an ocular irritant.⁸⁰⁻⁸² In an EpiOcular assay, a product containing Polyurethane-14 (10%) was tested at 20% (final concentration of Polyurethane-14 was 2%); the estimated Draize ocular irritation score of the test material at 100% was predicted to be 0 and Polyurethane-14 was predicted to be a non-irritant.⁸³ Polyurethane-21 (100%; 35% solids) was predicted to not be an ocular irritant in HET-CAM and BCOP assays.^{84,85} Polyurethane-42 was predicted to be a moderate irritant in a HET-CAM assay and a non-irritant in a BCOP assay.³⁶ Polyurethane-62 was predicted to not be an ocular irritation in an EpiOcular assay.⁶⁹

AnimalPolyurethane-1

Polyurethane-1 (30% in water and ethanol; 0.5 mL) was not an ocular irritant to rabbits.³² The test was conducted according to OECD TG 405 (Acute Eye Irritation/Corrosion).

Polyurethane-35

In an eye irritation study conducted in accordance with OECD TG 405, two of the rabbits (n = 3) exhibited redness in the conjunctivae in the treated eye of one rabbit 1 h after instillation of Polyurethane-35, and the remaining rabbit exhibited these effects in 1 treated eye 24 h after instillation.³⁸ All irritation responses were reversible within 48 h and were not sufficient to warrant classification of the polymer as an eye irritant.

Polyurethane-39

Polyurethane-39 (approximately 30% solids) was not irritating when instilled into the eyes of rabbits.³³ The test was conducted according to OECD TG 405.

Human

A 4-week use study of two mascaras containing Polyurethane-1 (30% and 28.5%) was conducted in subjects (n = 38) that either wore contact lenses or were self-assessed as having sensitive eyes.⁸⁶ Trace increases in redness of the palpebral conjunctivae were observed in three subjects during weeks 2 and/or 4; a trace increase in bulbar conjunctival redness was observed in one subject in week 2. There were no reports of subjective irritation. There were no increases in

lacrimation or eyelid inflammation. There were no changes in visual acuity or corneal tissue integrity. Both mascaras were found to be non-irritating.

SUMMARY

This is a review of the available scientific literature and unpublished data relevant for assessing the safety of polyurethanes as used in cosmetics. According to the wINCI, the functions of these 66 ingredients include artificial nail builders, binders, film formers, hair fixatives, plasticizers, and surface modifiers. The polyurethane ingredients in this report are copolymers, which comprise carbamate (i.e., urethane) linkages within the respective polymer backbone.

Several of these polyurethane ingredients, as defined, are the polymers dispersed in water (e.g., Polyurethane-17, -35, -36, -58, -60, -61, -70, -71, and -72). Polyurethane ingredients for which molecular weights were reported were all greater than 1000 Da.

The ingredients in this report are copolymers, each of which is synthesized, in part, from isocyanate analogs. Exposure to diisocyanates (monomers of the polymers in this report) in the work place is one of the leading causes of occupational asthma.

Polyurethane-36 and -60 are reported to be free of solvents and isocyanate groups; residual isocyanates are expected to react with water in trademark mixture dispersions and form polyureas. As supplied, a tradename mixture of Polyurethane-36 contains approximately 1.0% to 1.5% phenoxyethanol as a preservative and approximately 1.0% to 1.5% trimethylamine as a neutralizing agent. In tradename mixtures thereof, Polyurethane-60 and -61 contain approximately 0.0075% MI and 0.0075% benzisothiazolinone as preservatives, and approximately 1.3% and 1.5% by weight, respectively, dimethylethanolamine as a neutralizing agent. However, these non-polyurethane ingredients are components of the certain tradename mixtures, not components of the ingredients under review in this report. Accordingly, their safety is evaluated elsewhere. Polyurethane-62 is reported to contain no detectable residual unreacted isocyanate monomer (HDI).

According to VCRP survey data received in 2017, Polyurethane-11 was reported to be used in 315 formulations, including 303 in leave-on formulations and 12 in rinse-off formulations. The other ingredients that had reported uses were reported to be used in 33 or fewer formulations. The results of the concentration of use survey conducted by the Council in 2016 indicate that Polyurethane-1 has the highest reported maximum concentration of use; it is used at up to 15% in nail products. The highest maximum concentration of use reported for products resulting in leave-on dermal exposure is 7.5% Polyurethane-33 in the category of other skin care preparations.

The oral LD₅₀ of Polyurethane-1 in rats was reported to be > 2000 mg/kg. The oral LD₅₀ of Polyurethane-35 in rats was reported to be 4890 mg/kg. The oral LD₅₀ for Polyurethane-39 was reported to be > 2000 mg/kg for rats.

The inhalation NOAEC for Polyurethane-1 was 3 mg/m³ when administered to rats for 6 h/day for 5 days. The inhalation LC₅₀ of Polyurethane-14 for 4 h was 110 mg/m³ in a whole body chamber.

The oral administration of polyurethane particles at 5 and 10 mg/kg/day for 10 days generated inflammation in mice. The polyurethane particles had a diameter of 249 ± 5.7 nm and a PDI of 0.3 ± 0.04. There was increased visceral fat accumulation in the treated mice in all groups (2, 5, 10 mg/kg/d) compared to controls. The lungs of mice in the 5 and 10 mg/kg/day groups showed inflammation, and inflammatory infiltrate was observed in all treatment groups.

Polyurethane-14 caused alveolar histiocytosis in rats exposed for 6 h/day for 14 days in a whole body inhalation chamber at 30 and 100 mg/m³ in a dose-dependent manner. Multifocal, minimal alveolar histiocytosis was observed in the lungs of some of the rats in the control and 10 mg/m³ groups and was not considered to be an effect of exposure to Polyurethane-14.

Polyurethane-1 (30%) was not mutagenic in an Ames test; Polyurethane-1 was tested up to 16,000 µg/plate in both SPT and PIT assays, both with and without metabolic activation. Polyurethane-28 (concentration not specified) was not mutagenic in a bacterial reverse mutation assay conducted in accordance with OECD TG 471 using *S. typhimurium* and *E. coli*. Polyurethane-35 (concentration not specified) was not mutagenic in a bacterial reverse mutation assay. Polyurethane-42 (concentration not specified) was not mutagenic in a bacterial reverse mutation assay using *S. typhimurium* and *E. coli*. In an Ames mutagenicity test of Polyurethane-62 (up to 5000 µg/plate) using *S. typhimurium* and *E. coli*, no cytotoxicity or precipitation was observed with or without metabolic activation and there were no significant increases in the frequency of revertant colonies.

Polyurethane-35 and -62 were not corrosive to human skin cells in in vitro dermal corrosion assays.

Polyurethane-1 at 30% was not a dermal irritant in rabbits when exposed for 4 h under semi-occlusion. Polyurethane-39 was not irritating to rabbits when applied under semi-occlusion.

In a skin irritation study, Polyurethane-35 (40% in water) had a slight irritating effect to the skin of rabbits. All irritation effects were reversible within 7 days.

Polyurethane-62 was predicted to be non-sensitizing in a DPRA.

Polyurethane-1 was not sensitizing to guinea pigs in a Buehler assay. The induction was conducted at approximately 3% and the challenge at approximately 1.5%. In a guinea pig maximization test, Polyurethane-14 (23.4% solids) was not sensitizing. In Buehler and maximization tests, Polyurethane-35 (concentration not specified) showed no evidence of sensitization. Polyurethane-39 (up to 30%) was not sensitizing to mice in an LLNA.

In a cumulative irritation test, Polyurethane-14 (9.6%) was mildly to moderately irritating to human subjects and had similar results as ethanol (55%). In a human dermal irritation study, Polyurethane-21 had an average irritation score of 0.50 (out of 4); the saline control had an average score of 0.55. The irritation potential of Polyurethane-21 was low.

Mascaras containing 28.5% and 30% Polyurethane-1 did not demonstrate a potential for eliciting dermal irritation or sensitization in HRIPTs.

In an HRIPT of Polyurethane-21 (21% solids), no adverse reactions of any kind were observed during the course of the study. The study authors concluded that Polyurethane-21, as tested, was considered a non-primary irritant and a non-primary sensitizer. In an HRIPT of Polyurethane-21 (35% solids), no adverse reactions of any kind were observed during the course of the study. The study authors concluded that Polyurethane-21, as supplied, was considered a non-primary irritant and a non-primary sensitizer. In an HRIPT, Polyurethane-14 (10%) was not sensitizing and there were no adverse reactions observed at any time during the study. In another HRIPT, Polyurethane-14 (9.61% solids) was not sensitizing.

In in vitro tests of a mascara containing Polyurethane-1 at 30%, the test material was rated slightly cytotoxic in a NRR assay, HET-CAM assay, and a REC assay; when considering these three assays together, the authors concluded that the results might be equivalent to a Draize score of 0-15 (slightly irritating). In in vitro tests of another mascara containing Polyurethane-1 at 30%, the test substance was predicted to have practically no ocular irritation potential in a HET-CAM assay and a BCOP assay. In EpiOcular assays, a product containing Polyurethane-14 (10%) and Polyurethane-62 were predicted to not be ocular irritants. Polyurethane-21 (100%; 35% solids) was predicted to not be an ocular irritant in HET-CAM and BCOP assays. Polyurethane-42 was found to be a “moderately irritant” in a HET-CAM assay and a non-irritant in a BCOP assay.

Polyurethane-1 at 30% was not an ocular irritant to rabbits. In an eye irritation study conducted with rabbits, the irritant effects were not sufficient to warrant classification of Polyurethane-35 as an eye irritant. Polyurethane-39 (approximately 30% solids) was not irritating when instilled into the eyes of rabbits.

In a 4-week use study of two mascaras containing Polyurethane-1 (30% and 28.5%), the mascaras were found to be non-irritating.

DISCUSSION

The CIR Expert Panel examined the available data, which included method of manufacture and impurity data; acute and repeated dose oral and inhalation toxicity; genotoxicity; dermal and ocular irritation data; and sensitization data. These ingredients are expected to be large molecules. The assays for ocular and dermal irritation showed that there were no concerns that these ingredients would be irritating under the conditions of use.

Many of these polyurethanes are reported to be supplied, in tradename mixtures, as emulsions or in solutions with multiple non-polyurethane ingredients that may include sensitizers such as the preservative MI (e.g., as reported in some tradename mixtures containing Polyurethane-60 and -61). Cosmetics manufacturers and formulators are advised to be aware of the presence of potentially sensitizing constituents in these ingredients, as supplied, and to avoid reaching levels of potential sensitizers that may be hazardous to consumers, especially when combining these ingredients with other ingredients that may contain sensitizers. Levels that are unlikely to induce sensitization in consumers through the intended uses of such formulations may be estimated based on a QRA.

The Panel noted that these polyurethanes contain monomers that could be of concern if there were significant residual monomers present. For example, inhalation of the HDI monomer can cause occupational asthma, hypersensitivity pneumonitis, rhinitis, and accelerated lung deterioration. The Panel noted that these polyurethane ingredients are heterogeneous in their structures and monomeric components. However, these ingredients are all large molecules and will not be readily absorbed through the skin. These polymers are expected to be stable and any residual monomers would be either washed away in manufacturing or, because the monomers are reactive, consumed in reaction with solution or formulations. The Panel was comfortable that there would not be any significant residual HDI (or other isocyanate analogs such as isophorone diisocyanate, saturated methylene diphenyldiisocyanate, 1-isocyanato-1-methylethylbenzene, or hexamethylene diisocyanate) or other monomers in these ingredients, as supplied for formulation. However, producers and formulators should continue to use current good manufacturing practices (cGMP) and avoid creating conditions where monomers could be released into solution or formulation.

The Panel noted that Europe restricts the amount of residual amines, which may be present as residuals from the manufacturing process in Polyurethane-17 and -21, to 2.5% in ready for-use leave-on preparations. These amines are used in low concentrations. However, residual low molecular weight amines should be minimized in polyurethane ingredients to reduce risk of nitrosating reactions and should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

Because these polyurethanes are commonly only supplied as tradename mixture emulsions or solutions, there has been some confusion about the concentration of the polyurethanes in the safety data. These ingredients are reported to be supplied in emulsion or solution at 20% to 66%. It is not always clear in the submitted data if the concentrations tested are of the polyurethane or of the emulsion. The Panel asks that any such submissions make it clear at what concentration the polyurethane is tested.

The CIR Expert Panel recognizes that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at the concentrations provided indicate a pattern of use which was considered by the Expert Panel in assessing safety.

The Panel discussed the issue of incidental inhalation exposure from body and hand products, and hair sprays. The limited data available from inhalation studies, including acute and short-term exposure data, suggest little potential for respiratory effects at relevant doses. The mean aerodynamic diameter of the tested particles of Polyurethane-14 was $1.9 \pm$

3.21 µm. The Expert Panel believes that the sizes of a substantial majority of the particles of these ingredients, as manufactured, are larger than the respirable range and/or aggregate and agglomerate to form much larger particles in formulation. Thus, the adverse effects reported using high doses of respirable particles in the inhalation studies do not indicate risks posed by use in cosmetics. These ingredients are reportedly used at concentrations up to 6% in cosmetic products that may be sprayed and up to 3.2% in loose powder products that may become airborne. The Panel noted that droplets/particles from cosmetic products would not be respirable to any appreciable amount. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. The Panel considered other data available to characterize the potential for polyurethanes to cause systemic toxicity, irritation, sensitization, and genotoxicity and noted the lack of systemic toxicity in acute oral exposure studies, little or no irritation or sensitization in multiple tests of dermal and ocular exposure, the absence of genotoxicity in multiple Ames tests, and the lack of irritation or sensitization in tests of dermal exposure. In addition, these ingredients are large macromolecules, several are reported to be insoluble in water, and chemically inert under physiological conditions or conditions of use, which supports the view that they are unlikely to be absorbed or cause local effects in the respiratory tract. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at <http://www.cir-safety.org/cir-findings>.

CONCLUSION

The CIR Expert Panel concluded that the following ingredients are safe when formulated to be non-sensitizing in cosmetics in the present practices of use and concentration described in this safety assessment:

Polyurethane-1	Polyurethane-19*	Polyurethane-41*	Polyurethane-58*
Polyurethane-2	Polyurethane-20*	Polyurethane-42*	Polyurethane-59*
Polyurethane-4*	Polyurethane-21*	Polyurethane-43*	Polyurethane-60*
Polyurethane-5*	Polyurethane-23*	Polyurethane-44*	Polyurethane-61*
Polyurethane-6	Polyurethane-24	Polyurethane-45*	Polyurethane-62*
Polyurethane-7	Polyurethane-25*	Polyurethane-46	Polyurethane-63*
Polyurethane-8	Polyurethane-26*	Polyurethane-47*	Polyurethane-64*
Polyurethane-9	Polyurethane-27*	Polyurethane-48*	Polyurethane-65*
Polyurethane-10	Polyurethane-28*	Polyurethane-49*	Polyurethane-66*
Polyurethane-11	Polyurethane-29*	Polyurethane-50*	Polyurethane-67*
Polyurethane-12*	Polyurethane-32*	Polyurethane-51*	Polyurethane-68*
Polyurethane-13*	Polyurethane-33	Polyurethane-52*	Polyurethane-69*
Polyurethane-14	Polyurethane-34	Polyurethane-53*	Polyurethane-70*
Polyurethane-15	Polyurethane-35	Polyurethane-54*	Polyurethane-71*
Polyurethane-16	Polyurethane-36*	Polyurethane-55*	Polyurethane-72*
Polyurethane-17*	Polyurethane-39	Polyurethane-56*	
Polyurethane-18	Polyurethane-40	Polyurethane-57*	

* Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

TABLES**Table 1.** Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

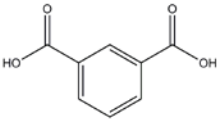
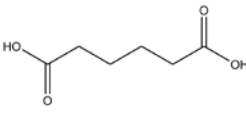
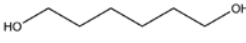
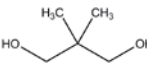
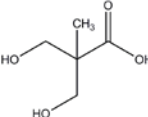
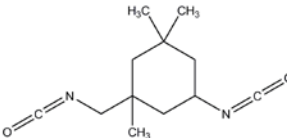
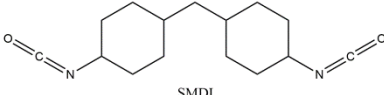

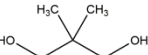
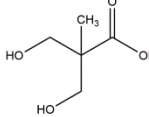
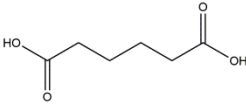
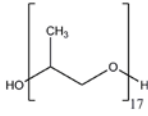
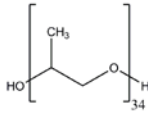
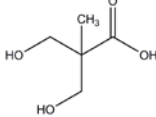
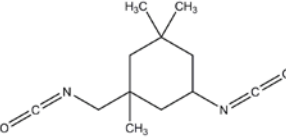
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-1	<p>Polyurethane-1 is a copolymer of isophthalic acid, adipic acid, hexylene glycol, neopentyl glycol, dimethylolpropanoic acid [DMPA], and isophorone diisocyanate monomers. [Monomers:]</p> <div>   </div> <div> <p>isophthalic acid</p> <p>adipic acid</p> </div> <div>   </div> <div> <p>hexylene glycol</p> <p>neopentyl glycol</p> </div> <div>   </div> <div> <p>dimethylolpropanoic acid</p> <p>isophorone diisocyanate</p> </div>	Binder; film former; hair fixative
Polyurethane-2	<p>Polyurethane-2 is a copolymer of hexylene glycol, neopentyl glycol, adipic acid, saturated methylene diphenyldiisocyanate (SMDI), and dimethylolpropanoic acid monomers. [Monomers:]</p> <div>  </div> <p>SMDI</p> <div>   </div> <div> <p>hexylene glycol</p> <p>neopentyl glycol</p> </div> <div>   </div> <div> <p>dimethylolpropanoic acid</p> <p>adipic acid</p> </div>	Film former
Polyurethane-4	<p>Polyurethane-4 is a copolymer of PPG-17, PPG-34, isophorone diisocyanate and dimethylolpropanoic acid [DMPA] monomers. [Monomers:]</p> <div>   </div> <div> <p>PPG-17</p> <p>PPG-34</p> </div> <div>   </div> <div> <p>dimethylolpropanoic acid</p> <p>isophorone diisocyanate</p> </div>	Film former

