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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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OPHTHALMIC DEVICES PANEL AND RISK COMMUNICATION ADVISORY COMMITTEE

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March 17, 2017
7:30 a.m.

Hilton Washington DC North
620 Perry Parkway
Gaithersburg, Maryland

PANEL MEMBERS:

JAYNE S. WEISS, M.D.	Panel Chair
STEPHEN D. McLEOD, M.D.	Panel Member
ANDREW J.W. HUANG, M.D., M.P.H.	Panel Member
BENNIE H. JENG, M.D., M.S.	Panel Member
SAM S. DAHR, M.D.	Panel Member
CYNTHIA OWSLEY, Ph.D., M.S.P.H.	Panel Member
KORT DELOST, RPh	Panel Member
DAVID M. BERUBE, Ph.D.	Panel Member
JAMES DILLARD, Ph.D.	Panel Member
SUSAN J. BLALOCK, Ph.D.	Panel Member
GARY L. KREPS, Ph.D.	Panel Member
PARTHASARATHY KRISHNAMURTHY, Ph.D.	Panel Member
CHARLES LEE, M.D.	Panel Member
RAJIV N. RIMAL, M.A., Ph.D.	Panel Member
JEANNIE SNEED, Ph.D.	Panel Member
MICHAEL S. WOLF, M.A., M.P.H., Ph.D.	Panel Member
H. SHONNA YIN, M.D., M.S.	Panel Member
MICHAEL E. PFLEGER, J.D.	Industry Representative
KIM WITCZAK	Consumer Representative
ANNIE ELLIS	Patient Representative
ADEN S. ASEFA, M.P.H.	Designated Federal Officer

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Free State Reporting, Inc.
1378 Cape St. Claire Road
Annapolis, MD 21409
(410) 974-0947

FDA REPRESENTATIVES:

MALVINA B. EYDELMAN, M.D.
Director, Division of Ophthalmic and Ear, Nose and Throat Devices
Office of Device Evaluation

JODI DUCKHORN
Director, Risk Communication Staff
Office of Planning
Office of the Commissioner

RON YUSTEIN, M.D.
Deputy Director for Clinical Affairs and Chief Medical Officer
Office of Surveillance and Biometrics

THERESA EISENMAN
Press Contact

FDA PRESENTERS:

J. ANGELO GREEN, Ph.D., DABT
Acting Branch Chief
Contact Lens and Retinal Devices Branch
Division of Ophthalmic and Ear, Nose and Throat Devices
Office of Device Evaluation

BERNARD P. LEPRI, O.D., M.S., M.Ed.
Division of Ophthalmic and Ear, Nose and Throat Devices
Office of Device Evaluation

CONSTANTINO CASTILLO, M.S., RN-BC
Nurse Consultant/MDR Analyst
Division of Postmarket Surveillance
Office of Surveillance and Biometrics

KATIE O'CALLAGHAN
Assistant Director for Strategic Programs
Office of the Center Director

GUEST SPEAKERS:

RUTH DAY, Ph.D.
Associate Professor of Psychology and Neuroscience
Duke University

ROLLIN J. "TERRY" FAIRBANKS, M.D., M.S., FACEP
Director, National Center for Human Factors in Healthcare
Associate Director, MedStar Institute for Innovation (MI2)

MANUFACTURERS OF HYDROGEN PEROXIDE CARE PRODUCTS:

MOHINDER MERCHEA, O.D., Ph.D., M.B.A., FAAO, FBCLA
Head, Medical Affairs
Alcon Vision Care, North America

CHRISTOPHER SMEJKAL, Ph.D.
Director, Global Regulatory Affairs
CooperVision

PROFESSIONAL ORGANIZATIONS:

MICHAEL R. COHEN, RPh, M.S., Sc.D. (hon.), D.P.S. (hon.), FASHP
President, Institute for Safe Medication Practices (ISMP)

SUSAN J. GROMACKI, O.D., M.S., FAAO, FSLS
American Academy of Optometry (AAO)

JEFFREY SONSINO, O.D., FAAO
Chairman, American Optometric Association (AOA) Contact Lens and Cornea Section

DEBORAH S. JACOBS, M.D.
Past President, Contact Lens Association of Ophthalmologists (CLAO)

OPEN PUBLIC HEARING SPEAKERS:

GLENN MORO
Vice President, Marketing
NovaBay Pharmaceuticals

SAMANTHA WATTERS, M.P.H.
Director, Communications and Outreach
National Center for Health Research

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M E E T I N G

(7:33 a.m.)

DR. WEISS: I would like to call to order the March 17, 2017 joint meeting of the Ophthalmic Devices Panel meeting of the Medical Device Advisory Committee and the Risk Communication Advisory Committee to order. It is now 7:34.

I'm Dr. Jayne Weiss. I'm Chair of this Panel. I am a cornea subspecialist and refractive surgeon. I'm Associate Dean of Clinical Affairs and Chair in the Department of the Ophthalmology at Louisiana State University Medical School.

And I note for the record that members present constitute a quorum as required by 21 C.F.R. Part 14. I would also like to add that the Panel participating in the meeting today has received training in FDA device law and regulations.

For today's agenda, the Committee will discuss and make recommendations regarding the potential risks of misuse of peroxide-based contact lens products. Specific issues to be discussed include adequate labeling and packaging of these over-the-counter products.

Before we begin, I would like to ask our distinguished Panel members and FDA staff seated at this table to introduce themselves. Please state your name, your area of expertise, your position, and your affiliation. Can we start --

MS. DUCKHORN: Good morning. I'm Jodi Duckhorn, and I'm the Director of the Risk Communication Staff.

DR. EYDELMAN: Good morning and welcome. I'm Malvina Eydelman, Director of the Division of Ophthalmic and Ear, Nose, and Throat Devices.

DR. McLEOD: Good morning. I'm Stephen McLeod. I'm the Chair of the Department of Ophthalmology at the University of California, San Francisco. I'm also a faculty member at the Francis I. Proctor Foundation, with expertise in cornea external disease and a

particular interest in infectious keratitis.

DR. HUANG: Hi. Good morning. I'm Andrew Huang. I'm from Washington University in St. Louis. I'm a Professor of Ophthalmology. I am a cornea specialist.

DR. JENG: Good morning. I'm Bennie Jeng, Professor and Chair of the Department of Ophthalmology, University of Maryland School of Medicine, cornea and external disease specialist.

DR. BLALOCK: I'm Susan Blalock. I'm a professor at the Eshelman School of Pharmacy at the University of North Carolina, Chapel Hill. I'm a behavioral scientist with expertise in medication risk communication.

DR. BERUBE: My name is David Berube. I am a Professor of Science Communication at North Carolina State University, and I'm also a Co-Director of the Research Triangle Nanotechnology Network.

DR. KRISHNAMURTHY: Good morning. I'm Partha Krishnamurthy, Director for Institute for Health Care Marketing. I'm Professor of Marketing at the University of Houston.

DR. LEE: Hi, my name is Charles Lee. I'm President and Founder of Polyglot Systems. My background is in medical informatics and communication across language barriers and health literacy.

DR. RIMAL: I'm Rajiv Rimal. I'm Professor and Chair of the Department of Prevention and Community Health at the Milken Institute School of Public Health at George Washington University.

MR. DELOST: Good morning. I'm Kort Delost. I'm a community pharmacist, Bountiful Drug, Bountiful, Utah.

MS. ASEFA: Good morning. My name is Aden Asefa. I'm the Designated Federal Officer for this meeting.

DR. OWSLEY: Cynthia Owsley, Professor of Ophthalmology, University of Alabama at Birmingham; patient-reported outcomes, age-related eye disease, and vision impairment.

DR. YIN: Good morning. I'm Shonna Yin. I am a general pediatrician and Associate Professor of Pediatrics and Population Health at the NYU School of Medicine, and my expertise is in health literacy.

DR. WOLF: Mike Wolf, Feinberg School of Medicine, Northwestern University, and my background is in risk communication and patient adherence.

DR. SNEED: I'm Jeannie Sneed. I'm currently a consultant, having retired from Kansas State University as a professor and department chair. I am a registered dietician, and my area of expertise is food safety, both with consumers and retail food safety.

DR. KREPS: My name is Gary Kreps. I am a University Distinguished Professor. I am Director of the Center for Health and Risk Communication at George Mason University. My area of expertise is in health information dissemination and reduction in health disparities.

DR. DILLARD: My name is James Dillard. I am a Professor of Communication Arts and Sciences at Penn State. I am a behavioral scientist with a research emphasis on persuasion and social influence.

DR. DAHR: Good morning. I'm Sam Dahr. I am a practicing ophthalmologist in medical and surgical retina as well as uveitis and inflammatory eye disease, and I hold a clinical appointment as clinical associate professor at the University of Oklahoma, College of Medicine, Dean McGee Eye Institute.

MS. ELLIS: I'm Annie Ellis. I am a Patient Representative and a longtime contact lens wearer.

MS. WITCZAK: Good morning. My name is Kim Witczak, and I am the Consumer Representative. I'm also a longtime contact lens wearer, as well as my background is in advertising communications.

