

DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. FOOD AND DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY AND APPLIED NUTRITION

PUBLIC MEETING: COSMETIC MICROBIOLOGICAL SAFETY ISSUES

WEDNESDAY, NOVEMBER 30, 2011

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PROCEEDINGS

MR. GASPER: Good morning, everybody. Welcome to the meeting. I've just got a minute or two of housekeeping notes here. I'm John Gasper. I'm in the Office of Cosmetics and Colors. I will be the moderator.

So, first thing to note, this public meeting is being transcribed and the transcription will be posted on the FDA's website when completed.

A short reminder, during the question and answer sessions that we'll have after the presenters, please clearly state your name and your organization to make sure that they are captured for the transcripts. The restrooms, both of them, are to the right as you exit the ballroom.

Now, you should have all received a folder. And inside your folder you should find the agenda; you should find copies of both Dr. Katz's and Dr. Hansen's slide presentations; there's a copy of the Federal Register notice. And as noted on the agenda, January 30th, 2012 is the deadline for submission of any written comments to the docket. And the docket's

address is listed there as well as in the Federal Register notice. We will be putting the slides to the docket later. And you also should have in the folder a list of attendees that have registered in advance.

Now, if anybody has any media or press contact questions, we do have somebody from our press office here, that's Miss Tamara Ward, she's standing in the back, waving, so if you have any question please contact her.

Now, for public comments, if there's anybody here who has not signed up to make a public comment today, and you would like to do so, please contact Juanita Yates. I believe she's still outside at the registration desk--oh, Juanita's right to your left here--or one of our staff members, by noon today, by the lunch break, and we can schedule you in.

If you need any -- have any more questions, or need some assistance, please talk to one of our personnel at the registration desk. Wendy Johnson is working outside; she should be able to answer any questions or help you.

With that being said, I'd like to start the

meeting with Dr. Linda Katz, who is the director of the Office of Cosmetics and Colors.

DR. KATZ: Thank you, John. Good morning and welcome. I'm glad to see that we have such a great turnout today to talk about the cosmetic microbiological safety issues. And we look forward to hearing from all of you, either here today who are presenters, or through public comments.

During the brief time that I have this morning, what I'm going to do is just to give an overview and talk a little bit about FDA's mission, talk a little bit about FDA's oversight for our cosmetic safety with regard to our regulatory authority programs and tools, and then talk a bit about the purpose of today's meeting, which, all of you are aware, is why you are here.

Let me start off with talking about FDA's mission. This slide is very simple. And it's simple because really the mission itself is fairly simple, to protect and promote the public health. And we do this by looking at and focusing on cosmetic safety.

FDA's authority for cosmetics is somewhat

limited. As probably all of you are aware, our authority is based on the Federal Food, Drug, and Cosmetic Act, and it states that cosmetics must not be adulterated or misbranded.

So what does this, basically, mean? It means that FDA's authority is post-market only. The law does not provide for FDA to have pre-market approval of cosmetics. Now, this is very different from drugs and devices in which an application will come into the agency for review and the agency will make a determination whether a product and ingredients are safe for use, as well as effective prior to marketing. For cosmetics, what we know about the products we learn after the products are out in the marketplace, in most cases.

So what is our responsibility at the FDA? Well, our responsibility is really to monitor safety and ensure the proper labeling of cosmetics. When a cosmetic gets marketed, industry has additional information and the responsibility to assure that products that are on the marketplace are safe.

So what does this, basically, mean? It means

that the cosmetics must be safe when used as labeled and under the customary conditions for use. So, our main concern is for the safety and the appropriate labeling, so that consumers who are using these products can use them safely.

So how does FDA determine and monitor the safety of cosmetics? We do this really by information that comes to us. We do it by the monitoring of adverse events that come into the FDA. As all of you know, adverse event reporting for cosmetics is voluntary, so it's somewhat limited. But, by the same token, we look for trends. If there are certain trends that come through that suggest that there may be a safety issue, it sets off a flag for us to delve a little more fully.

We also look at the scientific research. We look at what's published in the literature. We look at any additional information that may become available to us, and here CIR is often a valuable source for additional information.

We will do inspections of cosmetic manufacturing facilities, particularly if we have

concern about a product or a concern about ingredients. We examine imported products, again for their safety. And we will take enforcement action against cosmetics that are adulterated and/or misbranded. The ability to do that is in our regulations. And we also have guidances and other public communications to help industry to manufacture safe cosmetics.

This again leads to important information and part of the reason for why we're here today. When we talk about microbiological safety, the FDA's information is somewhat limited. But we do give advice for things that we would like to see as you market and manufacture products. We have GMP guidelines that provide fairly general directions that are available on our website. Even though we all know that GMPs are not required for cosmetics, we hope that manufacturers do follow them because, again, this is one of our ways to assure that products are being manufactured safely.

We have a compliance program and general manuals that are also available, which will give general information to manufacturers as to what kinds of information we're looking at, Warning Letters that

may have been issued, and why Warning Letters have been issued.

And we also have the *BAM*, which is the Bacteriological Analytical Manual, which is a technical manual. In the *BAM* itself, one chapter is dedicated to cosmetics and cosmetic ingredients. And Dr. Patricia Hansen will talk a little bit more about that in just a few moments.

So that brings us really to the goal of this public meeting. We're here really to talk about microbiological safety of cosmetics and to link them directly to FDA's public health mission. We're really here to hear from you, to find out more information, and to get more opportunities for us to see where we need to potentially modify guidances, what additional information we might need to make available to all of you, both in industry and academia. We need to assure that any time we change any information that we publish, that there's a sound scientific basis. And that, really, this session itself is designated primarily as a listening session. Again, I need to emphasize, we want to hear from you.

This slide section itself is just to let you know where you can find information about cosmetics and FDA's position about cosmetics and how we regulate them. On our home page we have multiple different listings. And we have question and answers to help to orient you about issues and questions that we get asked and what we think should be the answers. But again, the emphasis from this meeting will be to find out if any of our answers may potentially be incorrect because the science has changed. We need to know that.

So with that, I want to thank you and hope that this turns out to be a very productive meeting. And we look forward to hearing from you. Thank you.

MR. GASPER: Keith question: I need to make your slides larger. After we make this larger, Dr. Patricia Hansen will be giving you the FDA perspective. F5 didn't work.

DR. HANSEN: Okay. Little technical details. Good morning. It is really great to see so many of our stakeholders here this morning. And our office has really been looking forward to this day, the cosmetic program, and for those of you who are acquainted with

me, you know that personally I've really been looking forward to this day and to hearing from our stakeholders, your data, information, analysis, and perspective.

And I'm going to give, really, a brief, sort of overview and some context around FDA's perspective. I'm going to focus on safety and that will be a theme recurring. As Dr. Katz mentioned, safety really is our focus here--public health protection, and promotion of public health--and we're going to keep coming back to that.

We have a variety of current information sources, FDA sources, industry sources, others that address, in whole or in part, microbiological safety. I'm going to talk about those a little bit. I'm going to talk about our thoughts around updating and restructuring FDA information sources and getting to some of the themes that Dr. Katz mentioned. And also our information needs in this broad area and areas, excuse me, for stakeholder input, because we really want to hear from you. Again, you have valuable insight, information, and perspective and we need to

exchange that.

So microbiological safety and quality -- these are fundamental concepts and we believe they're important to all stakeholders. We also believe that stakeholder input into FDA's work and information sources is critical. We need current science. We need insight into current manufacturing and testing practices, suggestions about areas, future areas of research are also of interest, stakeholder needs and concerns, and other considerations.

Turning to the topic of information sources, there are various sources. FDA is one, industry importantly is another, standard setting organizations are again a source additionally of information relevant to microbiological safety. And there are other sources. Different sources emphasize different aspects of microbiological safety and/or quality.

FDA's information sources, Dr. Katz mentioned a couple of them, I'll go on a little bit more in depth. We have a cosmetic compliance program, which she mentioned, last updated in 2010 (and these documents are on a regular revision schedule). We have

the Cosmetic Good Manufacturing Practice Guidelines and Inspection Checklist, last updated in 2008, currently under revision now.

We have the Bacteriological Analytical Manual, familiar to many people in the audience, and Chapter 23, "Microbiological Methods for Cosmetics." This chapter has not been updated in some time. It was last updated in 2001.

Then we have consumer sources. Consumer updates is one vehicle we use and one of particular pertinence here is the one that addresses using eye cosmetics safely. And we're interested in hearing from all of our stakeholders too on information sources and topics that might be helpful for consumers.

There are industry information sources. There are the CTFA Microbiology Guidelines, 2007 update, CTFA Quality Assurance Guidelines, also 2007. And there are other information sources and guidelines out there, and many of you active in the field and in the industry will be well familiar with those. And my intent is not to give an exhaustive list but merely to highlight some of the critical ones.

Standard setting organizations are another source of information and guidelines. I'm highlighting ISO here, most prominent, in my view, but there are other bodies out there. There is the ISO Technical Committee 217 Work Group Six product, Cosmetic Good Manufacturing Practice, and I'll be taking up this particular information source in a little more detail later on in the presentation.

There is a draft International Standard, ISO, Evaluation of the Anti-microbial Protection of a Cosmetic Product. And that was out and last discussed at this year's meeting in March. Also at that meeting-- the 17th meeting of Working Group 1--a proposal was sent to the ISO advisory group for discussion. And that was to develop an international standard identifying objectionable microorganisms and setting microbial limits for cosmetics, considering current safety and quality standards. And I highlight this one to emphasize that these topics are of importance across the international scene. And there is some confluence of interest and priority, I think, across the group of stakeholders: Government, industry, consumers.

As many of you are aware, we are updating and restructuring FDA information sources and typically many documents do undergo periodic updating.

We need to align related FDA documents. This is very important: that we try to keep them, if they can't be absolutely synchronized, consistent and aligned. We don't need one pointing off to the right and one to the left. And so there's always that effort to keep things aligned.

We want our information sources to be up to date in terms of science and technology. And that is sometimes a real challenge in rapidly developing areas. And we really, again, want to hear from our stakeholders, particularly on science and technology.

In any library of information sources, you know, you pick one up off the shelf and when you're trying to use it things emerge. Things you thought were crystal clear are maybe not so crystal clear. So we need to clarify confusing or ambiguous areas and that is part of this effort that the agency is continually engaged in, in updating and restructuring its information sources.

We believe it desirable to align with international standards to the greatest extent possible within the existing legal framework, important parameter there, and without compromising safety, another critical parameter.

And we need to consider new information sources that may be needed. And here I'm harkening back again to Dr. Katz's remarks where we've been considering, given that some of our information sources are very general, there's a need to update. Do we need to develop new information sources, new guidelines, new consumer updates? What kinds of topics and what kinds of formats will be most useful?

So I'll talk about a few of the things that we're doing right now. You heard me speak about the compliance program, that that was last updated in 2010. And in that effort we removed a lot of obsolete material, clarified sections that had been found to be confusing or ambiguous to the users, and in general, really pulled it up to date.

We are presently engaged in revising the Cosmetic GMP Guidelines and Inspection Checklist.

Again, we are removing obsolete or extraneous information, clarifying ambiguous areas. We are also considering incorporating elements from the corresponding ISO guideline that I mentioned to the extent that's possible -- very important. And this document is very well developed, and it is in clearance. We do not have a date certain for its issuance. I will note that, but it's well along in the clearance process and we anticipate it issuing, hopefully, soon.

We're also revising Chapter 23 of the BAM. We're seeking greater alignment with more recently updated chapters. The BAM, in the main, focuses on foods and has chapters that are microorganism specific. Some of these chapters are more up to date in terms of methodology, so we are looking closely to, again, to align the cosmetics chapter, which is broader, to align with those chapters where it is needed, that are more specific to microorganisms and food products. And so, that's one thing that we're trying to achieve.