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

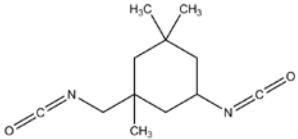
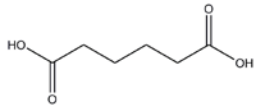
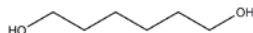
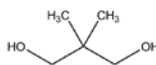
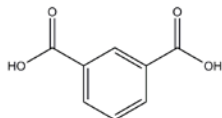
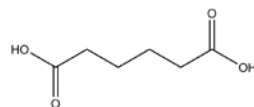
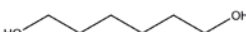
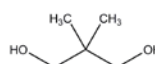
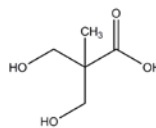
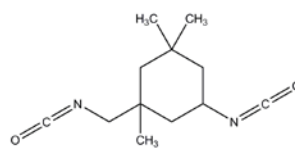
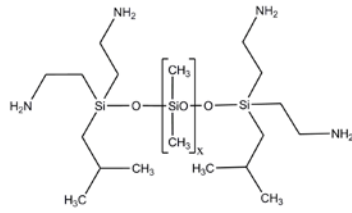
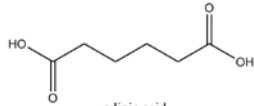
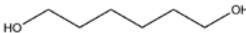
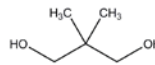
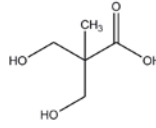
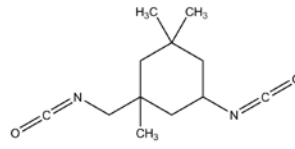
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-5	<p>Polyurethane-5 is a copolymer of hexylene glycol, neopentyl glycol, adipic acid and isophorone diisocyanate monomers. [Monomers:]</p> <div>  <p>isophorone diisocyanate</p>  <p>adipic acid</p>  <p>hexylene glycol</p>  <p>neopentyl glycol</p> </div>	Film former
Polyurethane-6	<p>Polyurethane-6 is a copolymer of isophthalic acid, adipic acid, hexylene glycol, neopentyl glycol, dimethylolpropanoic acid [DMPA], isophorone diisocyanate and bis-ethylaminoisobutyl-dimethicone monomers. [Monomers:]</p> <div>  <p>isophthalic acid</p>  <p>adipic acid</p>  <p>hexylene glycol</p>  <p>neopentyl glycol</p>  <p>dimethylolpropanoic acid</p>  <p>isophorone diisocyanate</p>  <p>bis-ethylaminoisobutyl-dimethicone</p> </div>	Binder; film former; hair fixative
Polyurethane-7	<p>Polyurethane-7 is a copolymer of hexylene glycol, neopentyl glycol, adipic acid, isophorone diisocyanate and dimethylolpropanoic acid [DMPA] monomers. [Monomers:]</p> <div>  <p>adipic acid</p>  <p>hexylene glycol</p>  <p>neopentyl glycol</p>  <p>dimethylolpropanoic acid</p>  <p>isophorone diisocyanate</p> </div>	Film former

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

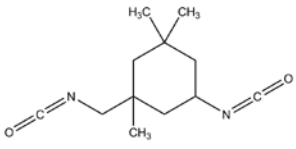
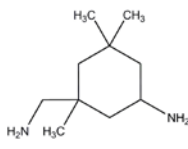
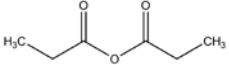
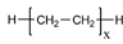
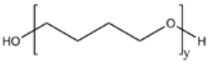
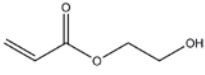
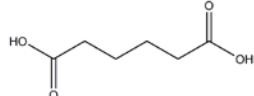
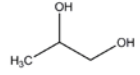
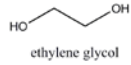
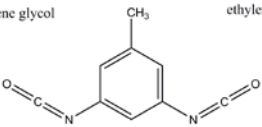
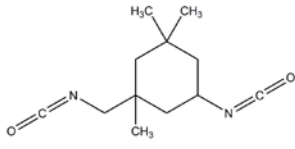
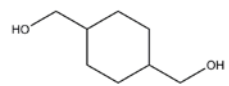
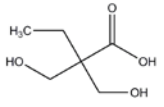
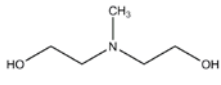
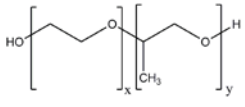
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-8	<p>Polyurethane-8 is a copolymer of polyethylene, poly(1,4-butanediol), propanoic anhydride, isophorone diisocyanate, and isophorone diamine.</p> <p>[Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>isophorone diamine</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>propanoic anhydride</p> </div> <div style="text-align: center;">  <p>polyethylene</p> </div> </div> <div style="text-align: center; margin-top: 10px;">  <p>poly(1,4-butanediol)</p> </div>	Binder; film former; plasticizer
Polyurethane-9 69011-31-0	<p>Polyurethane-9 is the copolymer of adipic acid, toluene diisocyanate, propylene glycol, ethylene glycol and hydroxyethyl acrylate monomers.</p> <p>[Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>hydroxyethyl acrylate</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>propylene glycol</p> </div> <div style="text-align: center;">  <p>ethylene glycol</p> </div> </div> <div style="text-align: center; margin-top: 10px;">  <p>toluene diisocyanate</p> </div>	Artificial nail builder
Polyurethane-10	<p>Polyurethane-10 is a copolymer of isophorone diisocyanate, cyclohexanedimethanol, dimethylolbutanoic acid, polyalkylene glycol and <i>N</i>-methyl diethanolamine monomers.</p> <p>[Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>cyclohexane 1,4-dimethanol</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>dimethylolbutanoic acid</p> </div> <div style="text-align: center;">  <p><i>N</i>-methyl diethanolamine</p> </div> </div> <div style="text-align: center; margin-top: 10px;">  <p>polyalkylene glycol</p> </div>	Film former; hair fixative

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2} CIR Staff

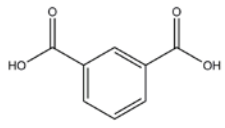
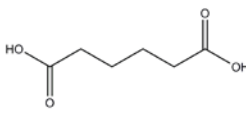
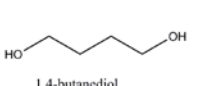
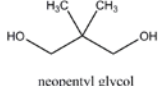
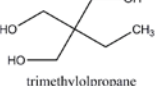
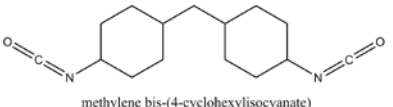
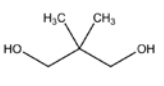
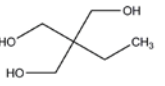
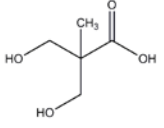
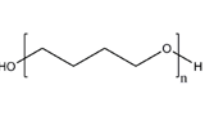
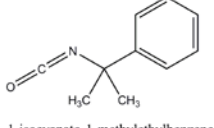
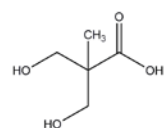
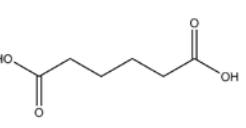
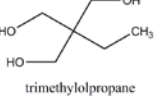
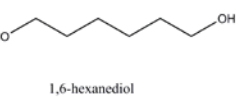
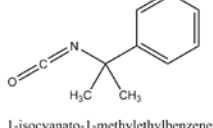
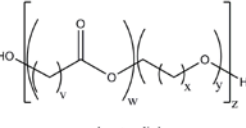
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-11 68258-82-2	<p>Polyurethane-11 is a copolymer of adipic acid, 1,4-butanediol, isophthalic acid, methylene bis-(4-cyclohexylisocyanate) [SMDI], neopentyl glycol and trimethylolpropane monomers. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>isophthalic acid</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>1,4-butanediol</p> </div> <div style="text-align: center;">  <p>neopentyl glycol</p> </div> <div style="text-align: center;">  <p>trimethylolpropane</p> </div> </div> <div style="text-align: center; margin-top: 10px;">  <p>methylene bis-(4-cyclohexylisocyanate)</p> </div>	Film former
Polyurethane-12	<p>Polyurethane-12 is a copolymer of trimethylolpropane, neopentyl glycol, dimethylolpropanoic acid [DMPA], polytetramethylene ether glycol and isocyanato methylethylbenzene monomers. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>neopentyl glycol</p> </div> <div style="text-align: center;">  <p>trimethylolpropane</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>dimethylolpropanoic acid</p> </div> <div style="text-align: center;">  <p>polytetramethylene ether glycol</p> </div> </div> <div style="text-align: center; margin-top: 10px;">  <p>1-isocyanato-1-methylethylbenzene</p> </div>	Binder; film former
Polyurethane-13	<p>Polyurethane-13 is a copolymer of trimethylolpropane, dimethylol propionic acid [DMPA], hexanediol, adipic acid, polyester diol, and isocyanato methylethylbenzene monomers. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>trimethylolpropane</p> </div> <div style="text-align: center;">  <p>1,6-hexanediol</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: flex-start; margin-top: 10px;"> <div style="text-align: center;">  <p>1-isocyanato-1-methylethylbenzene</p> </div> <div style="text-align: center;">  <p>polyester diol</p> </div> </div>	Binder; film former

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

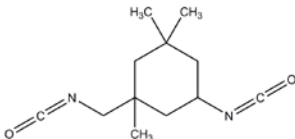
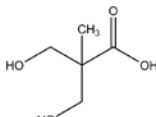
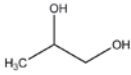
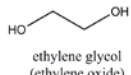
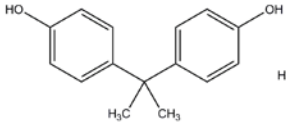
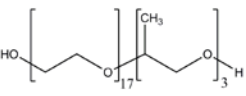
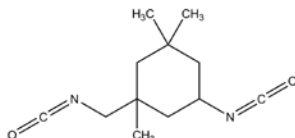
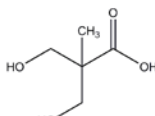
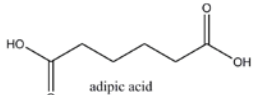
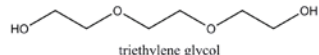
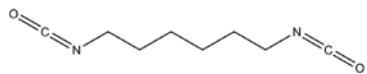
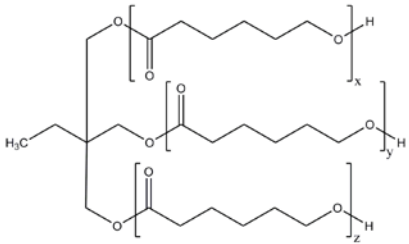
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-14	<p>Polyurethane-14 is a copolymer of isophorone diisocyanate, dimethylol propionic acid [DMPA], and 4,4'-isopropylidenediphenol reacted with propylene oxide, ethylene oxide and PEG/PPG-17/3. [Monomers:]</p> <div style="display: flex; flex-wrap: wrap; justify-content: space-around;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>propylene glycol (propylene oxide)</p> </div> <div style="text-align: center;">  <p>ethylene glycol (ethylene oxide)</p> </div> <div style="text-align: center;">  <p>4,4'-isopropylidenediphenol</p> </div> <div style="text-align: center;">  <p>PEG/PPG-17/3</p> </div> </div>	Film former; hair conditioning agent
Polyurethane-15	<p>Polyurethane-15 is a copolymer of isophorone diisocyanate, adipic acid, triethylene glycol, and dimethylolpropanoic acid. [Monomers:]</p> <div style="display: flex; flex-wrap: wrap; justify-content: space-around;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> <div style="text-align: center;">  <p>triethylene glycol</p> </div> </div>	Film former
Polyurethane-16	<p>Polyurethane-16 is a cross-linked condensation polymer formed from the addition polymerization of 2 [stoichiometric equivalents] of hexamethylene diisocyanate with 1 [stoichiometric equivalent] of polycaprolactonetriol terminated with 3 hydroxyl groups. [Monomers:]</p> <div style="display: flex; flex-wrap: wrap; justify-content: space-around;"> <div style="text-align: center;">  <p>hexamethylene diisocyanate</p> </div> <div style="text-align: center;">  <p>polycaprolactonetriol</p> </div> </div>	Anticaking agent; emulsion stabilizer; film former; slip modifier; surface modifier

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2} CIR Staff

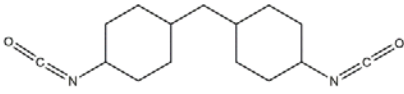
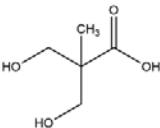
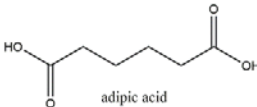
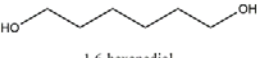
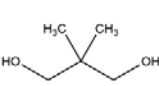
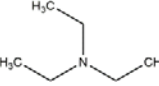

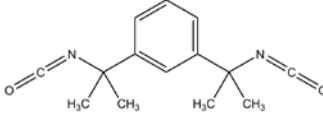
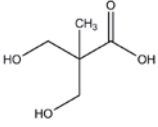
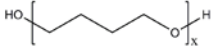
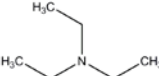

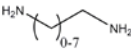
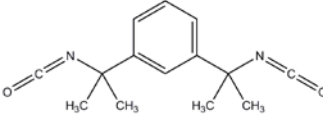
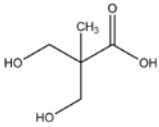
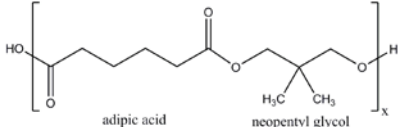

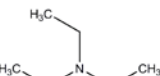
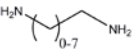
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-17 347175-78-4	<p>Polyurethane-17 is a complex polymer made by neutralizing hexylene glycol/neopentyl glycol/adipic acid/SMDI/DMPA copolymer with triethylamine in the presence of water. Further chain extension is achieved by reacting the polymer with ethylenediamine.</p> <p>[Monomers/reactants:]</p> <div style="display: flex; flex-wrap: wrap; justify-content: space-around;"> <div style="text-align: center;">  <p>SMDI</p> </div> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> <div style="text-align: center;">  <p>1,6-hexanediol</p> </div> <div style="text-align: center;">  <p>neopentyl glycol</p> </div> <div style="text-align: center;">  <p>triethylamine</p> </div> <div style="text-align: center;">  <p>ethylenediamine</p> </div> </div>	Film former
Polyurethane-18	<p>Polyurethane-18 is a complex polymer formed by the reaction of <i>m</i>-tetramethylene diisocyanate, polybutylene glycol and dimethylol propionic acid [DMPA]. The pre-polymer is neutralized with triethylamine and condensed with a combination of hydrazine and C1-8 diamines to achieve chain extension.</p> <p>[Monomers/reactants:]</p> <div style="display: flex; flex-wrap: wrap; justify-content: space-around;"> <div style="text-align: center;">  <p><i>m</i>-tetramethylene diisocyanate</p> </div> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>polybutylene glycol</p> </div> <div style="text-align: center;">  <p>triethylamine</p> </div> <div style="text-align: center;">  <p>hydrazine</p> </div> <div style="text-align: center;">  <p>C1-8 diamines</p> </div> </div>	Binder; hair fixative
Polyurethane-19	<p>Polyurethane-19 is a complex polymer formed by the reaction of <i>m</i>-tetramethylene diisocyanate, neopentyl glycol, trimethylol propane, dimethylol propionic acid [DMPA] and a polyester formed by condensing neopentyl glycol and adipic acid. The pre-polymer is neutralized with triethylamine and condensed with a combination of hydrazine and C1-8 diamines to achieve chain extension.</p> <p>[Monomers/reactants:]</p> <div style="display: flex; flex-wrap: wrap; justify-content: space-around;"> <div style="text-align: center;">  <p><i>m</i>-tetramethylene diisocyanate</p> </div> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>adipic acid neopentyl glycol</p> </div> <div style="text-align: center;">  <p>hydrazine</p> </div> <div style="text-align: center;">  <p>triethylamine</p> </div> <div style="text-align: center;">  <p>C1-8 diamines</p> </div> </div>	Binder; hair fixative

