Amended Safety Assessment of *p*-Hydroxyanisole as Used in Cosmetics

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The 2014 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

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MEMORANDOM

To: CIR Expert Panel and Liaisons

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

Date: November 14, 2014

Subject: *p*-Hydroxyanisole As Used In in Cosmetics

In September 2014, the Panel issued a Draft Final Amended Report of *p*-hydroxyanisole with the conclusion that it is safe for use in nail adhesives and in artificial nail coatings that are cured by LED light as a polymerization inhibitor; and unsafe for use in all other cosmetics because of the potential for dermal depigmentation. This conclusion supersedes the earlier conclusion issued by the Expert Panel in 1985, which stated that it was unsafe for use in all cosmetic products.

Comments from industry were addressed. No new data on this ingredient or UV nail lamps have been submitted by industry.

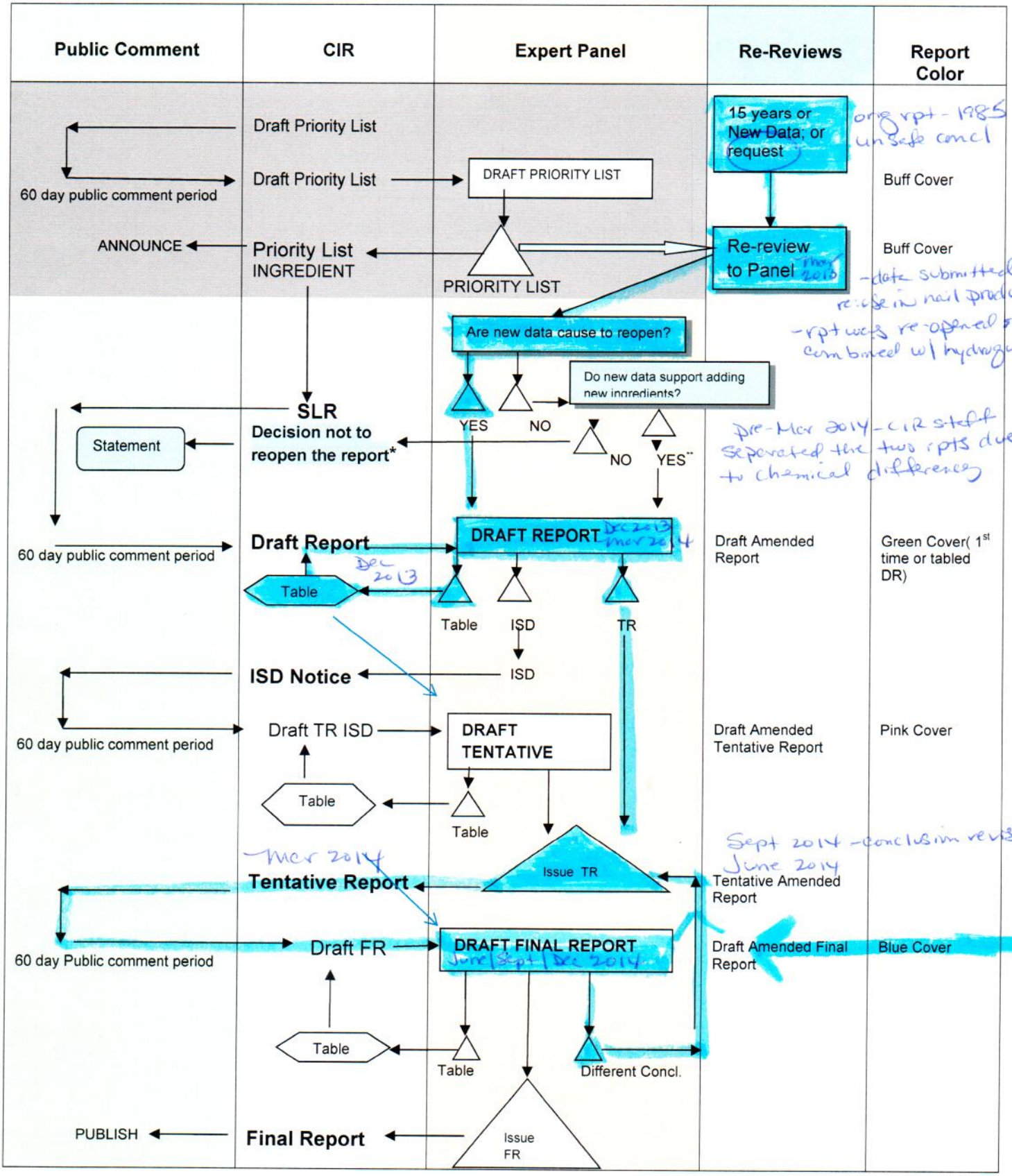
Since the discussion on hydroquinone and *p*-hydroxyanisole overlapped, especially with regards to UV exposure and application of nail gels, the transcripts of both ingredients from the September meeting are included in each Panel book.

The Panel is to review the Abstract, Discussion, and Conclusion to ensure that they reflect the Panel's thinking. A Final Amended Report is to be issued.

p-Hydroxyanisole

Dec 2014

SAFETY ASSESSMENT FLOW CHART



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

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

History of Hydroquonine and p-Hydroxyanisole

1985 – Safety assessment of p-Hydroxyanisole published with an unsafe for use as a cosmetic ingredient." This conclusion was based primarily on depigmentation of black guinea pig skin in studies in which concentrations as low as 0.25% or less (0.1% in some animals) were applied to the skin daily for 1 or more months (which were close to use concentrations up to 0.1% to 1.0% at the time of the FDA survey in 1981).

1986 - A safety assessment of hydroquinone and pyrocatechol was published with the conclusion that these two ingredients were safe for use in cosmetics at concentrations up to 1.0% in formulations designed for discontinuous, brief use followed by rinsing from the skin and hair.

1994 - An amended safety assessment of hydroquinone alone was published with the conclusion that hydroquinone was safe at concentrations of 1.0% or less for aqueous cosmetic formulations designed for discontinuous, brief use followed by rinsing from the skin and hair. Hydroquinone was not safe for use in leave-on, non-drug cosmetic products.

2010 – Safety assessment of hydroquinone published with a safe at concentrations ≤1% in hair dyes" and "safe for use in nail adhesives in the practices of use and concentration described in this safety assessment," although it "should not be used in other leave-on cosmetics." The Panel noted that, while absorption through the skin could be appreciable in leave-on products, hydroquinone in nail adhesives "is oxidized during use and is no longer present in the preparation and minimal dermal exposure and absorption is expected to occur from this application." The use concentration was reported to be 0.5% in nail adhesives at the time of the survey (2008). The Panel's discussion does not explicitly include a warning to avoid skin contact or specify that nail adhesives containing this ingredient should be for professional use only. The cosmetic use section of the CIR safety assessment noted that the EU banned the use of this ingredient in hair dyes in 2008 and approved its use in professional-use-only artificial nail systems up to a maximum of 0.02% after mixing with methacrylate monomers (hydroquinone at 0.02% in methacrylate monomer preparations was undetectable in the finished product).

March, 2013 - Data were submitted to the Panel with the request to reopen these two safety assessments with the purpose of changing the conclusion with regard to hydroquinone and *p*-hydroxyanisole's use in nail products using UV for polymerization and drying.

December, 2013 – The Panel tabled the report without a conclusion to have further information collected on UV nail lamps.

March, 2014 – The CIR staff split the report for these two ingredients due to their chemical differences. The Panel is to examine each report separately and come to independent conclusions.

New data on UV lamps and photo effects have been added.

The Panel examined the newly presented data and concluded that *p*-hydroxyanisole is safe for use in artificial nail coatings in the present practices of use and concentration described in this safety assessment. *p*-Hydroxyanisole is unsafe for use in all other cosmetics due to dermal depigmentation and irritation and sensitization potential

June, 2014 – At Industry's request, the Panel re-examined the Dowdy Sayre paper. The Panel became more concerned about the safety of the home use of UV nail lamps.

The Panel changed the conclusion to: hydroxyanisole is safe for use in artificial nail coatings in the present practices of use and concentration described in this safety assessment when photo-protective materials for the skin (e.g., gloves, sunscreen) are used in a professional setting; these

products are unsafe for the new in-home use. *p*-Hydroxyanisole is unsafe for use in all other cosmetics due to dermal depigmentation potential.

September, 2014 – David Steinberg presented new information on light bulbs and LED lights. The Panel was comfortable with the idea that all new nail gel-curing lights will contain LED lights and these are not harmful to the skin or eyes. The Panel rethought their approach to the conclusion.

The Panel changed the conclusion to: safe for use in nail adhesives and in artificial nail coatings that are cured by LED light as a polymerization inhibitor; and unsafe for use in all other cosmetics due to dermal depigmentation potential. This conclusion supersedes the earlier conclusion issued by the Expert Panel in 1985, which stated that it was unsafe for use in all cosmetic products.

December, 2014 - The Panel examines the Draft Final Amended Report.

Search Strategy – Hydroquinone & *p*-Hydroxyanisole

SciFinder – Searched by CAS No. Refined by date, publication type, and toxicity terms. 10 papers ordered.

ECHA – Data for hydroquinone.

Web Search – by CAS Nos. and ingredient names. Located FDA drug application documents; SCCNFP opinion; and NAILS Magazine.

UV Lamps

SciFinder – "UV nail lamp" – 4 hits.

Web Search – found www.hooked-on-nails.com and incorporated useful information.

Depigmentation in Manicurists

March 20, 2014 7:23 PM

Explore references by research topic: depigmentation in manicurists initiated, resulting in 2 candidates

March 20, 2014 7:24 PM

Explore references by research topic: nail polish depigmentation initiated, resulting in 1 candidate

March 20, 2014 7:25 PM

Explore references by research topic: nail gel depigmentation initiated, resulting in 2 candidates

Explore complete
Candidates Selected
    14 references were found containing all of the concepts "nail", "gel" and "depigmentation".
Explore results
    Answer set 1 created with 14 answers from CAPLUS
March 20, 2014 7:31 PM

Explore references by research topic: manicure depigmentation initiated, resulting in 1 candidate

March 20, 2014 7:41 PM

Explore references by research topic: manicure hazard initiated, resulting in 1 candidate

Explore complete
Candidates Selected
4 references were found containing the concept "manicure hazard".
Explore results
Answer set 2 created with
3 answers from CAPLUS
1 answer from MEDLINE

GOOGLE

"hydroquinone" – No hits. All possible hits were skin lighteners/brighteners

"hydroquinone cosmetics" – No hits. All possible hits were skin lighteners/brighteners

"hydroquinone cream" – No hits. All possible hits were skin lighteners/brighteners

GOOGLE

"UV nail lamp" – UV nail lamps available on Amazon, Salon Supply Store, Walmart, Sally Beauty, eBay, etc.
EXAMPLES:
http://www.amazon.com/Thermal-Spa-49135-Professional-Light/dp/B001RMP7M6
http://www.ebay.com/itm/310729068451
http://www.salonsupplystore.com/watt-nail-lamps-c-2717_2718_2959_2771.html?CAPCID=24941836456&cadevice=c&gclid=CMu2tfPK3r8CFQQQ7AodigwAOg&CA_6C15C=330011670000004245
http://www.walmart.com/c/kp/uv-lamp-for-nails
http://www.ebay.com/sch/Nail-Dryers-UV-LED-Lamps-/67653/i.html
http://www.premiernailsource.com/index.php?main_page=index&cPath=87
http://sale-fire.com/Uv%20Nail%20Lamp?p=gcp&gclid=CKShprPS3r8CFSdp7Aod8nAAUw

"Professional UV nail lamp" – UV nail lamps available from Amazon. More product line dedicated sources of lamps.
EXAMPLES:
http://www.tmart.com/UV-Curing-Lamp-Nail-Dryer/?cc=usd&gclid=CNjstpvM3r8CFQMT7AodilgA1w
http://www.sallybeauty.com/uv-lamp/SBS-156500,default,pd.html
http://www.nailiteinc.com/index.php?main_page=index&cPath=420

Of interest: Includes product descriptions of professional lamps that can be set for up to 15 or constant on.

"UV bulbs" – UV bulbs from Walmart, 1000bulbs,
Germicidal UV bulbs were available from 1000bulbs, Walmart, Home Depot, Top Bulb.
EXAMPLES:
http://www.walmart.com/c/ep/uv-bulbs
https://www.1000bulbs.com/category/ultraviolet-germicidal/
http://www.homedepot.com/b/Electrical-Light-Bulbs-Specialty-Light-Bulbs-Germicidal-UV-Light-Bulbs/N-5yc1vZc5sv
http://www.atlantalightbulbs.com/germicidal.asp

"UV nail lamp replacement bulbs"- Amazon and multiple product line dedicated sources.
EXAMPLES:
http://www.amazon.com/Light-Replacement-Extra-Dryer-Machine/dp/B005IHEC40
http://www.sallybeauty.com/uv-bulb/SBS-128450,default,pd.html
https://www.nailsuperstore.com/nail-supply/uv-gel-nail-lights
http://www.salonsupplystore.com/lamps-dryers-c-2717_2718.html

Minutes for Hydroquinone and *p*-Hydroxyanisole
September, 2014

Dr. Belsito's Team

DR. BELSITO: Anything else? Okay. So, we're going to hydroquinone. And, again, we got this mass of data in wave two. Basically, to sum up the data, I guess would be that we're now being told that these nail gels are not cured with UV lamps but with LED lamps that emit in a wavelength that is in the biswell [visible?] wavelength, and, therefore, one that we should not be concerned about, and that sunscreens will not help.

I think the CIR went online and did a nice little survey. I also went to one that was in the report of the two women with squamous cell carcinoma; that was Alibaba.com. And you can easily buy much cheaper UV lamps to cure these gels that take longer. They're cheaper.

When you do the cost analysis, they're probably not cost beneficial, but I really don't understand, since, presumably, the LED lamps last forever, and the product won't, why someone can't just buy the product, and then buy one of these cheaper lamps and use it. So, my concerns about the lamps remain the same, despite all the arguments that were put forth in wave two.

And, basically, that's all I have to say, and we'll open up to my team.

DR. LIEBLER: Well, if the -- so the memo that we got from David basically makes the case that the devices that are being sold and used for this purpose -- for products that contain hydroquinone or the anisole -- are LED-based and not UV-based, and that sources aren't changeable.

You know, if that were better documented, I'd be better comfortable with this, because I share your concern, Don, in our last discussions about the lamps and possibly --

DR. BELSITO: This is just Alibaba, Dan. You can buy LED lamps, and you can buy UV lamps.

DR. LIEBLER: Right.

DR. BELSITO: And the UVA lamps will work.

DR. LIEBLER: Mm-hmm.

DR. BELSITO: They just won't work as quickly. David?

MR. STEINBERG: Can I show something to everyone?

DR. BELSITO: Sure. There are multiple other sites where you can buy these lamps.

DR. SNYDER: (inaudible)

DR. BELSITO: No, leave it off (inaudible) I'm not quite sure what that means, but --

MR. STEINBERG: I had to do a lot of studying on light. I haven't taken a course in physics since 1962, and I really don't remember anything about (inaudible) light and everything else. So, I did a lot of self-education to find out.

This is the incandescent light bulb. This is what Edison invented, okay? I have a small one, because I'm limited by space. This gives off light all over. That's why they invented lampshades -- to direct the light. The radiation that's given off is all over the map, okay? They work when you turn your electricity on -- immediately, okay? They are very inefficient. They burn out fairly quickly, and we're constantly replacing them. These are dinosaurs. This size might stay in production, but the normal light bulb that you see in the lamp is disappearing.

This is what's replacing them. This is a fluorescent light bulb. Fluorescent light bulbs were invented back during World War II, because they're so much more energy-efficient -- around 10 times more energy-efficient than the standard light bulb. We can give -- have these give out energy in just about any wavelength you want.

The original fluorescent bulbs were these long tubes. Remember seeing them in our overheads? They are the exact same bulbs with energy or radiation restricted to 320 to 340 that are used in tanning salons. They put six, eight beds of lamps. You lie down, and you get exposed to tremendous amounts of damaging radiation. It's a different story.

They were not used, except for the overhead-type and some industrial applications, because we couldn't put them into a lamp. We couldn't put them right over here. It was the discovery that, if we bent the tube like this, we could get the distance far enough to create the light. You turn one of these on (inaudible) because I have four of them in my bathroom -- it takes about five minutes before you get the full intensity of light. It takes a long time. These are much more energy-efficient. They last much longer.

What replaced them is LED -- light-emitting diodes. And I can show you that LED light -- and when it was discovered, basically, it's always above 400. It is not below that. The problems that exist with this are many. We can't make a bowl [bulb?] like this.

This is an example of a flashlight that I bought. This is an LED bulb. This will last -- there are three bulbs, if you look at it. This will last -- oh, I don't know -- 10,000 years if I turn it on once or twice a day. It lasts forever. In fact, you cannot replace the bulb. I can take this apart. If you take the battery pack out, there's no way to get to the bulb. The bulb cannot be removed.

What are the instructions when you use an LED? If your bulb burns out -- which it takes forever to do -- you throw it out; you buy a new one.

This is the most popular nail lamp sold to consumers. If you look very carefully, you can see that it has about -- one, two, three, four, five, six -- six more bulbs. You cannot get the bulbs out. It is impossible. Oh, it's not impossible; you can take a sledgehammer, and smash it to bits, and get the bulbs out.

The way the bulbs are put in for LED is, they are soldered. This is (inaudible) bulb looks like. They have to be attached so they're not removable.

So, the consumer kit -- which is this -- will last forever. If you use it, you know, 100 times a day, it's still going to last 500 years. It's just not going to be something that you're going to replace the bulbs.

Now fluorescent bulbs were used in nail salons. Don is absolutely right. Why

were they used in nail salons? Nail salons classically start out for people -- women who want to get their nails professionally done using lacquers. Lacquers have nothing to do with MEHQ or HQ. They dry by evaporation of volatile solid.

What's the biggest time-consuming thing in a nail salon? The woman picking out what color polish she wants. The second biggest thing is waiting for the polish to dry. And they discovered that -- guess what accelerates the drying? Heat -- so they bought a lamp with a fluorescent bulb, and you could stick all ten fingers in it once. And you dried so much faster, you had more clients, et cetera, et cetera.

They, as Don says, may work to cure the gels. It depends on what the bulb is. If you have a 320 to 340 bulb, that will not cure the gel. Gels are cured at about 405 nanometers. They have to be in visible range.

Can you buy the lamps that these salons have? Yes, you can go online; you can buy them. You can go online and buy illegal drugs. You cannot buy lamps with the UV type of fluorescent bulb at the major retail outlets where people go to buy these. I went to both the high-end and the low-end stores. I went to Sally's Beauty Supply; they only have these lamps. I went to Sephora, which is the high-end part of the market; they only have these lamps.

You will notice that you can't stick your whole hand in; you can only stick your first four fingers. There is a separate lamp which is just for the thumb. You have to do each one separately. There isn't a huge one that you can stick all 10 fingers in, and expose yourself to more light. You just can't do it.