MR. PFLEGER: Good morning. Michael Pfleger. I'm the head of external affairs and regulatory policy for the Alcon division of Novartis, and I'm the Industry Representative.

DR. WEISS: Thank you.

If you've not already done so, please sign the attendance sheets that are on the tables by the doors.

Aden Asefa, the Designated Federal Officer for this meeting, will make some introductory remarks.

MS. ASEFA: Thank you.

The Food and Drug Administration is convening today's joint meeting of the Ophthalmic Devices Panel of the Medical Devices Advisory Committee and the Risk Communication Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. With the exception of the Industry Representative, all members and consultants of the Panel are special Government employees or regular Federal employees from other agencies and are subject to Federal conflict of interest laws and regulations.

The following information on the status of the Panel's compliance with the Federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 U.S.C. Section 208 are being provided to the participants in today's meeting and to the public.

FDA has determined that members and consultants of this Panel are in compliance with Federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special Government employees and regular Federal employees who have financial conflicts when it is determined that the Agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Related to discussions of today's meeting, members and consultants of this Panel who are special Government employees or regular Federal employees have been screened

for potential financial conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and, for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments; consulting; expert witness testimony; contracts/grants/CRADAs; teaching/speaking/writing; patents and royalties; and primary employment.

For today's agenda, the Committee will discuss and make recommendations regarding the potential risks of misuse of peroxide-based contact lens products. Specific issues to be discussed include adequate labeling and packaging of these over-the-counter products.

Based on the agenda for today's meeting and all financial interests reported by the Panel members and consultants, no conflict of interest waivers have been issued in accordance with 18 U.S.C. Section 208.

For the duration of the joint meeting of the Ophthalmic Devices Panel of the Medical Devices Advisory Committee and the Risk Communications Advisory Committee on March 17th, 2017, Ms. Annie Ellis, Ms. Kim Witczak, and Mr. Kort Delost have been appointed to serve as Temporary Non-Voting Members. For the record, Ms. Ellis, a Patient Representative, serves as a consultant to the Oncologic Drugs Advisory Committee at the Center for Drug Evaluation and Research (CDER). Ms. Kim Witczak, the Consumer Representative, serves as a member of the Psychopharmacologic Drugs Advisory Committee in CDER. Kort Delost serves as a consultant to the Drug Safety and Risk Management Advisory Committee in CDER. These individuals are special government employees who have undergone the customary conflict of interest review and have received the materials to be considered at this meeting.

These appointments were authorized by Janice Soreth, Associate Commissioner for Special Medical Programs, on March 7th, 2017.

Michael Pfleger is serving as the Industry Representative, on behalf of all related industry, and is employed by Alcon, Incorporated, a division of Novartis.

We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and their exclusion will be noted for the record.

FDA encourages all participants to advise the Panel of any financial relationships they may have with any firms at issue.

A copy of this statement will be available for review at the registration table during the meeting and will be included as a part of the official transcript.

Before I turn the meeting back over to Dr. Weiss, I would like to make a few general announcements.

Transcripts of today's meeting will be available from Free State Court Reporting, Incorporated.

Information on purchasing videos of today's meeting can be found on the table outside the meeting room.

The press contact for today's meeting is Theresa Eisenman.

I would like to remind everyone that members of the public and the press are not permitted in the Panel area, which is the area beyond the speaker's podium. I request that the reporters please wait to speak to FDA officials until after the Panel meeting has concluded.

If you are presenting in the Open Public Hearing today and have not previously provided an electronic copy of your slide presentation to FDA, please arrange to do so with AnnMarie Williams at the registration desk.

In order to help the transcriber identify who is speaking, please be sure to identify

yourself each and every time that you speak.

Finally, please silence your cell phones and other electronic devices at this time. Thank you very much.

And back over to Dr. Weiss.

DR. WEISS: At this time I would like to welcome Dr. Malvina Eydelman, who is the Division Director of Ophthalmic and Ear, Nose and Throat Devices at the Center for Devices and Radiological Health at the FDA. Dr. Eydelman will provide a short introduction, followed by Dr. Angelo Green, who will provide a presentation on the regulation and premarket review of contact lens products.

DR. EYDELMAN: Thank you, Dr. Weiss.

The safety and effectiveness of peroxide-based contact lens care products, when used as directed, has been well established for over 30 years. However, the number of adverse event reports related to misuse of these products have been increasing and causing alarm among some consumers. Given the persistence of these adverse events, we are here today to discuss additional measures to mitigate the potential risk for misuse of these devices. My division and I are eager to hear recommendations of this first-ever joint meeting of the Ophthalmic Devices Panel and the Risk Communications Advisory Committee. Thank you.

Dr. Green.

DR. GREEN: Good morning. My name is Angelo Green, and I am the Acting Branch Chief for the Contact Lens and Retinal Devices Branch.

The goal of today's Panel meeting is to bring together interested stakeholders to discuss and make recommendations on how best to mitigate the misuse of peroxide-based contact lens products. To that end, we hope to obtain your input on the adequacy of existing labeling and packaging.

I will give an overview on the regulation and premarket review of contact lens care products. Dr. Bernie Lepri will present on hydrogen peroxide care product history and use. Mr. Constantino Castillo will present on peroxide care product postmarket adverse events reported to the FDA. And Ms. Katie O'Callaghan will give an overview of CDRH's Patient Preference Initiative, which is related to our 2016-17 strategic priorities and relevant to today's meeting.

In the United States, the definition of a medical device is one that is intended to diagnose, cure, mitigate, treat, or prevent a disease or condition, or intended to affect the structure or function of the body, and does not achieve its intended use through chemical action or metabolism.

All accessories to articles that meet the definition of a device are also regulated as a medical device under the Food, Drug, and Cosmetic Act. Therefore, device accessories such as care products are medical devices.

A contact lens care product is an accessory device intended for use in the cleaning, rinsing, disinfecting/conditioning, lubricating/rewetting, or storing of a contact lens.

Greater than 70% of contact lens users reuse their contact lens and require care products to safely maintain them. Risks associated with use of contact lens care products therefore represent a significant public health impact. To help mitigate these risks, several FDA safeguards are in place. They include patient information and education materials on our FDA website and, for interested stakeholders, testing and labeling recommendations in our FDA guidance documents.

So types of contact lens care products include:

- Saline;
- Daily and weekly cleaners and protein removers;
- Multipurpose solutions which clean, rinse, disinfect, and/or store contact

lenses;

- Lubricants/rewetting drops; and
- Hydrogen peroxide solutions, which is the subject of today's Panel meeting.

Medical devices, including contact lens products, are regulated based on the risk classification. Devices are typically classified into three different risk categories: low, moderate, and high risk. Sunglasses are examples of low-risk Class I devices. Daily wear contact lenses and contact lens care products are examples of moderate-risk Class II devices. And intraocular lenses are examples of high-risk Class III devices.

Since the focus of this meeting today is on contact lens care products, specifically hydrogen peroxide solutions, I will discuss the regulatory controls that are applicable to these Class II devices.

The Medical Device Amendments of 1976 gave us the legal authority to regulate medical devices. Contact lens care products were initially categorized as Class III devices. This changed after 1990 with the Safe Medical Devices Act under which contact lens care products were down-classified to Class II in 1997. As a result of this down-classification, we issue a special control guidance document for contact lens care products to provide specific recommendations to interested stakeholders regarding what would be needed to regulate these products as Class II.

Care products, like most medical devices, are subject to general regulatory controls. They include provisions for prohibition of adulterated or misbranded devices; requirements to conform to good manufacturing practices; requirements to register manufacturing facilities and to provide to FDA a list of all devices they produce or process. They also require manufacturers to maintain records and reports on their devices, including adverse event reports, and to repair, replace, and refund the purchase price of devices that present unreasonable health risks.

Since care products are Class II devices, they are also subject to special controls. Special controls are device specific, and they include all the items listed on this slide, which include premarket data and labeling requirements typically submitted as part of a 510(k) submission. A device manufacturer may only market and sell a contact lens or care product after FDA has received and cleared a 510(k) submission.

The premarket notification, or 510(k), procedures are described in Section 510(k) of the Food, Drug, and Cosmetic Act. They are typically applicable for all Class II devices. A 510(k) allows a care product manufacturer to demonstrate that the special controls have been met. Most include performance data, which may include bench, animal, or clinical data.

Once the submission is received, the decision that allows a manufacturer to market is rendered in 90 days. The decision is based on whether FDA determines that a device is substantially equivalent to a predicate device. Substantial equivalence means that the new device is at least as safe and effective as the predicate. A predicate is a legally marketed device that has the same intended use and similar technological characteristics.

Information provided in a 510(k) submission for contact lens care products include the following:

- Materials/chemistry
- Manufacturing
- Sterility
- Shelf life information
- Biocompatibility information
- Labeling
- Nonclinical and clinical performance testing

With regard to labeling, manufacturers submit draft labeling before marketing but

are not required to submit the final printed labeling. This is true for all 510(k)s. The information is reviewed by an interdisciplinary team of FDA scientists, engineers, and clinicians. General testing and labeling recommendations and information to be submitted in the 510(k) submissions are described in our FDA guidance documents.