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

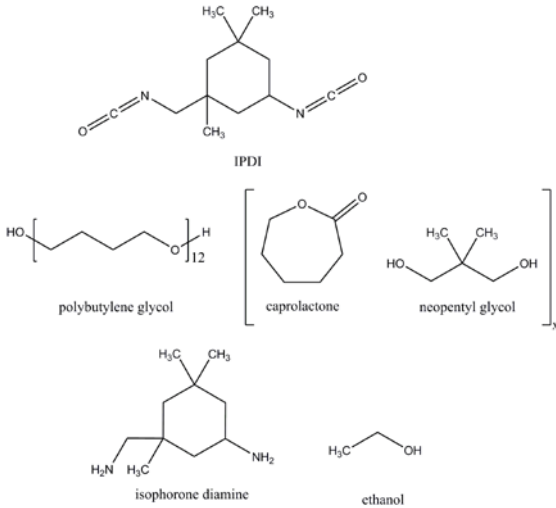
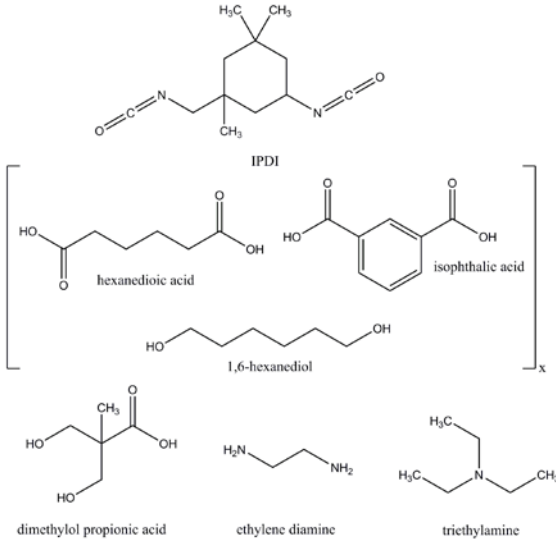
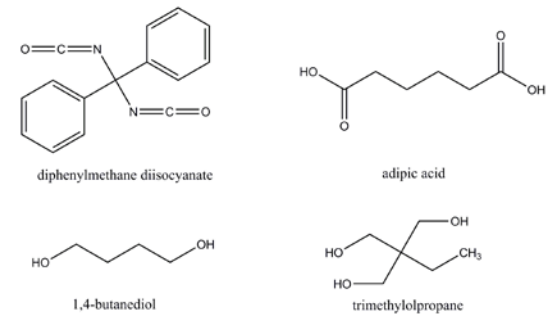
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-20	<p>Polyurethane-20 is a complex polymer formed by the reaction of isophorone diisocyanate (IPDI), and two polyols: The first polyol is polybutylene glycol containing approximately 12 butylene glycol units. The second polyol is formed by the reaction of approximately 10 [stoichiometric equivalents] of caprolactone [with 1 stoichiometric equivalent of] neopentyl glycol. The urethane polymer is then reacted with isophorone diamine to build molecular weight and the resulting polymer is capped with ethanol to eliminate residual isocyanate groups.</p> <p>[Monomers/reactants:]</p>  <p>The structures shown are: IPDI (isophorone diisocyanate), polybutylene glycol (HO-[CH₂CH₂CH₂CH₂O]₁₂-H), caprolactone (a seven-membered lactone ring), neopentyl glycol (HO-C(CH₃)₃-CH₂-OH), isophorone diamine (a cyclohexane ring with two methyl groups and two amino groups), and ethanol (H₃C-CH₂-OH).</p>	Binder; film former; plasticizer
Polyurethane-21	<p>Polyurethane-21 is a urethane copolymer prepared by reacting isophorone diisocyanate (IPDI) with dimethylol propionic acid (DMPA), a polyester of hexanedioic acid, isophthalic acid and 1,6-hexanediol, and ethylene diamine, neutralized with triethylamine.</p> <p>[Monomers/reactants:]</p>  <p>The structures shown are: IPDI (isophorone diisocyanate), hexanedioic acid (HOOC-(CH₂)₄-COOH), isophthalic acid (a benzene ring with two carboxylic acid groups in the meta position), 1,6-hexanediol (HO-(CH₂)₆-OH), dimethylol propionic acid (HO-CH₂-C(CH₃)₂-COOH), ethylene diamine (H₂N-CH₂-CH₂-NH₂), and triethylamine (H₃C-CH₂-N(CH₃)₂-CH₂-CH₃).</p>	Film former
Polyurethane-23	<p>Polyurethane-23 is a copolymer of adipic acid, 1,4 butanediol, diphenylmethane diisocyanate, and trimethylolpropane.</p> <p>[Monomers:]</p>  <p>The structures shown are: diphenylmethane diisocyanate (two benzene rings connected by a methylene group, with two isocyanate groups), adipic acid (HOOC-(CH₂)₄-COOH), 1,4-butanediol (HO-CH₂CH₂CH₂CH₂-OH), and trimethylolpropane (a central carbon atom bonded to three hydroxymethyl groups and one methyl group).</p>	Film former

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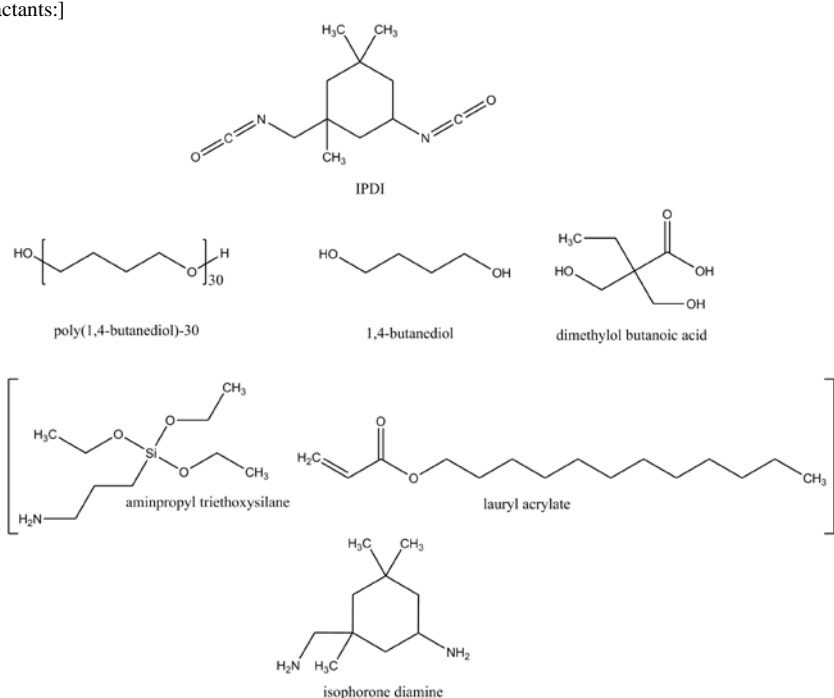
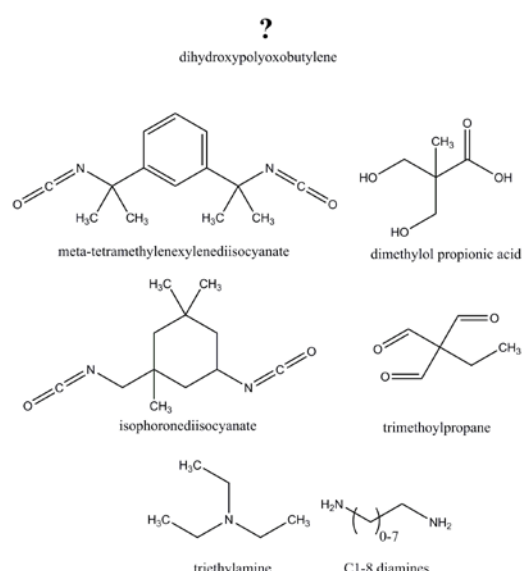
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-24	<p>Polyurethane-24 is a complex polymer prepared via the following multi-step synthesis. First, isophorone diisocyanate (IPDI) is reacted with three different polyols: poly(1,4-butanediol)-30, 1,4-butanediol, and dimethylol butanoic acid. This pre-polymer is then reacted with a reagent formed by the reaction between aminopropyl triethoxysilane and lauryl acrylate. The resulting polymer is subsequently chain extended by reaction with isophorone diamine in aqueous solution to produce Polyurethane-24. [Monomers/reactants:]</p>  <p>The structures shown are: IPDI (isophorone diisocyanate), poly(1,4-butanediol)-30, 1,4-butanediol, dimethylol butanoic acid, aminopropyl triethoxysilane, lauryl acrylate, and isophorone diamine.</p>	Hair conditioning agent; hair fixative
Polyurethane-25	<p>Polyurethane-25 is a complex polymer formed by the reaction of dihydroxypolyoxobutylene (degree of polymerization 12-30), dimethylol propionic acid [DMPA], meta-tetramethylenexylenediisocyanate, isophoronediiisocyanate and trimethoylpropane. The prepolymer is neutralized with triethylamine and chain extended with C1-8 alkyl diamine. [Monomers/reactants:]</p>  <p>The structures shown are: dihydroxypolyoxobutylene (represented by a question mark), meta-tetramethylenexylenediisocyanate, dimethylol propionic acid, isophoronediiisocyanate, trimethoylpropane, triethylamine, and C1-8 diamines.</p>	Binder; hair-waving/straightening agent; skin-conditioning agent-occlusive

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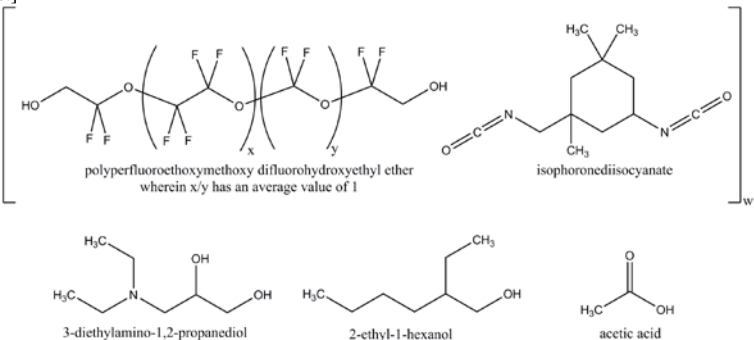
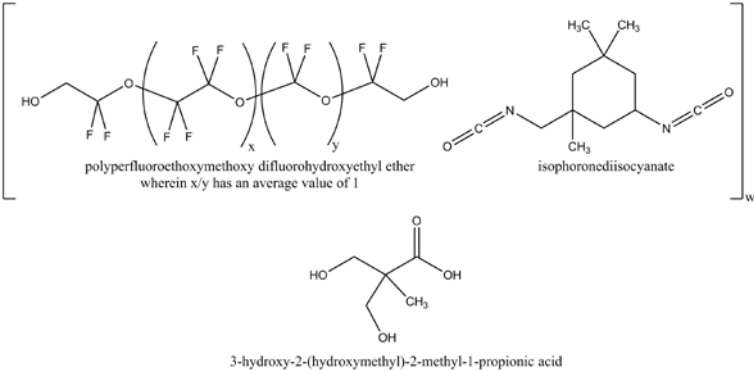
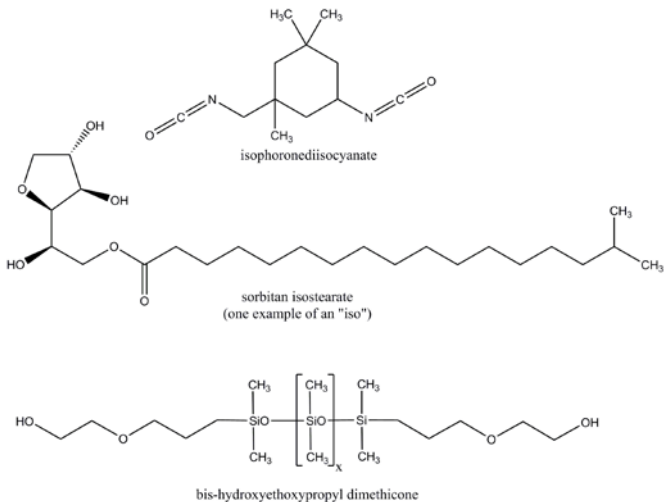
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-26 328389-90-8	<p>Polyurethane-26 is a complex polymer that is formed by the reaction of polyperfluoroethoxymethoxy difluorohydroxyethyl ether and isophorone diisocyanate (IPDI) to form a prepolymer. The prepolymer is further reacted with 3-diethylamino-1,2-propanediol followed by the capping of any residual isocyanate groups with 2-ethyl-1-hexanol. The resulting polymer is neutralized with acetic acid.</p> <p>[Monomers/reactants:]</p>  <p>polyperfluoroethoxymethoxy difluorohydroxyethyl ether wherein x/y has an average value of 1</p> <p>isophorone diisocyanate</p> <p>3-diethylamino-1,2-propanediol</p> <p>2-ethyl-1-hexanol</p> <p>acetic acid</p>	Film former; hair conditioning agent; skin protectant
Polyurethane-27 328389-91-9	<p>Polyurethane-27 is a complex polymer that is formed by the reaction of polyperfluoroethoxymethoxy difluorohydroxyethyl ether and isophorone diisocyanate (IPDI) to form a prepolymer. The prepolymer is further reacted with the triethylamine salt of 3-hydroxy-2-(hydroxymethyl)-2-methyl-1-propionic acid [DMPA].</p> <p>[Monomers/reactants:]</p>  <p>polyperfluoroethoxymethoxy difluorohydroxyethyl ether wherein x/y has an average value of 1</p> <p>isophorone diisocyanate</p> <p>3-hydroxy-2-(hydroxymethyl)-2-methyl-1-propionic acid</p>	Film former; hair conditioning agent; skin protectant
Polyurethane-28	<p>Polyurethane-28 is a complex polymer formed by the reaction of bis-hydroxyethoxypropyl dimethicone with isophorone diisocyanate (IPDI) and sorbitan isostearate.</p> <p>[Monomers/reactants:]</p>  <p>isophorone diisocyanate</p> <p>sorbitan isostearate (one example of an "iso")</p> <p>bis-hydroxyethoxypropyl dimethicone</p>	Surfactant-emulsifying agent

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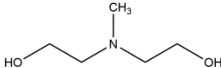
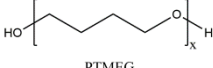
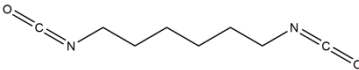
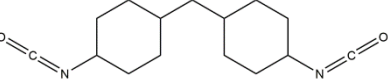
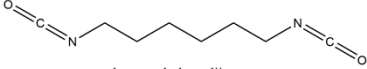
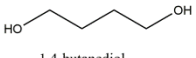
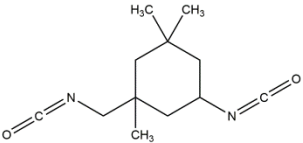
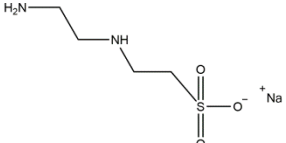

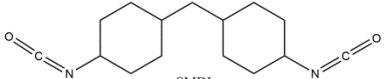
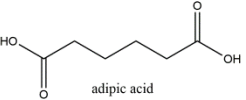
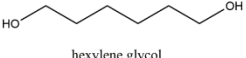
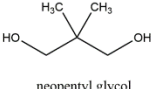
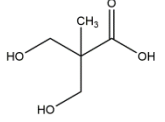
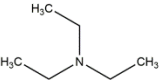

Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-29	<p>Polyurethane-29 is a copolymer of methyl diethanolamine (MDEA), polytetramethylene ether glycol (PTMEG), hexamethylene diisocyanate (HDI), and saturated methylene diphenyldiisocyanate (SMDI). [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>MDEA</p> </div> <div style="text-align: center;">  <p>PTMEG</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>HDI</p> </div> <div style="text-align: center;">  <p>SMDI</p> </div> </div>	Emulsion stabilizer; film former; hair conditioning agents; hair fixative
Polyurethane-32	<p>Polyurethane-32 is a copolymer of 1,4-butanediol, ethylenediamine, hexamethylene diisocyanate, isophorone diisocyanate, and sodium <i>N</i>-(2-aminoethyl)-3-aminoethane sulfonate monomers. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>hexamethylene diisocyanate</p> </div> <div style="text-align: center;">  <p>1,4-butanediol</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>sodium <i>N</i>-(2-aminoethyl)-3-aminoethane sulfonate</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p>ethylenediamine</p> </div>	Binder
Polyurethane-33	<p>Polyurethane-33 is a complex polymer formed by reacting dimethylolpropionic acid [DMPA] and a polyester composed of adipic acid, hexylene glycol, neopentyl glycol with methylene dicyclohexyldiisocyanate (SMDI) to form a prepolymer. The prepolymer is neutralized with triethylamine and then chain-extended with hydrazine. [Monomers/reactants:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>SMDI</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>hexylene glycol</p> </div> <div style="text-align: center;">  <p>neopentyl glycol</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 20px;"> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>triethylamine</p> </div> <div style="text-align: center;">  <p>hydrazine</p> </div> </div>	Binder

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

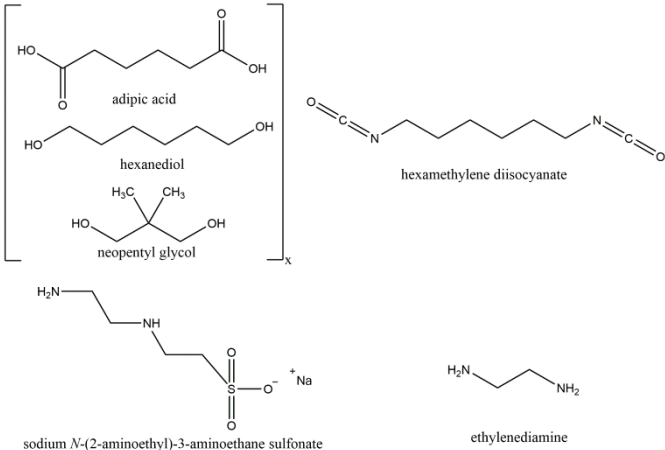
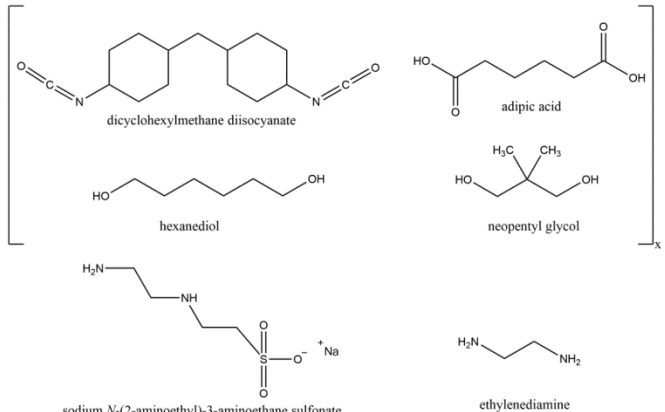
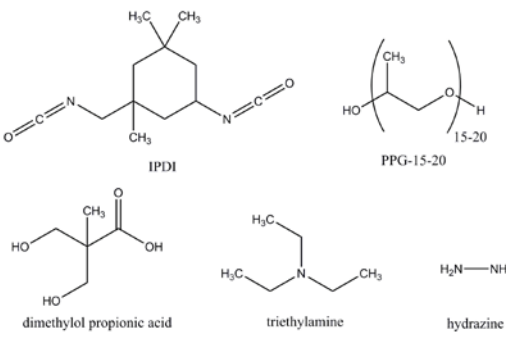
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-34	<p>Polyurethane-34 is a complex polymer that is formed in a multi-step reaction. A copolymer of hexanediol, neopentyl glycol, and adipic acid is reacted with hexamethylene diisocyanate. The resulting polymer is further reacted with <i>N</i>-(2-aminoethyl)-3-aminoethanesulfonic acid and ethylenediamine.</p> <p>[Monomers:]</p>  <p>adipic acid</p> <p>hexanediol</p> <p>neopentyl glycol</p> <p>hexamethylene diisocyanate</p> <p>sodium <i>N</i>-(2-aminoethyl)-3-aminoethane sulfonate</p> <p>ethylenediamine</p>	Binder
Polyurethane-35	<p>Polyurethane-35 is a complex urethane polymer that is made by reacting a polyester pre-polymer consisting of adipic acid, hexanediol, and neopentyl glycol with dicyclohexylmethane diisocyanate [SMDI]. The resulting urethane polymer is further reacted with sodium <i>N</i>-(2-aminoethyl)-3-aminoethanesulfonate and ethylenediamine and then dispersed into water.</p> <p>[Monomers:]</p>  <p>dicyclohexylmethane diisocyanate</p> <p>adipic acid</p> <p>hexanediol</p> <p>neopentyl glycol</p> <p>sodium <i>N</i>-(2-aminoethyl)-3-aminoethane sulfonate</p> <p>ethylenediamine</p>	Binder
Polyurethane-36	<p>Polyurethane-36 is a copolymer of isophorone diisocyanate (IPDI), PPG-15-20, and dimethylol propionic acid [DMPA], neutralized in the presence of water with triethylamine. Further chain extension is achieved by reacting the polymer with hydrazine.</p> <p>[Monomers/reactants:]</p>  <p>IPDI</p> <p>PPG-15-20</p> <p>dimethylol propionic acid</p> <p>triethylamine</p> <p>hydrazine</p>	Film former