We're seeking greater clarity in some of the sections of that chapter, especially regarding follow-

up on ambiguous results. We're removing extraneous non-technical material to have a tighter, more focused chapter.

And we see opportunities here, in periodic revision, to incorporate newer methodologies, perhaps as screening tools. And, if you recall from the Federal Register notice, we are particularly interested in hearing from our stakeholders on testing methods of all kinds.

And again, we're considering the possible development of new information sources. Should we be developing guidance to industry on cosmetic microbiological safety? What specific topics are most in need of addressing? We're really hoping to hear from you. What kind of formats will be most useful? Again, we're trying to keep these information sources current and there are a variety of different ways, formats, that would lend themselves, we believe, more easily to that. But we want to hear from you.

We're considering developing additional resources for consumers on cosmetic microbiological safety. We don't have an awful lot. Up there I gave

the one example of using eye cosmetics safely; that is the main one that we have. And we're looking for other topics that stakeholders believe are important to address, topics important to consumers, and what kinds of formats and presentation would be most useful for our stakeholders.

So, I've mentioned repeatedly that there are areas where information and input are needed. And I'll amplify some of those highlighted in the Federal Register notice. And I'm going to go through those and amplify a little bit on some of them here.

A number of things group under Product Manufacturing and Controls. We're very, very interested in hearing from stakeholders on microbiological testing of cosmetics, types of preservative systems, and methods for preservative efficacy testing, product and packaging characteristics that affect microbial growth as well as other factors.

We have a number of people here who have signed up to give presentations. We're hoping to have a great deal of technical information in this and other areas, and are hoping that people will also take full

advantage of the opportunity to submit written material to the docket.

We are very, very, interested in hearing from you on these factors I've outlined and other factors that you, from your perspective, believe are important to that broad umbrella topic of microbiological safety.

Some group under microbiological risk assessment. Here I want to emphasize that that's human health risk assessment. We're interested in the identity and prevalence in cosmetics of microorganisms that pose specific health risks, the question of frank pathogens, opportunistic pathogens, non-pathogens, and that whole continuum. And we're, again, interested in data and information, analysis and perspective. There are emerging pathogens. There are antibiotic resistant strains. All of these factors, we believe will be useful to hear from stakeholders and to consider as we move forward. Routes of exposure to microorganisms and the corresponding effective doses -- very important.

Particular sub-populations that may be at greater risk, we're very interested in this area and other considerations relevant to human health risk

assessment with microbial considerations.

We are also very interested in hearing about adverse events. You heard a little bit from Dr. Katz on the adverse event reporting system that FDA has. We have limited information. It's a passive system. And common to all passive systems, we believe there's significant underreporting; there's an awareness issue. We believe that consumers generally are not very aware of FDA's system for reporting cosmetic adverse events. So we are engaged, actually, in a separate effort to promote greater awareness amongst consumers and health professionals.

But we are very interested in hearing from you, our stakeholders, on topics relevant to this broad umbrella. The occurrence of adverse events in different product types, the occurrence of adverse events associated specifically with microbial contamination and other aspects of adverse events, including reporting and monitoring systems.

And this list, that I have been going through and that was enumerated in the Federal Register notice, is really not meant to be all inclusive. There are, we

believe, an abundance of other considerations that may be relevant to microbiological safety of cosmetics and protection of consumers. And we want to hear from you.

So again, to reemphasize, you know, we are really seeking to hear from you: Your data, your information, your scientific analysis, your perspective in the areas that I've outlined. And to recap them: the identity and prevalence of microorganisms, including antibiotic resistant strains, pathogens, frank or opportunistic non-pathogens; microbiological testing; preservative systems and preservative efficacy testing; product and packaging characteristics that may impact routes of exposure to microorganisms associated with cosmetics and infective doses; subpopulations who may be at greater risk; and the adverse event reporting topics that I just mentioned.

We also want to hear from you beyond those topics of what other topics you believe would be useful to stakeholders, useful to industry, useful to consumers, useful in the academic sense. And what types of formats and vehicles would be most practical, most useable, and helpful. And we need to hear from

you on that.

So, there are multiple opportunities for stakeholder involvement. That is a point I really want to emphasize. We're here today with really an early input kind of workshop, to gather from you, again, data, information, analysis, and perspective to help inform, really, our plan for moving forward. Setting some priorities around that, what topics do we need to address? What are most important? Should we proceed to formal guidance? That would be an area where there are further opportunities for stakeholder input and involvement built into the process.

But I hope that you realize, by our comments today, we really want to hear from you and want to offer as many opportunities for input and involvement as possible. We believe it will really strengthen the effort and ensure the very best and most useful of products in terms of information sources.

Today is a huge opportunity in this regard. And again, I'm really just so happy to see so many people here, to see the folks who have lined themselves up to present, very good. I hope that people who have

additional information to offer will sign up at lunchtime, as our moderator mentioned, to take their few minutes at the microphone.

Following up on this meeting there is a docket open, and a 60-day comment period. And I really want to encourage all of our stakeholders, whether they are formally presenting here today or not, to submit written material to the docket.

Information on the docket is contained in the folders that you have at the meeting. But it's here again for reference, up on the screen. And these comments, we're looking for them by January 30th in the coming year.

And more of just how to get hold of us. If you've got questions and information outside that docket process that you want to propose. And with that, I think I will close. Thank you.

MR. GASPER: Okay. Our first presenter is Mr. Etan Yeshua, from Environmental Working Group.

MR. YESHUA: Good morning. I don't have any slides for you all, so hopefully I'm enough to capture

your attention for the next 20 minutes.

Thanks for providing EWG the opportunity to comment on the issue of cosmetic microbiological safety. My name is Etan Yeshua, I'm the 2011 Stabile Law Fellow at the Environmental Working Group, where my work focuses on the regulation of cosmetic products.

EWG is a non-profit research and advocacy organization based in Washington, D.C. and Oakland, California. Our mission is to use the power of public information to protect public health and the environment. We appreciate FDA's interest in and commitment to ensuring the safety of cosmetics or personal care products.

The average consumer uses nearly ten different personal care products every day. That means there are ten opportunities daily for a microbiologically contaminated cosmetic product to spread infection to an unknowing consumer. Moreover, the 126 unique ingredients that the average person applies to his or her skin every day contain preservatives, chemicals that may often be toxic, and present hazardous health risks.

The federal government does not require the vast majority of these products to undergo health studies or pre-market testing. The information gap makes it all the more alarming then, in that young children, who are of course more susceptible to microbial and toxic contamination, are exposed to 61 unique cosmetic ingredients in a handful of different products every day.

Given the lack of regulatory authority provided FDA under the Federal Food, Drug, and Cosmetics Act, FDA guidance for industry would be one of the most effective ways to ensure cosmetic products to ensure that consumers are protected from microbial contamination.

EWG supports the agency's efforts to promote safe industry practices, especially given the narrow confines of FDA statutory authority. As a consumer advocacy group, and as a founding member of the Campaign for Safe Cosmetics, EWG has long backed the call for effective and efficient cosmetic safety regulation with sound scientific research.

To that end, EWG recommends that FDA develop

guidance for industry on the best methods for protecting consumers from both microbial contamination and exposures to harmful chemical preservatives to ensure the following:

That cosmetic products do not pose undue risks to consumers from microbial contamination.

That cosmetic products are formulated and their packages designed to minimize the risk of microbial contamination without toxic chemical preservatives.

That cosmetic products are safe for consumers, especially vulnerable populations, including pregnant women and young children, taking into account all sources of exposure, because health risks are not only from exposure to a single product but also the aggregated effects of repeated exposures.

And finally, that cosmetic products are labeled accurately, with expiration dates and information about the presence of all preservatives and chemicals, including those like formaldehyde that are often released into the product by the chemical breakdown of other ingredients.

In working to achieve these goals, our own

research has highlighted two specific areas of concern with regard to cosmetic preservation as well as a number of additional areas where further research is needed.

Since 2004, EWG's Skin Deep Database has provided consumers with a free, publically accessible, on-line tool with hazard profiles of almost 70,000 cosmetic products, and more than 8,000 cosmetic ingredients.

Our researchers continually compile and analyze information from more than 60 toxicity and regulatory databases to generate safety ratings for what has become the world's largest personal care products safety guide accessed every month by over one million people.

With eight years' worth of data, our Skin Deep Database serves as the basis for our research and policy conclusions about cosmetic product risk and regulation. The data we have amassed has revealed hidden health risks, spurred regulatory action, and led to changes in product formulation. The data also highlight the need for FDA guidance with regard to

preservation of cosmetic products.

Many products on the market contain preservatives that may be hazardous to human health; some may be over-preserved, while others may contain too little preservative ingredient to be effective. Still others, alarmingly, appear to contain no preservative at all. Information we have suggests that there's a gap in industry knowledge, or at least use of cosmetic preservation best practices. A gap, which we believe, FDA guidance would be well suited for.

Two topics stand out, first, a growing trend of products that do not protect against microbiological contamination. In evaluating the need for cosmetic preservative guidance, FDA should consider products that are unpreserved or under-preserved. Our database lists 943 such water-based products that do not contain any of the 1,159 preservatives we track. Products with high water content are of course especially susceptible to contamination. Shampoos, conditioners, lotions, liquid soaps, creams, and the like merit specific attention because their high water content increases the need for proper preservation, be it a chemical

agent, package design or product labeling.

Second, products with potentially toxic preservatives. Some 3,579 products in our database are preserved with one or more of 22 different preservatives for which there's evidence of toxicity and risk to human health, including the health of children and developing fetuses. The personal care products should not threaten consumers with infection from preventable microbial contamination. Neither should they force consumers to choose between microbial contamination and contamination due to harmful preservatives.

While FDA should guide industry toward anti-pathogenic and better preserved products, the agency should simultaneously promote safer, less toxic methods of preservation. Personal care products ought to be manufactured and used safely with minimal risk of microbial contamination, but without trading one risk for another.

For example, parabens are frequently used as preservatives in personal care products that contain a significant amount of water. Of the 40,000 currently

marketed products in our database, more than 12,000 include as an ingredient at least one of four parabens. Their widespread use is troubling because of evidence demonstrating that parabens may disrupt the hormone system.

Moreover, in a recent study traces of five different parabens were found in the breast cancer tumors of 19 out of 20 women examined. And other lab studies in the last decade have also linked parabens to cancer and to reproductive health problems.

Formaldehyde also prevents bacterial growth, but is a known human carcinogen and a proven immune system intoxicant. A 2011 investigation by the Campaign for Safe Cosmetics found quaternium-15, a formaldehyde-releasing preservative, in baby shampoo sold in the United States. The same product sold by the same company in several European countries contains another preservative instead of the formaldehyde-releasing agent.

The manufacturer's use of a safer preservative in its overseas products suggests that a safer formulation is indeed possible, and yet American babies

are exposed to this carcinogenic intoxicant. Even the industry-driven Cosmetic Ingredient Review Panel this year declared formaldehyde an unsafe ingredient in certain hair products. The carcinogenic chemical is a distinct ingredient in at least seven currently marketed products; 11,000 others contain formaldehyde-releasing ingredients such as quaternium-15 and DMDM hydantoin.

In light of these dangers associated with both under-preservation and preservation through the use of hazardous chemicals, more research is needed to determine the risks and benefits of different preservation systems. Where toxic chemicals can be reduced or replaced with product reformulations or careful package design, for example, they should be.

In addition, EWG suggests that FDA consider the following areas of investigation before issuing guidance on cosmetic microbiological safety. First is a comparative analysis of domestic and foreign markets. The European Union enforces more stringent regulations than the United States does with regard to cosmetic ingredient and product safety. Whereas FDA has banned

or restricted only a handful of ingredients, the European Union's 2003 Cosmetics Directive banned 1,100 chemicals from use in cosmetic products.