FDA guidance documents describe our interpretation of or policy on a regulatory issue. Guidance documents may provide product-specific testing recommendations or can provide general information with regard to labeling, manufacturing, or design of clinical studies.

Since our initial publication of our 1997 special control contact lens care product guidance document, we also published a 2010 labeling addendum which provides additional labeling guidance for safe use of care products.

Thank you for your time and attention. Dr. Bernie Lepri will now present on hydrogen peroxide care product history and use.

DR. LEPRI: Good morning, distinguished Panel members and guest speakers, FDA administration and staff, ophthalmic professional organization representatives, industry representatives, and members of the public. My name is Bernard Lepri. I'm an optometrist and expert clinical reviewer in the Office of Device Evaluation of CDRH, Division of Ophthalmic and Ear, Nose and Throat Devices, in the Contact Lens and Retinal Devices Branch. Today I'm here to provide you with a brief discussion of the regulatory and clinical history of peroxide-based contact lens care products.

The first hydrogen peroxide contact lens care products -- where are my slides? Okay. The first hydrogen peroxide contact lens care product was approved by FDA and developed and marketed by American Optical Corporation under PMA 820040 in 1983 as a Class III product and was specifically approved as the Septicon disinfection system for Softcon (vifilcon A) soft contact lenses. The Septicon system consisted of 3% hydrogen peroxide

solution, the disc, and the cup.

Since the first peroxide-based contact lens care product entered the market, these products were then classified to Class II in 1997, and other peroxide care products were introduced into the marketplace.

There are approximately 41 million contact lens wearers in the United States. According to a survey on lens care patterns published in *Contact Lens Spectrum* in 2015 by Jason Nichols, the vast majority of respondents reported using multipurpose chemical care systems. In 2009, 80% of contact lens wearers used multipurpose chemical systems, but now in 2015, that number has decreased to 72%. In 2009, 20% used hydrogen peroxide-based systems as compared to 27% in 2015 when the survey was conducted. The trend has been that there is an increase in the number of doctors who recommend and the number of contact lens wearers that are using hydrogen peroxide-based care systems.

Contact lens care products are formulated to clean and disinfect contact lenses by breaking up and removing trapped debris, protein, and lipid deposits.

In addition to differences in chemical composition, there are distinguishing differences between multipurpose solutions and hydrogen peroxide solutions. Multipurpose solutions include both a rub-and-rinse step prior to placing the contact lenses in the case containing the multipurpose solution for a disinfection cycle. Peroxide care products do not include a rub-and-rinse step because the 3% hydrogen peroxide solution is adequate for loosening debris.

Peroxide care products are preservative free, which is useful for individuals who are allergic or sensitive to preservatives found in some multipurpose solutions. There are also important differences in the methods of usage that are very important.

Contact lens consumer behaviors and proper care of contact lenses are directly related to their safe use. According to Ky et al., 80% of complications are due to deficient

compliance with wear and maintenance care. The patient's perception of their own behavior is essential to minimizing and preventing contact lens complications. Many patients believe their practices are safe when, in fact, they are not. In two other studies in this slide, the noncompliance rates ranged anywhere from 50 to 79%.

Donshik et al. identified several factors that may influence contact lens wearer compliance with care regimens, such as complexity of treatment, frequency, duration, and cost of regimen or treatment, as well as the nature of the condition. There is a higher incidence of noncompliance in conditions that are asymptomatic, prophylactic, or suppressive in nature.

For example, the literature regarding contact lens care regimen compliance reveals that 54% of patients considered themselves poor wearers. Of these, 44% reported that they are inadequate at cleaning of lenses or cases, and 15% reported noncompliance with medical instructions.

Regarding contact lens care procedures, 79% reported failing at implementation of care procedures, and 30% reported being poorly prepared for cleaning and awareness of maintenance procedures.

A striking finding by Turner et al. was that 91% of patients failed in following at least one procedure regarding the use of a multipurpose solution, despite the ease of use.

Compliance is even more critical when using peroxide care products. The method of cleaning and disinfection differs from that of multipurpose solutions. Many hydrogen peroxide products utilize a special case with an attached metallic neutralization disc. This case is provided with each bottle when purchased. Some hydrogen peroxide products don't use a metallic neutralization disc but rather the addition of a neutralizing tablet.

Hydrogen peroxide products cannot be used to rinse lenses prior to insertion in the eye, whereas multipurpose solutions can be. Direct exposure of the eye to peroxide can be

toxic to the corneal epithelium, and even more so to a slightly compromised corneal epithelium after contact lens wear.

So we'll see that hydrogen peroxide disinfecting processes can be either a one-step or a two-step process. The one-step process uses a metallic neutralization disc inside the case, whereas the two-step process requires the addition of a neutralization tablet to the case. Some products recommend a post-disinfection saline rinse of the lenses prior to insertion in the eye.

This slide provides a side-by-side comparison of the one- and two-step processes of some hydrogen peroxide products. One can see that the two-step process is somewhat more complicated than the one-step process but typically do include a saline rinse upon completion.

The one-step process, as you know, requires placing of the lenses in a provided basket, rinsing each lens for several seconds with Brand X over the sink or basin, filling the case to the line with Brand X and do not invert or shake the case, while the lenses soak in the case for either 4 to 6 hours depending on the product brand, and then remove the lenses and use, whereas the two-step process involves all of those steps but also involves the addition of the tablet for neutralization and rotating the case up and down several times to indicate the color change, and then finally, after sitting for at least 6 hours, to rinse the lenses with saline and wear them.

Safety and effectiveness of peroxide-based contact lens care products, when used as directed, have been well established for over 30 years. A major issue that's come to the forefront over the past few years, the number of adverse events reported related to misuse of these products has been increasing.

In 2009 a signal of the issue of adverse events related to use error of hydrogen peroxide products was raised by the Institute for Safe Medical Practice. This signal was

addressed by an FDA internal working group in conjunction with industry, resulting in FDA's recommended modified labeling to be assessed in structured focus groups. This modified labeling began entering the market in the summer of 2011 and was also recommended as a format for new products seeking FDA marketing clearance through the Class II 510(k) regulatory pathway.

The three most common sources of misuse of hydrogen peroxide-based contact lens care products identified were accidental use, such as while at a friend or a relative's home or mistaking bottles on the bathroom sink as saline, failure to follow the specific directions on the box and bottle for neutralization. Some consumers assume that peroxide care solutions are the same as multipurpose solutions and then use them incorrectly. And finally, erroneous purchases: Some consumers claim that the hydrogen peroxide care products' cartons are indistinguishable from multipurpose solutions on the store shelves.

FDA's strategies to enhance safe use of peroxide care products were directed towards labeling of the carton and bottle and patient education through publication and website page development.

On this slide you see the carton labeling strategy was to modify the uni-chromatic carton design, seen on the left of this slide, by changing to bold red-colored in the background to attract the consumer's attention to the specific instructions and warnings about proper use of hydrogen peroxide care solutions.

This is a close-up view of the enhanced warnings panel on the box and in the package insert. There are both pictures and accompanying verbal warnings, specifically:

- Do not use a flat lens case. This solution only works with the special case provided.
- Do not remove lenses from the case until at least 6 hours later. The solution needs time to neutralize.

- Do not rinse lenses with this solution prior to inserting lenses into your eyes. If you want to rinse lenses, use a sterile saline.
- Do not squirt solution directly into your eyes.

The front side of cartons in many of these products originally stated that they were no-rub products. The phrase "no rub" has been removed so that it would not be confused with other products portraying the no-rub label. Since that modification, even multipurpose solutions indicate rubbing and rinsing of lenses and are not primarily considered no-rub solutions.

Warnings had originally been on the cardboard collar that slipped over the red-tipped bottle, and these warnings were

- Misuse will result in burning and stinging.
- Use only the lens case provided.
- Red tip means do not put this solution directly in your eye.
- Do not rinse lens with solution prior to insertion in your eye.

Consumers complained that the collar would come off and then they would forget the warnings. To address this issue, the collar warnings were repositioned on a permanent band around the top perimeter of the bottle.

Regarding the strategies used to modify the bottle, the bottle already had a red tip on it to identify it as different from other lens care products, and subsequently, the cap was changed to bright red, also.

This slide is a summary of the carton and bottle changes that were implemented and recommended by FDA.

- "No rub" was removed from the carton labeling.
- Use only the lens case provided.
- Only use the special lens case for disinfection and neutralization.

- Do not use a flat lens case.
- Brand X only works with the special lens case provided.
- Specific safety instructions in bold font and red boxes.

FDA also utilized education as an approach to informing the public of the need to follow the specific instructions necessary for the safe use of peroxide care products. In April of 2016, an article entitled "Contact Lens Solutions With Hydrogen Peroxide: To Avoid Injury, Follow All Instructions" was published in the *FDA Consumer* magazine. In this slide you can see a summary of the points of the directions for safe use of the products.