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

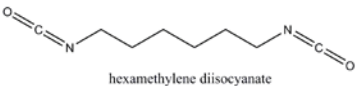
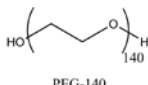
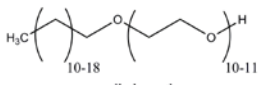
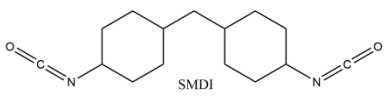
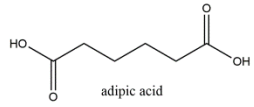
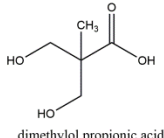
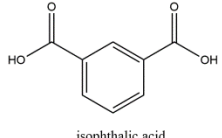
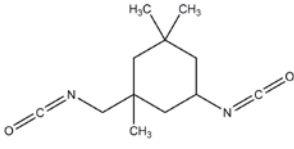
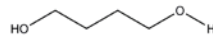
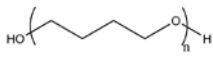
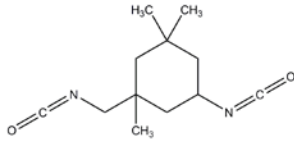
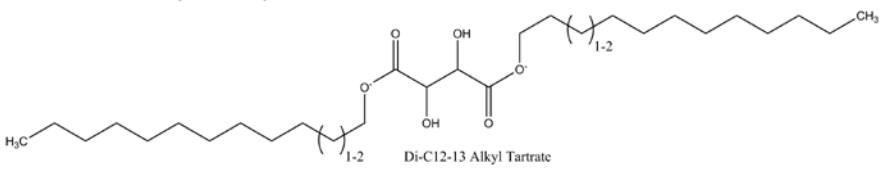
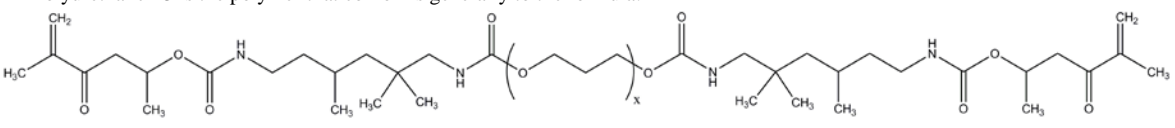
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-39	<p>Polyurethane-39 is a copolymer of PEG-140 and hexamethylene diisocyanate end-capped with C12-14 Pareth-10, C16-18 Pareth-11, and C18-20 Pareth-11. [Monomers:]</p> <div style="text-align: center;">  <p>hexamethylene diisocyanate</p> </div> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>PEG-140</p> </div> <div style="text-align: center;">  <p>alkyl pareths</p> </div> </div>	Hair conditioner
Polyurethane-40	<p>Polyurethane-40 is a copolymer of Adipic Acid, dimethylolpropanoic acid (DMPA), isophthalic acid and saturated methylene diphenyldiisocyanate (SMDI) monomers. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>SMDI</p> </div> <div style="text-align: center;">  <p>adipic acid</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>dimethylol propionic acid</p> </div> <div style="text-align: center;">  <p>isophthalic acid</p> </div> </div>	Film former; surface modifier
Polyurethane-41	<p>Polyurethane-41 is a copolymer of 1,4-Butanediol, polytetramethylene glycol and isophorone diisocyanate (IPDI) monomers. [Monomers:]</p> <div style="text-align: center;">  <p>IPDI</p> </div> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>1,4-Butanediol</p> </div> <div style="text-align: center;">  <p>polytetramethylene glycol</p> </div> </div>	Film former; hair conditioning agent; skin protectant
Polyurethane-42 1184186-26-2	<p>Polyurethane-42 is a copolymer of di-C12-13 alkyl tartrate, hydrogenated dilinoleyl alcohol and isophorone diisocyanate. [Monomers:]</p> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;"> <p>Hydrogenated Dilinoleyl Alcohol (not drawn)</p> </div> <div style="text-align: center;">  <p>Di-C12-13 Alkyl Tartrate</p> </div>	Film former
Polyurethane-43	<p>Polyurethane-43 is the polymer that conforms generally to the formula:</p> <div style="text-align: center;">  </div>	Film former

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

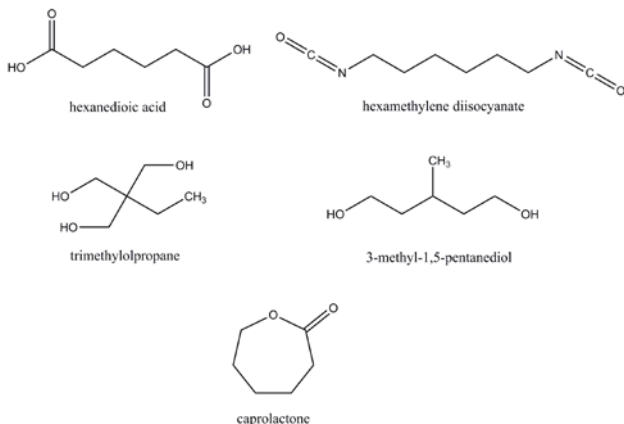
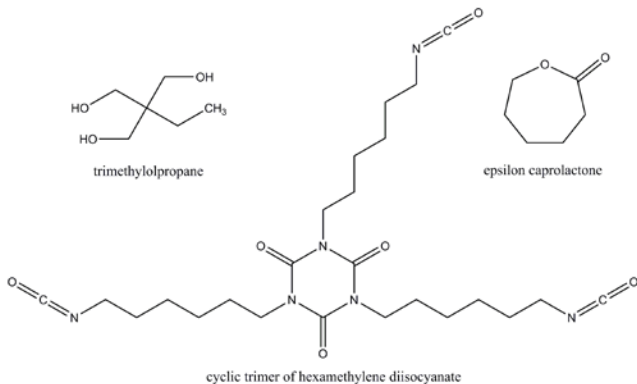
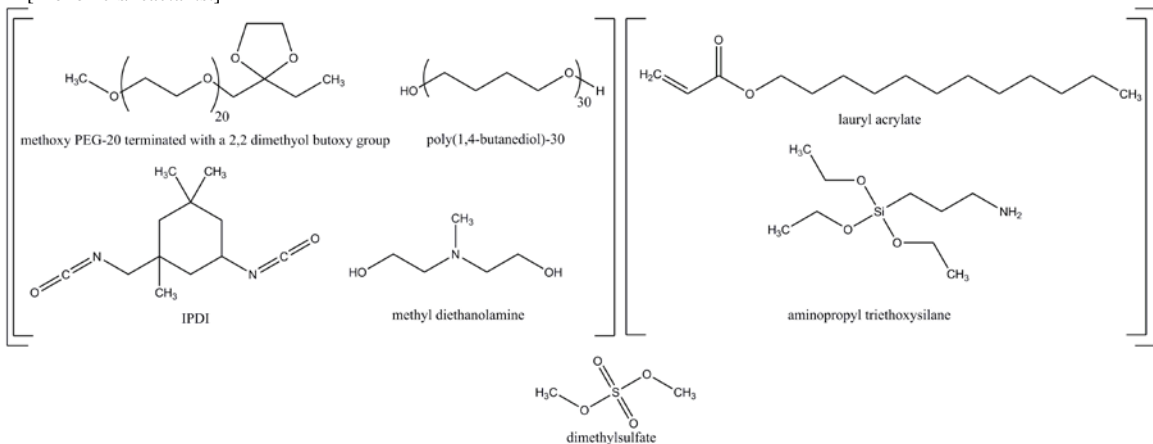
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-44	<p>Polyurethane-44 is a copolymer of hexanedioic acid, hexamethylene diisocyanate (HDI), trimethylolpropane, 3-methyl-1,5-pentanediol (MPD), and caprolactone monomers. [Monomers:]</p> <div>  <p>hexanedioic acid</p> <p>hexamethylene diisocyanate</p> <p>trimethylolpropane</p> <p>3-methyl-1,5-pentanediol</p> <p>caprolactone</p> </div>	Anticaking agent; bulking agent
Polyurethane-45	<p>Polyurethane-45 is a polymer made by the reaction of epsilon caprolactone and trimethylolpropane with the cyclic trimer of hexamethylene diisocyanate. [Monomers:]</p> <div>  <p>trimethylolpropane</p> <p>epsilon caprolactone</p> <p>cyclic trimer of hexamethylene diisocyanate</p> </div>	Film former
Polyurethane-46	<p>Polyurethane-46 is a complex urethane-based polymer. Initially, a pre-polymer is made by the reaction of isophorone diisocyanate (IPDI) with three different polyols. The polyols are poly(1,4-butanediol)-30, methoxy PEG-20 terminated with a 2,2 dimethyl butoxy group, and methyl diethanolamine. The pre-polymer is capped with the product formed by the reaction of lauryl acrylate and aminopropyl triethoxysilane (via Michael addition), and finally the amine groups from the methyl diethanolamine are quaternized with dimethylsulfate. [Monomers/reactants:]</p> <div>  <p>methoxy PEG-20 terminated with a 2,2 dimethyl butoxy group</p> <p>poly(1,4-butanediol)-30</p> <p>IPDI</p> <p>methyl diethanolamine</p> <p>lauryl acrylate</p> <p>aminopropyl triethoxysilane</p> <p>dimethylsulfate</p> </div>	Hair conditioning agent

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

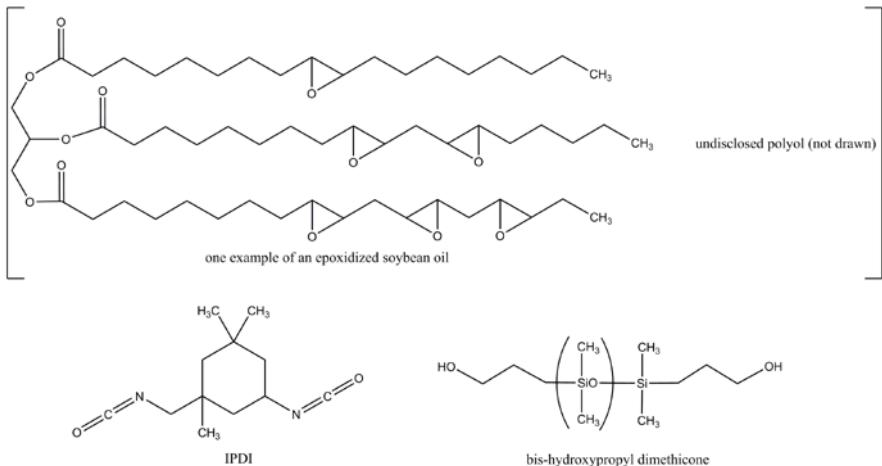
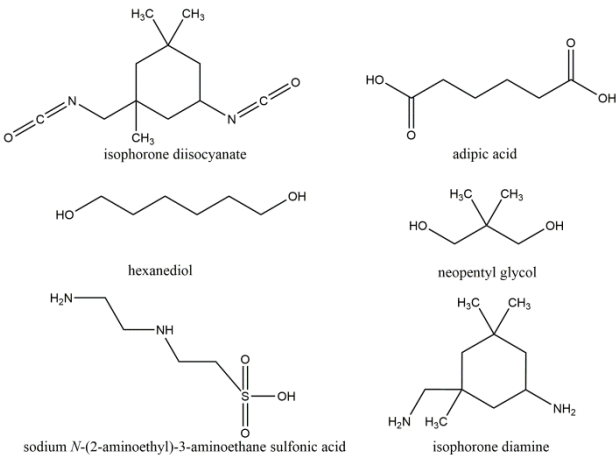
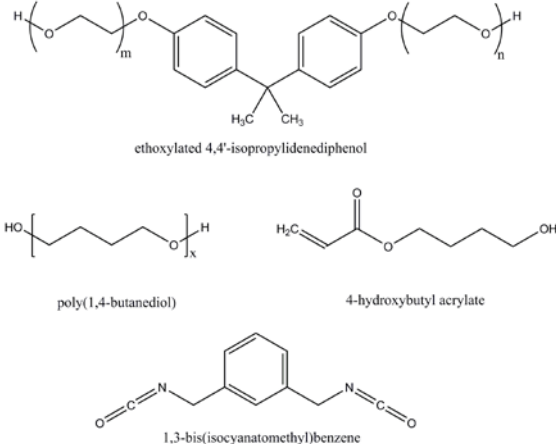
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-47	<p>Polyurethane-47 is a copolymer made by reacting a polyester polyol with isophorone diisocyanate (IPDI) and then bis-hydroxypropyl dimethicone. The polyester polyol is made by reacting epoxidized soybean oil with a polyol. [Soybean oil consists essentially of triglycerides of oleic, linoleic, linolenic and saturated acids. Monomers:]</p>  <p>undisclosed polyol (not drawn)</p> <p>one example of an epoxidized soybean oil</p> <p>IPDI</p> <p>bis-hydroxypropyl dimethicone</p>	Binder; film former; hair fixative; skin-conditioning agent-occlusive
Polyurethane-48	<p>Polyurethane-48 is a copolymer of hexanediol, neopentyl glycol, adipic acid, isophorone diisocyanate, isophorone diamine and sodium <i>N</i>-(2-aminoethyl)-3-aminoethanesulfonic acid monomers. [Monomers:]</p>  <p>isophorone diisocyanate</p> <p>adipic acid</p> <p>hexanediol</p> <p>neopentyl glycol</p> <p>sodium <i>N</i>-(2-aminoethyl)-3-aminoethane sulfonic acid</p> <p>isophorone diamine</p>	Film former
Polyurethane-49	<p>Polyurethane-49 is a copolymer of poly(1,4-butanediol), 1,3-bis(isocyanatomethyl)benzene, ethoxylated 4,4'-isopropylidenediphenol and 4-hydroxybutyl acrylate. [Monomers:]</p>  <p>ethoxylated 4,4'-isopropylidenediphenol</p> <p>poly(1,4-butanediol)</p> <p>4-hydroxybutyl acrylate</p> <p>1,3-bis(isocyanatomethyl)benzene</p>	Artificial nail builder

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}


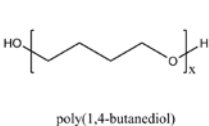
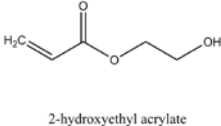
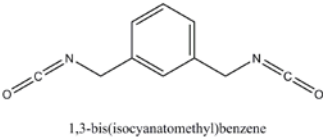
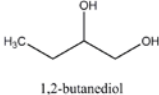
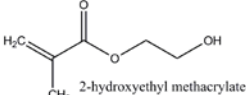
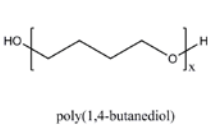
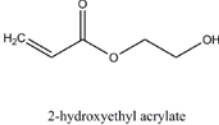
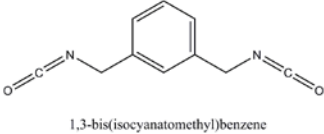
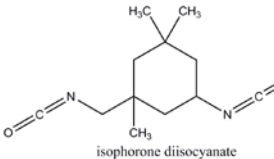
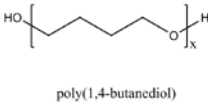
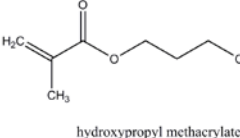
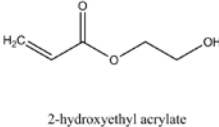
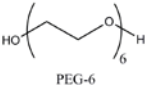
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-50	<p>Polyurethane-50 is a copolymer of poly(1,4-butanediol), 1,3-bis(isocyanatomethyl)benzene, ethoxylated 4,4'-isopropylidenediphenol and 2-hydroxyethyl acrylate. [Monomers:]</p>  <p>ethoxylated 4,4'-isopropylidenediphenol</p>  <p>poly(1,4-butanediol)</p>  <p>2-hydroxyethyl acrylate</p>  <p>1,3-bis(isocyanatomethyl)benzene</p>	Artificial nail builder
Polyurethane-51	<p>Polyurethane-51 is a copolymer made by reacting 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate (HEMA), 1,2-Butanediol, poly(1,4-butanediol) and 1,3-bis(isocyanatomethyl)cyclohexane. [Monomers:]</p>  <p>1,2-butanediol</p>  <p>2-hydroxyethyl methacrylate</p>  <p>poly(1,4-butanediol)</p>  <p>2-hydroxyethyl acrylate</p>  <p>1,3-bis(isocyanatomethyl)cyclohexane</p>	Artificial nail builder
Polyurethane-52	<p>Polyurethane-52 is a copolymer of poly(1,4-butanediol), isophorone diisocyanate, PEG-6, 2-hydroxyethyl acrylate and hydroxypropyl methacrylate. [Monomers:]</p>  <p>isophorone diisocyanate</p>  <p>poly(1,4-butanediol)</p>  <p>hydroxypropyl methacrylate</p>  <p>2-hydroxyethyl acrylate</p>  <p>PEG-6</p>	Artificial nail builder