So, basically, where we're going to -- and where we're coming from -- is, these bulbs can't be replaced. There is a blog -- now I'm not a fan of blogs; you can say anything you want in a blog. But there is an interesting one which I included in my comments. When you buy a kit -- the first time a consumer buys a gel kit -- you can't buy the gel until you have a lamp. And the blog said, your best results with your gel is to buy the lamp that comes with the gel in your first kit.

And that's what people do. They don't go out and spend $50 for a lamp and a kit, and then say, "Gee, I can go online. I can get another lamp for $30 or $20 which might be cheaper." They already have this. You don't buy the gel the first time without this, because it doesn't work. You can apply the gel from here to eternity; it will never dry until you expose it to the visible light for a period of time.

So, the idea that consumers are going to replace the bulbs is not possible, and the idea that consumers are going to specifically go online to buy a cheaper lamp doesn't make any sense, because they're not going -- you know, yes, you can go into CVS and buy gels. But they're basically specific for a lamp, and that's exactly what they have said all along. You get the lamp, and you use the gels with it. That's it. You don't go and say, "I'm going to buy company A's gel, and use someone else's lamp," because you just don't get the same results.

Is it possible? It's possible. Anything's possible. But it's just not recommended -- and the stupid blogs say that. So, the idea that people are going to go out

and buy a cheaper lamp doesn't make any sense. It doesn't make sense, because they don't even know if it will work on the gel polish that you're buying.

Now the one thing which I did check -- I have contacts, and I deal with the big-box stores on some totally different areas. Big-box stores -- there's one in Bangor -- and so I think you know where it is -- or who it is -- and there's one in Minneapolis, and there are three major drug chains. And I talked to the people who are very high up in the executive ladder at these companies, and I asked them the question that Don asked: Do they stock fluorescent lamps for nails? Answer is, no, we haven't had them for two or three years. Everyone went over to LEDs. They're now cheaper, they're more efficient, and that's what people buy.

Can you get it at distressed stores? Absolutely. I have a major project going on with sunscreens right now. I bought on Amazon 15-year-old sunscreens. Would I use it for sun protection? You've got to be kidding. For my work, I had to use it. So, online, just because it's available doesn't mean consumers are going to buy it.

I'll be glad to document any of these things. If you don't have -- if you want me to make copies of what the lamps look like -- the bulbs -- this is what an LED bulb looks like. You notice they have to be soldered. If they are not soldered in correctly, you don't get the radiation. They just don't work.

I'll be glad to answer any questions.

DR. BELSITO: David, I fully understand LED technology. We use it in dermatology. You're absolutely right. It's -- you can't remove the bulbs. You're absolutely right. It's not in the UV range.

However, in the little pamphlet (inaudible) that you sent us, it clearly states that UV is more affordable. When you go online, and you check out the prices, UV lamps are cheaper than the LED lamps. And under the pros and cons, they say for UV, costs more affordable; typical curing time two minutes. And for LED, generally more expensive; curing time 30 seconds.

So, again, I beg to disagree, but these UV lamps are still widely available. You can buy them on Amazon.com. You can buy them on Alibaba.com, and you can buy a kit at Walgreens, and have this lamp accessible. So, I don't -- you know, I don't disagree with what you're saying about the LED, but I think that my concerns about use of the UV lamps remain. That's all I'm saying. That's why I turned it over to the Panel.

MR. STEINBERG: Just one quick question, because Walgreens is one of the companies that I deal with, okay, and the kits they sell do not have UV lamps. They have LEDs. They haven't had the UV lamps now for two to three years. Can you buy it online? Yes, they're distressed stores. You can go to Dollar General and probably buy a UV lamp. Can you buy the kits? Most of the time, no. They're not -- you know, they're just not commercially available. The people making the gels are only selling the LED lamps.

So, if a consumer wants to go and take -- and buy a kit -- or just buy gels, and then go online and find some UV lamp, and hope that it works -- doesn't make sense to save

$5 now. The price of the LED lights have dropped. These lamps have dropped significantly in price.

I don't think it makes sense. Just because you can do it online -- it doesn't work, so why do it?

DR. BELSITO: Well, it works. It works more slowly.

MR. STEINBERG: Well, okay.

DR. LIEBLER: You know, when I read your --

DR. BELSITO: I -- you know, I'm not -- I've already formed my opinion; that's why I want to hear from my Panel members -- because I have to represent them tomorrow.

DR. LIEBLER: So, I read your memo, David. I thought that it would be great if we could get some, you know, more -- so your memo made a case for LED lamps. And if, indeed, LED lamps were all that were available -- or most of what's available -- to consumers, then I think you would have a very strong case.

But your memo was, you know -- we've gotten to know you, and we certainly respected your input over the years to this Panel; it's been very valuable to us. So, that was the approach I took when I read your memo.

And, as I mentioned to you earlier, you know, if there was some sort of survey of the availability of the different types of devices that use either UV versus LED technology, and if it was overwhelmingly LED, then perhaps I'd be a little more swayed. But, you know, the obvious thing is to just Google it, and, you know, Don just passed me the Alibaba thing, but I just Googled while you were talking UV -- I was listening to you, by the way -- but a UV nail lamp and LED nail lamp.

And when you Google LED nail lamp, you get some LED devices, and you also get UV devices. When you Google UV, you get a mixture of them. There were plenty of UV devices available, and it's not just, you know, distressedstore.com. I mean, it's -- they're widely available, they're easy to order, and the prices are cheap, and they "work" for the purpose -- as far as a consumer is concerned.

I think, you know, if we were to push the fast- forward button, you know, five years, perhaps, from now, and it's all LED lamps/devices that are available, then I think I would come down on a different side. But I think Don's basically, you know, under the conditions of use that are likely to be anticipated by consumers using these products, you're going to be having lots of people using UV devices. And it's not even an issue of changing bulbs.

MR. STEINBERG: Yeah. I mean, everyone agrees that you can't change the bulbs. The issue is, you're saying that people will go and buy a kit with a lamp which is an LED lamp, and then deliberately not use the lamp -- which will last forever -- to buy a cheaper lamp -- or the other reverse --

DR. LIEBLER: They buy the cheaper kit.

MR. STEINBERG: The cheaper kits are obsolete. No one's making them (inaudible) manufacturer -- could you tell me how many of those kits -- the people in back of you work for the largest supplier of the gels and the kits. Now ask them.

DR. LIEBLER: Just look at this, and scroll through the -- all you have to do is Google it, and scroll through the options.

MR. STEINBERG: Now I can Google and purchase right now online four-percent hydroquinone skin-bleaching creams, which are totally illegal in the United States, from major retail outlets. It doesn't make it right. It doesn't make it kosher. It's just something that you can do online now, where you can have this -- and we do this constantly.

I see it all the time. When I was given the sunscreen projects, and I was given the list of 50 different sunscreens to find -- of which at least 40 of them had not been on the marketplace for three years -- I was able to find, like, 90 percent of them online, from five, ten different sources. They're all terribly old. I would never think of touching them with my skin or using them. You can find them on the internet. That doesn't mean people are going to go out and deliberately change something like that. It isn't happening.

DR. LIEBLER: It's not an issue of changing anything. It's the kit you buy if you want to start doing this. It's right there.

DR. BELSITO: You don't even need to buy -- I mean, obviously, David, you will have to buy replacement gels. Is that correct?

MR. STEINBERG: Absolutely.

DR. BELSITO: And the replacement -- excuse me, David; I'm talking, okay?

MR. STEINBERG: I'm sorry.

DR. BELSITO: And the replacement gels will always come with an LED? No, because the LED lasts forever.

MR. STEINBERG: Right.

DR. BELSITO: So, I understand you probably can go online and buy cocaine. But I'm not going to legalize cocaine because you can do it online. If you can go to Walgreens and buy the replacement gels, and go to Amazon.com and buy a UV lamp, and you can get the same result in two minutes as you can in 30 seconds with an LED lamp, then I don't think allowing these gels on the marketplace is safe. That's all I'm saying.

MR. STEINBERG: Do you want to show them what size the gels are? I just gave him a bottle of gel that we had bought. This is how big the gels are, just so you can see.

DR. KLAASEN: Yeah, this is a bottle of gel that's available on the market right now.

MR. STEINBERG: This is a European --

DR. BELSITO: Mm-hmm.

DR. SNYDER: I think we're in a real conundrum here, because I really think that -- what is it, the FDA -- we don't have an FDA person? So, what does the FDA think about this issue before us?

DR. RUA: Are you talking about lamps -- or what is the question?

DR. SNYDER: About the -- I guess it really comes down to the intended use, because -- with it being -- the caveat that it can be used safely, if it's used with a specific bulb (inaudible) and it's not safe for use if it's used with an appropriate UV bulb -- or I guess even

that's --

MR. STEINBERG: It depends on the UV bulb (inaudible).

DR. ANSELL: Well, the FDA has a position on tanning beds, which is far less severe -- they're unsafe. But I think the -- what we're trying to -- well, what I think we would like to avoid is the whole discussion about UV lighting, because, you know, there's many devices which use UV light. The FDA themselves have had expert advisory committees talking about the use of UV lights, some lamps -- tanning beds with an exposure well in excess of anything which might be here.

I guess our concern is that we're not talking about UV light in the conclusion; we're talking about hydroquinone. And perhaps if we were to go back to where we were at the last meeting, which is, this is a legitimate concern that we discuss in the discussion. And to the extent it has to be brought into the conclusion, let's focus on UV lights, and not whether hydroquinone itself is unsafe. And that might --

DR. BELSITO: We didn't say that hydroquinone itself, Jay, was unsafe. We said that under the intended conditions of use, we were concerned about the use of these gels that require curing in a home setting. We said that they were fine for professional use. But I think that we had a very long discussion at not only the last meeting but the meeting before that, when we discussed this.

We heard from Rachel that, you know, inserts on packages, including very bold, you know, labeling of cigarettes have very little effect on consumer behavior, and that the best way to create a safe product for consumers is to create a product that, under no circumstances, can be misapplied.

I think that the issue here is that, yes, I have no concerns about consumers using LED. But the availability of this product out in the marketplace that could also be used with a UV lamp by the consumer, I do have concerns about. And the LED lamps are not the only lamps that can be used. The product is sold in and of itself in small bottles that will be consumed in less than a year, and I don't see how we have done anything to prevent the consumer from going into Walgreens, and buying the replacement kit, and using a UV lamp to cure it in two minutes, rather than 30 seconds.

So, all of the concerns that I voiced before have not been mitigated by what I'm hearing about UV lamps. That's all I'm saying.

DR. SNYDER: Can we find a middle ground, like we did with melena, where we said (inaudible) --

DR. BELSITO: We did. That's what we have here.

DR. SNYDER: Okay.

DR. BELSITO: We've said that it's safe for use in salons.

DR. SNYDER: Okay.

DR. BELSITO: And we can even go further and say, you know, safe for use in salons with LED, and safe for use in salons with UV-cured lamps if you use gloves or sunscreens. I mean, I'm fine with that. I'm just not fine releasing these nail gels out in the

consuming public.

MR. STEINBERG: Would you say that they're safe for use by the consumer when used with LED lamps? Just make it that simple.

DR. BELSITO: I would like to hear from Rachel on that, because I think Rachel will tell us that the consumer will totally ignore that.

MR. STEINBERG: I mean, you're saying that they're safe -- that the LED lamps are safe.

DR. BELSITO: I have no problems with LED lamps, Jay; I understand them very well.

DR. LIEBLER: So, I was going to suggest a possible compromise in which the conclusion is changed to read: "Hydroquinone is unsafe for in-home nail products in which curing is achieved with UVA light."

And in the discussion, the second-to-last paragraph of the discussion, we say, "The Panel stated that (inaudible) should manufacture lamps in which bulbs cannot be replaced, so that the lamps will be disposed of when bulbs no longer function, or develop unique sockets that ensure only use of appropriate narrow-band UVA. Recently marketed lamps that use LED lights would satisfy this requirement."

So, you know, it's true that Rachel's got a good point that people don't read the fine print on safety issues. However, if we say very clearly that anything with UV in it shouldn't be used with these products, any product that you can buy that says UV in it shouldn't be used in these products, but LED is okay, then that might be clear enough and interpretable enough to the consumer.

And our, you know, amended conclusion could simply say unsafe for in-home nail products in which curing is achieved with UVA light, or UVA lamps, or UV lamps -- because it deals with the issue that I think Don has very legitimate concern about. It makes clear to the consumer that there is an option, and the option should be pretty clear to anybody who can scroll through it and read two versus three letters.

So, that's a suggestion as a possible compromise here, because I think we're -- you know, this is -- I don't buy the argument that it's not our purview to regulate lamps. I got that, but under the conditions of use, the ingredients -- we have to -- we can't ignore the conditions of use. We dealt with the same thing with Brazilian Blowout. So, I think, you know, we can't ignore that.

DR. SNYDER: I think -- I mean, I've been going through this ever since I read the report, trying to figure out an iteration of how to do it, because we've always used this catch-all -- concentrates in use as a catch-all. But this really is, more specifically, an intended use; it's intended that they be used with a specific light source, and not with, you know, (inaudible).

But, again, it's a slippery slope, because, then, all of a sudden, we're back into the, you know, UV issue versus LED. And so I'm conflicted, because I think it can be used safely with the appropriate, intended light source. But then the potential does exist that we

have to be concerned about for the misuse of light sources that are not intended to be used -- or that shouldn't be used.

DR. ANSELL: You know, I --

MS. TORDO: Can I make a comment?

DR. BELSITO: Sure. Identify yourself, please.

MS. TORDO: I'm Lynn Tordo. I'm from Thor, but I'm speaking not from Thor; I'm speaking as a citizen. I totally understand the unsafe, because I can see where a consumer would buy just that little bottle, and then go to Dollar General or Ocean State Job Lot, and buy a UV lamp. But I also understand if you buy the kit, you wouldn't turn around and buy something that was not the proper light source.

And I guess the question is, just thinking outside the box, is there a way to say that it's safe in a consumer product if it's only put in a kit and not in the little ones that are sold? Do you know what I'm saying?

DR. BELSITO: I understand that, but then the consumer, every time they need to replace that little bottle, would have to buy the lamp, and they're not going to do that.

MS. TORDO: No, but what I'm saying is that that would be the only time that it would be put in the consumer product; otherwise, they'd have to use a different ingredient. I'm just thinking outside of the box.

MR. STEINBERG: I think some of these compromises, you know, seem quite reasonable. But to be precise, our objection is not that you guys specifically shouldn't be looking at noncosmetic applications; it's that these are very regulated, and no one's actually decided that the lamps exceed any of the regulatory standards, that they do not conform with household standards, that they are outside of what the advisory groups have found acceptable. I mean, we're just going with the assumption that this lamp can be abused and found not safe, and I'm not sure that's been demonstrated, either.

But I think you have raised a concern. It's in the discussion, and I think, Ron, your suggested compromise precises it nicely -- that it's the lamp that we're --

MS. TORDO: Dan.

DR. BELSITO: Dan.

MR. STEINBERG: I'm sorry.

DR. LIEBLER: That's okay, Jim (inaudible).

MR. STEINBERG: That's right; it was a statistical shot.

DR. SNYDER: Okay. So, what --

DR. GILL: No, I was just going to say, I really would not want us to get into consumer product packaging. That is certainly an FDA jurisdiction. It is well-known that even in a regulatory setting, FDA can put out the recommendations for safety, but they can't force the consumer to abide by them. They make their decision on safety, and they say, "This is how it is to be used," and then buyer beware -- and consumer -- you know, if they operate outside the safety requirements or the safety recommendations by FDA, then it's on the consumer.

So, I would not want to get into the only packaged as a kit -- it had to have that label. It's not our jurisdiction.

MR. STEINBERG: One of the problems with packaging is, you know, (inaudible) is, I think there are, what, 200 different shades of nail polish already available, and women change their nail polish to whatever clothes they want to wear or things -- I know my wife does.

But the whole -- I think it's ideal, you know, just to say that these can be used safely by consumers if they use non-UV light, or if they use (inaudible) -- whatever way you want to wordsmith it -- because that's what industry is going to.

The fact that there are people still offering products on the marketplace and the internet doesn't change what industry has done -- that the people who are in industry are selling LED lamps, period. The products are formulated to be cured using radiation in the max of 405 in the visible range.

Yes, they'll cure with a fluorescent light -- not one with 320 to 340; it'll take, you know, four days to cure. But, basically, you can't stop the consumer from buying things on the internet. It's not going to happen. But we can say that it's safe if you use it under LED or non-UV light. I think that makes sense.

DR. SNYDER: So, I think your conclusion still stands, with the caveat of adding at the end of the second sentence -- or the first sentence -- adding LED lamp issue -- because we just have the UV light; we don't have LED in there. Right? Professional settings for LED lamp (inaudible) unsafe for in-home use with nail products requiring curing by UVA light and unsafe for other (inaudible) cosmetic products. So, we're going to stay with that conclusion, correct?

DR. LIEBLER: Well, they don't require UVA (inaudible).

DR. BELSITO: If they require light, which can either -- I mean, the ideal is the early visible range, but they will cure with UVA -- high UVA.

DR. LIEBLER: Because they bleed over enough.

MR. STEINBERG: Yeah, you can't have that narrow of a band; it's impossible.

DR. ANSELL: I mean, that was purely editorial. They can't require UVA.

DR. LIEBLER: So, I think our recommended conclusion, as far as the words "professional settings," which, I think, is the first long sentence, which starts with the "CIR Expert Panel" and goes all the way through to "professional settings" -- I don't think there's a need to change that.

DR. SNYDER: Well, I think it had LED, because they're LED, right?

MR. STEINBERG: They're not UV.

DR. SNYDER: The salons are moving over to --

DR. LIEBLER: Well, now wait a minute -- but salons will -- right now, we can't know whether salons have sort of gotten LED religion and only use LEDs. They probably use both types of devices.

MR. STEINBERG: Yeah, I mean, they -- because they already have the heat lamps where you can stick 10 fingers in at a time --

DR. LIEBLER: So, we could change that to UV or LED light.

DR. SNYDER: Okay.

DR. BELSITO: Well, I mean, if it's LED light, then you don't need (inaudible).

DR. SNYDER: (inaudible).

DR. ANSELL: It said that are cured.

DR. SNYDER: Or LED lamps, at the end.

DR. ANSELL: So, I think that's precise to the UV -- that (inaudible) light.

DR. LIEBLER: Right, okay. So, all right, we don't need to change that.

DR. ANSELL: Right.

DR. LIEBLER: So, the issue, really, is the next sentence: "Hydroquinone is unsafe for in-home nail products," currently written as, "that require curing by UVA light." And my -- just to restate my suggested alternate language is, "Hydroquinone is unsafe for in-home nail products in which curing is achieved by -- with UV light." So, I'm not specifying UVA -- or UV lamps, rather than LED lamps. So, I'm a little more specific here.

DR. SNYDER: And I (inaudible) more specificity regarding the in-home use. I said, "Unsafe under conditions of use outside a professional salon."

DR. LIEBLER: That would be acceptable to me. It's --

DR. SNYDER: Because I just don't like the in-home. I think we should specifically say outside professional salons.

DR. LIEBLER: The key point is that we would essentially identify what's unsafe is the UV.

DR. ANSELL: Right.

DR. LIEBLER: It's the use with a UV device outside of a professional setting. And I guess, speaking for myself, I would be okay with a conclusion that was something like that, basically.