The more restrictive bans do not necessarily equate to smarter regulation and safer products. FDA should not ignore the data amassed and lessons learned from years of policy development by the European Union. Indeed, it was a comparative analysis by the Campaign for Safe Cosmetics that led to the discovery that a safer formulation was being used in foreign baby shampoos than in the same product marketed in the U.S.

Because manufacturers are faced with more stringent regulations in the European market, they may, and in at least one case most certainly have, already demonstrated an ability to reformulate their products to be safer while maintaining profitability.

The second area for further investigation is product labeling. Legible product labeling, including ingredient lists and expiration dates may be an effective means of encouraging safe use and timely disposal of personal care products. Whether seeking safer ingredients or avoiding known allergens, a

consumer should have access to information about the contents of their cosmetic products. And yet, a 2007 study found that, quote, "Forty-six percent of the study's participants had difficulties reading the labels of personal care products mainly because of the small font size and the long chemical names."

Indeed, FDA regulations currently allow for font sizes on ingredient labels to be as small as 1/32 of an inch. FDA ought to reconsider this regulation in light of its guidance that font size and style be, quote, "easily readable."

Manufacturers should be encouraged to include expiration dates on cosmetic products. Currently in the U.S. personal care products are not required to carry an expiration date. Consumers may not know when to dispose of their products. Cosmetics, especially those with high-water content and those that come in direct contact with the user's body run an increased risk of contamination if not disposed of before the product becomes contaminated.

Cosmetic products should be no less safe than foods and drugs, which are required to carry expiration

dates and which often contain the same preservatives used in cosmetics.

Comparative analysis would be useful here as well. The European Union recently introduced "best used before date" and "period after opening" labeling. Moreover, products with expiration dates may be able to contain safer preservatives because the shelf life of the product may be shorter than those of cosmetics lacking expiration dates. Of course, the contaminating effects on the environment of disposed cosmetic products should be considered as well.

Finally, concentration disparities. Studies of cosmetic products in the European market have revealed a great variation in preservative concentration among the investigated products. Though this variation may be attributable to variations in formula and to various combinations of different preservatives in a single product, it may also indicate that some products are over preserved while others under-preserved.

FDA should consider the disparities, if any, in cosmetic preservative concentrations in the United

States and provide industry with guidance regarding product design, formulation, testing and labeling, as well as the use of preservatives that would provide a reasonable certainty of no harm for vulnerable populations exposed to cosmetic products.

Given the many aspects of cosmetic safety for which more research is needed, EWG believes FDA guidance and analysis could go a long way to promote the safety of personal care products. EWG looks forward to working with FDA to address these issues and to ensure that personal care products are formulated, manufactured, labeled, and used so as to prevent contamination by both microbiological pathogens and toxic preservatives. Thanks.

MR. GASPER: Okay. We have scheduled ten minutes for any questions for Mr. Yeshua. And if you would, we have two people with hand-held mics. If you would just raise your hand, and as I stated earlier please state your name and your organization clearly, so it can be accurately caught in the transcript.

Is there anyone who has any questions? Okay. I guess we don't. Last call.

All right. Well, I believe we're scheduled for a twenty minute break now. So, I guess since it's just about quarter to, if we can reconvene at 10:05, all right. Okay. I'll see you here in 20 minutes.

(Recess)

MR. GASPER: Our next presenter is Jay Ansell from the Personal Care Products Council.

DR. ANSELL: Good morning, all. My name's Jay Ansell and I'm currently Vice President of Cosmetic Programs at the Personal Care Products Council, where I'm responsible for providing technical support for the council staff and various committees addressing the science and regulation of personal care products.

I previously led product safety and regulatory affairs at raw material suppliers and a finished products company. My academic training is as a chemist, completing my Ph.D. at the State University of New York at Binghamton, and I was first certified as a Diplomat by the American Board of Toxicology in 1986.

Based in Washington, D.C., the Council, formerly CTFA, is the leading national trade association representing the \$250 billion global

cosmetic and personal care products industry. Founded in 1894, the Council's more than 600 member companies manufacture, distribute, and supply the vast majority of finished personal care products marketed in the United States.

As such, we are most pleased to be able to provide these remarks and participate in today's public meeting on the microbiological safety of cosmetics. In addition to myself, Phil Geis and Richard Whiting will be speaking later. And of course, we will be filing additional detailed written comments by the January 30th deadline.

The U.S. cosmetic industry and the Council have a long history of working cooperatively with FDA in assuring the safety and quality of cosmetic products. In 1974, then Commissioner Alexander Schmidt said I know of no industry which has better -- a better record of voluntary accomplishments. Again, in 1980, Acting Deputy Commissioner Novitch cited Commissioner Schmidt, adding, what was true in 1974 is, if anything, more true today. We take pride in that history and strive to maintain that record of accomplishment.

Indeed, in the area of microbiology we've been working for more than 40 years developing, publishing, and updating microbiological guidelines for the industry.

Now, we know that in the '60s and '70s studies of topical drugs and cosmetic products in Europe and the United States raised concern about the microbiological quality of these products. Further, as the agency considered contaminated products with-- products contaminated with gram negative organisms to present a moderate to serious health hazard, any contaminated product would be considered adulterated within the meaning of the Food, Drug, and Cosmetic Act.

Findings from those studies were as concerning to the cosmetic manufacturers, and industry took action. In 1969 the then CTFA organized the microbiological committee and began publishing technical guidelines in CTFA's cosmetic journal. By 1973 the value and number of these guidelines had grown to the point that an independent volume was published to assist companies in establishing and maintaining a microbiological quality assurance program.

Between 1972 and 1975, CTFA undertook a

comprehensive national survey of the microbiological quality of cosmetics and published those findings in 1977. Of particular note, the survey found that of the 3,967 products tested, 97.7 percent were free of measurable microorganisms, and 99.6 percent were within the recommended microbiological limits.

In 1975, FDA conducted its own survey. And the findings of this and later surveys, in addition to the information from inspections of cosmetic manufacturers, led FDA to conclude that the contamination of cosmetics entering the market was no longer a major regulatory issue.

Thus, the main concern voiced by the agency then became the adequacy of product preservation, especially in the hands of the consumer. Industry agrees. And preservation of cosmetics is indeed an important consideration, and in fact, the original 1973 microbiological guidelines contain substantial information addressing the preservation and protection of cosmetic formulations.

Now, it should be noted that the state of science is not static. And so, the guidelines undergo

continual review and updating as new information becomes available. New guidelines are routinely added, while the existing guidelines are updated and revised to reflect the most current science. For example, guidelines specifically for aqueous eye area products were added in 1975, and included methods for testing water-based cosmetics, toiletries, and eye area cosmetics.

As another example, the 1993 edition included guidelines for the microbiological assessment of product quality after use, intended to assist manufacturers in assessing the microbiological quality of the products during use by consumers.

In fact, the ability of in-use tests to corroborate preservation efficacy test results has been the subject of several published studies. Most recently, the 2007 edition included new chapters on the determination of preservation efficacy in non-woven substrates. Methods for preservation of atypical products, rapid method preservation testing of water-miscible personal care products, and seven additional chapters underwent significant revisions.

Finally, as part of our long history of action, we should also mention the Council's participation, at the agency's request, in the development of a preservation efficacy test specifically for cosmetics. Through AOAC, a method was tested collaboratively in a study involving 19 laboratories, with the results being published in the 2001 Journal of the AOAC International. Today this method is still the only validated challenge test available.

Today the Council's microbiological guidelines are an important tool to assist manufacturers in establishing microbiological quality assurance programs and controls, to assure product quality, and consumer safety. Based on modern quality management techniques, including quality system approaches, the guidelines address assessing personnel qualifications, the microbiological evaluation of the physical environment including the plant, grounds, equipment, cleaning and sanitation, procedures for sampling, testing, assessing water quality, lab practices for method validation, documentation, and assessing the adequacy of product

preservation, including products after use.

The Council is also active in the development in international advancement of best biological practices through active participation in the ISO Technical Committee 217 we heard about earlier. The U.S. Technical Advisory Group representing the American National Standards Institute is chaired and administered by the Council and currently has 22 experts, including experts from FDA participating.

The U.S. experts, along with experts from 57 other national delegations have written nine international standards in the area of microbiology since 2005. These address general directions for microbiological examinations, methods for detection of aerobic mesophilic bacteria, *E. coli*, *Pseudomonas aeruginosa*, *Staph aureus*, *Candida albicans*, and a method for the enumeration of mold and yeast.

Of particular note, the experts have also published guidelines for risk assessment of microbiologically low risk products and established a standard for cosmetic good manufacturing practices that has now been adopted or referenced by authorities

worldwide. These include the U.S. FDA, the European Commission, Japan's Ministry of Health, Labour and Welfare, and Health Canada. Additionally, we are working currently on new standards for the evaluation of anti-microbial protection of a cosmetic product, microbiological limits, and preparing a technical report to assist in conducting microbiological risk assessment.

Now, those of you who are familiar with ISO know that the core mission of ISO is international harmonization to facilitate trade, allowing everyone to compete on an equal footing, everywhere. However, as a participant, I can say that the experts also firmly believe that advancing best practices through the standards, and with their adoption by the 160 members of ISO, including both advanced and developing countries, also has a direct impact on improving human health and safety.

Now, earlier I mentioned that the current Council guidelines rely on modern concepts of quality management and that our means to control the microbial content of a cosmetic begins during the earliest stages

of product development. Carl Brooke of FDA, in his 1971 paper, reminds us that man lives in equilibrium with a wide spectrum of microorganisms. Therefore, cosmetics are not required to be sterile, nor do they need to be. He then goes to describe those aspects that are common to cosmetic products of high microbiological quality. Highlighting three main criteria, specifically microflora, if present, are not harmful to the consumer or the product. They are processed with quality materials under sanitary conditions and products can tolerate microbial insult introduced by the consumer.

With that in mind, the microbiological research scientist will set microbiological limits based on consideration of the product's intended use, including application area and target populations. They will then develop an effective preservation and protection system, taking into account the raw materials used, the manufacturing procedures, information gained from the preservation of other products, the types of packaging, shelf life, and anticipated storage and shipping conditions.

Ultimately, with this information, we have a product preservation system designed to assure not only the product is adequately preserved to assure the quality at the point of purchase, but also ensure that the microbes introduced during normal and customary use of the product will not adversely affect quality and safety of the product.

With that said, I believe we can say with confidence that current industry practices assure that cosmetics are safe. However, as confident as we may be, a critical component of any quality system is post-market surveillance.

To that end, cosmetic manufacturers have in place robust systems for post-market surveillance. Here companies put in place systems where consumer calls are monitored, tracked, sorted into subcategories, like those formulation related, compliments on the effectiveness, packaging, or health, and conduct investigations initiated where appropriate.

These data show a very low incident rate, overall, consisting primarily of reports associated with irritation or sensitization. Indeed, those

attributed to microbiological affects are even lower. As examples, in 1971 and 1972, the FDA, at the request of CTFA, did establish voluntary programs for facility registration, filing of formulation information, and filing of cosmetic product experience reports. While the programs were discontinued in 1996, I should add parenthetically that the voluntary cosmetic reporting program has recently been reinvigorated with the completion of an on-line filing system.

However, certain data from FDA's product experience reports from the period of operation are available. A summary from the first six bi-annual reporting periods, from 1974 to 1976, showed an estimated 125 companies participating, with an estimated distribution of 9.75 billion units. With that, FDA reported an incident rate of 2.03 experiences per million units sold. Even given FDA's estimate that this may represent only 30 to 40 percent of cosmetic sales, it would still only represent five to seven unconfirmed experiences reported for every million units sold. This would give an incident rate of five ten-thousandths of a percent.