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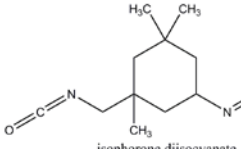
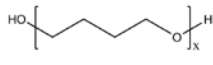
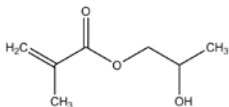
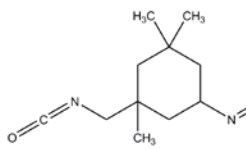
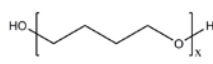
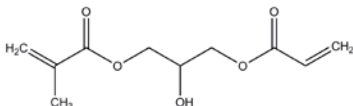
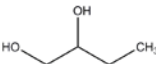
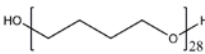
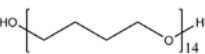
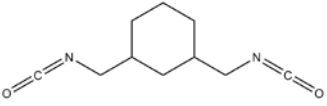
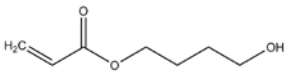
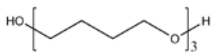
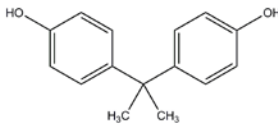
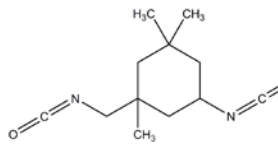
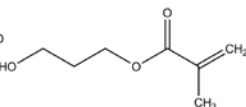
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-53	<p>Polyurethane-53 is a copolymer of poly(1,4-butanediol), isophorone diisocyanate, and 2-hydroxypropyl methacrylate. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>poly(1,4-butanediol)</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p>2-hydroxypropyl methacrylate</p> </div>	Artificial nail builder
Polyurethane-54	<p>Polyurethane-54 is a copolymer of poly(1,4-butanediol)-4, 1,2-butanediol, 3-(acryloyloxy)-2-hydroxypropyl methacrylate, and isophorone diisocyanate. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>isophorone diisocyanate</p> </div> <div style="text-align: center;">  <p>poly(1,4-butanediol)</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 20px;"> <div style="text-align: center;">  <p>3-(acryloyloxy)-2-hydroxypropyl methacrylate</p> </div> <div style="text-align: center;">  <p>1,2-butanediol</p> </div> </div>	Artificial nail builder
Polyurethane-55	<p>Polyurethane-55 is the polymer formed by the reaction of poly(1,4-butanediol)-28, poly(1,4-butanediol)-14, and 1,3-bis(isocyanatomethyl)cyclohexane. The polymer is capped with 4-hydroxybutyl acrylate. [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>poly(1,4-butanediol)-28</p> </div> <div style="text-align: center;">  <p>poly(1,4-butanediol)-14</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p>1,3-bis(isocyanatomethyl)cyclohexane</p> </div> <div style="text-align: center; margin-top: 20px;">  <p>4-hydroxybutyl acrylate</p> </div>	Artificial nail builder
Polyurethane-56 1342288-58-7	<p>Polyurethane-56 is a copolymer of 4,4'-isopropylidenediphenol, poly(1,4-butanediol)-3, hydroxypropyl methacrylate, and isophoronediiisocyanate (IPDI). [Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>poly(1,4-butanediol)-3</p> </div> <div style="text-align: center;">  <p>4,4'-isopropylidenediphenol</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 20px;"> <div style="text-align: center;">  <p>IPDI</p> </div> <div style="text-align: center;">  <p>hydroxypropyl methacrylate</p> </div> </div>	Binder

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2} CIR Staff

Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-57 930592-39-5	<p>Polyurethane-57 is a copolymer of ethylene carbonate, hexanediol, isophorone diisocyanate (IPDI), 1,5-pentandiol, and hydroxyethyl acrylate.</p> <p>[Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <chem>OCCCCCO</chem> 1,5-pentandiol </div> <div style="text-align: center;"> <chem>OCCCCCCO</chem> hexanediol </div> </div> <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 20px;"> <div style="text-align: center;"> IPDI </div> <div style="text-align: center;"> ethylene carbonate </div> </div> <div style="text-align: center; margin-top: 20px;"> <chem>CC(=O)OCC=C</chem> hydroxyethyl acrylate </div>	Binder
Polyurethane-58	<p>Polyurethane-58 is a complex polymer made by reacting polytetramethylene ether glycol, 2,2-dimethylolpropionic acid, and <i>meta</i>-tetramethylenexylenediisocyanate to form a prepolymer. The prepolymer is dispersed in water with 2-dimethylamino-2-methylpropanol as neutralizer and chain-extended with ethylenediamine.</p> <p>[Monomers/reactants:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> 2,2-dimethylolpropionic acid </div> <div style="text-align: center;"> <chem>HO(CH2)4OH</chem> polytetramethylene ether glycol </div> <div style="text-align: center;"> 2-dimethylamino-2-methylpropanol </div> </div> <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 20px;"> <div style="text-align: center;"> m-(tetramethylene)xylene diisocyanate </div> <div style="text-align: center;"> <chem>NCCCN</chem> ethylenediamine </div> </div>	Film former; hair fixative; plasticizer; skin protectant; skin-conditioning agent-occlusive
Polyurethane-59	<p>Polyurethane-59 is a copolymer of ethylhexylglycerin, PEG-240, tetradecyloctadeceth-100, and hexamethylenediisocyanate.</p> <p>[Monomers:]</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> ethylhexylglycerin </div> <div style="text-align: center;"> <chem>HO(CH2)4OH</chem> PEG-240 </div> </div> <div style="text-align: center; margin-top: 20px;"> tetradecyloctadeceth-100 </div> <div style="text-align: center; margin-top: 20px;"> <chem>O=C=NCCCCCCN=C=O</chem> hexamethylenediisocyanate </div>	Dispersing agent-nonsurfactant; emulsion stabilizer; viscosity increasing agent-aqueous

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2} CIR Staff

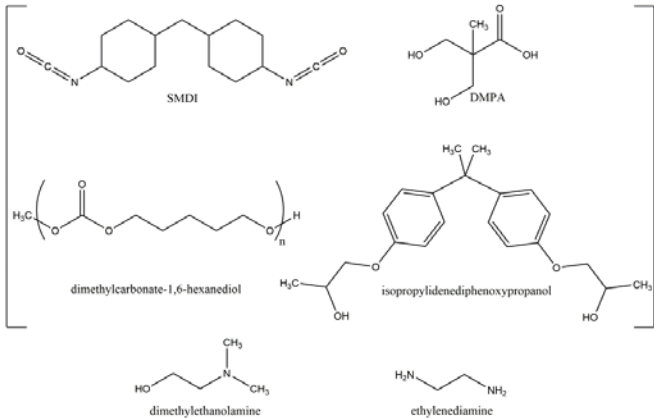
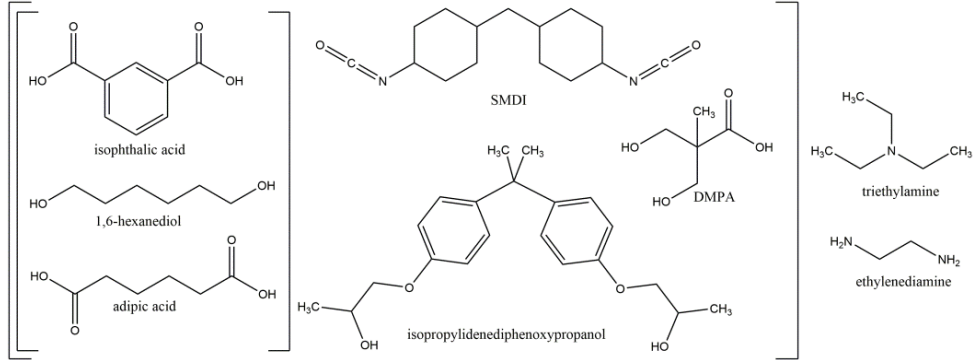
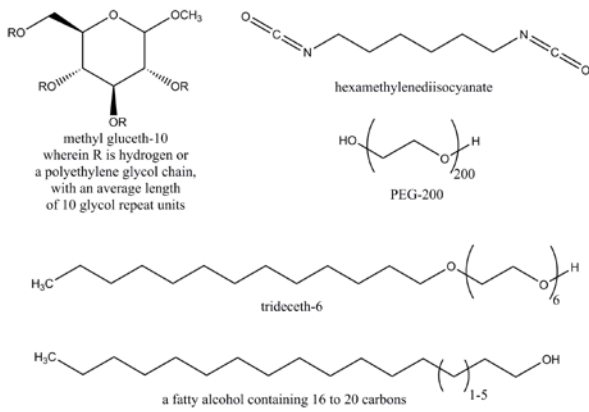
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-60	<p>Polyurethane-60 is the complex polymer made by first reacting saturated methylene diphenyl diisocyanate (SMDI), dimethylolpropionic acid (DMPA), bisphenol a bis-(2-hydroxypropyl) ether, and dimethylcarbonate-1,6-hexanediol to form a prepolymer, followed by dispersion in water with dimethylthanolamine and subsequent chain extension with ethylenediamine.</p> <p>[Monomers/reactants:]</p> 	Nail conditioning agent
Polyurethane-61	<p>Polyurethane-61 is the complex polymer made by first reacting saturated methylene diphenyl diisocyanate (SMDI), dimethylolpropionic acid (DMPA), bisphenol a bis-(2-hydroxypropyl) ether, and the polyester polyol derived from isophthalic acid/1,6-hexanediol/adipic acid to form a prepolymer, followed by dispersion in water with triethylamine and subsequent chain extension with ethylenediamine.</p> <p>[Monomers:]</p> 	Nail conditioning agent
Polyurethane-62	<p>Polyurethane-62 is a copolymer of hexamethylene diisocyanate, PEG-200, methyl gluceth-10 and trideceth-6 monomers, end-capped with a fatty alcohol containing 16 to 20 carbons.</p> <p>[Monomers:]</p> 	Binder; viscosity increasing agent-aqueous

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

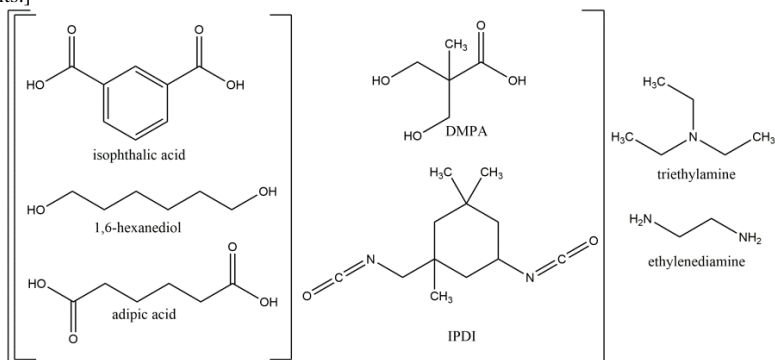
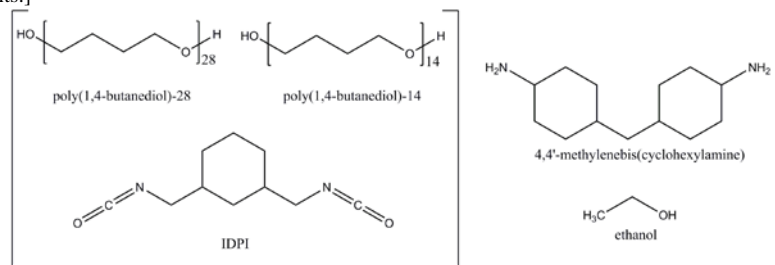
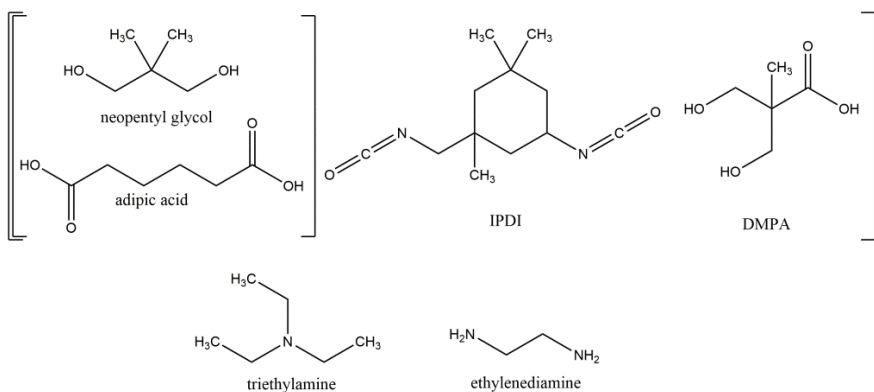
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-63	<p>Polyurethane-63 is a complex polymer formed by first reacting dimethylolpropionic acid (DMPA) and isophorone diisocyanate (IPDI) with a polyester diol made with adipic acid, isophthalic acid, and hexanediol. The resulting prepolymer is then neutralized with triethylamine and finally, chain-extended with ethylenediamine.</p> <p>[Monomers/reactants:]</p>  <p>The structures shown are: isophthalic acid (a benzene ring with carboxylic acid groups at the 1 and 3 positions), 1,6-hexanediol (a six-carbon chain with hydroxyl groups at both ends), adipic acid (a six-carbon chain with carboxylic acid groups at both ends), DMPA (dimethylolpropionic acid, a three-carbon chain with two hydroxyl groups and one carboxylic acid group), IPDI (isophorone diisocyanate, a cyclohexane ring with two isocyanate groups and two methyl groups), triethylamine (a central nitrogen atom bonded to three ethyl groups), and ethylenediamine (a two-carbon chain with amino groups at both ends).</p>	Film former
Polyurethane-64	<p>Polyurethane-64 is a urethane copolymer formed by a multi-step reaction. First, isophorone diisocyanate (IDPI) is reacted with a mixture of polytetrahydrofurans (PTHFs), also known as polybutylene glycols or polytetramethylene glycols. One of the PTHFs contains an average of 14 mols and the other an average of 28 mols of butylene glycol. The resulting polyurethane is reacted with 4,4'-methylenebis(cyclohexylamine) and finally the residual isocyanate groups are reacted with ethanol.</p> <p>[Monomers/reactants:]</p>  <p>The structures shown are: poly(1,4-butanediol)-28 (a long chain of repeating units with 28 units), poly(1,4-butanediol)-14 (a long chain of repeating units with 14 units), IDPI (isophorone diisocyanate, a cyclohexane ring with two isocyanate groups and two methyl groups), 4,4'-methylenebis(cyclohexylamine) (two cyclohexane rings connected by a methylene group, with amino groups at the 4 and 4' positions), and ethanol (a two-carbon chain with a hydroxyl group and a methyl group).</p>	Film former
Polyurethane-65	<p>Polyurethane-65 is a complex urethane copolymer made by reacting isophorone diisocyanate (IPDI) with a combination of dimethylolpropionic acid (DMPA) and a copolymer composed of neopentyl glycol and adipic acid. The resulting polymer is chain extended with ethylene diamine and neutralized with trimethylamine.</p> <p>[Monomers:]</p>  <p>The structures shown are: neopentyl glycol (a central carbon atom bonded to two methyl groups, two hydroxyl groups, and one hydroxymethyl group), adipic acid (a six-carbon chain with carboxylic acid groups at both ends), IPDI (isophorone diisocyanate, a cyclohexane ring with two isocyanate groups and two methyl groups), DMPA (dimethylolpropionic acid, a three-carbon chain with two hydroxyl groups and one carboxylic acid group), triethylamine (a central nitrogen atom bonded to three ethyl groups), and ethylenediamine (a two-carbon chain with amino groups at both ends).</p>	Artificial nail builders

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

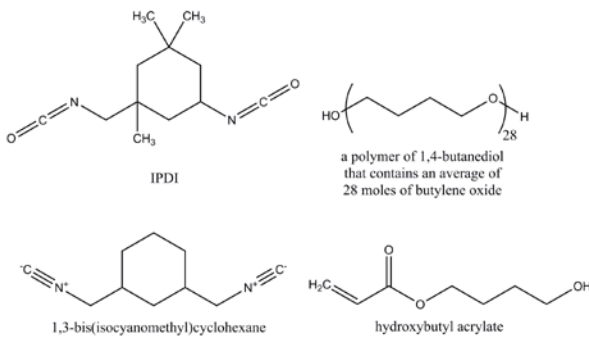
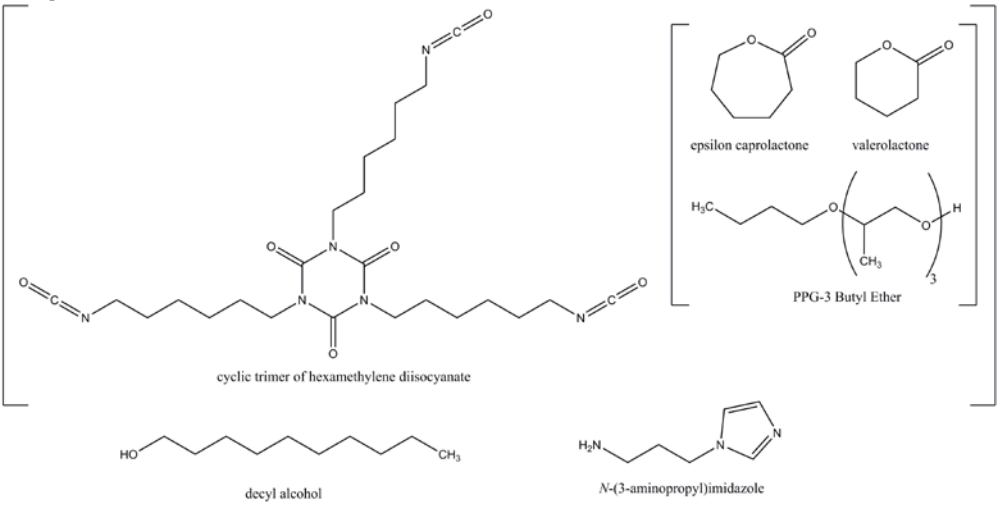
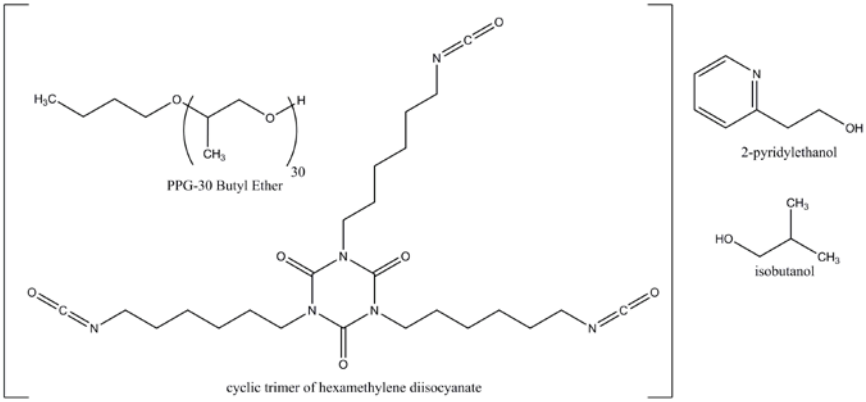
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-66	<p>Polyurethane-66 is a urethane polymer formed by reacting a polymer of 1,4-butanediol that contains an average of 28 moles of butylene oxide with a combination of isophorone diisocyanate (IPDI) and 1,3-bis(isocyanomethyl)cyclohexane. The polymer is end-blocked with hydroxybutyl acrylate.</p> <p>[Monomers:]</p>  <p>IPDI</p> <p>a polymer of 1,4-butanediol that contains an average of 28 moles of butylene oxide</p> <p>1,3-bis(isocyanomethyl)cyclohexane</p> <p>hydroxybutyl acrylate</p>	Binder
Polyurethane-67 1334242-38-4	<p>Polyurethane-67 is a complex polymer made by reacting the trimer of hexamethylene diisocyanate (HDI isocyanurate trimer) with a copolymer that is made by reacting PPG-3 Butyl Ether with a mixture of epsilon-caprolactone and valerolactone. Some of the remaining isocyanate groups from the first reaction are reacted with decyl alcohol and in a third step, the remaining isocyanate groups are reacted with <i>N</i>-(3-aminopropyl)imidazole.</p> <p>[Monomers:]</p>  <p>cyclic trimer of hexamethylene diisocyanate</p> <p>epsilon caprolactone</p> <p>valerolactone</p> <p>PPG-3 Butyl Ether</p> <p>decyl alcohol</p> <p><i>N</i>-(3-aminopropyl)imidazole</p>	Surface modifier
Polyurethane-68 157420-46-7	<p>Polyurethane-68 is a complex polymer that is made by reacting the trimer of hexamethylene diisocyanate (HDI isocyanurate trimer) with PPG-30 butyl ether. Some of the remaining isocyanate groups from the first reaction are reacted with 2-pyridylethanol and in a third step, the remaining isocyanate groups are reacted with 1-isobutanol.</p> <p>[Monomers:]</p>  <p>PPG-30 Butyl Ether</p> <p>cyclic trimer of hexamethylene diisocyanate</p> <p>2-pyridylethanol</p> <p>isobutanol</p>	Surface modifier