DR. ANSELL: And I think we would, too.

MR. STEINBERG: I think that works; good point.

DR. BELSITO: Okay. So, how is this being wordsmithed? So, we're -- polymerization inhibitor in artificial nail coatings that are cured by UV light when photo-protected materials under the gloves or sunscreen for the skin are used in professional settings or -- oh, Jesus -- or when curing is achieved by LED light.

DR. ANSELL: Right.

MR. LABA: Although it may be important that there are UV LED lamps, as well.

DR. SNYDER: Thanks a lot, Denny.

MR. LABA: (inaudible) how relevant it is. I don't know if it's just (inaudible) in terms of the availability and so on of a UV LED.

MR. STEINBERG: In theory, it's possible.

MR. LABA: I mean, it's something that's used in heavy industry and so on.

DR. LIEBLER: (inaudible)?

MR. LABA: No, I did not.

DR. LIEBLER: Okay, it's theoretically possible, but not commercially viable and probably wouldn't be sold.

MR. LABA: (inaudible).

MR. STEINBERG: You see the combination of automobile coatings.

DR. LIEBLER: Yeah, I mean, it's not --

MR. STEINBERG: It's not something (inaudible).

DR. LIEBLER: It's not going to be a device that you're going to be able to sell for less than $50 --

MR. STEINBERG: No, no.

DR. LIEBLER: -- which is the top-end --

MR. LABA: Mm-hmm.

DR. LIEBLER: -- products that we're looking at.

DR. BELSITO: Okay, so this is what I hear my teammates saying -- and let me just repeat the full discussion -- the CIR Expert Panel concluded that hydroquinone is safe at concentrations of less than (inaudible) to one percent for cosmetic formulations designed for discontinuous brief use, followed by rinsing from the skin and hair. Safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by UV light when photo-protected material -- that is, gloves, sunscreens -- for the skin are used in the professional setting, or when curing as (inaudible) by UV light -- by LED light.

Hydroquinone is unsafe for in-home nail products that require curing by UV light, and unsafe for use in other (inaudible) cosmetic products. This conclusion supersedes. Is that correct?

DR. SNYDER: Could you read that last sentence again? I'm sorry.

DR. BELSITO: Okay, so what's been changed is that it says, "Safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by UV light when photo-protecting material -- that is, gloves, sunscreens -- for the skin are used in professional settings, or when curing as achieved by LED light." If you want to be more specific, in all settings -- or in professional and nonprofessional settings.

DR. SNYDER: No (inaudible).

DR. BELSITO: Okay. "Hydroquinone is unsafe for in-home nail products that require curing by UV light, and unsafe for use in other (inaudible) cosmetic products."

DR. SNYDER: So, I don't like the in-home; I like this --

DR. BELSITO: (inaudible).

DR. SNYDER: -- unsafe for -- under conditions of use outside professional salons.

DR. BELSITO: It's unsafe.

DR. LIEBLER: How about, "Unsafe for use in nonprofessional settings" -- which is what I just wrote here on the copy.

DR. SNYDER: Okay.

DR. ANSELL: It's the required that bothers me. They don't require it. It's when

used with UVA. It isn't that the gel requires UVA; it's (inaudible).

DR. BELSITO: It does. So, it requires it to cure. It does require (inaudible).

DR. LIEBLER: My wording supersedes that, okay? So, hydroquinone is unsafe for use in nonprofessional settings in which curing is achieved with UV light. Okay, so it's not required. It's when you do it that way --

DR. ANSELL: Right, yes.

DR. GILL: Yes, that makes sense.

DR. BELSITO: Unsafe for use in nonprofessional settings --

DR. LIEBLER: In which curing is achieved with UV light.

DR. SNYDER: So, can we go back up to the first sentence? Do we need to -- since we -- it's a two-part sentence where we say it's safe for discontinuous use of less than one percent -- in the second half of it, we say safe for use (inaudible) but we don't give any limitation. The focus on it should be not (inaudible) safe for use as in this report, or -- because, I mean, we're not -- do you see what I'm saying?

DR. ANSELL: Well, it's linked to the polymerization inhibitor.

MR. STEINBERG: It's the same use in nail adhesives as the polymerization inhibitor.

DR. GILL: Mm-hmm.

DR. ANSELL: So, that (inaudible).

DR. SNYDER: Well, then, so (inaudible) that's what I said -- we need to either insert under current practices or as indicated in this report, so it's not open- ended, right?

MR. STEINBERG: (inaudible).

DR. GILL: So, it's really safe for use as a polymerization inhibitor in nail adhesives and artificial nail coatings.

DR. BELSITO: And so you want the word "and" -- and artificial nail coatings to be cured -- so it's clear that they're two separate products.

MR. STEINBERG: Yes.

DR. GILL: Because it's a polymerization (inaudible).

MS. BECKER: -- safe for use in nail adhesives --

DR. GILL: No, safe for use as a polymerization inhibitor --

DR. BELSITO: And --

DR. GILL: -- nail coating -- nail adhesives and nail coating (inaudible).

DR. BELSITO: Polymerization inhibitor --

MR. STEINBERG: No, it's polymerized by exposure to air.

DR. BELSITO: -- and nail adhesives (inaudible).

MR. STEINBERG: Crazy glue.

DR. BELSITO: So, safe for use in nail --

DR. SNYDER: Safe as a polymerization inhibitor --

DR. GILL: In nail adhesives.

DR. SNYDER: In nail adhesives.

DR. GILL: And in artificial nail coatings that are cured by UV light.

DR. BELSITO: Okay, so let me repeat this, so I make sure -- safe for use as a polymerization inhibitor in nail adhesives and as -- and in artificial nail coatings that are cured by UV light.

DR. SNYDER: And then go on -- read the last one, then. Just read the whole thing, from start to finish, please. Sorry.

DR. BELSITO: Okay, wow. Okay, so -- brief use following by rinsing from the skin and nail [hair]. Safe for use as a polymerization inhibitor in nail adhesives and artificial nail coatings that are cured by UV light when photo-protected materials -- gloves, sunscreen -- for the skin are used in professional settings or when curing as achieved by UV light. Hydroquinone is unsafe for use in nonprofessional settings in which curing is achieved with UV light, and unsafe for use in other (inaudible)[leave-on] cosmetic products. This conclusion supersedes.

DR. SNYDER: Thank you.

DR. LIEBLER: So, I also recommended an edit to the second-to-last paragraph of the discussion, because our considerations have evolved beyond bulb replacement and use.

So, I suggest there's an alternate wording that captures some new information, whenever you're ready to hear it, Don.

DR. BELSITO: Let me just get this conclusion all together (inaudible). Okay, Dan.

DR. LIEBLER: Okay. So, the second-to-last paragraph in the discussion, which is the top of the PDF page of the conclusion --

DR. BELSITO: Right.

DR. LIEBLER: The second sentence there says, "The Panel stated that industry should manufacture lamps," blah, blah, blah, and it's all about the sockets and stuff. So, we don't really need that. And I deleted that last sentence, and replaced it with a new sentence: "The Panel stated -- the Panel noted that curing lamps that use UV light are widely available to consumers. However, safer LED lamps are also widely available, and are expected to replace UV devices."

DR. BELSITO: Okay, so I'm just going to highlight this, state that we're going to delete it, and Dan has the wordsmithing.

DR. LIEBLER: Right.

DR. BELSITO: I'm not going to try and type (inaudible).

DR. LIEBLER: That's fine.

DR. SNYDER: Yeah, I think I said revised based on the new data regarding LED lamps and differences between LED and UV curing processes. So, I think that needs to be expanded more than just, you know, the different light sources, the time it takes to cure, et cetera, et cetera.

DR. LIEBLER: So, you want to say that the LED is more efficient at curing? I

mean, do you really want to get into that in the discussion or --

DR. SNYDER: Well, my -- I guess some of my concern is here, what message are we sending to the consumers? So, are these consumers that all have purchased these LED things that he has -- are they going to just throw them away and --

DR. LIEBLER: You mean the UV or the LED?

DR. SNYDER: The LED.

MR. STEINBERG: This is an LED lamp.

DR. SNYDER: The LED. I mean, so are we --

DR. BELSITO: No, the LED is safe (inaudible).

DR. SNYDER: (inaudible).

DR. LIEBLER: That's fine. Those are good. I think our discussion should alert the consumer -- or should alert the bloggers that alert the consumer -- that UV lamps for this purpose unsupervised are bad news.

DR. SNYDER: But equally important is just to say that the LED are okay, but they're not going to conflict with our outside the professional salon use.

DR. BELSITO: No, it doesn't, because it says, "and artificial nail coatings that are cured by UV light," so salons can continue to use the UV light.

DR. SNYDER: Or curing by LED.

DR. BELSITO: Or curing by LED. And if you think it could be confused, we could say, "or curing by LED light in professional and nonprofessional settings," if you want to add that, to make sure it's more --

MR. STEINBERG: That's more clear.

DR. SNYDER: I think that would be clearer, yeah, because --

MR. STEINBERG: Yeah.

DR. BELSITO: Anything else?

DR. LIEBLER: So, I've just revised that.

DR. BELSITO: You're doing the discussion --

DR. LIEBLER: Let me just read it to you. So, the Panel noted that curing lamps that use UV light are widely available to consumers. However, safer LED lamps are also widely available, and are expected to replace UV devices. The Panel felt that the use of UV lamps in nonprofessional settings was unsafe and should be discouraged.

DR. SNYDER: So --

DR. BELSITO: Potentially unsafe.

DR. SNYDER: Yeah, so I'm good -- so I don't care whether they're widely available; I only care that we consider that to be not a safe use. So, instead of saying -- I don't care whether they're widely available --

DR. LIEBLER: But I do (inaudible).

DR. BELSITO: (inaudible).

DR. SNYDER: No, the Panel recognizes that the use of the application of UV light sources for hardening is unsafe. I mean, that's what we're saying. I mean, it's nothing to

do with availability, right?

DR. LIEBLER: Right, but, I mean --

DR. SNYDER: So, we really need to say that it's -- we consider that to be unsafe.

DR. LIEBLER: The Panel -- this paragraph starts with --

DR. SNYDER: Or concerned regarding safety.

DR. LIEBLER: This paragraph starts with the sentence, "The Panel noted there is substantial research demonstrating the general public's inattention to product warning labels and operating instructions." So, the whole thing is about public perception, and that's why I indicated that these UV devices are widely available -- and they are -- and the widespread availability of these -- and they're often cheaper -- is going to lead people to want to choose these. And that's why I think it's important for us to explain why that's a bad idea.

DR. BELSITO: We're agreeing.

DR. SNYDER: Okay, I don't. I think it goes too far from the purview of the Panel. I think we just have to state what the facts are; that we think that it's unsafe use. And so availability, cheaper -- all that doesn't matter to me; it's just that -- I think that just goes beyond our purview, is all.

DR. LIEBLER: You know, I mean, we make conclusions that not only refer to the ingredient but also refer to the conditions of use. And all of this contributes to the conditions of use, in my opinion, which is why -- you know, that's why I feel that it should be at least part of the discussion.

DR. SNYDER: No, I think it is, but there's three paragraphs preceding that where I think we capture all of that, and that we've kind of (inaudible) we're drifting a little bit into things I think are less under the purview of us, but that's my opinion (inaudible).

DR. LIEBLER: Do you (inaudible) -- yeah, because we've still got this paragraph at the end of the previous page about UV sockets and stuff. And I think that's much less relevant now, based on what we've heard and discussed.

DR. KLAASEN: We are going to include statements related to the availability of UV. Is it also worthwhile to note that the industry typically provides an LED with the starter kit to (inaudible)?

DR. LIEBLER: No, if you buy -- okay, but if you buy the lamp, and if -- your starter kit has gels and a light, right?

MR. STEINBERG: Mm-hmm, right.

DR. LIEBLER: And then if you -- but if you can get the gels from your sister, and you order the lamp on the, you know, internet, then you're still in the same situation we're concerned about. It's true that if everybody buys the kit and goes with the kit to begin with, it's nice and tidy. But that just doesn't -- I mean, that doesn't take into consideration a reasonably likely circumstance in which somebody goes out and buys the cheapest available one -- the cheapest available lamp, which is most likely going to be a UV device at this point.

DR. KLAASEN: I just think it may capture the majority of use, as well as, you

know -- if we go back to the intended use, capturing that, as well.

DR. LIEBLER: It may be the majority, but then I don't think the minority in this case is insignificant. So --

DR. KLAASEN: Yeah, no, I agree.

MR. STEINBERG: I think we just leave it.

DR. BELSITO: We are going to need to insert in some point under the use section that these can be cured with UVA or with a currently-recommended or LED visible. So, that will need to be updated when we're talking about use. But it's --

DR. SNYDER: Yeah, we have a section on UV nail lamps, which --

DR. BELSITO: Right.

DR. SNYDER: -- now need to be expanded to include --

DR. BELSITO: So, we talk about LED on page 34 of the PDF. The other three devices were light-emitting diodes. So, I guess we probably already have that in there.

DR. LIEBLER: Paul, would you be comfortable if the language that I had that you're a little uncomfortable with was part of a revised paragraph at the last of page nine -- or of the report -- of 36 -- the PDF -- that bottom paragraph that was more about UVA, B, and C bulbs, and sockets, and stuff -- if we really took that out, and then re-approached it by talking about the availability of the devices -- that the complete kits are sold these days with LED, but UV lamps are still widely available, and could conceivably be used?

DR. SNYDER: Yeah, I mean, the discussion, I think, begins very nicely with our concern about the risk for squamous cell carcinoma regarding UV sources. And so I think that's good. I just think we drifted a little too far into the, you know, availability and all that kind of stuff. If we just stick to the facts related to that concern that we have -- and that, you know, the availability or the transitioning away from the UV light sources to the LED and that issue, instead of kind of where we drifted here -- so with the socket, and the (inaudible) and all that kind of stuff. That all needs to be just watered down.

DR. LIEBLER: We'll kick this over to Lillian, rather than --

DR. SNYDER: Yeah, yeah.

MS. BECKER: Okay.

DR. BELSITO: I mean, obviously, it's going to come back to us, but I think that we need to give Lillian some guidance.

DR. LIEBLER: Do you feel you're guided?

MS. BECKER: Just that last part -- I need a little more clarification of what you want --

DR. BELSITO: I think that if you go to page 36 of the PDF, okay -- so, you know, I think that, in a way, that should stay, because that's what's guiding our decision for if you're going to cure with the UV curing lamp that these need to be done in a professional setting.

So, I don't have any issues there, except that it's not only that if the bulb were replaced with UVC, which is germicidal -- but it's also with UVB, which would blind the retina -- so you need to say with UVB or UVC; that's the fourth line up from the bottom on page

36.

I think all of that should stay in, but I think, at that point, we need a comment that, you know, in recent years, there's been a change to the use of visible-light LED lamps, where bulbs cannot be replaced, where there is not a concern about carcinogenicity or ophthalmologic toxicity or damage, and these would be not an issue for home use -- so something to that effect, okay?

So, I think in that paragraph, what we need to go into is the notion that we have problems with the UV lamps -- not necessarily because of UVA, which is not an issue -- I mean, that comes through window glass; we're looking at UVA all the time, unless you've juiced your body up with serolins, and then we do know that UVA causes cataracts. But, you know, we get more from natural light than we'll get from these bulbs.

But it's UVB -- replacing with UVB or UVC that would be an issue -- and then a paragraph there about the change in technology to LED lamps, where bulbs aren't replaceable, where it's visible light, where we're not concerned about any toxicological endpoints - specifically skin cancer and ophthalmologic damage.

And then the next page is, you know, where we're talking about public's inattention to the product warning -- I'm not sure that we even need that if we just had the prior. I mean, we probably can delete that entire --

DR. SNYDER: So, I think the discussion should be --

DR. BELSITO: -- paragraph.

DR. SNYDER: I think the discussion in this aspect needs to be split into two parts: Professional use -- we should clearly state that they can be used safely under the conditions of the gloves, et cetera, et cetera -- and then the nonprofessional use, in which we say (inaudible) iteration that they cannot be safely used because of blah, blah, blah. But I think the professional/nonprofessional use -- we need that -- would drive this section more clearly, because --

DR. BELSITO: No, I think we do that in the conclusion. I mean, I think that -- or even, I mean, the issue with bulbs -- I mean, I'm assuming that professional use -- they'd realize that UVB and UVC aren't going to cure their products, and they wouldn't substitute the bulbs. I'm hoping they're a little bit more trained to understand this.

DR. SNYDER: But he says they put both hands in the --

MR. STEINBERG: Right now, the bulbs that they're using at salons are meant to dry. And that was because they (inaudible) --

DR. BELSITO: Right.

MR. STEINBERG: -- classical nail lacquers, not -- you know, not the gels that have MEHQ or HQ in them, but classical, nitrocellulose, solvent-based dryers. They dry them much quicker, okay? Do they work on the gels? Very, very slowly, and I think the salons -- at least -- I visit, too, and they're moving more and more to having one section for lacquers and one for gels. And the gels are using LEDs, because they're just so much faster.

The whole thing in the salon is, move the patients through. Do the nails; get

them out of here.

DR. BELSITO: I think they're customers, not patients.

MR. STEINBERG: Victims? I don't know. I don't get my nails done there.

DR. BELSITO: Okay. So, you have a sense of where we're going there, Lillian?

MS. BECKER: Yes, I do.

DR. BELSITO: Yeah, I would -- and I think -- I don't know -- let's see what Rachel has to say about that paragraph on public warnings.

Okay, just going back through the document, we've addressed everything we need to do about, hopefully, the light. We did get a request from NTP that we delay this.

DR. SNYDER: Well, it was -- I don't think it was NTP; it was Eastman (inaudible).

DR. BELSITO: Okay.

DR. SNYDER: (inaudible) --

DR. BELSITO: Okay.

DR. SNYDER: -- in person.

MS. BECKER: In person.

DR. BELSITO: Okay. That -- I don't think we need to. I mean, when the NTP study comes out, we can look at it, and change our mind. Everyone in favor of that? Okay.

I already told you page 36 of the document -- UVB or UVC. And -- well, we'll see whether we delete that entire paragraph -- first paragraph -- on page 37. If not, Dan has the wordsmithing for that.

Okay, I addressed all my concerns. Paul?

DR. SNYDER: I'm good.

DR. BELSITO: Okay. Are we done with this?

DR. LIEBLER: Yes.

DR. BELSITO: Okay.

MR. STEINBERG: Just change the necessary reports on the MEHQ --

DR. BELSITO: All right. Let me carefully organize it, then.

DR. SNYDER: So, the depigmentation issues are -- is a bigger risk factor than the carcinogenicity issue, right (inaudible)?

DR. BELSITO: Yeah. I mean, that's why we banned it in products before, was because of depigmentation.

MR. STEINBERG: (inaudible) you can buy prescription drugs with hydroxy (inaudible) as the active ingredient.

DR. BELSITO: Yeah, but --

MR. STEINBERG: I don't think anyone prescribes it, but, you know, (inaudible) the FDA's database.

DR. BELSITO: Okay. So, yeah, I mean, basically, it's -- I mean, it's going to be the same thing.