Today, more focused on eye area reports, a request for reported adverse events to FDA's CFSAN Adverse Event Database showed ten reports in the period 2004 to 2011. While comparison of the same eight-year sales period wasn't available, sales figures for the six-year period, 2005 to 2010, showed 2.7 billion eye makeup units sold during that period. From that, we see less than one reported adverse reaction for every 270 million units sold, or an incident rate of three ten millionths of a percent.

Now, while we do understand that incidents based comparisons of cosmetic and drugs are difficult, I think it is instructive to have some comparison. During the seven-year period, 2004 to 2010, the FDA's Adverse Event Reporting System for drugs and therapeutic drugs received 3.7 million reports. Similarly, the Center for Veterinary Medicine has an adverse drug experience system for domestic drug experiences that have been determined to be at least possibly drug related. The cumulative summary report for the period 1987 to 2011 exceeded 2,000 pages.

Now, while my comments have demonstrated that

the industry's quality programs are delivering safe cosmetics to consumers, I thought it might be useful to see how the microbial limits set by other international authorities compare. Perhaps not surprisingly, as the standards are science based, the U.S. recommendations are entirely consistent with worldwide standards. ISO TC-217 has just begun a program of work on new microbial standards that began with a comprehensive survey of objectionable organisms and microbiological limits.

The report included individual nations and community of nations that encompassed 71 separate nations. In brief, the report found that the limits recommended by the industry association on this slide are the same or lower than those set for baby and eye area products, with the single exception of Algeria, which had set a limit of 50 CFU for eye products.

The same net results may be found in identification of objectionable organisms. The organisms selected here are entirely consistent among all the authorities with minor deviations like the inclusion of a sulfite-reductor *Clostridium* in Algeria

and in talc products in the Miracor countries, as well as the addition of salmonella in Mexico and Chile.

With that said, industry does have a long history of effective cooperation with FDA in assuring that cosmetics are safe and we are committed to continuing this cooperative approach. To the extent that FDA believes additional guidance is needed, we are ready to participate in developing that guidance.

Consistent with the guidance that applies to modern quality management techniques, including implementation of quality systems approaches to all aspects of cosmetic production, and quality assurance that encourages implementation of risk-based approaches that focus industry and the agency's attention on critical areas, ensures that the regulatory review, compliance, and inspection policies are based on state of the art science, and enhances the consistency and coordination of FDA's cosmetic quality regulatory programs, in part, by further integrating and enhancing quality systems approaches into the agency's business processes and regulatory policies concerning review and inspection activities.

In conclusion, the industry practices do assure that cosmetic products are safe and meet consumer's quality expectations. We do this by using the best science and implementing the best quality management practices from start to finish. Industry practice had been proven effective with any type of adverse events being extremely rare and almost exclusively due to irritation and sensitization.

And finally, the industry is committed to continuous improvement and expects to continue to work cooperatively with FDA, ensuring world class performance in our industry. So with that, we'll open the floor for questions.

MR. GASPER: Any questions at all? We have time set aside for this.

DR. ANSELL: Thank you.

MR. GASPER: Okay. Our next speaker is Phil Geis from Geis Microbiological Quality.

DR. GEIS: Well, thank you. And thank the FDA for this opportunity to speak. I've been asked by the Council to speak to the scientific aspects of cosmetic micro quality.

But, let me first introduce myself, I'm Phil Geis. I am -- was trained initially as a medical microbiologist. After my undergraduate career at the University of Texas, I entered the Army, where I was trained as a medical microbiologist, my last assignment being establishment of a full microbiological capability for the Army's 45th Field Hospital. After the Army, I returned to the University of Texas, earned a Ph.D. in microbiology mycology, and then joined the Procter & Gamble company, where I spent the next 30 years studying microbiology, applied microbiology, especially in the context of cosmetics.

I retired about three months ago and formed this consulting group you see here in affiliation with the Advanced Testing Laboratory, and I'm an adjunct professor at the University of Florida, where I'll be teaching courses in microbiology, starting in the first of the year.

I've had the pleasure to be part of a dynamic industry, an industry that started to do its science in various focused manners. It wasn't one that discussed esoteric scientific principles; it was one that was

focused on applied micro. Basically, just a few subjects: Preservation, preservative testing, detection of microorganisms, detection of -- establishment of good manufacturing procedures, and understanding how consumers use and may have used our products in protecting against that.

The publication record goes back over 50 years for this industry. And if you look at it, it's somewhat surprising as to the detail that these guys went to. As Jay said, in the late '60s early '70s, agency concerns as well as industry concerns of contamination led us to form committees, and the PCPC, which was at that time the CTFA, was the organization that governed these committees. It brought the scientists together to combine their knowledge with the idea of forming some guidelines that would guide this industry to provide good quality products for consumers and lower the consumer risk for micro contamination.

The risk assessments in this context that led us to guidelines and compendial protocols and methods are the ones Jay mentioned. And these are very effective means, and they have brought us decades of

success.

The last method that Jay mentioned was in the AOAC. This is a preservative test method and if you examine this method, you'll see that we go well beyond what is traditionally true for drugs. He showed the four bacteria there, the Staph, the E. coli, the Candida albicans, Aspergillus. You examine this method, you'll see that there's a wide range of bacteria against which we try to control contamination.

Not only do we do guidelines and methods, but we also establish a greater level of capacity in our own colleagues. The PCPC committee has mentoring opportunities where the older folks, like myself, would mentor young microbiologists that are just entering this rather arcane field of cosmetic microbiology. We do training. We've conducted webinars, workshops, and scientific sessions to communicate what we understand about cosmetic microbiology. And we've enjoyed the FDA, who has joined us at these training sessions, to bring their understanding of policy and their understanding of the science so our young folks coming up will understand what the agency thinks.

Jay mentioned global harmonization. This is very important because I believe this industry in the United States is probably the most advanced in terms of quality in the world. And certainly our major companies, Procter & Gamble, Unilever, Johnson & Johnson, Estée Lauder and Avon, we manufacture around the world to the same quality standards that we make here in the U.S.

And by virtue of that passive presence outside the United States, we have established some additional knowledge in terms of what establishes quality. And now we are actively pursuing ISO harmonization to meet these same quality standards.

So I believe, as Jay said, we've established a superior quality record, not only just in the U.S., but one that both actively and passively influences the entire world. We've done this by understanding the entire scope of product quality.

And I hope this cartoon is not too goofy for you to see. What I try to portray here is this is not a matter of just preservation or testing products. Those things build -- attempt to build quality into the

product. What we've done here is attempt to control the whole scope of product quality from the first raw material to the last consumer use. Our industry has set up protocols, dynamic protocols, that change with the changing nature of our bacteria, changing nature of our products, that address each of these items from the vagaries of raw materials to the processes by which we combine these raw materials to make our finished product, to how the consumer will use it and how that product may be abused by the -- even the reasonable consumer.

The product left in the car to freeze in the winter, or to be baked in the summer in El Paso. The human bathroom where there's all sorts of mold floating around in a mildewed bathroom. We understand these elements and we've developed protocols to address these. And these are the things we teach each other as we go forward.

Let me go through the various aspects. The first one is product design. When our formulation chemists and our engineers first figure a product, they think of a consumer benefit that will delight our

consumers. The microbiologist is, at the same time, formulating a quality design that's consistent with his commitment to quality. Try and understand how they can make this product and give it to consumers so one, it's clean when they get it, and two, they won't contaminate it during use, during a long period of use, because again, this is years' worth of stability we build into our products.

It starts with the raw material qualification. When a raw material is identified, we go to that raw material supplier and determine how they will give us a high quality raw material consistently, batch after batch after batch. We don't take what they give us. It has to meet our standards. And to be successful in business we have to look at consistency of that supply. Often times, this means we have to go to this supplier or that supplier. But in order to establish the robust supply system we have, that is necessary for our product design microbiology.

Of course, there's preservation. And we have a small number of preservatives. You heard early today there are a bunch of preservatives. There aren't a

bunch of preservatives. We've lost preservatives. We have virtually a handful of preservatives left that are safe and effective, including parabens and formaldehyde releasers.

We use these to establish preservation in pilot plant batches, lab batches, and we demonstrate it in our manufacturing as well. And it's not just preservative capacity immediately, it's chronic preservative capacity that through the life of this product, the consumer's going to be protected.

That preservative system and that product quality also affects packaging. Packaging and the implements we use to apply the makeup to the face, apply the wipe to the hands, the various elements of delivery.

We do anticipate reasonable consumer use. We do this early in the process and indeed, if the consumer, in our early in-use testing, contaminates the product, we reformulate or repackage. We don't accept any level of contamination.

And finally, this is a part of the risk assessment. The overall risk assessment goes beyond

that--I'll tell you about that in a second--but this is the first step of our risk assessment.

The next aspect is in manufacturing, quality assurance, and quality control. I showed you that diagram that from beginning to end; we control the process by which we make products and make them clean, make them safe for consumer use. But it goes, again, to the design. Our construction and design of our manufacturing equipment is done in a manner that brings us a high level of hygiene, a high level of capability of removing and eliminating microorganisms.

It starts with raw material control. We've established by this time a reliable source of raw materials. That doesn't mean we stop testing. Our affirmative risk assessment says we had to establish quality upfront. We test to confirm that quality. Good manufacturing practices are, as mentioned before, are consistent across our industry.

We also borrow from other industries. HACCP, which is Hazard Analysis and Critical Control Point, is a concept adopted from the food industry. And here this concept identifies those areas in the making, in

that diagram I showed you, perhaps a pump, perhaps a heat exchanger where there's greater risk, we identified those and control the risk at that point. Environmental monitoring, which is something from the drug industry. We evaluate the bugs that may be appearing in our product stream, or adjacent to our product stream that can contaminate the product during making.

And finally, our QC testing, finished product testing. And all this is validated, validated to show that we can recover bacteria if they're there. Our finished product testing is well below the standards Jay mentioned. Those are governing standards. In a practical effect, the greatest percentage of product we make has no detectable microorganisms in our testing. Again, it's the product of an affirmative risk assessment. We built quality in. We expect to see nothing and we see nothing in our finished product.

The products are not sterile, and indeed, if we wanted to guarantee sterility it would have a major effect, and be unnecessary and not be worth it to consumers. But most of our products have less -- have

significantly less than one microorganism per gram.

In fact, we do most of our release testing in this industry by virtue of rapid methods. These rapid methods are go, no go. Detect, no detect. And they're very sensitive, down to less than one per gram.

Economically we could not sustain these rapid methods if we had multiple things that had any presence of microorganisms. So by and large, we have no microbes detectable in our products.

Consumer safety: Jay mentioned some of the protocols developed to understand consumer use and anticipate consumer contamination of our products. We are very well aware of this. And to do this, we establish stability of preservation through the various vagaries of consumer use and practices. In-use testing is a very common element. In the late '80s Procter & Gamble published a landmark study where we calibrated the level of preservation versus the level of consumer contamination. Of course, the objective was zero, zero consumer contamination. And that became the standard by which Procter & Gamble pursued preservation for cosmetics, in addition to safety and other elements, to

have zero contamination in the hands of the consumer, the reasonable consumer.

We continue to monitor, though; this is a dynamic industry. It's a scientific effort; we monitor the globe in terms of microbiology, the recalls of the European RAPEX Index, the recalls in Australia, China, Japan, Canada, to see how these products that are recalled failed. What made them fail? What was the nature of the microorganism that grew up in these products that substantiated the recall? And why did it happen? And we modify our protocols and address these in our own practices.

We look carefully at consumer comments and adverse reports. As Jay said, these are very rare. But when we have these, we follow these up, especially if they have anything that indicates microbiology, a bad smell, a bad color. If a consumer complains about this, we follow these things up. And this is consistent across our industry.