FDA also added a page to the contact lens website dedicated to highlighting the special instructions and warnings necessary for the safe use of peroxide care products. This page can be accessed at the web link at the top of this slide.

In summary, consumers have reported adverse events of burning sensations and stinging to FDA.

Consumers believe that the packaging is too similar to other contact lens care products, resulting in mistaken purchases and/or misuse of the product.

Consumers do not notice the warnings related to the directions for use on the carton and/or the bottle.

Despite updated and enhanced labeling instructions, use errors resulting in adverse events continue.

Why are we here today? To engage consumers, industry, and FDA to assess the adequacy of existing labeling instructions and packaging for peroxide-based contact lens care solutions; allowing industry to hear about the problems experienced by the consumers and hear their recommendations for making the packaging and labeling more user friendly; and finally, to obtain Panel recommendations regarding the labeling and packaging of peroxide-based contact lens care products.

Thank you for your attention.

DR. WEISS: Thank you, Dr. Lepri, of the Division of Ophthalmic and Ear, Nose and Throat Devices.

We now want to introduce our next presenter, Constantino Castillo, MDR analyst of the Office of Surveillance and Biometrics at CDRH, FDA, who will discuss the medical device reporting on misuse of hydrogen peroxide-based contact lens care system products.

MR. CASTILLO: Thank you. Good morning. My name is Constantino Castillo, and I'm an MDR analyst in the Office of Surveillance and Biometrics within CDRH at the FDA. I will be presenting the postmarket medical device reports, or the MDRs, of the adverse event data of misuse of the hydrogen peroxide-based contact lens care system products.

Before I present the data, I would like to give you a brief overview of the FDA's MDR reporting system. This slide provides important reminders of the limitations of the MDR data. Each year the FDA receives over a million MDRs reporting deaths, serious injuries, and malfunctions of medical devices. The FDA uses these MDRs to monitor postmarket performance, detect potential safety issues, and contribute to the benefit-risk assessment of medical devices.

Although MDRs are a valuable source of information, this passive surveillance system has its limitations, including underreporting, data quality issues like potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of any of them cannot be identified from this reporting system alone due to potential underreporting of events and lack of information about the frequency of device use. Lastly, it is difficult to know a causal relationship between an event and the device based on MDR data alone.

To provide the data for this Panel meeting, the Agency searched the FDA's MDR reporting system to identify medical device reports associated with misuse of peroxide-

based products entered between December 14, 2006 to December 14, 2016. In this search, misuse was defined as any instance of peroxide-based products that were not used properly, according to the instructions for use from the device labeling. This search yielded 370 pertinent MDRs across multiple manufacturers and product lines. In the following slides, I will provide you the results of our MDR review.

This graph provides the number of MDRs related to misused products received by the FDA per year for a 10-year time frame. Also note, in this figure is a significant increase in the number of medical device reports received for calendar year 2015, with 118 MDRs. This spike may be due to submission by an advocacy group of 74 voluntary reports on behalf of consumers during that calendar year.

In this slide, the first table provides the report source of the pertinent MDRs. Fifty-eight percent were submitted by voluntary reporters, and 42% were submitted by manufacturers. The FDA did not receive any reports from user facilities or healthcare providers.

The second table provides information on the type of events. The majority of reports, almost 97%, were reports of serious injury, with a small fraction of malfunction reports of 4%. There were no deaths reports submitted.

Here is the demographic data. The majority of MDRs come from countries of unknown origin; 161 MDRs were received from within the United States. Patient gender information was reported in 289 MDRs, of which the majority were female. Based on the information provided in 110 MDRs, the median age was 42.5 years.

This slide provides the three outcomes, which are misuse, reported eye problems, and personal burden, as our focus of clinical interest.

Misuse refers to the products that were used improperly.

The reported eye problems, which are the clinical outcomes, were further

subdivided into serious eye injuries, visual issues, eye infection or inflammation, and ocular signs and symptoms. "Serious eye injuries" refers to any serious injury to the eye region. Visual issues, these are complaints related to vision or visual acuity. Eye infection or inflammation refers to the eye conditions that are caused by pathogenic microorganisms or are localized eye protective responses elicited by an injurious agent. For ocular signs and symptoms, these are clinical signs and reported symptoms.

The outcome of personal burden represents qualitative measures of personally experienced burdens as described in the MDRs.

The following tables in the succeeding slides will provide more detail on the specific outcomes.

The different types of product misuse are presented in this slide. The top three types were accidental use with 168 reports; failure to follow neutralization method with 107 reports; and erroneous purchase with 40 reports. Accidental use was the most common type of misuse. Any consumer complaints that claimed accidental or inadvertent use were placed in this bucket. Failure to follow neutralization method appears to be the second most frequent type of misuse and was due to consumers not allowing adequate neutralization time or not using the special lens case that comes with the product. The third most frequently reported type of misuse was erroneous purchase. These were the narrative reports describing the consumers' erroneous purchase of the products. According to the reports, this was mainly due to the store's peroxide product placement in close proximity to other contact lens care products on the shelves. The narratives also indicate that the text label's "clean/disinfect/no rub" on the peroxide solution led consumers to purchase these solutions, thinking that this was the same as the saline or multipurpose solutions. There were 19 MDRs that did not provide a description of misuse. There were 15 reports of the use of expired solution.

Additional types of misuse include flawed reports of improper care of the lens case, in which tap water and broken lens cases were allegedly used. Nine MDRs report that the misuse was attributed to healthcare provider error. Within this type of misuse, there were three reports in which the providers soaked the lenses in the solution and had the patient reinsert the lens; one report in which the solution was dispensed without the neutralizing tablet; and another five reports of the healthcare provider failing to provide adequate instructions.

In the next four slides I will be discussing the four different subcategories for the reported eye problems as described by the reporter in the narrative of the adverse event. These are clinical outcomes of product misuse. Infection and inflammation are not included, since they are placed in a different table.

Based on the narrative descriptions, the most frequently reported serious eye injury was ulceration of the cornea with 11 clinical events. There were 9 events that described nonspecific corneal damage; the narrative descriptions in these events did not provide information on the extent of the damage to the cornea. There were 2 events which described loss of vision or blindness. In one of the events, the manufacturer reported a past medical history of uveitis and compromised cornea prior to product misuse. The second event, from a voluntary reporter, did not provide additional information.

The various visual issues mostly experienced by consumers are presented in this slide. Blurred vision was the most frequent complaint with 41 clinical events. Descriptions of blurred vision following exposure to the solution include visual acuity concerns, worsening vision, and unspecified visual problems. There were 7 events of temporary vision loss and 2 events of partial loss of vision. Limited information was provided on the severity of these issues.

This table provides the information on eye infection or inflammation. The most

frequently reported clinical event was chemical conjunctivitis with 12 events, followed by chemical keratitis with 9 events, and nonspecific eye inflammation with 8 events. Additionally, there were 7 events of nonspecific eye infection. Limited information on the infectious organisms causing the eye infections was provided. There were 2 events which mentioned bacteria as the source of infection and were allegedly caused by poor lens care. There was 1 event of fungal keratitis which mentioned fungus as the source of infection due to alleged improper care of the lens case.

This table provides information on reports of ocular clinical signs and patient-reported symptoms. Burning sensation with 210 clinical events was the most frequently reported symptom. The narrative event descriptions describe consumers' subjective complaints as a result of eye exposure to the peroxide solution. Other frequently reported events were chemical burn to the eye region with 186 events and reports of corneal abrasion with 33 events.

This slide identifies the different types of burden outcomes personally experienced by consumers as a result of product misuse. The burden outcomes consisted mainly of the consumers seeking medical help as described in 193 MDRs. This included visits to the ER, urgent care, eye clinic or eye care practitioner, hospital admission, and calls to poison control. These medical consults were allegedly needed as a result of the consumers' eye injuries sustained from chemical exposure to the solution.

As described in the MDRs, medical interventions included application of eye patches, prescriptions for pain relievers, eye irrigation, and treatment with topical antibiotics. Consumers were also advised to seek additional follow-up with their eye care practitioners. Limited information was provided in the five reports which stated that inpatient hospitalizations were required. There were 162 MDRs which did not report personal burden.

This slide provides information on reports of recovery outcome. These were obtained from the narrative event description section of the MDRs. Information on recovery was based on the most recent information received. The recovery post-injury was not reported in 243 MDRs. Among those where recovery status was reported, 83 MDRs provided limited information on the length of time to recovery figured by the consumer reporter.

There were 30 MDRs which described continuing eye issues. Based on the most current information received, the most frequent continuing eye issue described in the narrative was chemical eye burn. No additional information was provided on recovery status or duration of the ongoing events.

Fourteen MDRs stated that the consumer did not suffer any eye injury.

In summary, there were 370 MDRs that were associated with misuse of hydrogen peroxide products over a 10-year time frame.

More than half or 58% of the MDRs submitted to the FDA were from voluntary reporters.

Burning sensation and chemical eye burn were the most frequently reported patient problems described.