So, we're going to change the conclusion regarding the professional and

consumer for the UV gels, but unsafe for other uses.

Page 36 of the PDF -- again, it's -- top line was replaced with a UVB or UVC bulb.

DR. SNYDER: What heading are you please on?

DR. BELSITO: It's just -- it's in the discussions, just above the amended conclusion. Again, I mean, the concern would be a change with either UVB or UVC. And the eye damage would be both UVC and UVB.

That sentence, also -- there was concern that home users may be exposed to additional UV light exposure to hands if they increase the exposure duration -- there was a similar -- no, I'm sorry; the next comment was about the paragraph on public's inattention. I said I liked the one in the hydroquinone report better, but this may totally disappear now. So, if it doesn't, then we use the same as we used for the hydroquinone report, which Dan and -- I presume -- Rachel will wordsmith.

DR. SNYDER: So, a question for Lillian.

MS. BECKER: Mm-hmm.

DR. SNYDER: Do we have -- are you -- do you think it's necessary in the amended conclusion to put the last sentence, "This conclusion supersedes the earlier conclusion"? Is that necessary to put in the report?

DR. BELSITO: We've typically done that when we've changed the conclusion (inaudible). Well, no -- even when we changed the concentration limit (inaudible) to alert people that this is something new.

DR. SNYDER: So, we -- would it be better to state in there what is different, then, instead of just saying it supersedes? I mean, (inaudible) this conclusion.

DR. GILL: So, he wants more --

DR. SNYDER: Well, I'm just asking, yeah, so --

DR. GILL: He wonders about what the change is.

DR. SNYDER: Right -- what the change is, so it doesn't require them to go back, and see, and prepare -- to make it easier for the intended users to --

MS. BECKER: Well, the old conclusion is in the introduction.

DR. SNYDER: Oh, so it could say it was given in the introduction or something, instead of supersedes or --

DR. BELSITO: What we don't say, though, in the conclusion, is that it's unsafe for other uses -- which I think we --

DR. SNYDER: Have to.

DR. BELSITO: -- should say.

DR. SNYDER: Yeah.

DR. GILL: See, the earlier --

MS. BECKER: (inaudible) unsafe for use in all other cosmetics due to dermal depigmentation potential -- it's in the conclusion, just before this conclusion supersedes.

DR. SNYDER: Because the old report is not incorrect; it's that we have now new

product (inaudible).

DR. GILL: We have a safe use --

DR. SNYDER: Correct.

DR. GILL: -- for certain uses.

DR. SNYDER: Yeah, so I think --

DR. GILL: The old one said unsafe in all cosmetic --

DR. SNYDER: Right. So, I think we need to be careful that we're --

DR. GILL: Correct.

DR. SNYDER: Yeah.

DR. GILL: Correct.

DR. BELSITO: Okay. Then, again, this is a report that I worked on back on August, so there must have been a change. So, what is the new conclusion -- amended conclusions?

DR. SNYDER: Well, I think it's the same as the --

DR. BELSITO: Let me just see what you have, because I have a different one. I've been traveling the last two weeks (inaudible) a lot of this before.

It's the same. And the amended conclusion, really -- where does it say unsafe?

MS. BECKER: Very last part of the first -- of the sentence --

DR. BELSITO: I'm looking at the amended conclusion for this report.

MS. BECKER: Right. And unsafe for use in all other cosmetics due to dermal depigmentation potential --

DR. BELSITO: Oh, okay.

MS. BECKER: -- just before the supersede sentence.

DR. BELSITO: Okay, okay.

MR. STEINBERG: (inaudible) unsafe for home (inaudible) curing by UVA light.

DR. BELSITO: Right.

DR. SNYDER: So, we need to bring in some of the changes there that we did in the previous report. So, instead of in-home, outside a professional salon, da, da, da, da, da.

DR. LIEBLER: I think except for the reference to the dermal depigmentation potential, this conclusion and much of the discussion should be identical.

DR. SNYDER: Should be -- exactly. I agree; yeah.

MR. STEINBERG: (inaudible) the only caveat is that the hydroquinone was allowed in rinse-off products -- brief contact with (inaudible).

DR. LIEBLER: With that obvious exception -- right. I mean, the things that we're working (inaudible) be the same.

MR. STEINBERG: (inaudible) be the same.

DR. SNYDER: So, why -- I still -- I -- the statement that it can supersede the earlier conclusion -- the earlier conclusion's not incorrect, or it's not -- it's just this one's more expanded to include a different product category and then say --

DR. GILL: Correct. So, we're saying that it doesn't really supersede -- well, it

does. The decision in '85 says it's unsafe for use. This conclusion says there are safe uses; however, it is unsafe in all other uses.

DR. SNYDER: My preference would be to give some indication of how it's different, rather than just --

DR. GILL: Okay -- which said it was unsafe in all -- for all uses.

DR. SNYDER: Right.

MS. BECKER: So, change it to, "and continues to be unsafe for all use -- for use in all cosmetic products."

DR. GILL: Or if you wanted to leave the last sentence, "This conclusion supersedes the earlier issue by the Panel in '85, which stated that it was unsafe."

DR. SNYDER: Unsafe in all use -- yeah.

DR. GILL: Okay (inaudible).

DR. BELSITO: Which stated that it was unsafe for use --

MS. BECKER: In all --

DR. SNYDER: In all categories.

DR. GILL: In the back -- and make sure we use the exact wording.

DR. BELSITO: Okay. Anything else on (inaudible)?

Dr. Marks' Team

DR. MARKS: Okay. Hydroquinone; so in June, a tentative amended report for hydroquinone with a -- was issued with a conclusion that it's safe at concentrations less than, or equal 1 percent, formulaic for discontinuous -- brief use followed by rinsing from the skin and hair. Safe in nail adhesives as a polymerization inhibitor in artificial nail coatings that are cured by UV light when photo-protection materials in the professional settings, but unsafe for home use when used with UVA light -- that's going to creates discussion -- and hydroquinone should not be used in other leave-on products.

And the issue is the nail adhesives. That's why this was reopened to begin with. So Wave 2, David is here at the mic, and we can hear David's comments. He suggests changing the conclusion to make it simpler, safe for nail products. And, David you have the floor.

MR. STEINBERG: Thank you. Just two things I want to cover very briefly. One of them was light, which I haven't studied for 52 years, since I took physics in college, so I got a new education. And the other the use of radiation in the curing, which is what this whole issue is about, and the light bulbs and the lamps, and things like this.

Original light was burning when we oxidize something, whether it was wood, whether it was vegetable oils, whether it was fats. And then we got into petroleum, kerosene lamps, and then good old Thomas Edison invented the incandescent light bulb. A couple things about light bulbs, they go on instantaneously, you turn the switch and out comes light. The second thing is, they also admit heat. They get very hot.

Now there is one truism about all of these types of light bulbs, no matter what the

source. I haven't found anyone who replaces them until they burn out. You just don't buy a lamp or an office facility, or an automobile, take your headlights out and change the light bulbs, until they burn out.

Through the cost of energy, because of various things, we invented, or it was, discovered fluorescent light bulbs. And fluorescent light bulbs do not go on instantaneously when you turn the switch on in a fluorescent light bulb, it takes a while before you get the light.

Second thing is, they are long tubes. They had special appendages to them, and they lasted much longer, around 10 times longer than an incandescent bulb. They use about 10 times less energy, there were very good reasons for them, and the problem was we couldn't use them for lamps, it was that simple, until someone discovered that if we took that long tube, and coiled it, we could make a light bulb. And these are about all you can buy now. I understand that they basically phased out this size with this socket for incandescent bulbs. Okay.

The next thing that was discovered is LED, light emitting diodes. And LED, first, do not emit heat. They are just light; they can be very narrow-ranged, which is very important. First commercial use goes back -- at least that I knew of -- was in 1973, I was given one of the first Texas Instrument calculators, it weighed about 3 pounds, and had the red numbers, those were red LED bulbs. Okay.

Since then we've learned a lot more and there are several truisms. First is, they do not burn out, they last 20,000 years, 10,000 years, 5,000 years. The only way that they go is you throw the whole unit out. This I bought during Hurricane Sandy. This is a flashlight, and it has LED bulbs. There are actually three of them there, okay. You cannot take the bulbs out. I will unscrew it. You get a battery pack, you can't get to the bulb.

The only way I know of getting to the bulb is to take a sledge hammer and smash it to smithereens. Okay? The lamps that we use that are sold today for curing nail gels for consumer use, are LED lamps. This is the most popular one. If you can see it, you can see there are two, four, six bulbs, okay. It is used, you put four fingers in, there is a separate one bulb for the thumb. This is for home use. This is not what you use in beauty salons, they have different ones, because beauty salons are basically interested in having their clients processed faster. Okay.

The original nail polishes are lacquers, basically were polymers dissolved in volatile solvents with plasticizers and pigments. The woman, or if you are into it, put the nail polish on, and as my wife does at home, it takes forever for it to dry. You go to a professional beauty salon to get your nails done, and their concern is getting you out of there. The longest time it takes is for the woman to decide what color nail polish. But the second longest is, how long it takes to dry the nail.

They discovered, naturally enough, they did -- invented science; that heat will cause the volatile organic compounds to evaporate faster. So they took a fluorescent light bulb, stuck all 10 fingers in at once. And guess what? They drove the VIOCs off much more rapidly.

Out came nail gels. Nail gels came from the automotive industry to become solventless coatings which lasted far longer than nitrocellulose lacquers, and that's where we are today. They are used originally, professional nail salons, they found out that these are the types of things that consumers can do at home, and so in 2011, late 2011 starting 2012, the major suppliers of nail polish got into the nail gel business and sold kits. You bought a kit, you got a lamp, and you got half-a-dozen different nail polishes and extensive directions how to use them.

After that, whenever you needed a new nail polish, you just went to the store and you could buy millions of different nail polishes. I went and I bought lamps. I basically went to the two extremes, or at least I consider them the extremes of where a consumer can buy lamps.

I went to Sally's Beauty Products, which is basically the low-priced area, (inaudible) out. I went to Sephora, which is the high-priced area; the same thing. There are, as far as I know, no major retail outlets selling fluorescent bulbs. They don't work as well, there are safety issues, they break. These will last -- we will all -- we will never outlive the use of these. These are good for a -- you know, depending on your mathematics, anywhere that's between 1,000 and 5,000 years. I mean, they just don't burn out. We don't use them that much.

So the question that has been raised concerning the safety of the lamps, they were two separate things. One is that the consumers could replace the bulbs. Okay. You can't get to the bulb in these. Farther more, if you would like to see what these bulbs look like, I actually found a picture of them and this will explain one of the critical things. This is what the bulbs look like.

You don't screw them in, they have to be soldered in, they have to be permanently attached. If they are not permanently attached, they are not going to work. You will have to have these connections exactly lined up or else when you turn the juice on, you just don't get light. They do use the LED bulbs, by the way, right now are in traffic lights. If you ever see a green traffic light with those black dots, these are all LED green bulbs.

The one thing that's neat about the LED bulbs, we can really control the radiation that's given off. And you can see it if you want, I would be glad to send it to you, all the different bulbs, depending on the substrate, and all of them radiation above 400 nanometers, which is the visible light. The lambda max where you need to cure or do the polymerization, is at 405.

Now, an LED bulb will have a little at the 395, because that's life. Okay. Fluorescent bulbs, on the other hand, we can get them down -- we have them down at 320 or 340. Go to a tanning salon, and those tanning beds all have these (inaudible), and they are all 320, 340, very dangerous. I'm not a big fan of them.

But I think we have said, realistically these are something that consumers can use, they can use them safely. The question was raised; can you buy fluorescent bulbs, or fluorescent lamps? Like I said, I have checked various stores, they don't have fluorescent

bulbs -- fluorescent lamps anymore. I have checked the big-box stores. You know that one in Bentonville, Arkansas? I deal with them. There is one in Minneapolis, major drug chains, none of them are carrying the fluorescent drying lamps for -- or curing lamps for nail gels.

You can get them on the Internet. You just Google it, and you'll find various sellers who are selling these types of things, but none of the major stores are carrying them anymore. Why? The price of these have gone from about $100 now to, I think this s 19.95. Consumer buys the kit, usually the first time.

I know of very few consumers who will go into Walgreens, buy a bottle of gel, and then go online try finding a lamp that will cure it. Usually their introduction is to buy the kit, and that gives them the lamp, and there is one of my attachments was from a blog which I take with a grain of salt, which says, "Use the gel that works with the lamp." If you have a lamp that's made by OPI, use OPI's gels, it works best.

So, our conclusion should be that first, the issues that were raised back in December, were basically based on professional use lamps that were used to dry nails, as opposed to cure. Okay. But the lamps, the LED lamps are perfectly safe, there has been no reports of any injuries. These things that the consumer uses, and they can't replace the bulbs. So, for home use, we are of the opinion that MEHQ and HQ or hydroxyanisole, are safe for nail gels for consumer use, with, if you want to add the caveat that they be cured with LED lighting.

DR. MARKS: -- about professional here, because you addressed the unsafe for home use, and have a compelling argument why that isn't the case. How about UV light when -- further project the materials in the professional setting? So the professional setting is not switched over to LED lights.

MR. STEINBERG: Oh, they are. They are gradually -- now you start off with the -- Nail Salon started way back 20 years ago doing nail polish and then artificial nail extensions. The artificial nail extensions were all based on polymerization before it was applied to the nail, so we never thought about that. The nail polish was done by evaporation of solvents.

When the nail gels came into being, which I'm going to say is about four or five years ago, yes those lamps could be used, they don't work very well, it takes four to five times longer and time is not what they want, and they have all gradually switched to LED lamps, because it takes only, like 30 seconds to cure, where, using a fluorescent bulb it will take two-and-a-half to three minutes.

And when you are talking, these people, the faster they turn over the clientele the more money they make. So they are moving over in that direction, I would say, probably, in three to five years you won't see any fluorescent bulbs there. If they do, they will be strictly for the drying, not for the curing purposes. They don't cure very well.

The lamp -- like I said, the lambda max is about 405 in the visible range, the fluorescent that they are using is usually in the 380, 385 to 420 range, but the peak is around 400. So they are not really that -- you know, they are there for the heat, they are not there for the curing. They are just -- they are wide, these are focused, and will work much, much better.

DR. MARKS: That's close to the surette band. Is that right, David? Do you remember coming across that terminology, the surette Band?

MR. STEINBERG: No. No.

DR. MARKS: There are some rare skin diseases that are sensitive. Do you remember, Wilma? I wouldn't put that restriction down, that's too -- a great (inaudible).

MR. STEINBERG: I did meet -- there was a woman I met, I was visiting Holly Maybach, and we were making rounds, and there was a woman who was sensitive to visible light. And it was an adventure. It was.

DR. MARKS: Yes. Rachelle how -- so if I understand the way you would change the conclusion here, and I don't know if you have Lillian's memo in front of you, but the conclusion where it would be safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings, and you would end with that, and not put the restrictions in.

MR. STEINBERG: The only reason I would put the restrictions is that people -- as it would make a difference that people not use or not find on the Internet these fluorescent light bulbs to use in the cure. That we -- you know, basically the issue that always that always came up, was that this, the original two cases that were mentioned back in December --

DR. MARKS: Well that's -- yeah.

MR. STEINBERG: -- were based on a fluorescent light as opposed to the LED.

DR. MARKS: Which were just two cases; it's not like we've seen an epidemic, or.

MR. STEINBERG: No.

DR. MARKS: So the other way, David, could be where it has that last part of that sentence, you could just put artificial nail coatings that are cured by LED light, period. Rachel, from a consumer's point of view, would be interested, because that's what this has all come down to, really. And there are some questions even as, should the CIR be dealing with the devices that the ingredients are around. I think we have -- we should in this instance.

MS. WEINTRAUB: I think what's complicated is what you just said, that there were two incidents with fluorescent light, so that sort of seems inconsistent with what David just said, that these don't -- right. You are saying these--

MR. STEINBERG: The fluorescent -- the cases were back in 2009, these did not come onto the market until 2011, okay. These the consumer use, okay, started late 2011, 2012, when we were able to come up with kits which they could use without spending a fortune, and the directions.

What happened on the professional salon, it was -- it happened, it was reported. There were no other cases we -- I went to the FDA and couldn't find any reports of injuries report to the FDA for any nail-enhancement products -- until, there was in 2005, and that was an imported product. It wasn't a U.S.-made product.

So, you know, my feeling is, the professional salon, you have trained people, they should know what they are doing, that's part of their licenses, in every state as far as I'm

aware. They should know what they are doing, they should be able to follow the directions; and (inaudible), for the consumer we want something that is safe.

DR. MARKS: Just, Wilma has pointed out there's an article in Journal Investigation by Weinstock, it's the leading author, again with the conclusion that they are safe.

MR. STEINBERG: Yes. I have that here.

DR. MARKS: Dermatologists may reassure patients regarding the safety of these devices. And I think there's a difference, if I heard you correctly, David, that the LED is not fluorescent. So if -- it's not a fluorescent light so all that --

MR. STEINBERG: No. It's not.

MS. WEINTRAUB: That's what you were saying, right? In that --

DR. MARKS: Yes.

MR. STEINBERG: This is a fluorescent bulb, right. These are LEDs.

MS. WEINTRAUB: Right. So in that red light, they are LED.

MR. STEINBERG: Yes. These are only LEDs. See, take a look at it, you can see the little bulbs.

DR. MARKS: I guess that they are still on my mind, still concern about light exposure, and a potential of producing skin cancers, if in our conclusion we said, that are cured by LED lights, then there's no more concern.

MR. STEINBERG: Yes.

DR. MARKS: Because it's visible.

MR. STEINBERG: It's visible.

DR. MARKS: In things like a photo-protective material really don't apply, because as you mentioned in your memo, sunscreens aren't going to protect you.

MR. STEINBERG: Yes.

DR. MARKS: And in the other issue, is then, it's not a home issue either because you are only using LED lights at home. So, you can delete that part, and make it a simpler conclusion.

MR. STEINBERG: Yes.

DR. BERGFELD: Why not just visible light?

DR. MARKS: Well, I think it's -- well, fluorescent I'm not sure you can see fluorescent (inaudible) --

MR. STEINBERG: Right, but you are -- you can see the classical light bulb from Thomas Edison that gives you visible light, it also gives you radiation in the UV range and also in the IR range, where the OED doesn't. The LED has a very narrow range bulb.

DR. MARKS: So, Ron, Ron and Tom? We have David's presentation now, and obviously we have this article as background, and the other ones. Thank you, David.

MR. STEINBERG: You're welcome.

DR. MARKS: Yes.

MR. STEINBERG: That was a --

SPEAKER: Yes. He won, right? Why is that?

DR. MARKS: I don't know. Wilma wanted to take it home to cure her --

DR. BERGFELD: No. I can't do that. I'm sorry.

DR. MARKS: Yes. So, yeah; David, next time bring in lamps that have zebra stripes on them. Would you please?

DR. BERGFELD: Thank you. Then I will not take it.

[Laughter]

SPEAKER: Until they make them.

DR. MARKS: Yes. I'll sure that too. So, Ron, Ron and Tom, do you like the idea that, you know, is suggesting changing the conclusion to artificial, where it has that one part talking about protective materials, unsafe for homes, just say, artificial nail coatings, they are cured by LED light?