So let me give you an overview. I believe the cosmetic industry in the U.S. is a global leader. And I think that overall, the world has, frankly,

benefitted from the practices developed since the 1960s and 1970s by the PCPC groups. And it's very important you understand that because over-regulating this area is going to have a significant effect, and I'll discuss that in a second.

We have established and applied best practices. And these things have been copied around the world. And I believe these things will appear in the ISO guidelines. Through the many decades, we've established a very good record of safety.

And we have cooperated with the FDA. As I said, we welcome the FDA at our training sessions. And we're happy to be here today. We thank the FDA for giving us the opportunity to talk.

But all this quality, all this success is a product of affirmative risk assessment. I need to emphasize that. We don't test products, and see if it has bacteria, and throw that batch away if it does, and hope the next batch is good. We expect every batch to have no detectable microorganisms. Every consumer use has to be successful and can be safe because we built quality in from the very start. We've validated this

with data, with our testing data in the laboratory, with our consumer data, with monitoring stuff on the market. And we have decades of quality in this context.

As we go forward, I know the FDA will consider a number of standards here. And one of those standards -- and one of those considerations has to be safe and effective preservation; that includes parabens and formaldehyde releasers. We have very few preservatives to use. And clearly, failures in preservative -- failures in preservation have globally, outside the U.S. been shown to be very significant for consumer health.

As the agency considers other organisms, other microbes, especially the objectionable microbes, we have to carefully consider the risk assessment behind that. It's important to establish a technical justification and tap the industry's knowledge and experience in terms of risk assessment. Our current affirmative risk assessment means if there's a microorganism identified, we have to work against that. Mitigate it. Drive it out of our system.

And some of the bugs proposed so far have us concerned because those would drive us towards sterile products. And cosmetics do not need to be sterile. It does not serve the consumer at all to have them sterile. It will stifle the innovation and certainly limit consumer choice if they are required to be sterile.

I think it's important as we go forward, and I know the FDA's interested in this, and I welcome other groups as well, even the EWG, to cooperate with us on this risk assessment, because this is a relatively rare group. There is no school of cosmetic microbiology; there's no academic exercise here. This is learned. It's an arcane arts and science. And very few people know that. There's probably 20 people in this country that are experts at it. But they're all with companies that control major shares of the market. And they all are at the PCPC teaching new microbiologists how to do it.

I appeal to the agencies to continue this risk assessment with us and allow us to provide our experience and expertise as goes forward.

Again, thank you for this opportunity. I'm happy to take any questions. Scott?

MR. SUTTON: Phil, thanks. You've mentioned risk assessment at least five or six times. We're about three-eighths of the way through today's session and no one has yet commented on the current topic of bacillus cereus and risk assessment and where exactly is this going. Are we more concerned with hazard avoidance or in risk assessment? Thanks.

DR. GEIS: Certainly from my perspective, I'm more interested in risk assessment but maybe my colleagues from the FDA would like to answer that question.

MR. SUTTON: Yeah. I'm sorry. Just if I can interject? I've been asked to give my name and affiliation. My name is Scott Sutton. I'm the principal consultant with Microbiology Network. Thank you.

DR. GEIS: Let me make a shot at it first then Dave you can talk. I think the risk assessment is the important element. Not risk elimination. Risk elimination, especially in the context of B. cereus,

which for those of you that don't know, is a very common dust-born microorganism.

You mentioned *B. cereus*, and that, in some context, is a very serious pathogen, but it is also a very common dust-born organism. This room is full of *B. cereus*. So it's important that we do a risk assessment, because we can't eliminate *B. cereus* in this room.

The microorganisms in our -- as I said, in our cosmetic products are such a low concentration that whatever is in there is dwarfed by whatever you see on the skin when you apply it, by your face, by whatever intimate body surface you put it on. So that's why the risk assessment, I think, is the -- has to be the paradigm we use.

John, would -- you got a comment?

MR. GASPER: No.

DR. GEIS: Okay. Did that answer your question, Scott?

MR. SUTTON: Yes. Thank you.

DR. GEIS: Yes?

DR. KATZ: Actually, I have a question, and it

relates somewhat similarly, I guess, to the risk assessment question. When you're doing a risk assessment, which microorganisms are you looking at to assure that you've considered all concerns, because that wasn't explained in terms of your talk itself.

DR. GEIS: Yeah. I think the -- if you were to look at the AOAC documents you would see that. But in addition to the ones that Jay mentioned, Staph aureus, E. coli, Candida albicans, there's a wide range, especially, of Gram negative bacteria, Burkholderia cepacia, Serratia marcescens, Enterobacters, that we are very concerned with. And our preservative testing is designed to show that these bacteria, indeed, will not be present in our products. I can definitely get back to you with that list, but it is in the AOAC document.

DR. KATZ: Thank you.

DR. HANSEN: I guess I've got a question.

DR. GEIS: Yes?

DR. HANSEN: Again, on that risk assessment, which is admittedly a broad umbrella --

DR. GEIS: Yeah.

DR. HANSEN: -- many facets coming under that. We haven't heard from anyone yet on vulnerable sub-populations. Or, I guess, another area of interest would be products marketed for use in particular settings, a related topic. I know I've used the example before of products that are marketed for use in an institutional setting, particularly, say, a hospital or a nursing home. And what factors our stakeholders would look at in doing a risk assessment and what sorts of guidance they believe would be appropriate toward that end of protecting consumers in those particular settings and situations.

DR. GEIS. Yeah. I think it is an important consideration. Indeed one of the speakers to address this group shortly will talk about risk assessment. But one of the goals and understandings from our industry is that we have virtually nothing detectable in our products. That doesn't mean there's nothing there. But indeed, the practitioner, the people responsible for those institutions, those conditions, whether they're an isolation ward or a nursing home, have to consider what products are appropriate for

that. Is that what you were thinking, Dr. Hansen?

DR. HANSEN: Well, you've answered partially and you've promised that somebody else is --

DR. GEIS: I promise. I promise.

DR. HANSEN: -- is going to address, you know, in a little bit more detail, which is fair enough, fair enough. Thank you.

DR. GEIS: Thank you. If there's no more -- oh, there is another question.

MR. VAN NESS: John Van Ness, Chemaide Laboratories. I just want to ask one more time, you were saying that the parabens and the formaldehyde releasers --

DR. GEIS: Yes.

MR. VAN NESS: --you're contending that they are safe?

DR. GEIS: They are safe. I believe that the data are clear on that. And clearly, the concerns there dwarf in comparison to the consequences of contaminated products. We have very few preservatives to use. If you get rid of preservatives, if you limit their use because of concerns that don't have a lot of

foundation, we are putting our consumer at risk, clearly.

I'll defer for a second to an example in Saudi Arabia where a knock-off of a baby shampoo was not preserved appropriately, was not made appropriately to the right standards, clearly, had *Serratia marcescens* in it and resulted in the death of four or five babies in a hospital. The consequences are not so obvious, but when they are -- when they do happen, they are profound.

MR. VAN NESS: So in saying that, you had stated also that the practices and the things that have been studied by you and the PCPC, are used worldwide, and are the basis for a lot of the things. So would it be contrary to what the representatives of the EWG said? In other words, is the EU, are they so much more robust than what we're doing? Or --

DR. GEIS: We market the same products around the world. There's no difference. We get the same quality standards, the same efficacy standards are marketed around the world by all these companies, by Procter & Gamble, Estée Lauder, Avon. There's no

difference. We don't consider any population to be less deserving of protection.

MS. TALLENT: Hi, I'm Sandra Tallent from the FDA. You mentioned that you had rapid methods to detect one CFU per gram. Can you elaborate on your methods?

DR. GEIS: Sure. These are based on enrichment, enrichment of a quantity of product in a large vessel, in a large volume of broth. So, per -- so whatever volume of product is put in there, whether it's one gram of product or ten grams of product, anything viable in there will grow. So anything that grows in there, we'll say this product doesn't meet our standards.

And by virtue of our testing, by virtue of testing to that level -- and then we validate it, indeed to be -- to show that we can detect at that level -- by releasing by this method we have very vanishing levels of microorganisms at any level in our products. Is that what you were thinking? Okay. Well, thank you very much.

MR. GASPER: All right. Since we're running a

bit ahead of schedule, which is good, we'd like to have our next presenter, David Steinberg, up. And he's from the Cosmetic Preservative Council.

MR. STEINBERG: I have to change my speech, good morning, instead of good afternoon. Thank you very much for giving me this opportunity to speak. Just a little brief background, I got involved in the cosmetic industry in the '60s, that's why I have white hair, and been involved in the area of preservation shortly thereafter. In the early '80s I started teaching the chemistry of cosmetics in graduate school. I've lectured throughout the world. One of my specialties has been preservatives, I've invented preservatives; I've worked in this area for many years.

In 1995 I left the wonderful confines of industry and started consulting on my own. I was one of those people who voluntarily did this. And I'm here to talk on behalf of the Cosmetic Preservative Council. Now many of you have never heard of this and that's because we don't make a lot of publicity and we don't make a lot of noise. But we got together in 2006, the major producers of preservatives for cosmetics in the

world, to basically discuss about mutual problems and advocate the use of preservatives and to defend the use of preservatives.

We generally conduct most of our information through email. We do try to meet maybe once a year at the Supplier's Day of the Society of Cosmetic Chemists. Our current members include Dow, which also includes its acquisition of Rohm & Haas, Ashland, who purchased ISP and Sutton Laboratories, Clariant who had purchased Nipa Laboratories, Lonza, who also has now purchased Arch Chemical, Ueno Fine Chemicals from Japan, Sharon Laboratories from Israel, Schuelke & Mayr from Germany and Jeen. There are a couple of companies who sometimes attend meetings but haven't officially joined.

A couple comments, and these are very broad things, which everyone should be aware of, that preservation is the prevention of microbial -- or retardation of microbial contamination of our products from the time they are manufactured and the time they are used up by the consumer. We add chemical preservatives to a formulation to retard and prevent

this growth from consumer contamination. Preservatives are not a replacement for GMPs.

Regulations of preservatives vary throughout the world. In the United States the FDA does not preapprove preservatives, the FDA has the authority to prohibit preservatives, and they have prohibited some preservatives and we do not use these and have not used these. In fact, when I mention some of them when I teach the course, people say, "What is it? I've never even heard of it." We haven't used these in 50 years.

The European Union, on the other hand, has a preapproval list, currently under the Cosmetic Directive. It is called Annex-6 under the new cosmetic regulations which go into effect in 2013 this has been changed to Annex-5. Japan also preapproves preservatives and they break preservatives down by whether they are being applied for leave on, rinse off, general use or products that come in contact with mucous membranes.

As I said before, we add preservatives to products that have been produced under GMPs that are clean, so that they prevent contamination by consumers

under normal and foreseeable use. Now, previous speakers have talked about packaging, and let's understand some of the issues that cosmetic microbiologists and cosmetic manufacturers and people who manufacture preservatives understood full well.

Let's take a facial cream and package it in a typical jar with a nice wide mouth on it. And the consumer uses this by putting her absolutely sterile fingers into the jar and smearing the cream on to their face. If that product is not adequately preserved, it will grow and the problem is that we don't see bacteria. We might see mold, but we won't see bacteria.

Take the exact same product and instead of putting it into a wide mouth jar, put it into a tube with a very narrow orifice where the consumer can't stick her dirty fingers into, we have a totally different preservative issue and a totally different manufacturing and safety issues that you have to deal with.

Now, we have pretty much agreed in the world to establish the efficacy of preservatives by a

preservative efficacy test. And this is a simple test that basically we use and we'll talk about in a couple seconds. What did the FDA say about the adequacy of preservation? And again I'll date myself, because this goes back to the '60s and '70s, it went up until the '90s, the FDA had a cosmetic handbook. And I guess Stan Milstein and myself who still have original copies, I don't know whether anyone else does. I still have mine, I still use it very regularly.