Two reports described loss of vision or blindness. Due to the limited information provided post-injury, it is hard to know if these issues were permanent or if they were caused by misuse.

Based on the narrative descriptions, it appears that some consumers may have assumed that all contact lens care solutions are the same and safe to be applied directly to the eyes or for use with contact lens cleaning or disinfecting.

Included in the MDR narratives were suggestions from the adverse event reporters on how to avoid possible misuse. Some of these suggestions were

- Make the product appear less similar to the other lens care products.
- Have the product dispensed by the pharmacist.
- Create separate areas on the store shelves for the different lens care products so that there's less confusion among the different types of products.
- Provide better labeling in the box as well as on the bottle of solution.

That ends my presentation. Thank you for your attention.

DR. WEISS: Thank you, Mr. Castillo.

Our next presenter will be Kathryn O'Callaghan, CDRH Assistant Director, who will discuss the Patient Perspective Initiative.

MS. O'CALLAGHAN: Good morning to all those who are here in attendance today. My name is Katie O'Callaghan. I'm CDRH's Assistant Director for Strategic Programs in the Office of the Director, and I have the privilege of overseeing a variety of regulatory science and strategic partnership and patient engagement initiatives which are focused on how we can better involve patients in assuring safe and effective medical device use.

Whether you are a clinician or a regulator or a manufacturer or a patient, patients are really at the heart of all of what we do, and it's our common purpose. At CDRH, our vision is that patients in the U.S. shall have access to high-quality, safe and effective medical devices of public health importance, first in the world. And this series of initiatives that we've been engaged in over the last several years has really helped remind us how critical it is that despite all the complexity in terms of scientific, clinical, regulatory, and other challenges that we may face, it's really critical that we keep our focus on the patient at the heart of everything that we do.

Over the years, there's been a significant evolution on the role of the patient in healthcare and accordingly in the way that we engaged with them in our various roles. In the traditional medical model, providers made most of the decisions about diagnosis and

treatment. In the age of cancer and HIV patient advocacy, we saw a coalescing of patient forces with other stakeholder groups to really advocate for patient views to be considered before policy and other decisions are made. The internet age and all the information that's now available is empowering patients but also posing challenges as we try to raise communication as an important risk mitigation measure, as we're discussing today. And patient and provider partnership is gaining more and more traction in medical delivery and lots of decisions that we're making today, where patient perspectives are important to consider as we make decisions.

At CDRH, as has been mentioned by previous FDA speakers, our strategic priorities focus on partnering with patients, and recognizing that by interacting with them not simply as a data source or a beneficiary of the work and the decisions that we make, we're able to do a better job together in advancing the development, the evaluation, and the safe and effective use over the life cycle of marketed devices and accessories to devices.

This schematic is one that we use to depict the total product life cycle, from discovery and innovation stages through development, through regulatory decision making, and into the marketing phase. And the boxes that you see here that are transposed on top of that schematic indicate areas that we heard from the public in a series of meetings -- particular areas where patient input can add additional value to our decisions. It's important to note that patients still want the FDA to do our job. This is not to replace scientific evidence, but about combining scientific, clinical, and other information. With patient perspectives, we're able to draw broader insights.

For today's discussion, I think it's particularly important to think about the communication of benefit-risk information to patients, where we're using communication and labeling as measures to mitigate risks, but we also rely on patients to better understand how effective these measures might be.

I was asked to provide an overview of the activities that we're doing at the Center to promote patient involvement in regulatory decisions and actions. And so I'll start with the patient engagement efforts.

This is a model that we're using to depict our culture change efforts. We recognize that by promoting a culture of meaningful patient engagement throughout the Center, our staff and managers will be better equipped to incorporate the patient perspective and input and involvement in important phases of our decision making. And so it will be done by providing and facilitating for additional interaction between the FDA staff and the patients that are affected by our decisions, and some of these progress into more meaningful engagement and partnership opportunities, including our scientific partners in collaboration.

We have a variety of efforts that we've been building over the past several years to strengthen this culture, several of which I'll highlight today. This is a very good story of how we tapped into the enthusiasm and the expertise of our staff across the Center to help guide how we would proceed with this culture change throughout the Center.

We put together two competitions earlier last year, one focused around patient engagement and the second focused around patient science, things like patient-reported outcomes and patient preferences, where we challenged our staff to bring up regulatory and scientific clinical challenges that would be better solved with patient perspectives. We had over 75 staff competing and hundreds who participated in this contest, and it's really put a lot of momentum behind our engagement in science efforts in the Center.

In the course of our discussions with industry for the user fees in the MDUFA IV agreement in principle package, you will see a reflected shared agreement that it is worth investing further in these efforts. There are three particular areas that rose to the surface through our patient input in clinical trials, patient preference information, and patient-

reported outcomes.

Here is a just a sampling of some of the employee feedback that we've had in response to our patient engagement efforts.

Next, I'll switch gears and talk about some of the science of patient input initiatives that we have at the Center, and these are designed to increase the use and the transparency of patient input as evidence in the decisions and actions that we make.

There are a variety of different forms of patient input, just as there are a variety of different forms of clinical and other scientific data. We realize the importance of drawing parallels between these two frameworks. So, for instance, we all recognize that with clinical data, you have everything ranging from anecdotal case reports through observational or retrospective studies, and at the highest end of the spectrum would be the randomized clinical trial.

But the same is true of patient perspective data. So we don't have anecdotal reports of patient experience, but what a lot of our science efforts are working on is what is the higher end of that spectrum? What can we do to elevate the methodological and scientific rigor so that we're able to hold this patient experience data up alongside clinical and other scientific data of high rigor and use it for regulatory decision making?

These are the two areas that we have focused initiatives on: patient-reported outcomes, which many of you in this field will be very familiar with, as well as patient preference information, which is gaining more traction as a scientific field that can give us great information on how patients and other decision makers look at tradeoffs between various benefits and risks.

In a regulatory context, patient-reported outcomes can give us great information in terms of endpoints for regulatory studies. It can also be used to monitor outcomes in the postmarket phase and is increasingly of interest to payers, providers, and certainly to

patients.

Patient preference information can also be used to help us identify which endpoints are of most importance, or help us hone in on the effect size for regulatory studies based on the tradeoffs that patients or other decision makers would consider appropriate. It's also useful to inform subgroup considerations as well as labeling changes and expanded indications.

And so by combining the art of patient engagement and the science of patient input initiatives, we can move towards better regulatory decision making and ultimately more patient-centered healthcare.

So thank you for your attention.

DR. WEISS: Thank you, Ms. O'Callaghan. And I want to thank all of the FDA speakers for their very clear and coherent presentations.

We now have the ability to have questions from the Panel for clarification to the FDA. Remember that the Committee may also ask questions during the Committee deliberations this afternoon. Do any members of the Panel have any questions to the presenters? We'll start going around this way.

Dr. McLeod.

DR. McLEOD: I'm not quite sure the presenter to whom I should address this question, but one thing that would be helpful to do, to understand better the timeline of the implementation of the packaging changes that were outlined and whether or not there's been enough time to assess the impact on the incidence of the patient-reported adverse event.

DR. WEISS: Dr. Lepri.

DR. LEPRI: Yes. The timeline was that the signal was raised in 2009. FDA and some industry members, we responded together in an internal working group in 2010, and the

first rollouts were for 2011. So one would predict that there have been approximately 6 years of the rollout of the modifications in the type of labeling that FDA recommended and that some companies implemented from 2011 until now.

DR. McLEOD: Some.

DR. LEPRI: Some. Well, there are products that were out there that were, for example, some with a 510(k) application, a Class II device. Other companies can purchase the 510(k) rights and distribute others' products. For example, CVS and Walmart and Target can actually distribute other companies' products that have a 510(k). So we do not have access to their labeling or their products or those types of things. So that's why I can't tell you definitively everybody has done the right thing because we don't even know who everybody is.

DR. WEISS: Dr. Berube. If you could put on your microphone. Everyone, actually when you begin speaking, if you can identify yourself again. This will make it easier for the transcriptionist.

DR. BERUBE: Yeah, David Berube.

Mr. Castillo, on Slide 4 you talk about the blip that occurs in 2015, and you talked generally about some sort of advocacy-generated data blip. Could you explain this?

MR. CASTILLO: Yes. Constantino Castillo from FDA.

Yes. For the calendar year 2015, there were 118 MDRs on that, and the majority of those reports that we were seeing during that calendar year was from an advocacy group with 74 voluntary reports.

DR. BERUBE: So you received a package of 70 reports from one group is what you're saying?

MR. CASTILLO: Well, I would say it came in different times, and they were submitted directly to us.

DR. WEISS: Dr. Krishnamurthy.

DR. KRISHNAMURTHY: Yes, this is Krishnamurthy from the University of Houston.

I had a quick question. This spans two or three of our presentations that we heard today, and it centers on patient input. One of the things that we noted here was that you do focus groups to understand patient responses to labeling. That seems to be an odd choice to make. How else do patient voices get tracked or heard other than self-reports, because as mentioned earlier, it tends to underreport quite substantially. Not everyone who has a problem will actually take the avenues of MDR to report their troubles. Is there an active way of collecting patient responses after a drug goes on the market?