DR. SLAGA: Right.

DR. MARKS: Then it's very specific.

MS. WEINTRAUB: I just have one question.

DR. MARKS: Yeah. Go ahead.

MS. WEINTRAUB: Weren't there are products that used to have fluorescent lights?

MR. STEINBERG: There have been in the marketplace.

MS. WEINTRAUB: Yes.

MR. STEINBERG: That use fluorescent lights.

MS. WEINTRAUB: So the thing is, they haven't -- they haven't been recalled, right.

MR. STEINBERG: No. They are --

MS. WEINTRAUB: So it's possible they could still be in use.

MR. STEINBERG: They are still out there, and you can still buy them at distress stores on the Internet. If you Google it you'll find them. They are not sold retail; that I've been able to find. So, one of the comments, and the hopeful comment is that by the conclusion that you should be using LED lights, because they are safe, that will be the kiss of death for we think is -- what we know is happening in terms of the retail.

Now, none of the major and even minor players in the gel market are offering fluorescent bulbs at all, the only lamps they are offering now are the LED.

MS. WEINTRAUB: Right. But they are still out there?

MR. STEINBERG: But they are still there.

MS. WEINTRAUB: And a consumer could still purchase them, and people who purchased them before still have them, so it's, how to deal with that issue.

DR. MARKS: Well I don't think -- how we can deal with it as one with the conclusion points out that the only lamps that are safe at this point are the LEDs.

MR. STEINBERG: Are the LEDs.

DR. MARKS: And Tom nudged me saying, we need to have this in the discussion, largely what you presented, which I think is great, because it really brings this up to

date, in terms of the safety issues, so.

SPEAKER: Succinct?

DR. MARKS: Yes. Succinct, yeah. Tom, Ron?

DR. HILL: I was just going to let you know because I did a little (inaudible) -- If you had somebody who was surette-sensitive they would be sensitive probably to this. Yes.

DR. MARKS: That's rare.

DR. HILL: Except this is the visible light, I mean, would have to be sensitive to the LED because it's visible.

MR. STEINBERG: Yes.

SPEAKER: The surette is low, 400s.

DR. MARKS: So anyway, and then I -- so I think our team likes the idea of modifying the conclusion, or changing the conclusion that it will read, again, just referring to the nails, because that's where the issue was and why this was reopened. Hydroquinone is safe for use in the adhesives, and as a polymerization and inhibitor in artificial nail coatings that are cured by LED -- light or lamps? Which is more accurate? LED light?

MR. STEINBERG: It's LED light.

DR. MARKS: Light. Okay.

MR. STEINBERG: Yes.

DR. BERGFELD: Don't you think you should put in the nanometers too, is it 405?

MR. STEINBERG: The lambda max is 405, it's where curing takes place.

DR. BERGFELD: I think it's worth putting that in.

MR. STEINBERG: Okay. It's the possible --

DR. BERGFELD: In the discussion.

DR. MARKS: The discussion, yes. Not the conclusion.

MR. STEINBERG: Yes.

DR. MARKS: Okay. Does this warrant sending out another tentative amended report? To me it's a significant change in the conclusion.

DR. SHANK: Yeah. It would.

DR. MARKS: Yes.

DR. SHANK: You'd have to send it out again. But in fact, the conclusion as written is very well written, it says, the ingredient is unsafe home use when cured by UVA light, that's true. And now you are taking that out and you are saying it's safe if you use LED.

DR. MARKS: Yes.

DR. SHANK: What about UVA? If you use UVA, this says it's unsafe, if you don't use UVA you are okay. So I would leave it alone.

DR. MARKS: What, then you have to change home use, and then you can talk about other lights. To me, Ron, that can be put in the discussion.

DR. HILL: The discussion.

DR. MARKS: Ron, Tom? Tom, you did --

DR. HILL: So the idea would be -- the conclusion would not say LED?

DR. MARKS: Yes. This conclusion says it is safe when cured by LED light.

DR. HILL: Then it probably needs to go out again, right?

DR. MARKS: Oh, yeah. We made that decision.

DR. HILL: Okay.

DR. MARKS: Now the question. Ron liked the conclusion where you also stated, it's unsafe with UVA light. But I thought that could be handled in this discussion, but yeah.

MR. STEINBERG: The discussion is (inaudible) it is safe for home use, and is not limited to UVA because UVB can do -- you know, people -- as much as we know the difference, consumers don't.

DR. SHANK: Exactly what is the wavelength necessary for curing the nail?

MR. STEINBERG: 405 is the ideal wavelength. Curing starts -- usually we can go as low as 395, 398, and you'll get some curing. It's just, as you get closer to -- 405 is the quickest cure. Okay. If you go like to 500, you are going to cure much slower. If you go to 360 you are going to cure much, much slower.

DR. SHANK: And the UV -- LED lights?

MR. STEINBERG: I think it's -- in theory I guess it's possible to make an LED light, below 400, all the commercial ones are above 400 -- are 400 or higher. And they can be fairly narrow bands, which is why you see them in green, yellow and red traffic lights. They are a very narrow band to expose just that type of light.

In fact, the fun thing in researching this was they couldn't make a white LED bulb. They couldn't figure out how to do it, until it suddenly dawned on them that white consists of exactly what (inaudible) did, combine red, yellow and blue, and you got white.

DR. MARKS: Okay. Well, Lillian, you have a lot of background information to condense, as I think and Tom and Ron said, to a relatively brief but pithy discussion of why we arrived at LED light is safe. And why we deleted these other provisions which we had put in as a conclusion.

So tomorrow, it looks like I'm the one who will be presenting this, and I will move that we issue a revised tentative amended report with the revised conclusion that's safe by LED light, and obviously there are going to be changes in the abstract discussion; and adding the supporting documents which David has given us.

MR. STEINBERG: The only other comment is to quote someone from the other team, on any para-hydroxyanisole with a few editorial changes, ditto.

DR. MARKS: Okay. Let's -- any other discussion about hydroquinone? Okay. And Rachel, I assume that's -- from the consumer's point of view, this conclusion should be straightforward in the discussion?

MS. WEINTRAUB: I think so. But I think in the discussion it has to be clear about the fluorescence.

DR. MARKS: Right. Yeah. Well, that's my concern, they are still being used in a

professional setting.

MS. WEINTRAUB: Yeah. Exactly; they are being used, they are still available for sale. So that needs to be very clear.

DR. MARKS: And I think in the discussion you can put, if you're still using the fluorescent, that you do use protective, just to be on the safe side, UV protective --

MS. WEINTRAUB: Sunscreen and gloves.

DR. MARKS: Sunscreen, gloves, yes.

MS. WEINTRAUB: Okay. In the discussion?

DR. MARKS: In the discussion. Okay.

DR. HILL: And you are going to put the wavelength in the discussion as we well, right?

DR. MARKS: Yes.

DR. HILL: Because I think you could make a -- you could make an LED that kicks out 360 nanometer light. I'm pretty sure.

MR. STEINBERG: Yes. It's not for (inaudible).

DR. HILL: I know that.

MR. STEINBERG: But I think it can.

DR. HILL: Yeah.

DR. MARKS: Okay. Yeah. I think that's -- Ron Hill, I think that's important to put in there, that we talked -- that we know that we are (inaudible).

DR. HILL: Yeah. We want to be in the visible range, in the short visible range. Yeah.

DR. MARKS: Yeah. Okay. Do we have another memo from David on para-hydroxyanisole? This is the same issue. I think we could come to the same conclusion with the same tact, to issue another revised tentative report, with safe for nail coatings when using a LED light.

Ron, Ron, Tom, did you see any difference? It's unsafe for all other cosmetic uses, as the conclusion says. And it looks like the discussion will mimic the same.

SPEAKER: Copy.

DR. MARKS: Yes. You've got it.

MS. BECKER: Copy, paste.

DR. MARKS: Okay.

Day 2

DR. MARKS: So in June the Panel issued a tentative amended report of hydroquinone with the conclusion that it's safe at concentrations of less than or equal one percent for cosmetic formulations designed for discontinuous brief use, followed by rinsing from the skin and hair. The second sentence in this conclusion, we're going to propose a

change. Hydroquinone is safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by UV light when photo-protective materials, for example, gloves and sunscreens in professional settings, but unsafe for home use when used with UVA light, come back to that sentence. And then lastly, hydroquinone should not be used in other leave on cosmetic products. Yesterday we had an elegant presentation and supporting data that we could be reassured that the present use of LED lights for curing would be safe and so we would propose that the conclusion be changed in that the artificial nail coatings that are cured by LED light, and strike the remainder of that sentence. So we would propose to issue another tentative amended report with a change conclusion below. We thought it was significant enough to substitute LED light, that it should go back out for comment from industry and the public. So that's a motion.

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

DR. BELSITO: I'm not sure what the statement is. Let me read to you what our team came up with a conclusion -- that the CIR Expert Panel concluded that hydroquinone is safe at concentrations of less than one percent for cosmetic formulations designed for discontinuous brief use followed by rinsing from the skin and nails and for use as a polymerization (sic) inhibitor in nail adhesives and as -- and in artificial coatings that are cured by UV light where photo-protecting materials, that is gloves, sunscreens for the skin are used in a professional setting, or when curing is achieved by LED light in professional and non-professional settings. So basically what we're saying is, that curing by UV light in a home setting is not a safe approach. You can purchase both LED lights and UVA curing lights still online, so that's not the only option. You can walk into a Walgreen's, buy the polymers and purchase a separate UVA light and take it home. So I don't think that we want to give the impression that just because there's an LED light available, that home use for these products are safe. And then continued with hydroquinone is unsafe in home nail products that require a curing by UVA light, and unsafe for use in other leave on cosmetic products.

DR. MARKS: Don, I think we're saying the same thing.

DR. BELSITO: I just wanted to make sure.

DR. MARKS: Yeah.

DR. BELSITO: Because it didn't quite read a complete sentence and I want to make sure that theP is getting across that purchasing the gels and using a home UVA light would not be considered safe.

DR. MARKS: So we've addressed it making that second sentence, and it's all about this nail coatings and adhesives and use of light to cure them. So our sentence reads, "hydroquinone is safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by LED lights". It's very specific. That's the light you can use. Nothing else.

DR. BELSITO: Even in a professional setting.

DR. MARKS: Yeah. The idea is, when you use an LED light, it's safe. If you use any other light, it's not. And that can be covered in the discussion.

DR. BELSITO: Okay, so you're eliminating UVA lights even in professional settings.

DR. MARKS: Yes.

DR. BELSITO: I don't have a problem with that. I don't know that it's going to be done, but I don't --

DR. LIEBLER: That's good, that's actually good, because that gets you away from the whole gloves and sunscreens issue as well. That's -- I think we have all the same elements, we just have different wording. The only thing that's different is the LED only, which I think is a good idea.

DR. BELSITO: I would just like to hear Rachael's comments about the fact that these are now going to be out on the market and not necessarily have to be purchased with an LED light.

MS. WEINTRAUB: Well something that we discussed in the Belsito team is the fact that you could purchase these other types of products without an LED light. They are online and that's problematic. Probably should be recalled, given the specific use for nails and the problems, and the hazards it poses for consumers, but I think the conclusion I think is very clear in terms of a bright, pardon the pun, a bright line with LED lights. But I think -- but I do think in listening carefully to what you were both saying, I think you are both getting to the same place, but went about it differently, and I think that LED specific is a bit clearer and simpler, even though I think in your version, you go through sort of the elements of what's problematic and what's not.

DR. BERGFELD: That could be included in the discussion though.

MS. WEINTRAUB: Yes, and I think it should be.

DR. BELSITO: I actually like the idea of simply saying with LED light. I think we need to make it very clear in the discussion that with UVA light, we do not think it's safe.

DR. BERGFELD: Beth, do you have any comments?

DR. LANGE: We're in agreement.

DR. BERGFELD: Thank you. FDA has any comments?

SPEAKER: No, not at this point.

DR. BERGFELD: Thank you. Paul?

DR. SNYDER: So my only issue is that we have data, we have information that in professional salons they do use UV light to cure these nails. And so I think that we -- aren't we just kind of skirting the issue with not, it can be done safely, if they wear gloves, sunscreen, and appropriate precautions are taken, so I'm not certain that we're -- what are we -- I'm a little confused here, what we're doing. We're kind of setting guidelines on how they should be used, and ignoring that they could be used, because we know that salons exist that have the lamps right? And so I think that I'm not certain and just want to throw that out for discussion, because that's --

DR. MARKS: I think that can go in discussion Paul. I think we're very clear that if you're going to be safe, use LED lights.

DR. SNYDER: But then we're not going to bring that forward to say that's safe or unsafe? So we're going to say it's unsafe with any UV light source for curing?

DR. BELSITO: No we're not. Actually, in our conclusion we're not saying it's unsafe. We're just saying it's safe with LED lights. I'm very happy with that, because it makes it very very clear. Otherwise, I think it does get a little confusing when we start saying UVA in a salon with gloves and that. I mean, the LED lights are available for purchase and you know, as we know from the information we got, the gels certainly cure more quickly with an LED light, so -- and they're not that much more expensive and they last longer, that salons should just change over to LED lights.

MS. WEINTRAUB: I do think though, it's still important to have in the discussion the importance of using sunscreen and gloves in the case of florescent light.

DR. MARKS: Yes. Yes.

DR. BERGFELD: Any other things? Any other items that need to be discussed or put into the discussion? No? So this is a second? Did I hear a second?

DR. BELSITO: Yeah, I'll second it.

DR. BERGFELD: Anything else? Paul, do you -- are you satisfied or --

DR. SNYDER: Yeah, I'm still, I mean, we had an extra, another sentence that Don didn't read in our conclusion. We just, when we said that hydroquinone is unsafe for use outside of professional salons when nail curing is achieved by UV light and unsafe for use in other leave on products, so I think there was --

DR. BELSITO: Well, I said that, but now that we're not allowing it, only with LED, all we need is unsafe in other leave on products.

DR. SNYDER: Just as long as we capture the unsafe aspect, because I just don't want to ignore that.

DR. BELSITO: Yeah.

DR. SNYDER: Yeah.

DR. BERGFELD: Okay. All right. I wonder if you can re-read the conclusion so we're clear.

DR. BELSITO: So we want it to say in the conclusion that it's unsafe for use with UVA light in a home setting?

DR. SNYDER: I do.

DR. BELSITO: Okay. But since we say that's it safe with use for an LED light, that doesn't make sense. So what you're saying is --

DR. SNYDER: I mean it's a lot; it's different than what we concluded yesterday. To me, I think our conclusion is substantially different than -- I think the overall conclusion is the same. But I think the message that's delivered is different. I think we separated out the professional and non-professional. We said in professional it can be used safely and in the -- there is no safe use in the non-professional setting, other than the LED lights. And so, I'm trying to grasp that.

DR. MARKS: Well, that's why we lit on just saying it's safe for LED lights. Any

other use that can be used it, that can be addressed in the discussion, because if the salon uses florescent lights and they don't use photo- protective, we would not endorse that.

DR. SNYDER: So I guess it's, are they going to go beyond the conclusion to find that in the discussion, that safe use. It's a conclusion, so it should be in the conclusion.

DR. HILL: Yeah, and if you say unsafe with UV light, you're not ruling out LEDs at home, because LEDs are not kicking out UVA.

DR. BELSITO: Yeah, but Paul's point is --

DR. HILL: They're kicking out 405 plus minus ten.

DR. BERGFELD: You could include the wavelengths in your discussion language. So what is the conclusion please?

DR. MARKS: So at least the conclusion that our team proposed is really the change in the second sentence. The first sentence remains the same and the last sentence remains the same. And our second sentence would read very succinct and to the point, hydroquinone is safe for use in the nail uses and as a polymerization inhibitor in artificial nail coatings that are cured by LED light.

DR. BELSITO: But would you add, but not by UVA light?

DR. HILL: You could.

DR. MARKS: I would be interested in David Steinberg's comment on this because yesterday you did an elegant presentation of the, both the physics and the technical aspects.

DR. BELSITO: I'm just concerned that the consumer is not going to understand the difference between LED and UV, and at least if you point out that there are different types of lights, they might be more understanding. Because when you google, as Dan and I both did, when you google UV nail lamps, you get both UV and LED pop up with that search, and when you google LED, you get both UV and LED. So even the internet engines don't seem to have it straight.

DR. MARKS: I just want to make sure there's not a confusion between -- I don't have a problem with saying, and unsafe with UV light, but then, if you say that, you would have to go on and say, unsafe in UV light without photo protection.

DR. BELSITO: Yeah.

DR. MARKS: So we get back to an extended --

DR. BELSITO: But then you get back to the home versus salon use.

DR. MARKS: Yeah.

DR. LIEBLER: It's just, my problem with that is that it makes the conclusion unnecessarily complex.

DR. MARKS: Yes.

DR. LIEBLER: The thing that I like that's really elegant about the language that you initially proposed is that it's very clear and it says what's safe. The discussion I think, gives us ample opportunity to explain what the differences are between UV and LED based devices as used, and the differences between home and professional settings, and I think that

can be developed well. I respect Paul's point about our question of will somebody ready beyond the conclusion into the discussion.

DR. SNYDER: But I think the point is that you're going to have to conclude in the discussion that UV based curing is not safe and therefore, that's a conclusion and it's not brought forward in our conclusions, so that, to me, we're -- I full understand the discussion. We'll address it and deal with it, but there has to be a conclusion about UV sources to cure and harden, and if there is, it should be brought to the conclusion, in my opinion. Until yesterday, LED was not even on our radar. It was not even in discussion. So I think that we are kind of completely ignoring all the previous discussions we had about the issue with UV light source. And so I'm just a little surprised by that.

DR. BERGFELD: David, do you want to clarify?

SPEAKER: Yeah, I would like to, I, personally, I'd like the conclusion to be as simple as possible, because it eliminates a lot of the confusion. I'd like the discussion and the discussion part to go through the various professional versus non-professional use and one of the thoughts that came up was maybe saying in the conclusion that use of curing the nail gels which contain the hydroquinone or the MEHQ when we get to that one, should be cured for home use using LED lights only. Would that make more sense?

DR. BELSITO: Would we have to put the restrictions that we want for salon use of gloves or photo protection?

SPEAKER: Wouldn't you be covering that in the discussion, the salon use is by trained, licensed professionals who should in that training be made aware of this, as opposed to having it in the conclusion for the home use?

DR. BELSITO: Well, our conclusion is not just about home use. Our conclusion is about cosmetic use that can occur both in salons and in the home.

SPEAKER: We've not taken the approach --

DR. BERGFELD: I want to ask David, excuse me, Jim; do you want to ask David any specific questions?

DR. MARKS: No.

DR. BERGFELD: Okay. Go ahead Ron. What if we were to put in the discussion, or in the conclusion, just tossing this out, with LED light, and in parenthesis, see discussion.

DR. BERGFELD: No.

DR. LIEBLER: Parenthesis, call Ron Hill, here's his number. Sorry Ron.

DR. HILL: I don't mind having humor at my expense, but I think you're stuck between either, you stick with the really simple conclusion or you compound the conclusion, and I don't mind the compounded one. I think that's the right answer. Is LED at home and then exactly what Paul said in terms of the salon use and we're done, and it isn't as simple as people want it to be, but it gets it.