And it says there -- and it says that cosmetics and topical pharmaceuticals need not be sterile. And the reason for that is they're not applied to sterile surfaces. We have bacteria growing on our skin all the time, so applying a sterile product to a non-sterile surface really doesn't seem to make too much sense.

However, they say that our products cannot be contaminated with pathogenic microorganisms, bugs that can cause disease and illness. And further, that the other levels of microorganisms must be low, without really a definition of what that means.

Finally, the most important thing, which I

find which continues today is that cosmetics and their raw materials must be manufactured and stored under conditions that basically prevent adulteration, especially microbial contamination. And some of the most common types of contaminations that I am called upon to look at are products that are manufactured under clean operations, have adequate preservatives but are stored in such a way as they become contaminated.

The last one I was involved with was a company who made a bulk lotion, put it into a tote bin and left the tote bin sitting around for four days, uncovered. Naturally it became contaminated and naturally the product had to be destroyed. When management found out about it, they were rather upset, because their instructions were anything that is manufactured has to be filled immediately, not stored.

The European Union defines pathogens as three, *Pseudomonas aeruginosa*, *Staph aureus* and *Candida albicans*. Let me say one thing right now, which people who have taken my courses, have heard my lectures, for years and years and years I've said I've never been able to get *C. albicans* to grow in a cosmetic. I had

tremendous numbers of cosmetics that failed challenge testing for *C. albicans*, but I just never could get *C. albicans* to grow.

I always thought it was because cosmetics were hostile to *C. albicans*, but actually there is a real valid scientific reason and this came out in publication by a colleague of mine about 10, 12 years ago in a very obscure pharmaceutical journal. And basically what it said was that *C. albicans* need a very, very narrow range of water activity. Now water activity has been mentioned before. Water activity is not the amount of water present, water activity is the amount of water that's available for microbial growth.

And *C. albicans* needs a water activity of between .88 and about .91 and we just don't manufacture cosmetics in that water activity range, which is why we've never seen contamination.

Finally, about five years ago I was called into an account that had a contamination of *C. albicans*, it was actually growing, it was thriving there. We ran water activity, .9.

What does the FDA recommend? That each batch,

which is not self-preserving, should be tested for microbial contamination before it is released. We're going to talk a little bit more about that. And finally, that each batch, especially each cosmetic batch that is intended for eye area cosmetics, during their development, we check for adequacy of preservation under normal and reasonable foreseeable consumer conditions of use.

Challenge tests, we've already said a couple words. It's a short term test to see whether our product will withstand the contaminations that consumers do to our products.

This works very well for typical cosmetics, and you've heard that statement before. Let me say that typical cosmetics are products which have water as the solvent, water is the continuous phase. Challenge testing does not work well for atypical cosmetics and atypical cosmetics are products that do not contain water or do not have very high levels of water or water is not the continuous phase. For example, a water and oil emulsion. When we go and run a typical challenge test on a water and oil emulsion, we invert the

emulsion, so that water is the continuous phase. And when we try to do a standard test like this, all we have to do is formulate to pass the test, as opposed to adequately preserve it.

Now PCPC's micro committee has spent significant amount of time and effort to come up with ways in which we can adequately really understand atypical cosmetics and how they need or do they need to be preserved and how we test them and the information is available, just contact PCPC and they'll be glad to get you the information that we've developed.

Jay had talked about general microbial limits, Jay used a simple ten to the third, I'm using a thousand, that's ten to the third colony forming units per milliliter, eye and baby products in the absence of pathogens. Many years ago Don Orth and myself coauthored a paper which was sort of like a contest between the two of us as to whether this was appropriate. And we both agreed on one thing, that these tests are appropriate on one important condition, that if you turn up with a positive number of colony forming units, you define what happens to it 24 or 48

or 72 hours later.

So, if you turn up with a count of let's say 50 CFUs, you are taking a snapshot at one moment of time. Come back 24 hours later and see what numbers you have. Could it be too numerous to count? Then you have a product that's inadequately preserved and should not be shipped. Has it died off so we can't detect it? Or is it stasis, meaning it's staying the same?

And this is what we concluded. The most common test for this plate count is USP-61, I won't go into details to it, just that this seems to have been adopted as the universal standard. When we talk about preservatives, I have written several books on this, and please save your money, the third edition is coming out next year. Please buy it. I define preservatives by their chemical structures. And I'm going to go through them very briefly here. We have a lot of acids that are used, they're principally active against fungi. Many of the acidic preservatives are also allowed in foods, these would include things like benzoic acid and sorbic acid.

Aromatic alcohols are mostly active against

bacteria, these are extremely common, we'll talk about them in a few minutes. And methylol groups are often referred to formaldehyde donors or formaldehyde releasers, they're mostly active against bacteria.

When we put a halogen group onto most molecules, they tend to become very strongly anti-fungal, so most of our strong anti-fungal bacteria agents happen to have a halogen group on them.

We have a whole classification of two actual used preservatives which are based on isothiazolinone chemistry, and because of the way they're produced, we'll talk about that in a second, they are active against both fungi and bacteria.

There are some preservatives which are quaternium compounds, they're mostly active against bacteria. We tend not to use them very frequently in cosmetics, they have more important uses in terms of disinfectants.

And finally, one of the more important groups that's growing in popularity are the 1,2-diols which are mostly effective against bacteria.

Preservatives that tend to be active against

bacteria generally are not active against fungi. Preservatives that are active against fungi tend to not be active against bacteria. So, we combine them, we put them together to give us a broader coverage, so we take care of all microorganisms.

The following are the most popular preservatives used in the United States, as of my last publication, which was two years ago. Back in the early '70s, the FDA issued a publication on the frequency of use of preservatives, this was updated from the voluntary cosmetics registration base. When I started consulting in the mid-90's I was asked to take over this project and about every three years I updated this list. I want to thank Don Havery for his support in getting me the information.

The last time -- well, I published last year, but three years before that I also obtained the exact same information from Health Canada. Now, the difference between Health Canada and the United States is Health Canada has mandatory registration of cosmetic formulations. So, the numbers there actually represent what is in Canada, where what we have in the United

States are voluntary. And guess what, they're the exact same order. We use the exact same preservatives whether we force people to register or we don't, we get the same information.

And the trends also track the same. Most popular preservative continues to be methylparaben and number two is propylparaben. Both of them happen to be universally permitted in foods, not very frequently used, but universally permitted in foods. They also are permitted in ingestible and injectable drugs. Phenoxyethanol is a very popular preservative, it's also a solvent, followed by butylparaben, ethylparaben, we'll talk a little bit more about that and isobutylparaben, in a couple minutes.

MCI/MI are just my abbreviations for methylchloroisothiazolinone and methylisothiazolinone. This is a mixture, but it's not really a mixture, it's produced this way, a three to one ratio of the methylchloro to the methyliso. It was introduced to the cosmetic industry in Europe in the '70s, in the United States around 1981, 1982. It is the most popular preservative for shampoos and rinse off

cosmetics. It is also the most powerful preservative. We typically use this in the total of ten to fifteen parts per million range.

This is followed by DMDM hydantoin, one of the N-methanol groups, followed by imidazolidinyl urea, another N-methanol group. Finally, benzyl alcohol rounds off the top ten. Benzyl alcohol could be questioned, because besides being a preservative, benzyl alcohol is a fragrance component and it's a solvent, so we don't know how it's functioning. In fact, I've always wondered, the European Union permits benzyl alcohol as a preservative up to one percent, and they permit it up to 100 percent as a solvent. And I've always wondered, when I'm making a formulation, does the benzyl alcohol know what's doing in the formulation? Do I ask it or does it tell me? Good question.

Caprylyl glycol, growing in popularity. One (1),2-diol, diazolidinyl urea one of the N-methanol groups. Sorbic acid, a food grade preservative, strongly anti-fungi. Benzoic acid, another food grade preservative. Finally, number 15, chlorphenesin, we'll

talk about that a little later. Halogenated group, it gives it anti-fungi properties.

Sixteen, dehydroacetic acid, another product that's also allowed in foods, but it's rather obscure. I believe the only food application that was approved was for yellow squash. I haven't quite figured out why yellow squash needs to be preserved.

Number 17, IPBC, I again abbreviated this so it would fit on the slide, Iodopropynyl butylcarbamate, very strong anti-fungi preservative. Number 18, ethylhexylglycerin which is used more as a solvent. Number 19, pentylene glycol, another 1,2-diol and finally, rounding out the top 20 is quaternium-15.

If I look at the next 80 preservatives and add them together, the number of uses doesn't equal where we are with the last one on the list. So, although we might have a hundred different preservatives, we're basically using only about 15 to 20. Our list is very, very narrow.

We use combination products, we call them cocktails. Okay, why? First, it gives us broader activity. Second, it gives us an easier way to

incorporate the methylchloroisothiazolinone, methylisothiazolinone. Can you imagine weighing out ten parts per million of a powder accurately? Well, maybe the plant can do it, because you're making a big batch, but I know in the lab, when I worked in the lab, if I could measure out a tenth of a percent it was a miracle. Ten parts per million, never would get it in correctly. But it's sold in solution so that it's easier to incorporate and it's easier to weigh in the lab. And finally, that was why we dilute it.

Okay. The most popular mixtures, now I have this in an order for a reason. This is a chronological order, the first combination which really became popular was the methylchloroisothiazolinone, methylisothiazolinone, around 1981, 1982, for rinse off products. It is manufactured at a three to one ratio. Can they make it pure? Yes. Do they? No, there's no reason for it. Recently, five years ago, they introduced just the methylisothiazolinone, very strongly antibacterial, needs an anti-fungal agent, a number of combinations.

Okay. The second one was one which I was

deeply involved, I invented it was the combination of the diazolidinyl urea with parabens predissolved in propylene glycol. The big reason it achieved popularity, it was easy to use, you just dumped it in, instead of worrying about how to dissolve things. This was promptly followed by the parabens dissolved in phenoxyethanol.

And if you look at the first slide in which I had the different preservatives, the combination of parabens and phenoxyethanol is why you see methyl, ethyl, propyl, butyl and isobutyl. That was what was in this combination and it attests to the popularity of, again, a liquid which is much easier to incorporate into formulations.

The latest one has been the use of caprylyl glycol and because of its limited solubility it is usually offered in combination with phenoxyethanol as a solvent.

With one exception, all of the preservatives in that top 20 list have been reviewed and re-reviewed for safety by the Cosmetic Ingredient Review. The only preservative on that list which has not been reviewed

yet by the Cosmetic Ingredient Review is chlorphenesin and in two weeks I will be back in Washington when we will have the first review of chlorphenesin.

So, all of our preservatives are being reviewed or have been reviewed by independent people, people who have no connection to cosmetic companies or anything else, they're only interested in reviewing the safety of these products.

They've also been reviewed and re-reviewed by the European independent group of safety assessors called the SCCS, the Scientific Committee on Consumer Safety.

Many of these preservatives we have been using safely for 90 years. Parabens were introduced in 1920's, and used safely since then.

The biggest problem and the biggest injuries and biggest concerns of safety of preservatives has always been sensitization. Preservatives function to kill bugs. When we apply too high a level or very high levels we can cause sensitization or reaction to the human skin. A lot of the industrial preservatives are not used in cosmetics because of this reason. The

preservatives that are used in cosmetics are tested constantly for sensitization and most of the time when we have reports of sensitization they usually occur because people have higher levels than what are needed.

All cosmetic companies, that I'm aware of, test their finished formulations for sensitization. Yes, I can know a preservative that's very sensitizing and I can formulate it so it's not sensitizing. If I can't, I won't use it.