DR. EYDELMAN: Malvina Eydelman, FDA.

So as was summarized by a number of speakers, we try to help to obtain as much patient input as possible. Obviously, all the avenues are open to all of the patients. Unfortunately we can't control the amount of reports that we do receive, and I think we've heard from our OSB colleagues that there tends to be a great underreporting for all product areas, not just for this one. When we identify a particular problem and we feel that we need to be more proactive to seek the patient input, we employ a number of different avenues, and a focus group was one of those that was identified as a potential useful solution.

DR. WEISS: Dr. Lee.

DR. LEE: This is Charles Lee.

Do you have any educational requirements among eye care practitioners when patients pick up their contact lenses?

DR. EYDELMAN: I'm sorry, we didn't hear your question.

DR. LEE: Are there any educational requirements that are required of eye care practitioners around this issue, when they get their contact lenses?

DR. EYDELMAN: So FDA regulates medical devices. As such, we regulate the labeling, we clear the labeling that's associated with a product, and we hope that the practitioners discuss its content with the patients. However, then we get into the practice of medicine, which we cannot, which we do not regulate.

DR. LEE: Okay. So they don't have to describe any of this to patients? As far as you know.

DR. WEISS: Speaking as an ophthalmologist, this is standard of care. So there are certain things that are standard of care in terms of practice of ophthalmology or optometry, and this would be one of them. If you're dispensing contact lenses, part of that is to instruct the patient on how to care for their contact lenses.

DR. LEE: Okay.

DR. WEISS: If someone had instruction in contact lenses 10 years before, and then on follow-up with their practitioner and they go autopilot, that's something that can happen.

DR. LEE: Okay, so that's out of the purview of the FDA. Okay.

DR. WEISS: Since we're going around this way, I have a couple of questions myself. So do we have -- three questions. Do we have any information whether one- or two-step have more MDRs? Any ideas why there's a disproportionate number, the majority were female reporting? Is that what's usually found? Those are the first two, and then I have a last one.

DR. LEPRI: I can address the demographic portion of the question. The majority of contact lens wearers are female, and that may be why they're represented in the higher proportion in the data that was presented by Mr. Castillo. Okay.

DR. WEISS: So hydrogen peroxide solutions are 27% of the market. Do we know the number of MDRs for multipurpose solutions to compare?

MR. CASTILLO: Unfortunately, we don't have that information in the database.

DR. WEISS: And then the last question, following up on Dr. McLeod's question. So we don't have a way to have any idea of what was -- the changes that were put into place some years ago to effect change, whether they did or didn't effect change, because we don't know what percentage of the labeling out there for boxes actually -- where you made the change. And going forward, will any changes, if they were recommended by FDA, have to be used by Walmart, CVS, Costco, whatever, if they then get the solutions from the original manufacturers?

DR. EYDELMAN: Well, we can certainly recommend it, and we can recommend it for the products that are coming in for clearance, and we can certainly strengthen the education through the website, etc., and we're actually looking for advice from you today. It's the best place to do it.

DR. WEISS: Thank you.

Dr. Yin.

DR. YIN: Hi, this is Dr. Yin.

I was wondering, just to clarify for the eye care products that use hydrogen peroxide, is there any level of testing that's expected with patients and consumers related to usability and understandability of the labeling for each product? Is there any sort of protocol around that?

And then my second question was around the typical shelving practices for the hydrogen peroxide products. Are they just intermixed in with all the multipurpose solutions, or is it like next to each other but still on the same shelf? What are the typical practices around that?

DR. LEPRI: This is Bernard Lepri.

Dr. Yin, I'll answer your question in regards to the first part, is that we have no

control over where items are placed on pharmacy store shelves or retail areas, and our experience and my experience, having a son who's a contact lens wearer, is that all the products are presented as contact lens care products and the solutions, and they're all together on the shelf. That part is true. But we do not regulate that.

And I would like to ask you to please repeat the first part of your question so that I address it properly.

DR. YIN: I was just wondering if there's any particular protocol that needs to take place in terms of the understandability of labeling for patients before it goes onto the market.

DR. LEPRI: We do not assess patients' interpretation of the labeling. When these modifications were recommended and we worked with a couple of the industries, they conducted their own focus groups with patients to determine if the patients would be responsive to it, and they did have a very positive response. But that is not done with all contact lens care products that are put onto the market.

DR. EYDELMAN: Let me just add to that. As Dr. Lepri said, that's not standard practice. We don't usually do that. However, should we identify a particular complicated issue, there is precedent for doing focus groups to try to assess if the labeling truly conveys correctly -- or let me rephrase it, if the labeling is interpreted by the patients in a way that that they intended.

DR. YIN: Great.

DR. EYDELMAN: So if the Panel recommends it, that is something we can explore.

DR. YIN: Great. In the conduct of the focus groups that were done, or is there some thought about which kinds of patients in terms of -- that you would enroll like patients with a cross-section of socioeconomic status or health literacy levels, etc.?

DR. EYDELMAN: We would seek your guidance, and then we can try to see the best

way to implement that.

DR. WEISS: Dr. Wolf.

DR. WOLF: I was actually going to follow up on two pieces, one on the question you asked that was about whether or not there were differences between the multi-step and the -- or two-step versus one-step. If that data is not available, I understand. But I mean, we have learned from other, like on other devices that, you know, when you do reduce the number of steps, you do see greater success and completion or at least proper compliance. So I didn't know if that data existed.

DR. LEPRI: We do not have that data comparing the two types of systems from review of the reports that were provided. In this analysis conducted by OSB, there did not appear to be any major differences between one-step and two-step.

DR. WOLF: Okay. And this is more of maybe a comment, but just for clarification. So just so I'm understanding this right, there are 370 reports of adverse events that have occurred over a 10-year period. And then the data that we saw before at the beginning of the presentation, I mean, I'm just trying to get a sense of scale on things because the rate of patient-reported noncompliance or misuse or accidental use is pretty substantial. You know, I was just looking at the numbers.

So in terms of patients who are reporting errors or improper use, in terms of how it trickles down to actually the report of an adverse event, I'm assuming, like many things in the medication realm, which I'm more familiar with, we do know that there are a lot of unreported adverse events or errors. So I'm assuming part of that capture is -- I didn't know if also part of the uptake on some of these things in 2015 or post-2011 was associated with changes in the reporting besides the advocacy group.

DR. LEPRI: No, I can't provide you with any -- Bernard Lepri.

We don't have any data to show that there were any changes in the amount of

errors reported, but in consideration of the complaints and what they identify as their causes of misuse were that most of it were the mistaken purchases, mistaken use when visiting relatives or friends and just assuming that the contact lens bottle on the counter is the same as theirs. So there is no way, based on those reports, to identify whether that was associated with the change. No, those were not assessed.

DR. WEISS: Dr. Kreps.

DR. KREPS: So there appears to me to be a big emphasis on health education through labeling for these devices, which is a relatively passive form of communication. I was wondering if there was any emphasis on multimedia types of health education, particularly a point of referral or purchase. For example, use of videos to illustrate the issues, concerns, or they demonstrate the utilization and then access to those multimedia through websites later on. But I think at the point of purchase it's particularly critical. I wonder if there has been any thought of doing that or experience with doing that, other things delivering health education. Anybody?

DR. EYDELMAN: So for our FDA website, we spend an enormous amount of time trying to maximize all ways of communicating the risk and there are some videos that are live on our website. However, I'm very interested to hear what exactly you suggest at the point of purchase. I guess I'm not clear. How can we better suggest to consumers to go on our website at the point of purchase? I'm very interested in your thoughts on that.

DR. KREPS: Do you want me to follow up on that?

DR. EYDELMAN: Please.

DR. KREPS: Recently, I guess, I went to a dental surgeon for a dental implant, and while I was in the waiting room -- they wheeled me into another room and showed me a video describing the process and how it would happen, what I needed to do, and I found it to be extremely educational, and it really helped me understand the process and probably

improve my compliance. And I suspect that perhaps if there were videos available for people waiting to get their referral for contact lenses or to purchase, that might be helpful as well. I think -- mention on the FDA website is a good idea, but it's got to get people to come there and -- people that go the website, they may go as a follow-up. But I know that they're already at the doctor's office getting the prescription, you're getting a referral for the contact lenses, and so that might be really a wonderful place to provide more moving visual information.

DR. WEISS: One thing I will add to that, now with internet and the ability to get contacts on your own and such, and maybe some of the speakers will address that, with the good standards of medical care, an individual practitioner might choose to do that up front, but I don't know if any of our speakers have any estimates on what percentage of contact lens wearers are new or entry and what percentage are return, in which case they're not necessarily going into that doctor's office. It's sort of what I call the autopilot and how to get those individuals. We're going to keep on going around so everyone has a chance.

Dr. Dillard.

DR. DILLARD: Thank you. Jim Dillard, Penn State.