MS. WEINTRAUB: I'm wondering if there's a way to sort of merge the two as well, because I think what Dr. Mark's group tried to do was focus on the type of light as

opposed to the location of the application, but I think the phrase that you said which I think is important and everyone agrees with, is sort of just another perspective on the conclusion, so if we add to that the phrase that you mentioned, what's unsafe to what is safe in terms of LED, does that do it, or is it because it's not exact corollaries? Is that the problem?

DR. BELSITO: Well I'll read you what we suggested, okay? So we'll get rid of the brief discontinuation, the brief discontinuance used from the skin and safe for use in nail adhesives and as polymerization inhibitor in artificial nails that are cured with UV light when photo-protective materials, for instance, gloves, sunscreen, for the skin are used in a professional setting, or when curing is achieved by LED light in professional and non-professional settings. Hydroquinone is unsafe for use in non-professional settings in which curing is achieved with UV light and unsafe for use in other leave on products.

MS. WEINTRAUB: What if we add that last sentence? Do you think it's confusing?

DR. BERGFELD: It's very confusing.

MS. WEINTRAUB: One other question I had and I don't think there was -- I don't recall seeing any data -- has there been any survey in terms of what type of protective measures are taken in salons when there is -- you know, are people are actually having sunscreen and gloves or what, we don't even know?

DR. BERGFELD: No.

DR. BELSITO: No.

MS. WEINTRAUB: Right.

DR. BERGFELD: It's not practical. It's not used. Not even mentioned to them. Jim, do you have a --

DR. SNYDER: I'm not hard and fast on this, because we're sending the correct message; it's just that I think we're leaving a not insignificant message out of the message, with the UV light source. We're kind of skirting that when prior to yesterday and learning about the light sources, we would have had a very different --

DR. MARKS: Well, that's why it would be issues as another tentative amended report, so we have a few months to think about it more and say if we want to change the conclusion --

DR. BELSITO: Yeah, but we better get this conclusion right, because if we amend with just LED and change our mind in three months, it goes out again.

DR. MARKS: Exactly.

DR. BELSITO: So do we just go with LED? I mean, I see Paul's point, because --

DR. SNYDER: It also goes to the fact, excuse me, it also goes to the fact that David shared with us yesterday, that they do use these large UV lamps where they can put their -- put all of their ten fingers in and get it all cured at once rather than the small --

DR. BELSITO: Yeah that's where our -- drying position.

SPEAKER: That's drying; excuse me, that's drying lacquers which do not

contain MEHQ and HQ. That's just strictly heat to dry.

DR. MARKS: So I guess one of the things, if we go in the real world and even though we recommend and we'll say that in the discussion, photo protective materials -- if that's not being done, it's sort of like us making a recommendation in our conclusion, which has no real world relevance. Whereas if we say, use only LED light, that's what's safe; use only that, put in.

DR. BELSITO: But our goal is not to make conclusions that do or do not have real world relevance. Our goal is to make conclusions that provide a safe environment for consumers to use products. And a nail salon reading this has two choices. If they are currently curing these gels with UV light, they should either purchase gloves or sunscreen. Or if they don't want to do that, then they purchase LED lights. Clear. Well, what we hear is it takes two minutes to cure with a UV lamp, it takes 30 seconds. These people want to move customers in and out, and they'll probably switch, but at least we've made the point on safety that if you want to continue to use your old UV lamp, then to do it safely in a professional setting you need to start providing gloves or sunscreen.

DR. MARKS: So let me read Lillian's conclusion, because she's sitting right --

DR. SNYDER: Just one other comment, I mean, we have a whole large section of the document talks about UV nail lamps, so again, we're kind of skirting it I think if we're not going to address that.

DR. MARKS: So let me read what Lillian wordsmiths here. "Safer use in (inaudible) and as a polymerization inhibitor in artificial nail coatings that are cured by LED light or by UV light when photo-protective materials, for example, gloves and sunscreens for the skin are used in professional setting."

DR. BELSITO: Right, that's what we said.

DR. LIEBLER: And?

DR. BELSITO: Safe for home use when cured by LED light, but not UV light.

SPEAKER: Isn't that thing redundant?

DR. BELSITO: No, I mean it's restricting it only to professional settings now. It's back to what we had originally.

DR. GILL: Yeah, my next sentence takes care of that.

DR. BERGFELD: Any comments Jim? Tom?

DR. SHANK: I guess, kind of can maybe we weigh the other extreme as, why don't we have it just for everybody, you need to -- you know, just get rid of the UV light. I mean, what you're saying with the UV light is if we put a sunscreen on, we'll decrease the amount of cancer. I mean, it doesn't stop it. It just decreases the risk. So why not use the new bulbs, so that there's zero risk.

SPEAKER: It's not a new bulb. It's a new lamp. You can't just substitute bulbs. It doesn't work that way.

DR. SLAGA: If we were assured that even under professional they would use the protective thing but we're not and I agree that LED light is the best approach.

DR. BERGFELD: So are you suggesting that it should be the simplified conclusion, or the added inclusion of photo protection?

DR. SLAGA: I'd like to simplify it and put everything else in the discussion.

DR. BELSITO: I guess in a sense it's like what we did for formaldehyde methylene glycol where we saw that yeah, if you use the proper ventilation, you could reduce the formaldehyde (inaudible) and it could be safely used, but in practice in fact, that wasn't happening.

SPEAKER: Right.

DR. BELSITO: I'm okay with that. I mean we can have a big long discussion about that it theoretically could be used but the reality is that the typical nail salon is not doing it. I have three daughters who occasionally get nail gels and I've asked them. They've been advised and they never get gloves or coating.

DR. SLAGA: So it's important for us to all see the discussion and how do we deal with that, that's --

DR. BELSITO: I'm okay with that.

DR. SLAGA: Yeah.

MS. WEINTRAUB: Also practically, I'm sure most salons have no idea what kind of light. Like someone working a salon doesn't know what kind of lights they have either.

SPEAKER: I would slightly disagree. There's a lot of time and effort being spent by the professional beauty association and nail manufacturer's council to education the nail salons in all aspects of the nail treatments, whether they be polishes or nail extensions, or cleansing or, you know you can go down the whole list of all the services that are offered there, and that these training manuals are in English, Spanish and Vietnamese. There are videotapes that are available. There are CDs that are on the websites. They are spending a significant of effort to continuing to upgrade the nail salon industry, including such areas as ventilation, because you do have fumes that come off when you use conventional lacquers and things like this. So yes, industry is aware of this. Industry has been working on this and spending considerable time to educate them. If you go to any of the PBA shows, you will see actual demonstrations of safe use of products there, for the visiting nail salon techs.

MS. WEINTRAUB: I think that's a positive thing but there is a huge disconnect between what you described and what's in most salons across the country.

DR. BERGFELD: Any other comments, and if we don't have any, I'm going to have Jim summarize what we've actually done here.

DR. MARKS: We, I think, we now are at a consensus. And I say consensus because I'm not sure we're unanimous at this point, that we'll issue another tentative amended report with a change conclusion. And the everything in this report has, since we've reopened it, it is around the safety and nail adhesives and the artificial nail coatings and that sentence will read, hydroquinone is safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by LED light.

DR. BERGFELD: And then, what will go in the discussion?

DR. BELSITO: Hydroquinone is unsafe for other leave on products.

DR. MARKS: Yes, exactly. Yeah, the first sentence and last sentence remains the same. It's just that one reference to nail coatings. And in the discussion will be what we've discussed for the last however long we have, and yesterday, about UV lights and the potential, although it's just a few case reports but the alert of the possibility of introducing skin cancers and the use of proto-protection.

DR. BELSITO: And we can go in the discussion that it potentially could be safely used but LED seems to be a more effective technology, and therefore we're just simply eliminating UV as a potential way of curing.

DR. MARKS: Right. And the good thing is we don't compromise the end product by recommending LED light.

SPEAKER: I just have one thought or suggestion and that is that the last sentence, that hydroquinone is not safe for other leave on applications -- shouldn't that go right after the first sentence in where we said it was safe for discontinuous use and then just move the nail polish and nail adhesives to a separate conclusion?

DR. BELSITO: No. Because those are leave-ons, so I think we need to say that they're safe in the nails and then, but for anything else that's leave on, they're not safe, so I think the order is correct.

DR. BERGFELD: Okay.

SPEAKER: Okay, thank you.

DR. BERGFELD: Any other discussion points, because we're going to move the question now?

DR. BELSITO: No.

DR. BERGFELD: Seeing none, I'm going to call the question. All those in favor of the conclusion that was read? Thank you, unanimous. Now we're moving on to the next ingredient which has some of the similar problems, that hydroxyanisole, Dr. Belsito.

DR. BELSITO: Okay, so let me try to wing this based upon the discussion that we just had here.

DR. MARKS: Just make it a simple conclusion.

DR. BELSITO: So, CIR expert Panel concluded that para-hydroxyanisole is safe for use in artificial nail coatings when cured with LED light, and unsafe for use in all other cosmetic products due to the de-pigmentation potential.

DR. MARKS: Second.

DR. BERGFELD: Any other discussion? I would assume that the discussion that we had for the hydroquinone would appear in this one as well?

DR. BELSITO: Yes.

DR. BERGFELD: All right. Seeing none, I'll call the question. All those in favor of safe? Thank you.

Amended Safety Assessment of *p*-Hydroxyanisole as Used in Cosmetics

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The 2014 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

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ABSTRACT

The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed *p*-hydroxyanisole to address the new uses in nail gels reported by industry, which require curing by light. The Panel reviewed the relevant animal and human data related to this ingredient, as well as data on the possible adverse effects of using nail products that require curing by light. The Panel concluded that *p*-hydroxyanisole is safe for use in nail adhesives and in artificial nail coatings that are cured by LED light as a polymerization inhibitor. *p*-Hydroxyanisole is unsafe for use in all other cosmetic products because of the potential for dermal depigmentation.

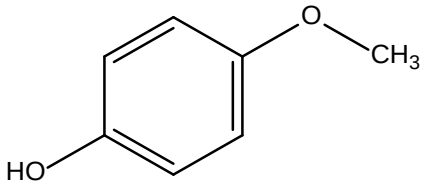
INTRODUCTION

This is an amended safety assessment of *p*-hydroxyanisole. Use in artificial nail coatings and adhesives that requires curing using a light source has been identified by industry as a new use and represents a change from the previous CIR safety assessment of this ingredient.[1] *p*-Hydroxyanisole and hydroquinone are used interchangeably or in combination as polymerization inhibitors in nail gels and adhesive products. Hydroquinone is the focus of a separate amended safety assessment addressing this new use.[2]

p-Hydroxyanisole (CAS No. 150-76-5) is defined in the *International Cosmetic Ingredient Dictionary and Handbook* as the substituted phenolic compound that conforms to the formula in Figure 1.[3] It is currently reported to function as an antioxidant, fragrance ingredient, and reducing agent. *p*-Hydroxyanisole is a common name for 4-methoxyphenol.

In 1985, the Panel concluded that *p*-hydroxyanisole is unsafe for use in cosmetics due to dermal depigmentation.[4] The summary of that report is provided below. The use categories in this safety assessment included dermal products but did not include nail products.

This report presents new data pertinent to the new use in nail products, as well as new toxicity data that have become available since the initial review of this ingredient.



p-Hydroxyanisole

Figure 1. *p*-Hydroxyanisole

SUMMARY FROM 1985 *P*-HYDROXYANISOLE SAFETY ASSESSMENT

p-*Hydroxyanisole is a waxy solid prepared by the reaction of hydroquinone with dimethylether.*[4] *When used for cosmetic purposes, the compound typically has a purity of 99.5%. Impurities consist of hydroquinone dimethylether (about 0.1%) and an unidentified compound with a "high boiling point" (about 0.4%).*

p-*Hydroxyanisole has acidic properties characteristic of phenols. It binds by hydrogen bonding to itself, water molecules, and various proteins. The compound is readily oxidized and can undergo a variety of reactions, including alkylation, halogenation, and other substitutions on the aromatic nucleus. Peak absorbance of UV light by* p-*hydroxyanisole occurs at about 340 nm.*

Noncosmetic uses of p-*hydroxyanisole include applications as an antioxidant, as a polymerization inhibitor, as a chemical intermediate, and as a stabilizer. It is used in cosmetics as an antioxidant.*

Data submitted to the FDA by cosmetic firms participating in the voluntary cosmetic registration program indicated that this antioxidant was used in 31 cosmetic products during 1981 at concentrations of >0.l% to 1.0% (8 products) and ≤ 0.1% (23 products). Cosmetic formulations containing this compound, such as eye makeup, sachets, makeup bases, and skin care preparations, are normally applied to or have the potential to come in contact with the skin and eyes.

Results of numerous studies indicated that p-*hydroxyanisole is a skin-depigmenting agent. Unpublished data strongly suggested that this cosmetic ingredient was a depigmenter of the skin at concentrations approximating those used in cosmetic products. Skin depigmentation was observed in guinea pigs exposed 6 weeks to 0.25% of the antioxidant and in guinea pigs exposed 6 months to 0.5% and 1.0%* p-*hydroxyanisole. Exposure for 6 weeks to 0.1% produced depigmentation at the site of skin application in 1 of 6 guinea pigs. Associated with the skin-depigmenting action of this compound was a selective cytotoxic effect on the melanocyte. The melanocytotoxic effect was dependent upon both antioxidant concentration and duration of exposure. No cytotoxic effects on human melanocytes or morphological changes in human keratinocytes were observed following a 45-minute exposure to either 10^{-2} M or 10^{-3} M* p-*hydroxyanisole in disperse tissue culture. However, whole epidermis (human) exposed in vitro to 10^{-l} M for 1, 5, and 24 hours had extensive damage to melanocytes*

and keratinocytes. Concentrations as low as 10^{-8} and 10^{-9} M were cytotoxic to guinea pig melanocytes in vitro. These latter concentrations are lower than p-*hydroxyanisole concentrations typically used in cosmetics.* p-*Hydroxyanisole given orally to rats and mice caused induction and inhibition of various enzymes in the esophagus, nonglandular stomach, and microsomal fraction of the liver. In vitro studies with isolated rat liver suggested that the antioxidant interferes with ribonucleic acid synthesis, protein synthesis, and mitochondrial respiration. The compound inhibited growth or was microcidal in studies with bacteria and fungi. Chromosomal aberrations in plants and denaturation of DNA in bacteriophage were observed following* p-*hydroxyanisole exposure.*

p-*Hydroxyanisole was absorbed by guinea pig skin in vitro. Oral doses of the antioxidant were excreted by rabbits primarily as conjugates of glucuronic and sulfuric acids; small amounts were demethylated and excreted as hydroquinone.*

The acute oral LD_{50} of p-*hydroxyanisole in rats was estimated as 1630 mg/kg. The oral LD_{50} in rats of 50%* p-*hydroxyanisole in corn oil was 740 mg/kg. The acute LD_{50} of the antioxidant when administered by intraperitoneal injection was 250 mg/kg and 430 mg/kg for mice, 730 mg/kg for rats, and 720 to 970 mg/kg for rabbits.*

Undiluted p-*hydroxyanisole was a severe skin and ocular irritant in rabbits; a single exposure to the compound produced extensive skin edema and necrosis and cornea1 injury. Minimal irritation was observed in the eyes of rabbits exposed to a 0.1% aqueous solution of the antioxidant and on rabbit skin treated with 5%* p-*hydroxyanisole in sweet almond oil. Skin sensitization to* p-*hydroxyanisole (0.5 M and 1.0 M) was observed in guinea pigs in both the "maximization test" and the "Freund's complete adjuvant test." Cross skin sensitization of guinea pigs to hydroquinone (1 M) and* p-*hydroxyanisole (3 M) was also reported. No photosensitization was observed in guinea pigs exposed to both* p-*hydroxyanisole (0.1% and 1.0%) and UV irradiation. Application of a water-oil emulsion containing 1.0%* p-*hydroxyanisole to the skin of guinea pigs for 30 days produced hyperemia, edema, and desquamation. Skin irritation and depigmentation were observed in guinea pigs and mice treated for 4 weeks with 20%* p-*hydroxyanisole in petroleum jelly and in guinea pigs treated 1 to 6 months with antioxidant concentrations of 0.25 M or 1.0 M in acetone, 0.5 M in dimethylsulfoxide, and 5.0 or 10.0 percent in hydrophilic ointment. Application of 20%* p-*hydroxyanisole in lanolin base to guinea pig skin for up to 6 months and to hamster cheekpouch 3 times a week for 45 days caused encroachment of basal cell pseudopodia into the dermis. In addition, the hamster cheekpouch had erythema, hyperkeratosis, epithelial hyperplasia, bullae, and muscular degeneration. Rats and rabbits fed diets containing 5% and 10%* p-*hydroxyanisole and dogs fed up to 12 g daily for 2 weeks had growth inhibition and changes in hematological parameters and organ weights; no other significant toxicological effects were noted.*

p-*Hydroxyanisole was nonmutagenic in the Ames assay with and without metabolic activation. No local toxic changes or tumors were observed following application of 5% and 10%* p-*hydroxyanisole in acetone to the skin of mice and rabbits in a lifetime study. The antioxidant (13.1% in benzene) was inactive as a tumor promoter when applied for 20 weeks to the 7,12-dimethylbenz(a)anthracene (DMBA)-initiated skin of mice. Application of a bleach cream containing 5%* p-*hydroxyanisole and a water-oil emulsion containing 25 percent of the antioxidant to the skin of pregnant rats produced embryotoxicity but not teratogenicity.*

In clinical studies, p-*hydroxyanisole at a concentration of 2.0% in petrolatum and 2.0% in sweet almond oil was, at most, minimally irritating to the skin. A 5.0% concentration of the antioxidant in sweet almond oil was both nonirritating and nonsensitizing to humans. Several cases were reported in the literature of individuals who developed skin depigmentation following exposure to products containing* p-*hydroxyanisole or following occupational exposure to the antioxidant.*

CHEMISTRY

p-Hydroxyanisole is a substituted phenol that is reported to function as an antioxidant, fragrance ingredient, and reducing agent in cosmetics.[3] This aromatic ether is a waxy solid prepared by the reaction of hydroquinone with dimethylether.[4] As noted in the original report, *p*-hydroxyanisole has acidic properties characteristic of phenols. It interacts by hydrogen bonding to other molecules of *p*-hydroxyanisole, water molecules, and various proteins. The compound is readily oxidized and can undergo a variety of reactions, including alkylation, halogenation, and other substitutions on the aromatic nucleus. Peak absorbance of UV light by *p*-hydroxyanisole occurs at about 340 nm.

USE

Cosmetic Use in Nail Products

Data on ingredient use are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP).[5] In 2014, it was reported by the VCRP that *p*-hydroxyanisole is used in 3 basecoats and undercoats and 2 nail extenders. A survey was conducted by the Personal Care Products Council (Council) of the maximum use concentrations for this ingredient.[6] No uses were reported for *p*-hydroxyanisole by the Council. An internet search for "*p*-hydroxyanisole" and "cosmetic ingredients" showed that there are more nail gel products available on the market than those reported to either the VCRP or the Council. While a full inventory of the results was not taken, multiple professional and home-kits were available for sale that included nail gels containing *p*-hydroxyanisole requiring UV curing. Because industry is not required to register products with the VCRP, the database represents a sampling of cosmetics that are available on the market.