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2} CIR Staff

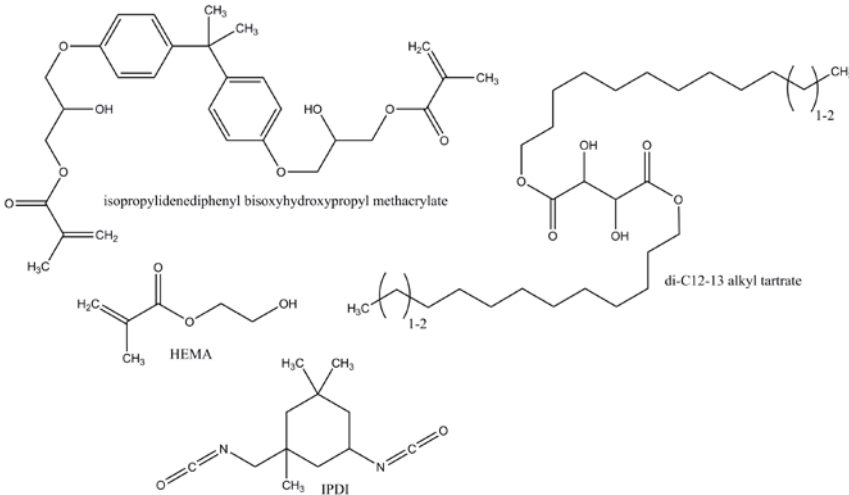
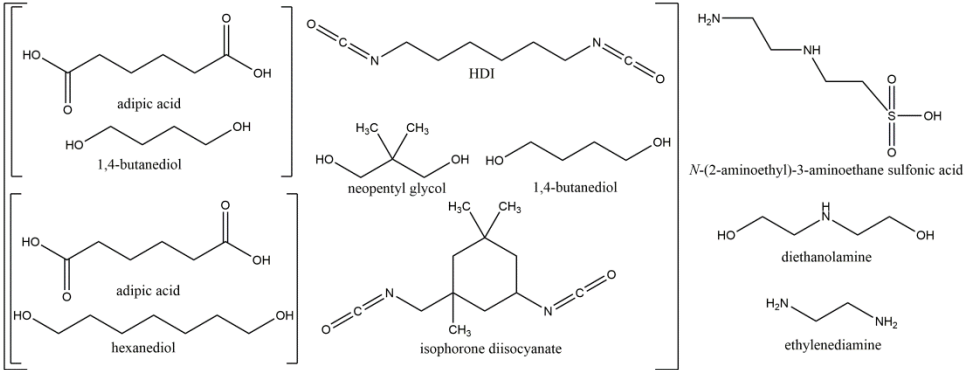
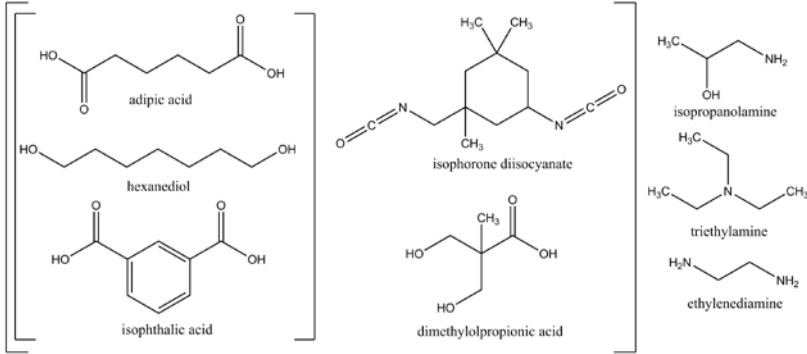
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-69 1668562-30-8	<p>Polyurethane-69 is a copolymer of isopropylidenediphenyl bisoxyhydroxypropyl methacrylate, isophorone diisocyanate (IPDI), and di-C12-13 alkyl tartrate, end-capped with hydroxyethyl methacrylate (HEMA). [Monomers:]</p>  <p>The structures show: isopropylidenediphenyl bisoxyhydroxypropyl methacrylate (a central isopropylidene group connected to two phenyl rings, each with a bisoxyhydroxypropyl methacrylate chain), HEMA (hydroxyethyl methacrylate), and di-C12-13 alkyl tartrate (a long-chain alkyl tartrate derivative).</p>	Skin-conditioning agent-miscellaneous
Polyurethane-70	<p>Polyurethane-70 is a complex polymer that is formed by a multi-step synthesis. First, a mixture of polyester diols (a copolymer of adipic acid and 1,4-butanediol; and a copolymer of adipic acid and hexanediol; and neopentyl glycol and 1,4-butanediol are reacted with isophorone diisocyanate and hexamethylene diisocyanate (HDI). The resulting urethane polymer is reacted with the sodium salt of N-(2-aminoethyl)-3-aminoethanesulfonic acid, ethylene diamine, and diethanolamine. The final polymer is dispersed in water. [Monomers/reactants:]</p>  <p>The structures show: adipic acid, 1,4-butanediol, hexanediol, neopentyl glycol, isophorone diisocyanate, HDI (hexamethylene diisocyanate), N-(2-aminoethyl)-3-aminoethanesulfonic acid, diethanolamine, and ethylenediamine.</p>	Film former
Polyurethane-71	<p>Polyurethane-71 is a complex polymer that is formed by a multi-step synthesis. First, a polyester diol made by condensing hexanediol, adipic acid, and isophthalic acid is reacted with isophorone diisocyanate and dimethylolpropionic acid [DMPA]. The resulting pre-polymer is neutralized with triethylamine. The neutralized polymer is dispersed in water with isopropanolamine and ethylene diamine. [Monomers/reactants:]</p>  <p>The structures show: adipic acid, hexanediol, isophthalic acid, isophorone diisocyanate, DMPA (dimethylolpropionic acid), isopropanolamine, triethylamine, and ethylenediamine.</p>	Binder; film former

Table 1. Definitions, idealized monomer structures, and functions of the ingredients in this safety assessment.^{1,2, CIR Staff}

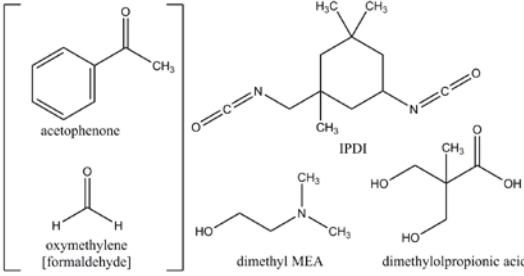
Ingredient CAS No.	Definition & Monomer Structures	Function(s)
Polyurethane-72 502761-95-7	<p data-bbox="256 216 1312 289">Polyurethane-72 is a urethane polymer made by reacting hydrogenated acetophenone/oxymethylene copolymer with isophorone diisocyanate (IPDI), dimethylolpropanoic acid, and dimethyl MEA. The resulting polymer is dispersed in water. [Monomers/reactants:]</p> <div data-bbox="537 289 1057 562">  <p>The image displays five chemical structures of monomers and reactants used in the synthesis of Polyurethane-72. On the left, acetophenone (a benzene ring with an acetyl group) and oxymethylene [formaldehyde] (a methylene group between two hydroxyl groups) are enclosed in brackets. To the right, the structures of isophorone diisocyanate (IPDI), dimethyl MEA (N,N-dimethylethanolamine), and dimethylolpropanoic acid are shown individually.</p> </div>	Binder; film former; nail conditioning agent

Table 2. Previous reports on precursors, monomers, moieties, and related ingredients of polyurethanes in this safety assessment.

Moiety	Conclusion; year	Relevant to	Reference
Acetic Acid	Safe as used; 2012	Polyurethane-26	²³
Adipic Acid; Hexanedioic Acid	Safe as used; 2012	Polyurethane-1, -2, -5, -6, -7, -9, -11, -13, -15, -17, -19, -21, -23, -33, -34, -35, -40, -48, -61, -63, -65, -70, -71	⁷
Alkyl PEG Ethers	Safe when formulated to be non-irritating; 2012	Polyurethane-39, -62	²⁴
Butylene Glycol, Hexylene Glycol	Safe as used; 1985, 2006	Polyurethane-1, -2, -5, -6, -7, -17, -33	^{4,6}
1,4-Butanediol; 1,5-Pentadiol; Hexanediol	1,4-Butanediol-Insufficient Data; 1,5-Pentadiol and Hexanediol-safe as used; 2017	Polyurethane-8, -11, -13, -21, -23, -24, -32, -34, -35, -41, -46, -48, -49, -50, -51, -52, -53, -55, -56, -57, -60, -61, -63, -66, -70, -71	³
1,2-Butanediol	Safe as used; 2012	Polyurethane-51, -54	¹¹
Diethanolamine	Safe when formulated to be non-irritating; 2011	Polyurethane-10, -29, -46, -70	¹⁶
Ethylhexylglycerin	Safe as used; 2013	Polyurethane-59	¹³
Glycine Soja (Soybean) Oil	Safe as used; 2011	Polyurethane-47	²⁵
HDI Polymers	17 are safe as used, 2 insufficient data; 2016	All	³¹
Bis-Hydroxyethoxypropyl Dimethicone	Safe as used; 2014	Polyurethane-28	^{8,9}
Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer	Safe as used; 2016	Polyurethane-9	²²
Hydroxypropyl Methacrylate; Isopropylidenediphenyl Bisoxhydroxypropyl Methacrylate; HEMA (Hydroxyethyl Methacrylate)	Safe in nail enhancement products when skin contact is avoided	Polyurethane-51, -52, -54, -56, -69	¹²
Isopropanolamine	Safe as used if not used in products containing N-nitrosating agents; 1987, 2006	Polyurethane-71	^{4,17}
Isostearic Acid (Sorbitan Isostearate)	Safe as used; 2014	Polyurethane-28	¹⁰
Methyl Gluceth-10	Safe as used; 2013	Polyurethane-62	²⁶
PEGs; Triethylene Glycol	Triethylene Glycol and PEGs ≥ 4 are safe as used, 2010	Polyurethane-14, -39, -46, -52, -59, -62	¹⁴
Polyethylene	Safe as used; 2007, 2015	Polyurethane-8	²⁰
PPG-3 Butyl Ether; PPG-30 Butyl Ether	Safe when formulated to avoid irritation; 2001 Insufficient Data Announcement; 2016	Polyurethane-67, -68	^{18,28}
Propylene Glycol; PPGs	Propylene Glycol and PPGs ≥ 3 are safe when formulated to be non-irritating, 2012	Polyurethane-4, -9, -14, -36, -67, -68	¹⁹

Table 3. Precursors, monomers, moieties, and related ingredients of polyurethanes in this safety assessment that are either cosmetic ingredients that have not been reviewed or chemicals that are not cosmetic ingredients.^{1,2}

Acetophenone*	<i>N</i> -(3-Aminopropyl)imidazole	Aminopropyl triethoxysilane
bis-Ethylaminoisobutyl-dimethicone monomers	Bisphenol A bis-(2-hydroxypropyl) ether	Butylene oxide
Caprolactone*	Cyclohexanedimethanol*	Decyl Alcohol*
Di-C12-13 Alkyl Tartrate*	3-Diethylamino-1,2-propanediol	Dihydroxypolyoxobutylene
Dilinoyleyl Alcohol*	2-Dimethylamino-2-methylpropanol	Dimethylcarbonate-1,6-hexanediol
Dimethyl MEA*	Dimethylolbutanoic acid	Dimethylolpropanoic acid
Dimethylolpropionic acid (DMPA)	Dimethylsulfate	Ethoxylated 4,4'-isopropylidenediphenol
2-Ethyl-1-hexanol	Ethylene Carbonate*	Ethylene diamine
Ethylene glycol*	Ethylene oxide	Hydrazine
4-Hydroxybutyl acrylate	3-Hydroxy-2-(hydroxymethyl)-2-methyl-1-propionic acid	Hydroxypropyl dimethicone*
Hydroxybutyl acrylate	Hydroxyethyl acrylate	1-Isobutanol
Isophthalic acid	Isophorone diamine	4,4'-Isopropylidenediphenol*
Lauryl Acrylate*	4,4'-Methylenebis(cyclohexylamine)	<i>N</i> -(2-Aminoethyl)-3-aminoethanesulfonic acid
Neopentyl glycol*	Oxymethylene	Poly(1,4)-butanediol
Polyalkylene glycol	Polybutylene glycol	Polycaprolactonetriol
Polyester diol	Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether*	Polytetrahydrofurans (PTHFs)
Polytetramethylene ether glycol	Polytetramethylene glycol	Propanoic anhydride
Propylene oxide	2-Pyridylethanol	Sodium <i>N</i> -(2-aminoethyl)-3-aminoethane sulfonate
Tetradecyloctadeceth	Trimethylamine*	Trimethylolpropane*
Valerolactone*		

*Cosmetic ingredient or closely related to a cosmetic ingredient listed in the wINCI that has not been reviewed. These are largely highly reactive molecules and not likely to be a significant component in final formulation and not likely to be released following polymerization and formulated in a cosmetic product.

Table 4. Diisocyanates used in manufacturing polyurethanes in this safety assessment.^{1,2}

bis(Isocyanatomethyl)benzene	1,3-bis(Isocyanatomethyl)cyclohexane
Diphenylmethane diisocyanate	Cyclic trimer of hexamethylene diisocyanate
Hexamethylenediisocyanate	Isocyanato methylethylbenzene
Isophorone diisocyanate (IPDI)	Methylene bis-(4-cyclohexylisocyanate) (HMDI)
<i>m</i> -Tetramethylene diisocyanate	meta-Tetramethylenexylenediisocyanate
Saturated methylene diphenyldiisocyanate (SMDI)	Toluene diisocyanate

Table 5. Chemical and physical properties of polyurethanes.

Property	Value	Reference
Polyurethane-11		
Molecular Weight g/mol	> 1000,000	37
Polyurethane-14		
Molecular Weight g/mol	> 1000	35
	20,000-35,000	66,67
Water Solubility g/L	Miscible	35
Polyurethane-21^a		
Viscosity kg/(s m) @ 25°C	0.160	34
Water Solubility	Miscible	34
Other solubility		
Propylene glycol	Insoluble	34
Ethanol	Insoluble	34
Dimethicone	Insoluble	34
Polyurethane-28		
Molecular Weight g/mol	> 30,000	36
Polyurethane-35		
Molecular Weight g/mol	> 1000	38
Disassociation constants (pKa, pKb) @°C		
pKa	0.5-4.5 est.	38
Polyurethane-36^b		
Physical Form	Liquid	43
Color	Whitish	43
Molecular Weight g/mol	> 50,000	43
Density @ 20°C	~ 1.04	43
Viscosity kg/(s m)	0.02-0.20	43
Vapor pressure mmHg @ 20°C	17.25	43
Melting Point °C	~ 0	43
Boiling Point °C	100	43
Water Solubility	Completely miscible	43
Polyurethane-42		
Molecular Weight g/mol	> 36,000	36
Polyurethane-59		
Molecular Weight g/mol	25,631	45
Polyurethane-60^c		
Physical Form	Liquid	39
Color	Light yellow	39
Molecular Weight g/mol	> 50,000	39
Density @ 20°C	~1.06	39
Viscosity kg/(s m)	0.05-0.5	39
Vapor pressure mmHg @ 20°C	17.25	39
Melting Point °C	~ 0	39
Boiling Point °C	100	39
Water Solubility	Completely miscible	39
Polyurethane-61^d		
Physical Form	Liquid	40
Color	Light yellow	40
Molecular Weight g/mol	> 50,000	40
Density/Specific Gravity @ 20°C	~ 1.05	40
Viscosity kg/(s m)	0.02-0.5	40
Vapor pressure mmHg @ 20°C	17.25	40
Melting Point °C	~ 0	40
Boiling Point °C	100	40
Water Solubility	Completely miscible	40

Table 5. Chemical and physical properties of polyurethanes.