What's happened in our marketplace? Since the late '70s the consumers have been inundated by advertising and selling of consumer products, and I'm not just talking about cosmetics, I'm talking about foods, I'm talking about other consumer products, for what they do not contain. I remember one time, probably about 15 years ago, going to the supermarket and there was a little stand and a woman was selling frozen boil-in-bags of soup. And she was telling everyone, "Please try it. It's preservative free." Now, for someone who is deeply interested in preservatives, this always arouses my curiosity.

So, I took some of the soup and I tasted it

and I said, "Yum, you're right. I don't taste any preservatives." I tasted it again, I said, "You know, I don't taste any automobile tires in here either." I tasted it again, I said, "Hey, boy, I don't taste any dynamite. Why don't you say they're dynamite free?" And the woman says, "Look, I'm just hired to say this."

What was the implication? There was something wrong with preservatives. And I told her, I said, "Your issue is you're selling a frozen product, that is how it's preserved. And if you put a preservative in a frozen product someone is wasting someone's time and effort."

The FDA took action in the '70s against a company who advertised their vegetable oil was cholesterol free. Well, there was never ever cholesterol in vegetable oil, cholesterol comes from animal fats, not vegetable fats.

In the early '90s, not far from here, I attended a meeting of what we called Anti-microbial 2, which was one of the monographs from the Division of Drug Evaluation and Research. And they had made the announcement that they were going to divide Anti-

microbial 2 into what we commonly call now healthcare antiseptics and first aid antiseptics.

But the speaker made the comment that one of the things he was disturbed about was the use of alcohol in mouthwashes. And he wanted to put the percent alcohol into mouthwashes on the label. And I spoke to him privately and I said that this will only have the effect of demonizing alcohol and the function of alcohol in mouthwash is the preservative. The removal of this will cause companies to advertise and market alcohol free mouth rinses.

Well, back when he said this, the only time you ever saw an alcohol free mouthwash was the little bottles you were given when you went into the hospital. I remember my wife getting one when she gave birth to our son. Now it's a mass marketed consumer item. If you look at the FDA's voluntary recall of contaminated products, the most common one that you see are alcohol free mouthwashes. But that's a GMP problem, correct? Because it's manufactured under conditions in which it was contaminated. Well, let's ignore that. Let's assume we make it properly under good GMP and it's not

contaminated. How do consumers use mouthwash (gulping sound). Do you think that bottle is now not contaminated?

Marketing quickly picked up on this and suddenly everything was free of whatever we could sell product for. Preservatives became a prime target, whether it be paraben-free, formaldehyde-free, triclosan-free. These organizations are constantly attacking preservatives. So what do we do? Marketing turns to the microbiologist and said, "I don't want you to formulate with these." Well, if you look at our list of characters of what we can use, we start using them at higher levels.

I go back to the '60s when potassium sorbate and sorbic acid were one of the most common anti-fungal agents used in cosmetics. And the number of sensitizations to sorbic acid was high, they were one of the highest that was reported from the constant dermatology group. We almost discontinued using sorbic acid, even though it's natural and it's food grade, it's not so great on your skin.

Well, what's happening now, we're back to

using it because parabens were our big anti-fungal preservative and you want to be paraben-free you need an anti-fungal agent. And you want it to be halogen-free. I expect to see probably higher levels as we have to use higher levels of sorbic acid.

The organizations basically talk about several things. If it's natural it's safe. I have no concept or no idea why consumers believe this. If it's natural, it's safe. Arsenic is natural, cyanide is natural. Next thing, if it's chemical it's toxic. I hate to tell everyone, but everything's a chemical.

I was at a meeting and someone used the term chemical free and I said, "Chemical free is a damn good vacuum. What are you talking about?" "Oh, I mean natural." "What do you mean natural? They're chemicals also."

Industry doesn't care about safety. You just heard two speakers talk about how much time and efforts are spent to justify the safety. I have a question for everyone in the audience, how many of you buy unsafe cosmetics? Oh, where's my market then? Adam Smith's Invisible Hand, if you took economics, the marketplace

says cosmetics have to be safe because people won't buy them and companies can't sell them.

One of the other comments here, government is paid off by industry. The pharmaceutical industry spends a fortune in fees to the FDA to approve new drugs. They're called user fees. Congress mandates them. The law is up for review. Should we eliminate user fees for drugs? We approved -- the FDA approved more new drugs in 2011 than they did for the past two or three years combined. Why? Because they have user fees and have resources without having to raise taxes to pay for it.

If the first attacks against you on a preservative don't work there's another one, but keep attacking it and finally everyone will believe that whatever you're attacking is true and is bad. Canada addressed this. Advertising Standards Canada in cooperation with Health Canada considered all of these free claims to be inherently false and misleading. So, if you want to claim your product is hydrogen cyanide free, that is a false and misleading claim.

They did say there are times when it's

important to the consumer to know that the product doesn't contain something, for example, if you're a diabetic and your food contains sugar, you should know that it contains sugar.

So they set up some rules and regulations as to when you can make this claim. The first thing is the product has to have been sold with this in it. So, your product had to have been registered, had been on the market in Canada and then you have to notify the government that you're removing the ingredient. We're taking the parabens out of our creams and lotions. You must then also submit an outside laboratory analysis showing that the new formulation contains no detectible paraben, none. If our detection limit is one part per quadrillion, then that's what we have to find absent.

At this point you're allowed to make a paraben-free claim for one year. And at the end of one year, not only are you no longer allowed to make the claim, you must go to the store and remove all products which make this claim. What's happened in Canada? You don't see free claims anymore. What you do see is saying the product has not been formulated with

hydrogen cyanide or it contains no hydrogen cyanide, or we do not have hydrogen cyanide in the product.

However, these all have to be true and provable.

In 2008 I was asked to speak on what was going on with the different preservatives and I said every single one of them is under attack. Most of the attacks are silly, most of them are not based on science whatsoever. We have the science that says they are safe. The Cosmetic Ingredient Review has said they were safe. The European SCCS said they were safe. Cosmetic companies would not use them if they weren't safe.

Are there going to be new preservatives, the answer to that question is no. I'll go back to 1960, a new preservative was developed, the company who invented it took it to a major user and said, "What safety data do you need for us to sell this preservative to you?" And they said, "Well, we want you to do an LD-50," feed this to rats until you've killed half of them. "We want you to do a rabbit eye irritation test to be sure it doesn't irritate the eyes." And finally, "We want you to do a skin

irritation sensitization on guinea pigs." Total cost was about \$2,000.

Same company, in the '80s, that I worked for, when they came out with my brand new cocktail that I invented, even though every single ingredient in the cocktail had been safety tested for ages, it cost us over \$100,000. And that was in 1980, that was 30-some years ago.

The latest one that was approved took five years to get approval in Europe, five years to get approval in Japan. The costs were in the seven to eight figure range. That's just cosmetic safety, now we have to deal with environmental issues like REACH and the DSL list in Canada and NICNAS in Australia. It's too expensive, our market's not that big. It's not that big.

So, what's happening? We're seeing more and more non-preservatives offered to the marketplace. What's a non-preservative? It's a product that's not on the European approval list. The glass is half full or the glass is half empty. If it's a preservative, the glass is half full. If it's not a preservative,

the glass is half empty. It's an emulsifier, it's a skin conditioning agent, it's whatever else you want to call it. And that makes our products self-preserving.

Let's go back to the FDA's comments.

Cosmetics that are not inherently self-preserving need to be tested and challenge tested, et cetera. They're in conflict with each other.

One of the things that marketing asks, "Well, give us something that's natural, that will self-preserve our products." Well, what happens is if you ask for it there will be people who give it to you.

Just like dietary supplements, which claim drug activity but are dietary supplements and the FDA constantly is recalling these because they contain real drugs that are not disclosed. Just about every botanical extract that I have looked at has had one of those top 20 preservatives in them.

Caveat emptor, let the buyer beware. So what can we do? The manufacturers of cosmetic preservatives, we believe in a strong FDA. We believe in strong public relations. We believe that the public has to know that their products that we are selling are

safe and that they're safe for the consumer to use, that we have excellent safety standards and that we have had this evaluated, not by ourselves, but by independent scientists who have no vested interest in this.

The history has supported that the cosmetics are sold are safe and that the preservatives that we use today are safe.

And I thank you. I'll be glad to take any questions.

MR. GASPER: We're going to take a break for lunch but first a few little housekeeping notes. In addition to the hotel restaurant on this level, there are a number of places on the mall level serving sandwiches, salads, et cetera.

Another reminder, if you have not signed up yet to make public comments, but would like to do so, please see Juanita Yates before going to lunch. That was something I mentioned in the morning.

And if any of you drove in today and are parked in the hotel parking garage, please see Juanita before going to lunch.

I guess with that we'll break for lunch till one o'clock. Thank you very much.

(Lunch break)

MR. GASPER: Thank you all for coming back. Next up we have Dr. Richard Whiting from Exponent.

MR. WHITING: Thank you. I'm Richard Whiting. I'm a microbiologist and a microbial risk assessor. Prior to joining Exponent I spent a career with the U.S. Department of Agriculture and with the FDA.

Exponent has conducted microbial risk assessments in food products and we are just in the process of collaborating with the Personal Care Products Council in the cosmetic area, in microbial risk assessment.

We noted in the Federal Register Notice for this meeting, that FDA noted a variety of factors affecting microbial safety and requested information on organisms that posed specific health hazards and requested stakeholder input in the development of guidance.

So, what I'd like to do in this presentation is discuss the microbial risk assessment process

itself, look on it as a necessary procedure to develop guidance and that this should be done in collaboration with industry and consumer stakeholders. And I noticed on Dr. Hansen's slide this morning that she had one on risk assessment and I think actually we're very much on the same page with this and I hope this will prove to be the case.

As someone who has done a lot of microbial risk assessments, I've noticed the word is used a lot, it's been kicked around here today on many presentations, but I also have seen that people do not really have a good understand of exactly what is involved with microbial risk assessments and what it's all about. So, that's what I would like to present today, is looking at microbial risk assessment as a process to help you come up with guidance.

My objectives here, briefly, are to describe the risk analysis process and I'll present sort of a hypothetical case to help describe that. To present risk assessment as a tool for making informed decisions in evaluating potential hazards and to describe the risk assessment process as a foundation in developing

guidance, by providing structure, transparency, objectivity and as a basis for good risk communications.

Now risk analysis is the broader picture here. And again, it's a tool here to make a systematic evaluation of the relative scientific knowledge to help the risk managers make an informed decision. And there are three basic activities within this. The risk management, within the context of this meeting, would be FDA and making decisions on what guidance they would put out. The risk assessment is the scientific gathering of information and data and evaluation of that. And then risk communication refers to the necessary actions of collecting information from various stakeholders, it could be from the industry, could be from the public, for doing the risk assessment, but also getting this information back out again afterwards.

The classic structure of a risk assessment has four different components. Called first the hazard identification, which describes what the purpose of the risk assessment is, which bacteria, which products,

which people are concerned and the subject of the risk assessment. The exposure assessment then is determined how many bacteria are actually exposed to the consumer, what are the numbers what are the frequencies of exposure. And it's important to realize, of course, this is to the consumer, not necessarily at the end of manufacture or some other time when regulatory control might be applied. The hazard characterization or as they sometimes call it the dose response, looks at the organism itself and asks what the potential for illness of that organism or the virulence of that organism.

The risk characterization part then brings these last two together and looks at a specific product with its contamination, the exposure to the consumer and the risk characterization from the organisms, says what is the risk of this product to the consumers.

And again, the overall purpose of this is to, you know, inform the risk managers for the decision. The risk assessment does not actually determine or calculate the safety. It provides information to the risk managers that they can make their decision.