The *p*-hydroxyanisole content was reported to be 223.2 ppm (0.02232%) for soft nail gels for coloring, 142.6 ppm (0.01426%) for soft gel top coats, 426.3 ppm (0.04263%) for hard gel no cleanse top sealer, and 147.2 ppm (0.01472%) for hard gel sculpting before curing.[7]

p-Hydroxyanisole, alone or in combination with hydroquinone, serves as a stabilizer or inhibitor that stops the reaction in the liquid component of 2-component methacrylate artificial nail systems.[8] When used as a stabilizer/inhibitor the maximum concentration for hydroquinone or *p*-hydroxyanisole is 200 ppm (0.02%). After mixing 2 parts liquid to 1 part powder the final concentration is reduced to approximately 133 ppm (0.0133%).

When used as a nail adhesive, a brush is wetted in the liquid component which contains the stabilizer(s) and acrylate monomers. The wetted brush is then dipped into the powder which contains the initiator to produce an "aspirin sized" bead. The liquid:powder ratio is approximately 2:1. The 2 components are mixed into a "slurry bead", which is applied to the center of the nail plate and then shaped. The polymerization is complete in 5-15 min. Contact is to the keratin of the nail plate and not to the skin or cuticle.[8]

p-Hydroxyanisole is added to the monomer as oligomer (e.g., dimer, trimer, tetramer) preparations during manufacturing to prevent polymerization.[1] This preserves the integrity of the monomers or oligomers until they are used to produce polymers or other derivatives. For polymerization to occur, the inhibitors must either be destroyed or inactivated. Some *p*-hydroxyanisole is destroyed during polymerization (using light) and any residual inhibitor is enclosed in the hardened polymer. Nail polish gels, containing *p*-hydroxyanisole, alone or in combination with hydroquinone, are cured using nail lamps with either a UVA light source or a LED light source (in the visible light range).[9]

In a guide to using UV gel enhancements, the manicurist is instructed to carefully prepare the nail bed by removing the cuticle from the area of the nail where the product is to be applied.[10] If the cuticles are not cleared, natural oils and moisture under the nail gel or the enhancement adhesive prevents the product from adhering to the nail and the product will peel off, creating an unsatisfactory result.

The nail gels and adhesives are removed by the application of a solvent (that is provided on a presoaked pad) for 15 to 30 min.[11,12]

p-Hydroxyanisole is listed in Annex III of the European Council Directive with the following precautions and restrictions: only for use in artificial nail systems, maximum concentration of 200 ppm after mixing, for professional use only, avoid skin contact, and read use directions carefully.[8]

Health Canada[13] has restrictions for the use of p-Hydroxyanisole in cosmetics. This ingredient is permitted at concentrations equal to or less than 0.02% (after mixing), for professional use only, in artificial nail systems. Additionally, the inner label and the outer label of the cosmetic shall carry statements to the effect: "For professional use only", "Avoid skin contact", and "Read use directions carefully."

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Dermal/Percutaneous

The permeability coefficient, for skin and receptor fluid, of *p*-hydroxyanisole (35 mg/mL in water; 469 µL/cm^2) was 9.39 x10^{-3} cm/h; the flux at 10 min was 283.0 µg/cm^2/h and at 60 min was 223.0 µg/cm^2/h.[14] The experiment was performed in accordance with the Occupational Safety and Health Administration (OSHA) procedures. [Federal Register Vol. 69, No. 80] These procedures include the use of only abdominal cadaver skin that is either dermatomed or heat separated using a minimum of 3 donors and 6 replications. The dose applied to each skin replicate was ''infinite", which provides an undepletable reservoir.

There was low systemic exposure to *p*-hydroxyanisole (2%) when administered to human subjects (n=8) in a cream that also contained tretinoin (0.01%; a prescription drug) twice/day for 21 days.[15] The test material was administered to 400 cm^2 of the back. After the last treatment, the subjects received a single topical application of 2% *p*-hydroxyanisole/0.01% (^{3}H)tretinoin solution. After 12 h, the radiolabelled dose was removed and treatment with the non-radiolabelled 2% *p*-hydroxyanisole/0.01% tretinoin solution was continued for 7 days. Plasma was analyzed for *p*-hydroxyanisole by gas chromatography/mass spectrometry (GC/MS). The C_{max} at 2 h for *p*-hydroxyanisole was 9.92 ± 7.48 ng/mL with AUC_{0-12} 33.43 ± 14.30 ng h/mL.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

In a dermal teratology study in New Zealand White rabbits (n not provided), there were no effects observed that could be attributed to treatment in rabbits topically administered a depigmentation cream containing *p*-hydroxyanisole (40 mg/kg; 440 mg/m^2) and tretinoin.[16] In a repeat of this study of this depigmentation cream containing only *p*-hydroxyanisole, the no observed effect level (NOEL) for teratogenicity was 4 mg/kg (0.22 mg/m^2). The authors stated that this is in the range of the maximum possible human daily dose. The maximum human daily dose is defined as the amount of solution applied daily to 5% of the total body surface area. There were no differences among treatment groups in fetal malformation data. The test material (12, 40 mg/kg; 132, 440 mg/m^2 *p*-hydroxyanisole, respectively) was administered dermally to the rabbits. The summary of the study does not provide details on timing, length of study, or the concentration of the low-dose group.

In a study of the same depigmentation cream containing both *p*-hydroxyanisole and tretinoin, it was not teratogenic

in Sprague-Dawley rats (n not provided) when given in topical doses equal to 80 mg/kg (480 mg/m^2) *p*-hydroxyanisole (or 11 times the maximum human daily dose).[16] No further information was provided about this study.

In another study of a depigmentation cream containing *p*-hydroxyanisole (2%) and tretinoin (0.01%), the maternal, neonatal, and developmental no observed adverse effects levels (NOAEL) for *p*-hydroxyanisole were 40 mg/kg/d (0.240 mg/cm^2/d).[17] *p*-Hydroxyanisole (0, 0.6, 2.0, 6.0 mL/kg/d; 0, 0.072, 0.240, 0.720 mg/cm^2/d) was administered dermally to 10% of the body surface of pregnant Crl:CD (SD) Br rats (n=25/sex) for 6 h/day 7 days/week (assumed through entire pregnancy). At post-natal day 4, the litters were culled to 8 pups. At age 8-13 days, pups were randomly selected for physical and functional development (n=10/sex), and reproductive performance (n=15/sex). The F_1 generation was not treated. Dams in the F_1 generation underwent laparotomy on gestation day 20 and the fetuses were evaluated. F_1 rats were necropsied.

There were no deaths in any group. Clinical signs in the F_0 rats were very slight to severe erythema (first noted on study day 8), very slight to moderate edema, including fissuring (especially at the high dose), desquamation (first noted on study day 13), eschar, and focal eschar and exfoliation (first noted on study day 14) at the treatment sites. Vocalization was observed on application of the test material in mid- and high-dose groups. High dose animals exhibited decreased body weight on gestation day 20 and lactation day 1, in mean body weight gain during gestation, and in food consumption during gestation days 9-12. Increased food consumption in the first few days of lactation was observed in those animals before they were killed for humane reasons.

Six dams in the mid- and high-dose groups failed to deliver by post-mating day 25, as compared to 2 each in the control and low dose groups; all but 1 of the controls were found to be gravid. Four high dose females had total litter loss between lactation days 1 and 5. Gross necropsy revealed reddening, thickening and scabbing of skin at treated sites in the F_0 dams.

Clinical signs in the F_1 rats were only observed at the maternally toxic high dose. There was increased pup mortality, decreased pup body weight, and an increased incidence of clinical signs. Clinical signs in the high dose pups included small size, hypoactivity, cool to the touch, and paleness in appearance.

There was reduced F_1 pup survival and a higher rate of missing or cannibalized pups in high dose litters after postnatal day (PND) 1. There was an increased incidence of F_1 pup clinical and necropsy findings. Balanopreputial separation and vaginal patency were unaffected by treatment. Auditory startle testing on or about PND 21 and 60 revealed no treatment-related effects. Motor activity (total and ambulatory) measurements were made on or about PND 60 and there was no effect of treatment on total or ambulatory counts. Testing in the water maze was initiated between PND 20-23 and between PND 57-62 and evaluated; no effect of treatment on swimming ability, learning and memory was demonstrated. Estrous cycling in F_1 females and reproductive performance in F_1 animals were unaffected by treatment. Gravid uterine weights and the fetuses were also unaffected.

In F_1 pups found dead or euthanized, gross findings in the high dose group included absence of milk in the stomach, renal papilla not developed or not fully developed and/or distended ureters or urinary bladder. One external malformation (anury) was noted in 1 animal in 1 litter. At the low dose, 1 pup was found to have the renal papilla not fully developed. In F_1 euthanized surplus pups, high dose animals were again noted with the absence of milk in the stomach, and 1 litter had pups in which the renal papilla was not developed or not fully developed and/or ureters or urinary bladder were distended. In the high dose group, there was 1 pup in 1 litter with a hemorrhagic ring around the iris. In F_1 adults, no findings were seen that could be attributed to treatment.[17]

GENOTOXICITY

In Vivo

No genotoxic effects were observed when Sprague-Dawley rats (n and sex not specified) were dermally administered *p*-hydroxyanisole (4, 12, 40 mg/kg in ethanol) in a depigmentation cream for 6 months.[18] No further details were provided.

CARCINOGENICITY

p-Hydroxyanisole (2% in feed) was carcinogenic to the forestomach of male and female F344 rats (n=30/sex) when administered for 104 weeks.[19] Histopathological findings included atypical hyperplasias (male, 67%; female; 37%), papillomas (50%; 23%) and squamous-cell carcinomas (77%; 20%) in the forestomach. The body weights as well as the liver and kidney weights were reduced for both sexes in the treatment group compared to controls.

p-Hydroxyanisole (0, 0.4% in feed) was carcinogenic to F344 rats (n=30-31) when administered for 104 weeks.[20] An increase of forestomach papillary or nodular hyperplasia incidence as compared to the control group was observed. There were no incidences of glandular stomach submucosal hyperplasia or adenoma observed. The final average body weight of the treatment group was lower than the controls. Relative liver and kidney weights were similar between the 2 groups.

In a second study, F344 rats were pretreated with *N*-diethylnitrosamine, *N*-methylnitrosourea, 1,2-dimethylhydrazine, or *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine for 2 to 4 weeks, and then fed a diet containing *p*-hydroxyanisole (0, 0.08%, and 0.4%) for 24 to 26 weeks.[20] There were increased incidences of forestomach papillary or nodular hyperplasia and papilloma in the high-dose group. There were no additive or synergistic effects seen in the groups

receiving a combination of chemicals.

In a synergistic test where *N*-methyl-*N*'-nitro-*N*-nitrosoguanidine- (MNNG; 150 mg/kg) was administered to male F344 rats (n=15) in a single dose followed by *p*-hydroxyanisole (0, 0.25%, 0.5%, 1.0%, 2.0% in feed) for 51 weeks, *p*-hydroxyanisole did not increase the incidence of either papillomas or squamous cell carcinomas caused by the prior administration of MNNG.[21] There was no increase in MNNG-initiated forestomach carcinogenesis caused by the *p*-hydroxyanisole. Increased epithelial damage and hyperplasia in a dose-dependent manner in the forestomach epithelium was observed. The control rats (administered *p*-hydroxyanisole but not MNNG) had reduced body weights in a dose-dependent manner and increased relative kidney and liver weights. All rats in the 2% *p*-hydroxyanisole, without MNNG pretreatment, had large forestomach ulcers without tumor formation.

IRRITATION AND SENSITIZATION

Irritation

Dermal – Non-Human

Dermal administration of *p*-hydroxyanisole (0, 0.6, 2.0, 6.0 ml/kg/d) to Crl:CD (SD) Br rats (n=25/sex) for 6 h/day 7 days/week (assumed through entire pregnancy) resulted in extreme irritation at the application site.[17] The dams and offspring in the high-dose group were killed within the first week of lactation because of the resulting irritation.

When *p*-hydroxyanisole (5% in propylene glycol/ethanol, 50:50) was dermally administered to multiple sites of the backs of Yucatan miniature pigs (n=2), *p*-hydroxyanisole was rated as mildly irritating.[22] The test substance was administered twice daily, 7 days/week, for 90 days. Microscopic examination of biopsies of the test area showed reduction in pigment and number of melanocytes.

Sensitization

Dermal – Human

In multiple human repeated insult patch tests (HRIPT) of nail products, there were no signs of potential cuticle irritation or allergic contact sensitization (Table 1).[23-34] The test materials were administered to a fingernail of the subjects and removed by wiping with a proprietary remover solution after 10 minutes 3 times per week for 9 applications. The nail gels were not dried using a UV nail lamp. Two weeks later, the test material was administered to the same fingernail in the same manner. The amounts of *p*-hydroxyanisole were not provided. The inhibitor in these gels can be hydroquinone or *p*-hydroxyanisole or some combination of these ingredients.

NAIL LAMPS

There have been several studies on the potential effects of using UV and LED nail lamps to dry artificial nail coatings. This is an overview of these studies as well as other information pertaining to using these nail products.

UV lamps are used to cure nail gels, acrylic nails, and nail fill-ins, and to dry traditional nail polish and UV top sealers/topcoats.[41]

The UV nail lamps produce light mostly in the UVA-1 range with little UVA-2, and there is virtually no UVB or UVC radiation emitted.[42] UVA-1 is the least erythemic and photocarcinogenic range in the UV spectrum. The bulbs in UV nail lamps have internal filters to eliminate UVB.[43] The UV bulbs were also reported to emit in the 390-420 nm range.[4]

Estimates of exposure to UV light duration per visit to a professional nail salon vary with the specified procedure and number of applied acrylic coats. In 2010-2011, over 87% of professional nail salons reported using UV nail lamps.[44] Typical client usage is 1–4 times/month for 2 min or less per visit.[43] Another researcher stated that typical salon exposures are 10 minutes or less per hand and with exposures occurring only twice per month.[45]

An instructional pamphlet for the application of nail polish directs, that in the course of applying a base coat, color coat, and top coat, the polish is to be cured for 30 sec for each coat using the proprietary UV light (for a total of 90 sec) or for 1min, 2 min, and 3 min, respectively for a total of 6 min using another UV light.[46]

Typically, 3 or 4 separate thin coats of nail gel are applied and cured for 3 min each coat to achieve the desired results.[41]

In a study of 2 UV nail lamps (for salon use; each from a different nail product company) cumulative exposure measured as minimal erythema doses (MED) were low.[47] However, measured in J/m^2, cumulative exposures were equivalent, in less than 10 min, to the recommended limit of 30 J/m^2 for 8 hours of outdoor work and recreation by the International Commission on Non-Ionizing Radiation Protection. Dosimeters that measure DNA damage caused by UV irradiation of viable spores were used to make these measurements. Manufacturer's instructions for curing acrylic nails using UV light were followed. It was assumed that the nails would be refinished every 3 weeks or 17 times per year; the dosimeters were exposed for the equivalent of the cumulative dose that would be expected over 1 year of using such lamps. The UV lights yielded 0.6 MED/h for phototype II skin. The curing time recommended by the manufacturers yielded from 0.06 to 0.09 MED per treatment and yearly cumulative exposures estimated between 1.1 and 1.5 MEDs. Total exposures were estimated to be 285 and 386 $J/m^2/y$ from 15 and 22.5 J/m^2 per nail session, respectively (Table 2).

In the same study, a spectrometer calibrated to measure absolute UV irradiance was used to compare solar radiation with radiation emitted from the lamps. The spectra indicated that the lamps emitted 4.2 times more energy ($\mu W/cm^2/nm$)

than the sun (UV Index=6) in the 355-385 nm range. The authors recommended the use of full spectrum sun block to the hands 30 minutes before exposure.[47]

In an evaluation of 6 UV nail lamps, the authors concluded that total exposure following programmed times and steps, analogous to nail polish application, accumulates to only a small fraction of the recommended practice (RP)-27 permissible daily occupational exposure of UV.[48] The UV nail lamps, submitted by the Nail Manufacturers Council on Safety (NMC), were representative of major US manufacturers; it was not clear if these were lamps for salon, home use, or a combination. They were evaluated for radiant hazards as defined in the American National Standards Institute/Illuminating Engineering Society of North America Recommended Practice-27 (ANSI/IESNA RP-27), the Recommended Practice for Photobiological Safety. Lamps were evaluated at 3 positions: 1 cm above the inner surface, which approximated exposure to the hand; 20 cm directly in front of the box opening; and 20 cm outside the box and 45° above the hand opening.

Three of the devices were fluorescent UV nail lamp systems with 2, 3, or 4 small 9 W lamps. Lamps were of 2 base types with tubes oriented either perpendicular (in the case of the t2-lamp device) or parallel to the fingers of a hand undergoing a procedure. The tubes in the 3- and 4-lamp units were arrayed in an arc-like configuration to irradiate from above and from the sides of the hand while the perpendicular-oriented tubes of the 2-lamp unit were in a planar configuration above the fingertips. The other 3 devices were light-emitting diode (LED)-based with arrays of 6 or 32 LEDs or, in the case of a single finger unit, 1 LED. These LED arrays were mounted in planar configurations oriented generally perpendicular to the fingers in approximately equidistant arcs above the fingertips. The 32 LED devices had 4 of their LEDs oriented in 2 lateral pairs positioned on either side. The entrance aperture of the spectroradiometer was positioned to receive the full intensity expected at each of the 3 different measurement positions chosen to approximate expected intensities to which a user's skin or eyes might be exposed.

Hazard to skin at intended-use distance enabled classification of these devices into Risk Group 1 (low risk for 1 LED lamp tested) or 2 (moderate risk for the other 5 lamps) based on S(λ)-weighted (ie, relative spectral effectiveness-weighted, where S(λ) ranged from 0.2–1.7 μW/cm²) effective UV irradiances that yielded permissible daily exposure durations ranging from 29.8-276.25 min. At 20 cm on center and at 45° from center, UV risk to skin and eyes were within the "exempt" classification. Actinic UV ranged 0.001–0.078 μW/cm² and unweighted near UV (320-400 nm) range was 0.001-0.483 mW/cm². The retinal photochemical blue light hazard and retinal thermal and cornea/lens IR were also exempt. One device using fluorescent bulbs was found to be an aphakic eye hazard slightly rising into Risk Group 1 (low hazard). There were no other photobiological risks to normal individuals. The potential risks estimated in this study are likely to be substantial overestimates of any actual risks in realistic non-occupational use scenarios because such exposures to these lamps would unlikely be a daily occurrence.