Property	Value	Reference
Polyurethane-62		
Physical Form	Powder	41
Color	White to off white	41
Molecular Weight g/mol	> 70,000	41
	~ 100,000	42
Density kg/m ³ @ 23°C	1500	41
Water Solubility	Dispersible	41

est.=estimated

^a Polyurethane-21 at 35% in an aqueous dispersion.^b Polyurethane-36 in an aqueous dispersion with approximately 1.0%-1.5% phenoxyethanol and triethylamine.^c Polyurethane-60 in an aqueous dispersion with approximately 0.0075% methylisothiazolinone (MI) and benzisothiazolinone and 1.5% triethylamine.^d Polyurethane-61 in an aqueous dispersion with approximately 0.0075% MI and benzisothiazolinone and 1.5% triethylamine.**Table 6.** Methods of manufacture for polyurethanes.

Ingredient	Method of manufacture/monomers	Termination	Notes	Reference
Polyurethane-28	Condensation of an isocyanate component and molecules containing hydroxyl groups (sorbitan isostearate)	Addition of ethyl alcohol		36
Polyurethane-42	Condensation of an isocyanate component and molecules containing hydroxyl groups (di-C12-13 alkyl tartrate and hydrogenated dilinoleyl alcohol)	Addition of ethyl alcohol		36
Polyurethane-62	A proprietary anhydrous reaction		The resulting solid is then ground to the desired particle size.	42
Polyurethane-69	Condensation of an isocyanate component with di-C12-13 alkyl tartrate and isopropylidenediphenyl bisoxhydroxypropyl methacrylate.	2 added to react with terminal isocyanate groups. The reaction is carried on until free isocyanate groups are not detected.	-H	36

Table 7. Polyurethanes that are reported to be supplied in tradename mixtures as dispersions or solutions.

Ingredient	Percentage Solids	Solvent/medium	Reference
Polyurethane-1	30%	Water ~60%, ethanol (denatured) ~ 10%	32
Polyurethane-14	20%	Water	35
Polyurethane-21	35%	Water	34
Polyurethane-28	25%	Cyclopentasiloxane	36
Polyurethane-35	40%	Water	38
Polyurethane-36	39.0% - 41.0%	Water, approximately 1.0% - 1.5% (by weight) phenoxyethanol as a preservative and approximately 1.0% - 1.5% triethylamine as a neutralizing agent	43
Polyurethane-39	~ 20%	Water, ~ 1.2% preservative mixture of phenoxyethanol, phenylpropanol, 1,3-propane diol, caprylyl glycol, and α -tocopherol	33
Polyurethane-42	47.50%	Isododecane and ethanol	36
Polyurethane-60	37.0% - 39.0%	Water, approximately 0.0075% MI and benzisothiazolinone as preservatives, and approximately 1.3% (by weight) dimethylethanolamine as a neutralizing agent	39
Polyurethane-61	38.0% - 40.0%	Water, approximately 0.0075% MI and 75 ppm benzisothiazolinone as preservatives, and approximately 1.3% and 1.5% by weight, respectively, dimethylethanolamine as a neutralizing agent	40
Polyurethane-69	66%	Butyl acetate and ethanol	36

Table 8. Frequency of use according to duration and exposure of polyurethanes.^{47,48}

Use type	Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)	
	Uses		Uses		Uses		Uses	
	Polyurethane-1		Polyurethane-2		Polyurethane-6		Polyurethane-7	
Total/range	19	0.15-15	13	0.63-9	16	3-6	14	NR
<i>Duration of use^a</i>								
Leave-on	17	0.5-15	12	0.63-9	13	3-6	14	NR
Rinse-off	2	0.15	1	NR	3	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
<i>Exposure type</i>								
Eye area	10	0.9-4.6	8	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	4;2 ^b	0.5-5	1 ^b ; 3 ^c	NR	8	3-6	NR	NR
Incidental inhalation-powders	NR	NR	3 ^c	0.63; 1.1 ^c	NR	NR	6	NR
Dermal contact	2	2.3	7	0.63-1.1	NR	NR	14	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	9	0.5-5	NR	NR	16	3-6	NR	NR
Hair-coloring	NR	0.15	NR	NR	NR	NR	NR	NR
Nail	NR	15	NR	9	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR
	Polyurethane-8		Polyurethane-9		Polyurethane-10		Polyurethane-11	
Total/range	1	NR	1	NR	NR	0.098-3	315	0.0015-5.2
<i>Duration of use</i>								
Leave-on	1	NR	1	NR	NR	0.098-3	303	0.0072-5.2
Rinse-off	NR	NR	NR	NR	NR	NR	12	0.016
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	0.0015
<i>Exposure type</i>								
Eye area	NR	NR	NR	NR	NR	0.098	195	0.051-1.5
Incidental ingestion	NR	NR	NR	NR	NR	NR	2	0.058
Incidental Inhalation-sprays	NR	NR	NR	NR	NR	3 ^c	2; 1 ^b ; 2 ^c	0.0072-0.086
Incidental inhalation-powders	NR	NR	NR	NR	NR	NR	2; 2 ^c	3-3.2; 0.024 ^c
Dermal contact	1	NR	1	NR	NR	2	235	0.0015-3.2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	NR	NR	NR	NR	3	NR	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	0.086
Nail	NR	NR	NR	NR	NR	NR	78	0.06-5.2
Mucous Membrane	NR	NR	NR	NR	NR	NR	14	0.0015-0.058
Baby	NR	NR	NR	NR	NR	NR	NR	NR

Table 8. Frequency of use according to duration and exposure of polyurethanes.^{47,48}

Use type	Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)	
	Uses		Uses		Uses		Uses	
	Polyurethane-14		Polyurethane-15		Polyurethane-16		Polyurethane-18	
Total/range	33	0.18-2.8	2	0.01-0.2	1	0.98	11	0.8
<i>Duration of use</i>								
Leave-on	31	0.28	2	0.01-0.2	1	0.98	11	0.8
Rinse-off	2	0.18	NR	NR	NR	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
<i>Exposure type</i>								
Eye area	NR	0.62	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	0.036	NR	NR	NR	NR
Incidental Inhalation-sprays	10; 15 ^b	0.6-2.4; 0.6-2.8 ^c	NR	NR	NR	NR	3; 7 ^b	NR
Incidental inhalation-powders	NR	NR	1	0.2	NR	NR	NR	NR
Dermal contact	2	0.62-1.5	2	0.01-0.2	1	0.98	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	31	0.18-2.8	NR	NR	NR	NR	10	0.8
Hair-coloring	NR	0.63	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	0.036	NR	NR	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR
	Polyurethane-24		Polyurethane-33		Polyurethane-34		Polyurethane-35	
Total/range	NR	0.0018-2	27	0.04-7.5	9	0.36-3.2	18	0.84-7
<i>Duration of use</i>								
Leave-on	NR	0.0018-2	27	0.04-7.5	8	0.36-3.2	18	0.84-7
Rinse-off	NR	NR	NR	NR	1	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
<i>Exposure type</i>								
Eye area	NR	NR	2	0.5-1.8	8	3.2	17	2-7
Incidental ingestion	NR	NR	NR	NR	NR	2.9	NR	NR
Incidental Inhalation-sprays	NR	0.0018	NR	0.04	NR	0.36-0.75; 0.5 ^c	NR	NR
Incidental inhalation-powders	NR	NR	NR	NR	NR	NR	NR	0.84 ^d
Dermal contact	NR	NR	1	0.5-7.5	1	NR	4	0.84-2.9
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	0.0018-2	NR	0.04	NR	0.36-0.75	NR	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	25	0.3-7.5	NR	NR	1	NR
Mucous Membrane	NR	NR	NR	NR	NR	2.9	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR

Table 8. Frequency of use according to duration and exposure of polyurethanes.^{47,48}

Use type	Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)	
	Uses		Uses		Uses		Uses	
	Polyurethane-39		Polyurethane-40		Polyurethane-46			
Total/range	8	NR	9	NR	NR	0.2		
<i>Duration of use</i>								
Leave-on	5	NR	9	NR	NR	NR		
Rinse-off	3	NR	NR	NR	NR	0.2		
Diluted for (bath) use	NR	NR	NR	NR	NR	NR		
<i>Exposure type</i>								
Eye area	NR	NR	3	NR	NR	NR		
Incidental ingestion	NR	NR	NR	NR	NR	NR		
Incidental Inhalation-sprays	3 ^b	NR	2 ^b	NR	NR	NR		
Incidental inhalation-powders	NR	NR	1	NR	NR	NR		
Dermal contact	1	NR	9	NR	NR	NR		
Deodorant (underarm)	NR	NR	NR	NR	NR	NR		
Hair-noncoloring	7	NR	NR	NR	NR	0.2		
Hair-coloring	NR	NR	NR	NR	NR	NR		
Nail	NR	NR	NR	NR	NR	NR		
Mucous Membrane	NR	NR	NR	NR	NR	NR		
Baby	NR	NR	NR	NR	NR	NR		

NR = Not Reported; Totals = Rinse-off + Leave-on + Diluted for Bath Product Uses.

^a Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.^b It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.^c Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.^d It is possible these products may be powders, but it is not specified whether the reported uses are powders.**Table 9.** Polyurethanes that have no reported uses in the VCRP or from an industry survey.^{47,48}

Polyurethane-4	Polyurethane-5	Polyurethane-12
Polyurethane-13	Polyurethane-17	Polyurethane-19
Polyurethane-20	Polyurethane-21	Polyurethane-23
Polyurethane-25	Polyurethane-26	Polyurethane-27
Polyurethane-28	Polyurethane-29	Polyurethane-32
Polyurethane-36	Polyurethane-41	Polyurethane-42
Polyurethane-43	Polyurethane-44	Polyurethane-45
Polyurethane-47	Polyurethane-48	Polyurethane-49
Polyurethane-50	Polyurethane-51	Polyurethane-52
Polyurethane-53	Polyurethane-54	Polyurethane-55
Polyurethane-56	Polyurethane-57	Polyurethane-58
Polyurethane-59	Polyurethane-60	Polyurethane-61
Polyurethane-62	Polyurethane-63	Polyurethane-64
Polyurethane-65	Polyurethane-66	Polyurethane-67
Polyurethane-68	Polyurethane-69	Polyurethane-70
Polyurethane-71	Polyurethane-72	

Table 10. Precursors and monomers of the polyurethanes in this safety assessment that may be used in polyurethane resins that are used in adhesives that may come in contact with food in accordance with the FDA. [21CFR175.105]

1,4-Butanediol	1,4-Butanediol modified with adipic acid
1,4-Cyclohexanedimethanol [part of a polyester resin]	1,6-Hexanediol (CAS Reg. No. 629-11-8) [part of a polyester resin]
2-Hydroxypropyl methacrylate	4,4'-Isopropylidenediphenol
Dehydroacetic acid	Diethanolamine
Diethylene glycol adipic acid copolymer	Diethylene glycol copolymer of adipic acid and phthalic anhydride
Dipropylene glycol copolymer of adipic acid and phthalic anhydride	Ethylene glycol
Ethylenediamine	Ethylenediaminetetra-acetic acid, calcium, ferric, potassium, or sodium salts, single or mixed
Fats and oils derived from animal or vegetable sources, and the hydrogenated, sulfated, or sulfonated forms of such fats and oils	Hydroxyacetic acid
Isobutyl alcohol (isobutanol)	Isophthalic acid
Isopropanolamine (mono-, di-, tri-)	Monochloroacetic acid
Octylphenoxypolyethoxy-polypropoxyethanol (13 moles of ethylene oxide and propylene oxide)	Polybutylene glycol (molecular weight 1,000)
Polyester of adipic acid, phthalic acid, and propylene glycol, terminated with butyl alcohol	Polyethylene glycol (molecular weight 200-6,000)
Polyethyleneadipate modified with ethanolamine with the molar ratio of the amine to the adipic acid less than 0.1 to 1	Propylene Glycol and <i>p,p'</i> -isopropylidenediphenol diether
Tetramethyl decynediol plus 1-30 moles of ethylene oxide	Toluene
Tridecyl alcohol	Triethylene Glycol

Table 11. Genotoxicity studies of polyurethanes.

Ingredient	Concentration/dose	Method	Results	Reference
Polyurethane-1	0 and 64-16,000 µg/plate of 30% Polyurethane-1 in water and ethanol	Ames test, SPT and PIT. <i>Salmonella typhimurium</i> (TA98, TA100, TA1535, and TA1537) and <i>Escherichia coli</i> (WP2 uvrA).	Not mutagenic	³²
Polyurethane-21	100%; 35% solids	Ames test using <i>S. typhimurium</i> (strains TA97a, TA98, TA100, TA102, and TA1535)	Not a potential mutagen with and without metabolic activation	⁸⁷
Polyurethane-28	Not specified	OECD TG 471 (Bacterial Reverse Mutation Test)	Not mutagenic	³⁶
Polyurethane-35	Not specified	OECD TG 471 (Bacterial Reverse Mutation Test)	Not mutagenic	³⁸
Polyurethane-42	Not specified	OECD TG 471 (Bacterial Reverse Mutation Test) using <i>S. typhimurium</i> and <i>E. coli</i>	Not mutagenic	³⁶
Polyurethane-59	0, 312.5, 625, 1250, 2500, and 5000 µg/plate	Ames test, SPT and PIT, using <i>S. typhimurium</i> (TA98, TA100, TA1535, and TA1537) and <i>E. coli</i> (WP2 uvrA)	Not mutagenic	³³
Polyurethane-62	Up to 5000 µg/plate (tested without trideceth-6 solvent; not specified if tested in water or other neutral solvent)	Ames test using <i>S. typhimurium</i> (strains TA98, TA100, TA1535, and TA1537) and <i>E. coli</i> (WPluvrA)	No cytotoxicity or precipitation was observed with or without metabolic activation. There were no significant increases in the frequency of revertant colonies.	⁶⁹

PIT- pre-incubation test

SPT- standard plate test

Table 12. Human sensitization assays of polyurethanes.

Ingredient/test article	Concentration/Dose	Procedure	Results	Reference
Polyurethane-1	30% in a mascara	HRIPT (n=103)	Did not demonstrate a potential for eliciting dermal irritation or sensitization.	⁷⁵
Polyurethane-1	28.5% in a mascara	HRIPT (n=103)	Did not demonstrate a potential for eliciting dermal irritation or sensitization	⁷⁴
Polyurethane-14	9.61% solids in 54.9% ethanol. Control was 55% ethanol.	HRIPT (n=104). Semi-occlusion to upper arms of subjects 3 times per week for 3 weeks. Challenge was administered at same concentration. Test material was applied to the patch pad 15-30 min before application to the subjects.	Mild erythema was observed in both treatment and control groups in a few subjects at various evaluation periods during induction. No reaction was observed in any subject during challenge phase. Test material did not yield evidence of delayed contact hypersensitivity response in human subjects.	⁷⁶
Polyurethane-21	60% in corn oil; 21% solids; 0.2 mL/0.2 g	HRIPT (n=50). Applied under occlusion	No adverse reactions of any kind were observed during the course of the study. Considered a non-primary irritant and a non-primary sensitizer.	⁷⁷
Polyurethane-21	35% solids; 0.2 mL	HRIPT (n=100). Applied under occlusion	No adverse reactions of any kind were observed during the course of the study. Considered a non-primary irritant and a non-primary sensitizer.	⁷⁸

Table 13. In vitro ocular assays of polyurethanes.

Ingredient	Concentration	Method	Results	Reference
Polyurethane-1	30% in a mascara tested at 0, 5%, 15%, 25%, 35%, and 50%; effective concentrations: 0.015%, 0.045%, 0.075%, 0.105%, and 0.15% Polyurethane-1	NRR using rabbit cornea fibroblasts	NR ₅₀ > 50%; equivalent to a Draize score of 0-15 (slight irritant)	⁷⁹
Polyurethane-1	30% in a mascara	HET-CAM	Mean scores: Hyperhemia - 3.5; hemorrhage-5.0; coagulation-0; overall-8.5. Equivalent to a Draize score of 15.1-30 (moderate irritant)	⁷⁹
Polyurethane-1	30% in a mascara	REC	Cumulative SMCI-0.71. Slightly cytotoxic; equivalent to a Draize score of 0-15 (slight irritant)	⁷⁹
Polyurethane-1			Considering the 3 assays above (NRR, HET-CAM, and REC), the estimated Draize classification of the test material might be a slight irritant with an estimated Draize score of 0-15.	⁷⁹
Polyurethane-1	30% in a mascara tested at 50%; effective concentration-15%	HET-CAM	Mean cumulative score-1.25; predicted to be practically no irritation potential at 100%.	⁸²
Polyurethane-1	30% in a mascara	BCOP	Mean score-1.0; minimally irritating. Estimated Draize score approaching 0 (non-irritant).	⁸¹
Polyurethane-1	30% in a mascara; tested at 20%; effective concentration-6%	EpiOcular™	Viability at 20 min-105%; 1 h-102%; 4 h-92%. ET ₅₀ > 256 min. Estimated Draize score approaching 0 (non-irritant).	⁸⁰
Polyurethane-14	10%, tested at 20%, final concentration 2%	EpiOcular™	ET ₅₀ was > 256 min. Estimated Draize ocular irritation score of the test material at 100% was 0 and Polyurethane-14 can be predicted to be a non-irritant.	⁸³
Polyurethane-21	100% with 35% solids	HET-CAM	Mean cumulative score-0.50, predicted not to have ocular irritation potential	⁸⁵
Polyurethane-21	100% with 35% solids	BCOP	Average score of 1.7. Predicted to be a non-irritant and expected to elicit a Draize score approaching 0.	⁸⁴
Polyurethane-42	100% with 35% solids	HET-CAM	Moderate irritant	³⁶
Polyurethane-42	100% with 35% solids	BCOP	Non-irritant	³⁶
Polyurethane-62	Tested without trideceth-6 solvent; not specified if tested in water or other neutral solvent	EpiOcular™ assay using the reconstructed human cell epithelial (RhCE) model (conducted in accordance with OECD Draft Guideline titled Reconstructed Human Cornea-Like Epithelium (RhCE) Test Method for Identifying Chemicals Not Requiring Classification and Labelling for Eye Irritation or Serious Eye Damage)	Treated cells had 63% survival. Survival > 60% is considered negative for ocular irritation. The control had expected result.	⁶⁹