I'm a contact lens wearer. In 2014 I woke up a little bit fuzzy, and I used my wife's peroxide solution, and I experienced that burning sensation. It was a very educational experience for me, and I don't think I'll repeat that.

(Laughter.)

DR. DILLARD: But I mention that only because the data you presented here, there are 371 cases, and I know you're underreported by at least one.

(Laughter.)

DR. DILLARD: But it wouldn't surprise me if the underreporting is a hundred-fold or a thousand-fold difference. And so I mean, I raise that question because, first of all, the

reason we're meeting is the assumption that there was a problem, and I don't know, do we have the data? First, do we have the data to demonstrate that this really exists? The chart also shows us that the problem is increasing like this, but you know, generally in an increasing direction. Is that real? I don't think we can infer that on the basis of these 371 cases.

Yes, this is for Mr. Constantino. Sorry. And when you start to break it down into the different types of problems, accidental misuse, I can verify that happened, but when you start to subdivide the data, it becomes much more difficult to say these problems are real or the categories are really different from one another. So I guess what I want to ask you is are there other sources of data, other reasons to believe that this is a problem, that the problem is getting worse, that the specific types of problems exist and may be amenable to human intervention, or are we just operating on assumption and kind of feel scary?

DR. EYDELMAN: So you're absolutely correct in that 374 are certainly not the number of adverse events that we'll anticipate that are occurring in the U.S., and I think that's why the first few minutes of our OSB colleague's presentation was intended to summarize all the shortcomings of our current system to capture the adverse events. We're well aware of the tremendous underreporting and inaccuracies of reporting.

Having said that, it is a database that we can analyze, but we do have to acknowledge all of its shortcomings. In addition to the MDRs, we have patients and patient groups who write directly to us or complain directly to the FDA staff. There are a number of avenues to convey their concerns about a particular health issue, and this was the case for this. So we do believe there is a signal in addition to the MDR analysis that we're presenting today.

DR. WEISS: Thank you, Dr. Eydelman.

Dr. Dahr.

DR. DAHR: I have two questions I'd like to ask one at a time. Sam Dahr.

The first for Dr. Lepri, possibly with some input from our cornea colleagues. The vast majority of these MDR reports are transient with self-recovery. Is there any potential with these exposures of the peroxide solution to the surface of the eye for a more permanent type of damage? Is there any potential for limbal stem cell damage or any other type of event, or are these principally just transient with good self-recovery?

DR. LEPRI: Bernard Lepri.

I'm speculating here, being a clinician and having worked in this area. Typically, once a patient has this experience of misusing the peroxide solution, it is not something that is done repeatedly. So I would hope that there was no limbal stem cell damage from them repeatedly doing this. So, you know, that's a projection on our part, of course. But does that address your question? I mean, I don't think you would hear of repeated use. Now, we do not have any data with respect to that occurring with proper use of the device, okay? I mean, it's been around for 30-some years, and it's actually probably the most highly recommended from practitioners of contact lens dispensing because of its effectiveness as a cleaning and disinfecting agent. So when used properly, there have not been any reports, to the best of my knowledge and our knowledge, that there's been any corneal damage from its repeated use because once it's neutralized, the H_2O_2 just becomes H_2O; it becomes water when it's properly neutralized.

DR. EYDELMAN: If I may add, we have a number of distinguished cornea experts around this table. Perhaps they want to pipe in if they're aware of any such.

DR. WEISS: Well, my only comment is if a patient made this repeated mistake, with the amount of pain it causes, I think that would actually be being reviewed by the psychiatry panel, not us.

(Laughter.)

DR. WEISS: Dr. Jeng or Dr. Huang or Dr. McLeod, any maybe more erudite comments than --

DR. DAHR: So a one-time exposure, the concentration is not enough from a one-time exposure to cause an issue?

DR. WEISS: Not typically, no. No. So if you looked at the -- there were a few patients there who had more damage, but a one-time, as was described by Dr. Dillard, it hurts, it burns, you say, oh, why did I do that, maybe on a shorter framework than what I just said. And that's it.

DR. DAHR: So my second question, just trying to look at these scenarios whereby someone uses his or her -- his wife's solution by mistake on the bathroom countertop, is it ever the custom whereby patients are either counseled or of their own volition might use a mixed modality approach to their contact lens cleaning, whereby they may use the peroxide-based solution once or twice a week for that extra degree of cleaning, but then use the multipurpose solution the other 4 or 5 days of the week for the simplicity and quickness? Is there ever that mixed modality pattern of clinical use or not really, because that seems like a scenario whereby that confusion could occur on the bathroom countertop.

DR. LEPRI: Bernard Lepri.

Dr. Dahr, as I mentioned in one of my slides, one of the factors that has to do with compliance with contact lens care, and any medical care for that matter, is the expense of the products. And so patients, you do not typically -- and I have never known anyone to prescribe both modalities. If someone has heavy buildup on their contact lenses, they are oftentimes recommended to use a protein remover once a week or twice a week, but that is in addition to their regular multipurpose solution regimen.

Many problems with contact lenses do not come from having mixed use, but rather from being abused in terms of reusing the product, topping off the product, not exchanging

it, and using too little of a product in order to effectively clean and disinfect lenses.

DR. WEISS: Dr. Owsley.

DR. OWSLEY: Cynthia Owsley.

My comment has to do with the perceptual features of the packaging for the multipurpose solutions versus the hydrogen peroxide products. Is FDA aware of any movement from the companies and manufacturers to make the packaging more distinctive? It kind of seems like, as a visual psychophysicist, it's sort of, from my perspective, it would seem like a simple approach. Is FDA aware of any movement in that direction, and if so, has it been effective?

DR. EYDELMAN: So for today's meeting, we have extended an invitation to all of the manufacturers to come and present their point of view, and those who have chosen to accept our invitation will be presenting shortly, and I believe several will be addressing your question.

DR. WEISS: We're only going to have a couple more minutes, so I'm just going to address those on the Panel who have not asked a question before we wrap up. There will be an opportunity this afternoon to ask more questions.

Dr. Ellis.

MS. ELLIS: Just Annie Ellis, I'm a Patient Representative.

My earlier question was going to be were there multiple reports from the same reporter, and along with an earlier question, with each report, is there an assumption or a sense of how come the number of one reported instances happened? But I do want to -- I am someone who has experienced accidental misuse, and my husband and I both use the same peroxide, which kind of brought us together, but --

(Laughter.)

MS. ELLIS: And it's excruciating. You know, it's not just a little burning sensation; it

is a paralyzing, excruciating pain. And I noted laughter. You know, you would think one would just do this once, but what I would like to submit to you is that when people are using these products, think about the timing. You're waking up first thing in the morning. You may be groggy. You may be on automatic pilot in your daily routine. If something is not in the right place or in a different thing, there's the possibility that you're going to reach blindly for another thing or splashing can occur. So I fortunately have not had subsequent misuse, but there have been close calls, and I'm thankful to have one bathroom and a partner who can tell me hey, hey, hey, wrong one. So that being said, it does not keep me from continuing to use peroxide-based cleaning solutions because I do have sensitivity to the preservatives, and I do appreciate how much cleaner it does feel. I have tried them and I use them when traveling, and I've had to give up my peroxide at TSA, but it's not my first choice. But, you know, I'm very concerned with safety, and I'm very concerned with access.

DR. WEISS: Dr. Rimal and then Dr. Sneed, and I think then we will go on in -- yes, next. And then we'll -- those three, and then we'll go on in this portion.

DR. RIMAL: Rajiv Rimal.

I guess this is a question sort of to the FDA in general. I'm wondering if the FDA has the authority to require sponsors to conduct observational studies postmarket, if that would be our recommendation.

DR. EYDELMAN: We do conduct postmarket studies very frequently. If there's a definitive safety issue that needs to be dealt with, then that is the least burdensome way to do it.

DR. WEISS: Dr. Sneed does not. Ms. Witczak.

MS. WITCZAK: One follow-up on that FDA authority. Do you have the authority to have a manufacturer change the labeling, like on the outside of the boxes, how they're packaging or the actual bottle itself? Does the FDA have authority, or do you just basically

recommend, suggest, or can that be put into some type of regulations?

DR. LEPRI: It is not a regulation. The regulations state that you must have carton labeling, a package insert, professional labeling, and patient instruction booklet. But we review the draft labeling, and we look at the carton and how things are presented, and we make sure that they utilize the universal symbols and verbal instructions to go with things. And so we review the draft labeling, and we tell the sponsors, the industry, what our recommendations are about what they should change, and they are cooperative. However, once products are out on the market, we don't see the final labeling, and we have to understand that this labeling does not always go through the regulatory staff at industry but also reaches their marketing departments. And so they have a different approach to presenting some of these types of things, and sometimes there may be modifications of that. But we don't have any regulations that they have to show us the final product and --

DR. EYDELMAN: If I can just ask Director Yustein to make a comment.

DR. YUSTEIN: Hi, Ron Yustein. I'm Deputy Director for the Office of Surveillance and Biometrics and also Deputy Director in the Office of Device Evaluation.