Now the risk managers would then commission a

risk assessment, because they have some issue that they need scientific information to help them make a decision on. And the risk assessment, therefore, is tailored specifically for each situation, each one is unique. And there are several different forms or levels that it can take. The first here is a risk profile, which is really quite similar to what you might think of as a white paper.

If you're interested in comparing two products or two treatments, you might want to do a risk ranking, determine whether one was greater or lesser than the other. If you don't have a lot of quantitative information you might move into what we call a qualitative risk assessment where the frequency might be considered high, medium and low or frequent, rare, something like this.

And the finally, a fully quantitative risk assessment where you have numerical values for levels and various other parameters and I'll show you an example later.

Obviously as you go down towards the quantitative risk assessment, there's a need for more

data, better quality data in order to make the calculations. It also means that the quantitative risk assessment will be probably more time consuming and expensive to conduct. But again, what you do will depend on partly the information that's available but also what is necessary to provide the information that the risk managers need to make their decision.

It's important, in the risk management process, that the risk managers define very specifically what the particular issue or question is that they want guidance on. And some of the things I threw out here that might be of concern to the risk managers: Which particular products, what specific products do you want a risk assessment on or perhaps products that have certain types of applications, what particular microorganisms are you interested in, are you interested in the numbers of the bacteria or the numbers that might be above or below a certain level. You might want a basis on virulence factors, not all strains of a certain bacteria are equally virulent. And then finally, you may have a risk assessment for different users. You might be interested in all people

or you might be just interested in children, for example.

For an example, today I've put together just an outline of a hypothetical risk assessment here. Looking at sort of the question of what is the likelihood that a facial product could cause an eye infection and how often and why will the product exceed the specific criteria that leads to that.

In the hazard identification section, you can see some of the things that you will be looking for information on. And I might just add, as a side thing here, I've put the word pathogen up there, but that's a very general term that I'm using it today, it's really the organism that you are concerned with that may have a public health impact. And in fact, it may turn out that the risk assessment shows that it does not have a public health impact.

So, again, you're looking at contamination levels, where is it coming from, what does the pathogen do in the particular product. Will it grow? Is it inactivated? And then, what's the epidemiology? What does the pathogen do when it is used by the consumer?

A typical step here is to develop a flowchart. In this case we've got our ingredients, one of which may be contaminated with our organism of concern. We have our bulk processing, processing, packaging, which is another opportunity for contamination. Then there's distribution and consumer storage, and again, it's very important in a process like that to consider what the consumer is doing with the product.

And then finally, on the right side, the risk assessor's -- risk managers may ask for different outputs. They may ask what's the likelihood of illness per serving or per use, or how frequently does the contamination exceed a certain level. And that can be looked on as an individual basis or if you have a population, what are the total numbers for a population.

So, this is our flowchart then that we are going to populate with data which we need for each step of the process. And what occasionally will happen here is that you do not have good data for a particular step and in this case, if it proves to be a very critical step in the process, this is now a research need that

you need to go out and collect data, then come back and do the risk assessment.

Just very briefly here, some of the types of data that you would use in populating this risk assessment. What's the thermal inactivation of spores? In this case you've got D-values time for one log of inactivation. What do you know about growth? Is it inhibited by water activities below a certain level? What about the inhibitors that are added to the product, are they effective?

During the storage period of the product, what's the organism doing? Does it decline at a certain rate?

Consumer use, here's examples of some of the information that you would need. How long does the consumer store the product? Is it used daily or less frequently? How much is applied? If, in this case, a concern about the eye, what's the likelihood that some of this could get into the eye and how much, if that happens?

Looking at the dose response part of it, here's some of the factors. Are we talking about a

competent or susceptible population? Do we have simultaneously an injury to the eye at the time we're concerned about it or not? And if there are say certain standards, like 100 CFUs, are we above or below that at the time of exposure?

So just to kind of summarize all of this back up here. The risk assessment here is really your only way to really take a complex process like this, with a lot of different steps, a lot of different factors, and try to put it all together to see how those steps actually affect your public health outcomes that you're concerned with.

In a case like this you could say, which one of these locations of contamination would be the most important? Or, is a processing step sufficiently severe to have the desired public health? Or, what is the organism doing during the storage period and how does that affect the public health?

So, to just summarize this, quick look at this. What we're using the risk assessment process here is to try to develop effective guidance. And in order to do that you need to have this full risk

assessment process. The risk assessment provides, you know, a structured and transparent way of collecting all the data that everybody can see and evaluate and it can show how this complex process interacts and what particular parts of this process are particularly important.

And then finally, the risk assessment process provides a mechanism for stakeholder involvement and it's also a very effective way, when it's done, to communicate the results back to the various stakeholders.

So, you know, as FDA goes forward in developing guidance I certainly encourage them to use this risk assessment approach to its fullest advantage. So, with that I'd like to thank you and I'll be happy to answer any questions.

MR. SCHNITTGER: My name is Steve Schnittger, I'm a microbiologist, part of the PCPC Micro Committee. I work for Estee Lauder. My question to you, or I guess my observation is that your risk assessment scheme can really be broken down into two parts. The risk of the product itself to support microbial growth,

which we use preservatives in our products to make sure that there is no possibility that those bugs could grow to high levels. And then there's also the risk to the consumer, of that bug potentially becoming a concern or developing into an adverse reaction to the consumer.

And but what your -- the way your scheme is laid out there, it looks at, like you'll look at the overall picture as far as the overall risk assessment of that product plus bacteria, in the same light.

And I think what we've tried to do in the industry is really look at what the potential or what the risk is of a certain product type to support microbial growth and that's why we add preservatives, that's why we look at packaging. And that's done just pretty much on a daily basis with every product that we make.

So, as I think that this scheme can be used for the FDA or for whomever to look at the different types of organisms of concern, this is something that is done on a daily basis by each of our companies. So, it's nothing new, but it does help in overall look at the different types of bacteria and those of concern.

MR. WHITING: Several comments. Yes, first of all, the risk assessment process is not new. What I think is new with this is we are becoming much more quantitative about all the calculations, before it was a little more of a subjective process.

And, in your example you're looking at part of the whole process and then you've made certain judgments on other parts of it. You know, you look at what's the contamination level, you're kind of assuming, okay, that's perhaps at certain levels.

MR. SCHNITTGER: But --

MR. WHITING: Is that true or not? And this is just a way of getting all of the information together and on the table.

MR. SCHNITTGER: My only concern is, again, we set these limits and Phil and Jay talked about the limits that we use for the industry, and as long as those limits are set and that the products that are sold within those limits, then that chance of an adverse reaction of that product to the consumer really is minimal. Because we're not putting out products that exceed that limit of 100 CFU or 1,000 CFU. And we

know, based on those specifications, that those products are safe.

MR. WHITING: Well, in this case the risk assessment should back that up. And by going through this process now you've put out, on the table, all of your data and all of your reasoning to support the conclusion that you have.

MR. SUTTON: Scott Sutton, Microbiology Network. One of the aspects that we've found really useful over the past few years in looking and investigating issues is CAPA, corrective and preventive action plans. And usually you start with a problem and you identify a root cause for this problem, you identify a fix for the root cause and then you demonstrate the fix was effective.

I guess my question is more of one for the industry and FDA as a whole. What's the problem we're correcting here? Is there a serious issue with microbiological safety of cosmetics. Thank you.

MR. WHITING: I'm not sure I'm quite following your question. You say you found the problem, corrected it and --

MR. SUTTON: What's the problem with testing?

MR. WHITING: The problem with testing?

(Speaking off the microphone)

MR. WHITING: You're not on here.

MR. SUTTON: We're addressing the general topic of microbiological safety of cosmetics, which infers that there's a problem with microbiological safety of cosmetics. And I'm just asking, what is that problem?

MR. WHITING: Well, I think I would put it back to FDA here for calling the meeting. I'm talking about the process, not specifically any particular organism or product. I'm trying to talk about the general process, the general way you would approach developing guidance and developing standards.

DR. KRAEMER: Axel Kraemer from Schwan. Maybe I'm going to rephrase your question. Somehow industry and FDA lost, how to put it, the mutual understanding of what is a microorganism which is objectionable. And I'm wondering how we are getting back to mutual understanding which microorganisms which are to be considered as objectionable microorganisms. And that's

basically a comment or a question to your direction.

DR. HANSEN: This is Pat Hansen, Office of Cosmetics and Colors. That's one of the purposes of us holding this public meeting - is to gather information, to share information. We are really looking for, as I said before, is data, information, analysis, and perspective to help inform our approach to these issues.

And I guess I would say also that, in part in response to Scott Sutton's question, that we're really on a preventive perspective here. Preventive perspective, and that's in large part what guidance is intended for, is to put out, as industry's own guidelines do, best practices, and points to consider in taking a preventive approach. And I think that informs FDA's approach across the vast range of products that we regulate, and cosmetics is one of them. This is not a different approach that we're taking.

MR. GASPER: Okay. Now we're going to move on to our closing remarks with Dr. Linda Katz.

DR. KATZ: Thank you. And actually my closing

remarks are fairly brief. I'm posting a slide that I posted earlier this morning for the goals of this public meeting. And as Pat Hansen said, the purpose of this meeting is for us to gain information from you, from others who are concerned, and interested parties.

As we went through the history and even listening to the history that was presented to us by industry, a lot of the guidances and recommendations that we've used are old. We've revised some of the information that we've received, but others are probably in need of being revised. Part of the reason is that science changes. Hopefully this isn't a static process but one that's an active process, where we can constantly gain new information - a wealth of information that all of you can provide to us. So as we look at the guidances that we have on our website, both from GMPs and from our BAM chapter, this is probably the right time to go back and see what needs to be changed.

It doesn't necessarily imply, from the questions that have been asked, that we have to change anything. But if science has changed and if we have

moved forward, now is the time to do make changes.

Some of the information that we have and some of the information that we rely upon, is close to ten years old. Some is less than that, but again, it's time for us to gain information, to look at the science once again to make the determination, whether our guidances are current, and if they are up to date.

So, basically, the bottom line is that as we've listened to today's presentations, we know that there probably is other information that all of you may have. We hope that you'll be able to share that with us in the form of written comments that will go to the docket, so we can go back and look to see if we need to revise anything, or if our current guidances and practices are appropriate, so that we make the determination if modifications are needed.

So, the basic bottom line is, we want to hear from you. We've heard from some of you earlier today, but we'd like to hear, hopefully from all of you or from all of you who have any interest in this area, and to provide us with written information, comments to the docket.

As John mentioned, all comments need to be submitted by January 30th. And so that way, as soon as the information becomes available after the docket's closed, the comment period closes, we'll go back and we'll reassess and make a determination as to what we need to do and how we can go forward.

With that being said, it may be that we may need another meeting; it may be that we don't. The information that we receive will make that determination. But I do want to thank all of you for coming.

And I will turn over to John, so John can go through our final information and some of the logistics that need to be taken care before the meeting closes. Thank you again for coming and sharing with us.

MR. GASPER: Okay, I've just got three simple things here, since we're obviously moving up the break. Feel free to enjoy the refreshments we have provided for you outside.

We have gotten a few questions about receiving a copy of the slides from the presenters today. If you want a copy, give either like I say your card or your

contact information to either Juanita Yates or Wendy Johnson or Shirley Turpin outside, or other FDA staff, and we can get you a copy of the slides.

I mentioned about the refreshments. We do have this space till five o'clock this evening, so if anybody -- you want to stay, possibly have some short discussions, whatever, the space is available to you till five o'clock today.

That's basically all I have to say. Thank you again.

(End of Meeting)

CERTIFICATE OF NOTARY PUBLIC

I, Natalia Thomas, the officer before whom the foregoing meeting was taken, do hereby certify that the proceedings were taken by me in audio recording and thereafter reduced to typewriting under my supervision; that said transcription is a true record of the proceedings; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

Natasha Thomas

Notary Public in and for
The District of Columbia