The authors noted that improper UVB medical phototherapy, broad band full spectrum-type, narrow-band 311 nm phosphor, and 9 W short wavelength UVC germicidal bulbs easily fit into the UV nail lamps. They expressed concern about potential ocular hazard, even at arm's length, from the UVC bulbs. It was also noted that these bulbs were easily obtainable and inexpensive.[48]

In a survey of 17 commercial UV nail lamps in use at 16 different salons, the amount of irradiance was not consistent among these devices and the irradiance was different for the possible hand placements.[49] UVA irradiance ranged from 0.6-15.7 with an average of 10.6 mW/cm^2. UVA energy ranged from 0-8 with an average of 5.1 J/cm^2. It was calculated that it would take an average of 11.8 exposures (visits applying gel nails at a nail salon) to attain the threshold of the amount of irradiance to cause DNA damage (600 KJ/m^2; 60 J/cm^2). Higher wattage sources correlated with higher UVA irradiance emitted in the lamps. The survey was conducted using a UVA/UVB light meter (280-400 nm) in 5 different positions within each lamp to mimic possible hand positions.

When compared to the UV output of tanning bed lamps, UV nail lamps are vastly less hazardous.[45] The results indicate that a person could in their workplace, once every day, put their hand under a UV nail lamp for 25 min and remain within the permissible daily occupational exposure limits for workers, according to the applicable international ANSI/IESNA RP-27.1-05 standard.

The carcinogenic-effective irradiance from 3 different UV nail lamps used 10 min/week was estimated to be over 250 years.[50] The UV nail lamps tested were reported to have wave-lengths of 365-370 nm. Three common UV nail lamps were tested, but it was not clear if they were professional or home use units. The first contained 9-W UV fluorescent bulbs (36W total). The second contained a 9-W UV fluorescent bulb (9W total). The third contained 6 1-W light-emitting diode UV lights (6W total). The UV nail lamps primarily emitted UVA with no detectable UVB or UVC (lower detection limit of 0.1-0.2 mWm^2). There was a difference in the spectral emission between the UV nail lamps containing fluorescent lamps (1 and 2) and the light-emitting diode lamp (3). The first 2 lamps had peak emission at wavelengths 368 and 370 nm, respectively, whereas the diode lamp had a peak emission at a wavelength of 405 nm.

A concern exists that it is possible to insert an incorrect replacement lamp/bulb into the UV nail lamp (eg, emitting UVB or UVC), which could be harmful to the skin if used.[45] The replacement bulb should be the exact same original manufacturer's UV lamp bulb that was supplied with the UV nail unit when it was purchased. There was also concern that special care should be taken in cases where potential users are taking medications that increase UV sensitivity. People who have been advised against venturing into natural sunlight without proper protection should also be cautious about using UV nail lamps.

Newer nail lamps, introduced in 2012, are manufactured with LED instead of fluorescent bulbs.[11] These bulbs are manufactured so that they emit a narrow range of light, 380-420 nm, encompassing the optimum wavelength for curing nail gels, 405 nm. These bulbs are soldered into place and cannot be easily replaced. Replacement from normal wear and tear should not be necessary since LEDs last for 50k h of use.[51] LED nail lamps are reported to cure nail gels in 30 sec, faster than the 2 min that it takes fluorescent nail lamps.[52]

Risk Analysis

In a risk analysis, it was concluded that 72,709 women would have to use UV nail lamps to cure their nail gels at 8 min/application, every 3 weeks, for 20 years to increase the chance that 1 more individual might develop squamous cell carcinoma on the back of the hand, compared to individuals who were never exposed to UV nail lamps (Table 3).[47] The model UV nail lamp used in this analysis had an unweighted UV irradiance of 115 W m^2 with an erythemally weighted output of 1.58 SED/h. It was not clear if this was for professional or home use. The authors stated that the estimated risk of squamous cell carcinoma could be reduced to virtually zero by wearing fingerless gloves when the hands are being exposed to UV radiation from such lamps.

FINGER NAILS

UVB light did not penetrate the finger nails of a cadaver (n=10).[48] Only an average of 1.65% of UVA light penetrated the nails in this study.

Five women aged 28- 59 years (average, 36.4 years) presented with severe pseudoleukonychia as a result of superficial nail plate desquamation and severe onychoschizia lamellina.[49,50] All subjects reported using gel polish and having difficulty in its removal. To remove the gel, their nails were soaked in acetone for 10-15 min and, in some cases, the polish had to be manually peeled off. All subjects noted that their nails became noticeably thinner after the manicure. All 5 manicures were done professionally in a salon but it is not known if the gel was removed at a salon or by the subject. The brand of nail gel or ingredients of the nail gel were not provided.

To evaluate the impact of gel polish on nail thickness, 1 of the authors measured the thickness of a thumb nail before and after receiving a profession UV light cured nail gel manicure at a salon and removing the gel at home with acetone. Measurements were taken using ultrasound and reflectance confocal microscopy (RCM).

Both ultrasound and RCM showed thinning of the nail plate after the removal of the gel manicure. The ultrasound measured an average thickness of 0.063 cm before the manicure and 0.050 cm after removal. The RCM measured a thickness of 588.90 µm (0.059 cm) and 298.57 µm (0.030 cm), respectively. In all subjects, the clinical appearance of the nails improved with time. For the author, pseudoleukonychia resolved in approximately 3 weeks; onychoschizia and subjective brittleness were still present 5 weeks after removal.[49,50]

Case Reports

Non-melanoma skin cancers were observed on the dorsum of the hands of 2 women who reported exposure to UV nail lamps.[51] The first woman was 55 years old, in good health, and was not taking immunosuppressive medication. She had an indoor occupation and participated in little outdoor recreation. Her family had no history of skin cancer. She had been exposed to a UV nail light twice monthly for 15 years. She presented with an erythematous plaque on the dorsomedial aspect of her right index finger. Biopsy revealed a squamous cell carcinoma.

The second woman was 48 years old, in good health, and not taking immunosuppressive medication. She had an indoor occupation with moderate outdoor recreational exposure to UV. She had no personal or family history of skin cancer except for a previous squamous cell cancer that had been removed from the dorsum the left finger 3 years earlier. She presented with a scaly papule on the dorsum of her right hand. Biopsy revealed a squamous cell cancer. Over the next 4 years, 2 further squamous cell cancers on the dorsum of both hands were treated. She had had exposure to UV nail lights 8 times within a year several years before the first appearance of the skin cancer.[51]

SUMMARY

The Panel concluded in 1985 that *p*-hydroxyanisole was unsafe as a cosmetic ingredient.

This amended safety assessment of *p*-hydroxyanisole addresses a new use in nail gels and adhesives that require curing by light. Because these products are marketed as direct sales to consumers, they are being offered for “at home” use; this constituted the new use. *p*-Hydroxyanisole is used interchangeably and in combination with hydroquinone to control polymerization in nail gels and nail adhesives. *p*-Hydroxyanisole was reported to be used in the liquid component of 2-component artificial nail systems at a maximum concentration of 200 ppm, which decreases to approximately 133 ppm after mixing with the solid component just before application. Polymerization was reported to take 5-15 min in a nail adhesive product.

The VCRP reported that *p*-hydroxyanisole is used in 5 nail products. A Council survey reported no uses for *p*-hydroxyanisole.

In an in vitro assay, the permeability coefficient for the skin of *p*-hydroxyanisole was 9.39 x 10^{-3} cm/h; the flux at 10 min 283.0 µg/cm^2/h and 223.0 µg/cm^2/h at 60 min. There was low systemic exposure to 2% *p*-hydroxyanisole when

administered in a cream to human subjects.

Dermal administration of a cream containing *p*-hydroxyanisole at 4 or 40 mg/kg caused no teratological effects in rabbits. The maternal, neonatal, and developmental NOELs for *p*-hydroxyanisole were 40 mg/kg/d (12 µL/cm^2). The same depigmentation cream was not teratogenic in rats when given in topical doses equal to 80 mg/kg (480 mg/m^2) *p*-hydroxyanisole.

In a 2-generation study of a depigmentation cream containing 2% *p*-hydroxyanisole, the maternal, neonatal, and developmental NOAELs for *p*-hydroxyanisole were 40 mg/kg/d (12 µL/cm^2) in rats. Clinical signs in the F_0 rats were very slight to severe erythema, very slight to moderate edema, including fissuring, desquamation, eschar, focal eschar and exfoliation at the treatment sites. Vocalization was observed on application of the test material in the 2.0 and 6.0 mL groups. There was reduced F_1 pup survival and a higher rate of missing or cannibalized pups in litters after PND 1 in the 6.0 mL group. F_1 pups in the high-dose group had reduced body weights and an increased incidence of F_1 pup clinical and necropsy findings.

No genotoxic effects were observed when rats were dermally administered *p*-hydroxyanisole up to 40 mg/kg in a depigmentation cream for 6 months.

p-Hydroxyanisole at 0.4% and 2% in feed was carcinogenic to the forestomach of rats when administered for 104 weeks.

When *p*-hydroxyanisole at 0.6, 2.0, and 6.0 mL/kg/d was administered dermally to rats for 6 h/day 7 days/week (assumed through entire pregnancy), the dams and offspring in the high-dose group were killed in the first week of lactation because of extreme irritation at the application sites. *p*-Hydroxyanisole was rated as mildly irritating at 5% in miniature pigs.

In multiple HRIPTs of nail products, there were no signs of cuticle irritation or allergic contact sensitization when products containing hydroquinone or *p*-hydroxyanisole or a mixture of both were administered to the fingernails (the exact inhibitor[s] used were not provided).

UV lamps are used to cure nail gels, to cure acrylic nails and nail fill-ins, as well as to dry traditional nail polish and UV top sealers/topcoats.

In a study of UV exposure from different professional UV nail lamps using 2 different measurement methods, the cumulative MED were low. However, in less than 10 minutes, the exposure measured in J/m^2 was equivalent to the day-long recommended limit for outdoor work and recreation.

In tests of multiple types of professional UV nail lamps used as intended, the estimated UV exposure was below levels associated with potential carcinogenicity. The carcinogenic-effective irradiance from 3 common UV nail lamps used 10 min/week was estimated to be over 250 years.

UV bulbs were reported to emit in the 390-420 nm range. In 1 study, the UV nail lamps tested were reported to emit wave-lengths of 365-370 nm. Another study reported 355to 385 nm.

A risk analysis of the use of UV nail lamps concluded that tens of thousands of women would have to use UV nail lamps to dry their nail gels 8 min/manicure, every 3 weeks, for 20 years to increase the chance that 1 more woman would develop squamous cell carcinoma on the back of the hand, compared to women who were not exposed to UV nail lamps.

UVB light did not penetrate finger nails; very little UVA light penetrated fingernails.

There were 2 case reports of squamous cell carcinomas on the dorsum of the hands of 2 women who used UV nail lamps.

It was recommended that fingerless gloves or full-spectrum sun block be used when UV nail lamps are to be used. It was also recommended that special care should be taken in cases where potential users are taking medications that increase UV sensitivity. People who have been advised against venturing into natural sunlight without proper protection should also be cautious about using UV nail lamps.

A concern exists that it is possible to insert an incorrect replacement lamp/bulb into the UV nail lamp (eg those emitting UVB or UVC).

Newer professional and home-use nail lamps are manufactured with LEDs instead of fluorescent bulbs. These bulbs are manufactured so that they emit a narrow range of light, 380-420 nm, encompassing the optimum wavelength for curing nail gels, 405 nm. These bulbs cannot be easily replaced and are reported to last for 50k h of use. LED nail lamps are reported to cure nail gels in 30 sec, faster than the 2 min that it takes fluorescent nail lamps.

DISCUSSION

In a safety assessment published in 1985, *p*-Hydroxyanisole was found to be unsafe as a cosmetic ingredient due to skin depigmentation at 0.25%. That conclusion did not contemplate the new use in artificial nail coatings that are cured under light.

The Panel noted that there is no dermal exposure to *p*-hydroxyanisole when artificial nail coatings are properly used and that the amount of *p*-hydroxyanisole in the nail gels are well below the concentrations that cause depigmentation. Users are advised to promptly remove any accidental application to the surrounding skin for best visual results and adherence as well as to minimize exposure. The Panel concluded that when following these instructions, there is no risk of more than a momentary exposure that should not result in skin depigmentation. However, the Panel stressed that contact with the skin is to be prevented and that professionals be properly trained in the application of these products. The Panel also noted that

p-hydroxyanisole is either consumed during the curing process or is trapped within the polymerized matrix, so post application exposure is not an issue.

p-Hydroxyanisole is an ingredient in nail products, marketed as "home kits," that are now available to the consumer. The Panel considered the greater likelihood of accidental skin and nail bed exposure when nail products are applied by consumers compared to experienced salon personnel and emphasized that directions be followed carefully by consumers so that contact with the cuticle or skin is avoided.

The concentration of *p*-hydroxyanisole was not indicated in the series of sensitization studies conducted by applying the nail gel to the fingernails and not to the skin. Although these studies do not demonstrate the dermal sensitization potential of these products as in the usual HRIPT, the lack of observed sensitization when administered to the nail does demonstrate how unlikely it is for sensitization to develop when these products are used properly.

The Panel reviewed estimates of risks of developing squamous cell carcinoma in individuals who are placing their hands under a fluorescent UV light source. The Panel acknowledged that there is controversy about the potential carcinogenicity of UVA light under the conditions of use, indicating that a slightly elevated risk of developing squamous cell carcinoma exists. The Panel noted that the potential risk of photo-carcinogenicity warrants the precaution to use a broad-spectrum sunscreen or photo-protective covering, such as light-impermeable gloves, during the gel-curing process. These lights should only be used in a professional setting and are not safe for home use.

Nail lamps used to cure nail gels, as previously designed, were manufactured using universal light bulb sockets. The UVA bulbs used in nail lamps emit UVA light (390-420 nm), but can be easily replaced with UVB and UVC bulbs. The Panel had several concerns based on the possibility of the incorrect bulb being used upon replacement. First, the Panel discussed the damage that could occur to the eyes; it is possible that, in a home-use setting, an individual could look into the lamp and, if the bulb was replaced with a UVB or UVC bulb, incur eye damage from that light. Additionally, the Panel was concerned that these lamps might be used at the eye level of small children. Also, there was concern that home users may be exposed to additional UV light exposures to the hands if they increase the exposure duration when the nail gel does not set properly because the wrong bulb is used.

The Panel noted that there is substantial research demonstrating the general public's inattention to product warning labels and operating instructions, and discussed the possibility that an improper replacement bulb could be inserted into the UV lamp. The Panel noted that curing lamps that use UV light are widely available to consumers. The Panel felt that use of UV lamps in non-professional settings was unsafe and should be discouraged.

Recently, however, safer LED lamps are also widely available and have largely replaced UV lamps in nail gel kits sold to consumers. The bulbs in the LED nail lamps emit a narrow band of light (380-420 nm, encompassing the optimum wavelength for curing nail gels, 405 nm; very little in the UVA range), are long lasting (expected to last for 50k h of use), and cannot be replaced by the consumer. The Panel concluded that these lamps will not cause squamous cell carcinoma and are safe to use for curing artificial nail coatings.

The Panel emphasized that it is important for companies to report their ingredient usage to the VCRP program, as well as to respond to the concentration of use surveys conducted by the Council, to facilitate the development of safety assessments that are based on accurate and representative ingredient use information. The Panel noted that the VCRP collects data only on products sold to the general public, not on professional-use-only products.

AMENDED CONCLUSION

The CIR Expert Panel concluded that *p*-hydroxyanisole is safe for use in nail adhesives and in artificial nail coatings that are cured by LED light as a polymerization inhibitor; and unsafe for use in all other cosmetics due to dermal depigmentation potential. This conclusion supersedes the earlier conclusion issued by the Expert Panel in 1985, which stated that it was unsafe for use in all cosmetic products.

TABLES

Table 1. HRIPTs (n=50 or 51) of nail products containing *p*-hydroxyanisole and/or hydroquinine administered to the fingernails (not the skin) by trained technicians. The amount of *p*-hydroxyanisole in the products was not provided. All tests resulted in no signs of potential cuticle irritation or allergic contact sensitization.

Product	Reference
UV gel top coat nail polish	[28]
UV gel top coat nail polish	[27]
Builder gel	[26]
Clear overlay gel	[25]
Soak-off sealer	[24]
Soak-off gel lacquer	[23]
Gel system-thick gel sealer	[29]
Base gel	[30]
No-cleanse overlay gel	[31]
Soft white sculpting gel	[32]
Pink builder gel	[33]
Luminous white overlay gel	[34]

Table 2. Ultraviolet nail lamp measurements.[41]

Lamp	Exposure time (min)	Total MED/yr	Total J/m^2	MED/h	Total MED/manicure	Total J/m^2/manicure
OPI lamp	150	1.5	386	0.62	0.09	22.5
CND lamp	108	1.1	285	0.63	0.06	15.0

Table 3. The number of individuals who would need to be exposed to ultraviolet A (UVA) nail lamps[a] for 1 individual to develop squamous cell carcinoma who would not have done so otherwise.[47]

Age when UVA nail lamp use begins	Number of years of use			
	5	10	20	40
20	218 604	125 629	72 709	44 254
30	271 521	155 688	89 435	52 952
40	332 747	189 670	107 287	60 863
50	395 768	223 255	123 290	-

[a] Assumes a typical level of exposure of 8 min per hand, once every 3 weeks with no sun block agents..

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Personal Care Products Council
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Memorandum

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

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

DATE: October 1, 2014

SUBJECT: Comments on the Revised Tentative Amended Report: Amended Safety Assessment of p-Hydroxyanisole as Used in Cosmetics

p.2 - Cosmetic Use - As there is only one subsection in the Cosmetic Use section, the sub-heading Use in Nail Products should be deleted. It is not correct to state that the uses of p-Hydroxyanisole were reported to the FDA in 2014. The FDA VCRP information was obtained from FDA in 2014.

p.3 - Please delete "may only" - as the VCRP is voluntary, it is only a sample of the products that are on the market.

p.3 - When describing the depigmentation cream containing p-Hydroxyanisole and tretinoin, please indicate that it is a prescription drug product.

p.4 - Were both male and female rats used in the carcinogenicity study in rats fed 0.4% p-Hydroxyanisole in feed (reference 20)? The summary of this study says that the final body weights of the treatment groups were lower than controls - but there was only one dose used. Therefore, does "treatment groups" represent male and female rats?

p.4-5, Summary - On p.5, in the summary of reference 17 found in the Irritation section it states: "The dams and offspring were killed within the first week of lactation because of the resulting irritation." How can this be true? The description of this study on p.4 indicates that "Motor activity (total and ambulatory) measurements were made on or about PND 60..." Based on the information on p. 5, there were no animals alive at PND 60. The summary in the Irritation section needs to be revised to indicate which dose groups were sacrificed within the first week of lactation.

p.5 - Please clarify the following sentence: "Estimates of exposure duration per visit vary with the specified procedure and number of applied acrylic coats." To what is the subject exposed? Where are they visiting?

Please revise: "separate thin coats of nail gel be applied..."

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p.6 - The study described in reference 47 examined 6 different nail lamps, 3 with fluorescent bulbs and 3 with LED bulbs. The results indicated low risk for one of these lamps. Did this lamp have fluorescent or LED bulbs? What was the bulb type in the device found to be an "aphakic eye hazard"?

p.8 - In the last paragraph of the summary, it should be noted that home use nail gel kits are sold with LED nail lamps.

p.9, Discussion - As nail application was used in the sensitization studies, "administered to the skin" should be revised to "administered to the nails".