BCOP = bovine corneal opacity and permeability assay; ET₅₀ = The estimated time at which the percent viability would be 50%; HET-CAM = chorioallantoic membrane of the embryonic hen's egg assay; NR₅₀ = The amount of test substance that will cause a 50% decrease in neutral red uptake measured by optical density; NRR = Neutral red release assay; REC = Reconstituted human epithelial culture assay; SMCI = Simplified mean cytotoxicity index

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2017 VCRP Data for Polyurethanes

03B - Eyeliner	POLYURETHANE-1	1
03C - Eye Shadow	POLYURETHANE-1	1
03F - Mascara	POLYURETHANE-1	8
05B - Hair Spray (aerosol fixatives)	POLYURETHANE-1	4
05G - Tonics, Dressings, and Other Hair Grooming Aids	POLYURETHANE-1	2
05H - Wave Sets	POLYURETHANE-1	2
05I - Other Hair Preparations	POLYURETHANE-1	1
		19

03D - Eye Lotion	POLYURETHANE-2	1
03E - Eye Makeup Remover	POLYURETHANE-2	1
03F - Mascara	POLYURETHANE-2	6
07C - Foundations	POLYURETHANE-2	1
12C - Face and Neck (exc shave)	POLYURETHANE-2	3
12F - Moisturizing	POLYURETHANE-2	1
		13

05B - Hair Spray (aerosol fixatives)	POLYURETHANE-6	8
05H - Wave Sets	POLYURETHANE-6	3
05I - Other Hair Preparations	POLYURETHANE-6	5
		16

07B - Face Powders	POLYURETHANE-7	6
07C - Foundations	POLYURETHANE-7	7
07F - Makeup Bases	POLYURETHANE-7	1
		14

07C - Foundations	POLYURETHANE-8	1
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12J - Other Skin Care Preps	POLYURETHANE-9	1
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03B - Eyeliner	POLYURETHANE-11	29
03C - Eye Shadow	POLYURETHANE-11	160
03G - Other Eye Makeup Preparations	POLYURETHANE-11	6
04E - Other Fragrance Preparation	POLYURETHANE-11	2
07A - Blushers (all types)	POLYURETHANE-11	2
07B - Face Powders	POLYURETHANE-11	2
07E - Lipstick	POLYURETHANE-11	2
07I - Other Makeup Preparations	POLYURETHANE-11	12
08E - Nail Polish and Enamel	POLYURETHANE-11	77
08G - Other Manicuring Preparations	POLYURETHANE-11	1
10A - Bath Soaps and Detergents	POLYURETHANE-11	11
10E - Other Personal Cleanliness Products	POLYURETHANE-11	1
12D - Body and Hand (exc shave)	POLYURETHANE-11	2
12F - Moisturizing	POLYURETHANE-11	1
12J - Other Skin Care Preps	POLYURETHANE-11	7
		315

05B - Hair Spray (aerosol fixatives)	POLYURETHANE-14	10
05F - Shampoos (non-coloring)	POLYURETHANE-14	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	POLYURETHANE-14	15
05H - Wave Sets	POLYURETHANE-14	1
05I - Other Hair Preparations	POLYURETHANE-14	4
07I - Other Makeup Preparations	POLYURETHANE-14	2
		33

07A - Blushers (all types)	POLYURETHANE-15	1
07B - Face Powders	POLYURETHANE-15	1
		2

07C - Foundations	POLYURETHANE-16	1
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05B - Hair Spray (aerosol fixatives)	POLYURETHANE-18	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	POLYURETHANE-18	7
07H - Makeup Fixatives	POLYURETHANE-18	1
		11

03B - Eyeliner	POLYURETHANE-33	1
03F - Mascara	POLYURETHANE-33	1
08E - Nail Polish and Enamel	POLYURETHANE-33	24
08G - Other Manicuring Preparations	POLYURETHANE-33	1
		27

03F - Mascara	POLYURETHANE-34	8
12H - Paste Masks (mud packs)	POLYURETHANE-34	1
		9

03B - Eyeliner	POLYURETHANE-35	1
03F - Mascara	POLYURETHANE-35	13
03G - Other Eye Makeup Preparations	POLYURETHANE-35	3
08E - Nail Polish and Enamel	POLYURETHANE-35	1
		18

05A - Hair Conditioner	POLYURETHANE-39	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	POLYURETHANE-39	3
05I - Other Hair Preparations	POLYURETHANE-39	1
07I - Other Makeup Preparations	POLYURETHANE-39	1
		8

03D - Eye Lotion	POLYURETHANE-40	2
03G - Other Eye Makeup Preparations	POLYURETHANE-40	1
07A - Blushers (all types)	POLYURETHANE-40	1
07B - Face Powders	POLYURETHANE-40	1
12C - Face and Neck (exc shave)	POLYURETHANE-40	2
12F - Moisturizing	POLYURETHANE-40	1
12G - Night	POLYURETHANE-40	1
		9

03C - Eye Shadow	POLYURETHANE	1
03F - Mascara	POLYURETHANE	1
05B - Hair Spray (aerosol fixatives)	POLYURETHANE	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	POLYURETHANE	1
05I - Other Hair Preparations	POLYURETHANE	3
07E - Lipstick	POLYURETHANE	1
07I - Other Makeup Preparations	POLYURETHANE	1
08A - Basecoats and Undercoats	POLYURETHANE	1
08E - Nail Polish and Enamel	POLYURETHANE	1
08G - Other Manicuring Preparations	POLYURETHANE	1
12A - Cleansing	POLYURETHANE	1
12C - Face and Neck (exc shave)	POLYURETHANE	2
		17

There were no reported uses in the 2017 VCRP for:

Polyurethane-4	Polyurethane-52
Polyurethane-5	Polyurethane-53
Polyurethane-10	Polyurethane-54
Polyurethane-12	Polyurethane-55
Polyurethane-13	Polyurethane-56
Polyurethane-17	Polyurethane-57
Polyurethane-19	Polyurethane-58
Polyurethane-20	Polyurethane-59
Polyurethane-21	Polyurethane-60
Polyurethane-23	Polyurethane-61
Polyurethane-24	Polyurethane-62
Polyurethane-25	Polyurethane-63
Polyurethane-26	Polyurethane-64
Polyurethane-27	Polyurethane-65
Polyurethane-28	Polyurethane-66
Polyurethane-29	Polyurethane-67
Polyurethane-32	Polyurethane-68
Polyurethane-36	Polyurethane-69
Polyurethane-41	Polyurethane-70
Polyurethane-42	Polyurethane-71
Polyurethane-43	Polyurethane-72
Polyurethane-44	
Polyurethane-45	
Polyurethane-46	
Polyurethane-47	
Polyurethane-48	
Polyurethane-49	
Polyurethane-50	
Polyurethane-51	

Memorandum

TO: Dr. Bart Heldreth, Ph.D., Interim Director
COSMETIC INGREDIENT REVIEW (CIR)

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

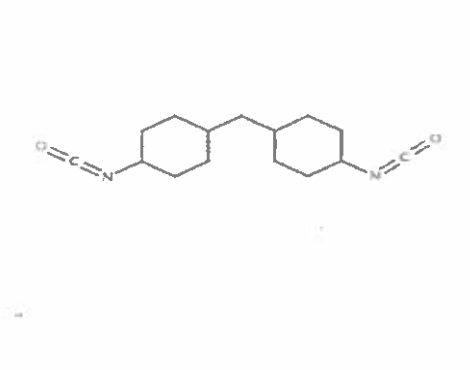
DATE: August 14, 2017

SUBJECT: Monomer Structures: Polyurethanes

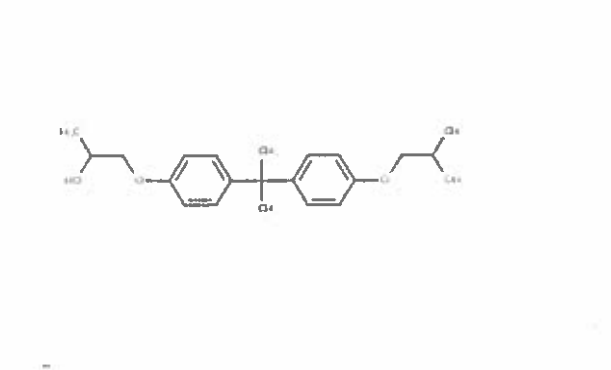
A supplier has indicated that dimethyl aminopropylamine (DMAPA) in Polyurethane-60 and -61 is not correct. This monomer should be dimethylolpropionic acid (CAS 4767-03-7).

The structures for the monomers, saturated methylene diphenyldiisocyanate (SMDI) (CAS 5124-30-1) and isopropylidenediphenoxypropanol (CAS 116-37-0; also called Bisphenol A bis-(2-hydroxypropyl)ether) are also incorrectly drawn for Polyurethane -60 and -61. The correct structures are shown below:

SMDI



isopropylidenediphenoxypropanol



The SMDI structures shown for Polyurethane-2 and -29 also need to be corrected (the double bond in the rings need to be deleted).

It was also noted that the Dictionary did not consistently use the same name, saturated methylene diphenyldiisocyanate (SMDI) (CAS 5124-30-1) in the definitions of Polyurethane ingredients. This has been corrected for Polyurethane-11, -33, -35. Corrected monographs are attached.

08/14/2017

Monographs Proof Report

- P -

POLYURETHANE-11

INCI Monograph ID: 16603

CAS No.: 68258-82-2

Definition: Polyurethane-11 is a copolymer of Adipic Acid (q.v.), 1,4-Butanediol (q.v.), Isophthalic Acid (q.v.), Saturated Methylene Diphenyl Diisocyanate (q.v.), Neopentyl Glycol (q.v.) and trimethylolpropane monomers.

See Sections 20 to 22 for the Japanese, Chinese, and Korean translations of this INCI Name.

Information Source: TSCA

Chemical Class: Synthetic Polymers

Reported Function: Film Former

Ingredient Source: Synthetic

Trade Name:

WSR Coating (Glitterex Corporation)

Trade Name Mixtures:

Daiya Hologram UC Type (Daiya Kogyo)

Daiya Hologram UC Type, Gold (Daiya Kogyo)

Diamond Piece CO-UC Type, Black (Daiya Kogyo)

Diamond Piece CO-UC Type, Blue (Daiya Kogyo)

Diamond Piece CO-UC Type, DG Gold (Daiya Kogyo)

Diamond Piece CO-UC Type, Green (Daiya Kogyo)

Diamond Piece CO-UC Type, LG Gold (Daiya Kogyo)

Diamond Piece CO-UC Type, Pink (Daiya Kogyo)

Diamond Piece CO-UC Type, Red (Daiya Kogyo)

Diamond Piece CO-UC Type, Violet (Daiya Kogyo)

Diamond Piece H/UC Type, Black (Daiya Kogyo)

Diamond Piece UC Type, Black (Daiya Kogyo)

Diamond Piece UC Type, DG Gold (Daiya Kogyo)

Diamond Piece UC Type, LG Gold (Daiya Kogyo)

Diamond Piece UC Type, Pink (Daiya Kogyo)

Diamond Piece UC Type, Red (Daiya Kogyo)

Diamond Piece UC Type, Silver (Daiya Kogyo)

Diamond Piece H-UC Type, Silver (Daiya Kogyo)

Illuminate (Daiya Kogyo)

Neon Color Orange (Daiya Kogyo)

Neon Color Pink (Daiya Kogyo)

Neon Color Yellow (Daiya Kogyo)

POLYURETHANE-33

INCI Monograph ID: 23560

Definition: Polyurethane-33 is a complex polymer formed by reacting dimethylolpropionic acid and a polyester composed of Adipic Acid (q.v.), Hexylene Glycol (q.v.), Neopentyl Glycol (q.v.) with Saturated Methylene Diphenyl Diisocyanate (q.v.) (SMDI) to form a prepolymer. The prepolymer is neutralized with triethylamine and then chain-extended with hydrazine.

See Sections 20 to 22 for the Japanese, Chinese, and Korean translations of this INCI Name.

Chemical Class: Synthetic Polymers

Reported Function: Binder

Ingredient Source: Synthetic

Trade Name Mixture:

Bondthane P-6250 (Bond Polymers)

POLYURETHANE-35

INCI Monograph ID: 22952

Definition: Polyurethane-35 is a complex urethane polymer that is made by reacting a polyester pre-polymer consisting of Adipic Acid (q.v.), Hexanediol (q.v.), and Neopentyl Glycol (q.v.) with Saturated Methylene Diphenyl Diisocyanate (q.v.). The resulting urethane polymer is further reacted with sodium N-(2-aminoethyl)-3-aminoethanesulfonate and ethylenediamine and then dispersed into water. See Sections 20 to 22 for the Japanese, Chinese, and Korean translations of this INCI Name.

Chemical Class: Synthetic Polymers

Reported Function: Binder

Ingredient Source: Synthetic

Trade Name:

Baycusan C 1004 (Bayer MaterialScience)

POLYURETHANE-60

INCI Monograph ID: 29196

Definition: Polyurethane-60 is the complex polymer made by first reacting Saturated Methylene Diphenyl Diisocyanate (q.v.) (SMDI), Dimethylolpropionic Acid (q.v.) (DMPA), Bisphenol A Bis-(2-Hydroxypropyl) Ether (q.v.), and dimethylcarbonate-1,6-hexanediol to form a prepolymer, followed by dispersion in water with dimethylethanolamine and subsequent chain extension with ethylenediamine.

Chemical Class: Synthetic Polymers

Reported Function: Nail Conditioning Agent

Ingredient Source: Synthetic

Trade Name:

Alberdingk U 6150 (Alberdingk Boley GmbH)

POLYURETHANE-61

INCI Monograph ID: 29198

Definition: Polyurethane-61 is the complex polymer made by first reacting Saturated Methylene Diphenyl Diisocyanate (q.v.) (SMDI), Dimethylolpropionic Acid (q.v.) (DMPA), Bisphenol A Bis-(2-Hydroxypropyl) Ether (q.v.), and the polyester polyol derived from isophthalic acid/1,6-hexanediol/adipic acid to form a prepolymer, followed by dispersion in water with triethylamine and subsequent chain extension with ethylenediamine.

Chemical Class: Synthetic Polymers

Reported Function: Nail Conditioning Agent

Ingredient Source: Synthetic

Trade Name:

Alberdingk U 5200 (Alberdingk Boley GmbH)



Memorandum

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

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

DATE: April 4, 2017

SUBJECT: Draft Report: Safety Assessment of Polyurethanes as Used In Cosmetics (draft prepared for the April 10-11, 2017 CIR Expert Panel Meeting)

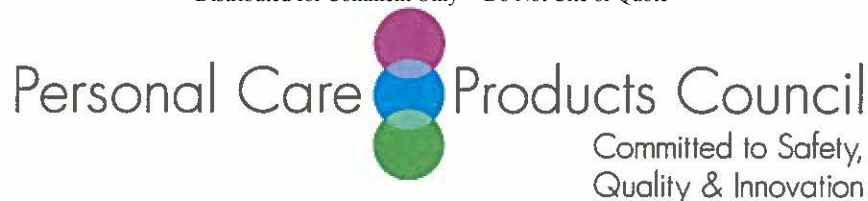
Introduction/Chemistry - In either the Introduction or Chemistry section, it would be helpful if the naming convention for these ingredients was described. Polyurethane-type ingredients with 4 or more monomers are named "Polyurethane-x". Polyurethane ingredients with 3 or fewer monomers are named based on the monomers.

Physical and Chemical Properties - So far there is no evidence that these polymers have molecular weights less than 1000 Daltons. Therefore, in the Physical and Chemical Properties section the following should be deleted: "and non-penetrating to readily penetrating the skin."

Impurities/Constituents - Based on information provided by suppliers, it appears that neutralizing agents are important residual constituents in these polymers. This should be stated in the Impurities/Constituents section.

Cosmetic Use - As the EU limitation is for trialkylamines, rather than stating that "Polyurethane-17 and -21 are restricted in Europe" it would be more accurate to state that trialkylamines (which may be residuals in Polyurethane-17 and -21) are restricted in Europe.

Non-Cosmetic Use - Reference 35 should be cited for the statement that Polyurethane-36 is exempt from TSCA. The CFR citation (40CFR723.250) is the polymer exemption, so it is likely that many of the polymers in this report are exempt from TSCA..



Memorandum

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

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

DATE: May 5, 2017

SUBJECT: Tentative Report: Safety Assessment of Polyurethanes as Used In Cosmetics

Non-Cosmetic - Please indicate that the supplier stated that Polyurethane-36, -60 and -61 are not in compliance for use in food contact adhesives.

Inflammatory Response - Rather than using the trade name Tween 80, please use Polysorbate 80.

Sensitization, *In Vitro* - When discussing the DPRA, it would be helpful to have the value for the positive control (78.04%) with the statement that "The control had the expected result."

Ocular Irritation Studies - Please correct "an ocular irritant in and neutral red release assay.."

Summary - In describing the molecular weights, it would be more accurate to state:

"Polyurethane ingredients for which molecular weights were reported were all greater than 1000 Da."

Please correct: "Polyruethane-60"

The concentration not associated with any adverse effects (10 mg/m³) in the inhalation study of Polyurethane-14 should also be stated in the summary.

Particle size of an ingredient as tested in an animal study does not equate to the particle size of a product. To be a relevant animal study, the particles must be respirable. The inhalation section of the summary should not say: "a substantial majority of the particles of these 'ingredients', as manufactured..." The majority of particles of spray products are larger than the respirable range.

Table 2 - The report on the Butyl Polyoxyalkylene Ethers (PPG-3 Butyl Ether and PPG-30 Butyl Ether) was finalized at the April 2017 meeting with a conclusion of safe when formulated to be non-irritating. This needs to be corrected in Table 2. It is not clear why toluene is included in this table for Polyurethane-9. A monomer in Polyurethane-9 is toluene diisocyanate. This does not mean that it contains toluene.

Table 3 - This table contains both "Ethylene diamine" and "Ethylenediamine". As these appear to be the same, one of these names should be deleted.

Table 5 - Please correct "Polyruethane-21" and "Polyruethane-28". It should be indicated that reference 33 concerning Polyurethane-21 was for a 35% emulsion in water (solvent-free). The viscosity for this emulsion was provided in reference 33 and should be added to Table 5 as viscosity values are included in this table for other emulsions.