So to answer your question, we do have various mechanisms to address labeling for products that are already on the market, and we have done this in the past. We can issue a guidance document which recommends that specific items appear on certain parts of the labeling. A guidance document is recommendation, and we have done those recently.

But as Dr. Lepri was mentioning, to make it a more formal requirement would require a regulation, and I think you understand the regulatory environment we currently live in as well as the fact that issuing a regulation isn't something that can happen overnight. Issuing a regulation comprises of issuing an order, then it's actually put in the *Federal Register* for comment, and it has to be left open for comment. So making the end product of the regulation occur can be years down the line. Can it be done? Yes, it can. Is

it done? Very infrequently. But those are options that we do have, but there are limitations. The guidance can be done quicker, but as a recommendation; a regulation can be -- it takes a lot longer, but it can be "a requirement."

DR. EYDELMAN: And let me just add one more thing. You know, while my colleagues have delineated our regulatory boxes in which we live, I do believe that most of industry is very eager to try to maximize patient safety. So I think recommendations from this Panel will be widely disseminated and heard by most of industry. So I do urge you to continue sharing all your thoughts with us.

MS. WITCZAK: I was just going to ask one. When you say labeling, does that also go to the actual bottle itself, like packing, the actual packaging?

DR. LEPRI: Yes, it does.

MS. WITCZAK: Okay.

DR. LEPRI: And I would like to add that our guidance documents for contact lenses and contact lens care products provide specific lengthy sections on recommendations for labeling. So it isn't just a matter of us looking at it. There actually are guidelines that are presented for industry.

DR. WEISS: Mr. Pfleger, I'll let you have the last word before we go on --

MR. PFLEGER: It's just, I think, if we go through the industry presentation, I think some of these questions may be addressed, and I think it will be a much fuller discussion this afternoon, then. But obviously, industry listens very closely when FDA makes suggestions.

DR. WEISS: Thank you very much.

We're now going to go on to introducing Dr. Ruth Day, who is Director of the Medical Cognition Lab at Duke University. Dr. Day is presenting Labeling Comprehension: Effects of Standard versus Enhanced Displays. Dr. Day, you will have 25 minutes to present, and you

can now begin your presentation.

DR. DAY: Good morning, everyone. So the topic is Labeling Comprehension: Effects of Standard versus Enhanced Displays. My name is Ruth Day, and I direct the Medical Cognition Laboratory at Duke University where we study comprehension, memory, and use of drug and device information.

Our basic approach has three prongs. In the cognitive analysis phase, we look at information that's provided in hard copy on the internet, video, other means, and we obtain quantitative measures of the information and calculate cognitive accessibility, which I'll tell you more about in a moment.

And then what we do is we make some enhanced displays of the same information but based on cognitive principles and then conduct cognitive experiments to test the effects on attention, comprehension, memory, problem solving, decision-making behavior, and ultimately health outcomes.

Today we're focusing on the labeling for contact lens care products containing hydrogen peroxide, and we'll look at some enhanced displays and cognitive experiments in progress.

Cognitive accessibility is the ease with which people can find, understand, remember, and use information, and hopefully, in a safe and effective manner. Cognitive inaccessibility occurs anytime people have trouble with one or more of these things.

Here's a sample experiment from our lab, not on contact lens care products but from over-the-counter drugs, and it's an example of hidden warnings. Basically, we have people read some information, and we test their knowledge of uses, warnings, etc. And here's the excerpt from aspirin, and there is a hidden warning here. This is the warning section complete. See if you can find it. And if you haven't found it, here it is. The last line says, "Aspirin may cause stomach bleeding." Well, if you start reading the section on alcohol

warning, and it says "If you consume three or more alcohol drinks every day," and you might not keep reading. So it is really buried and it's hidden, and it can cause stomach bleeding even for people who aren't heavy alcohol users.

So we did an experiment where we compared the original version where "stomach bleeding" is hidden at the end of the alcohol warning, and we made a new enhanced version where we just pulled out "stomach bleeding," and it had its own chunk down below with its own subtitle, and then we asked people what are the warnings that you just read, and we looked at how well they did for the two conditions. And we found that the people who studied the original version were only a little above 30% correct, with a big increase for those who had the enhanced version. So this is a 100% increase. That's a very simple case here. The point is that warnings can be physically present but functionally absent. Physically present but functionally absent. If they're functionally absent, they're not being helpful. Any information can be physically present but functionally absent.

So the principle here is chunking, the chunking, putting things all together that goes together and separating it from other information. It enhances what we can see at a glance, how much we're being engaged, how well we will understand and remember the information.

One more sample experiment with precautions. Here is the original version for something, which starts out "Tell your doctor, nurse, or pharmacist if you." Okay, take a look at that. It looks simple and clear with bullets, and if I were to ask you a question, how many things should you tell your doctor, nurse, or pharmacist, the typical answer is seven. Why did people say seven? Because that's what it looks like, there's seven bullet points.

Let me take this standard way of showing a list of things with bullets and now show an enhanced version. We pulled it out, and we've chunked the separate topics, and we're giving each topic a name. As you count up all the individual things you should tell your

doctor, etc., there are 18 things. And so the takeaway is what people -- what do people get and what their takeaway means later. So the principle here is coding, that when you have it chunked and you name it, if it's important, it will enhance comprehension, memory, solidification of the chunks, what's in it, and then the use of the information.

Turning now to contact lens care products, as Dr. Lepri this morning has indicated, there are three main sources of misuse: accidental use, failure to follow the neutralization directions on the box and bottle, and erroneous purchase. For now, I'm going to focus on the failure to follow, but not just neutralization directions but everything that's on the labeling, all right, failure to understand, remember, and use labeling information.

So let's look at some labeling for contact lens solutions containing H_2O_2 and a typical one looks like this. This is an actual labeling for a given product, and it is current; it's been there since 2011. All identifying information has been removed. It's now Brand XYZ. Everything else is the same, the same content, format, colors, etc. Let's take a look at it.

This is an excerpt from just the warning section, and as you can see, there's red and there's black, and there's a little bit of spacing. But if you look at that block in the upper right-hand corner, it's just a lot of text, and it's very hard to find out what are the topics and what are the warnings in this display.

Just so you can see it a little better here, here you can actually read some of what's written, and that's that block I was just telling you about there. And this block would jump across topics. There might be something along the way of Topic D and then E and then F, and then it goes back to D and so on. So there isn't good clustering of the information. And here's some of what the rest of it looks like.

So we took this, and we kept everything the same and made an enhanced version, and this is just an excerpt. One of the problems we found in some of our testing was people mix up what the directions are for soft lenses versus RPG lenses with this same product, all

right? And so what we did was to do the practices, what I've already shown you about, about chunking and coding, but we put them side by side so that you can see, for example, the one on the right, rubbing is involved, whereas the one on the left, rubbing is not involved, etc.

And you can also see, if I were to step back and show you a wider view, that the one on the left, the soft lenses, has a much longer set of directions than the steps on the right. We asked people about how many steps are there, what are they? And when people see these two side by side, they do much better. And so they can use this information more effectively.

And here it is just so you can read it a little bit better. That's the beginning of the soft lenses section, and there it is with the RPG lenses, and you can see the individual steps standing out more fully.

Here is the top of what it looks like, and you'll notice, in this approach, I guess I will go a little bit farther here, you can see that we have done something different with having the titles and the actual text be in different fonts and they're contrasted. Everything in traditional labeling is all the same kind, and it kind of all runs together. So we've done some things like that to make a spatial way out and the contrast more distinctive.

Here's the warning section from the enhanced version, and you can see it goes way down the page. You can't see all of it, but there is a warning about lens insertion, there's something about soaking lenses; it pops out. Another pop-out is the contrast between daily wear lenses versus extended wear; and so on it goes down the page. And here are some of the other pages.

So our current study is in progress, and let me tell you about it. We used the original labeling that I've shown you and the enhanced labeling prepared for this study that I've also shown you. And I just want to point out, the enhanced labeling has not enhanced

everything. We basically looked at the spatial layout of the information.

All right. So the demographics and participants, there's a wide range, and all of them, their range in age is from 23 to 55 with a mean of 35, 70% male, from 28 states across the United States, education varies from some high school to advanced degree, but mostly high school grads, some college, and college grad.

And in terms of having ever worn corrective lenses, 55% have, whether it's glasses or contacts, and 23% are either currently wearing or have worn contact lenses.

The sample size so far we're continuing to correct, and I'm sure today we're going to correct it more back home. But in the sample I am able to show you today, there are 64 participants, 32 in each labeling condition.

Here's the basic procedure. Testing was done by a screen, and here is the welcome screen. Welcome, good vision study. And then they went on and used the procedure that they followed. First of all, they studied the labeling and then we tested them. They studied either the original or the enhanced, and participants were randomized to conditions. So about half of them saw the original, and half saw the enhanced. When we tested, we tested on all content, warnings, directions, ingredients, etc., and we used multiple tasks that would tap attention, what do they notice, comprehension, and memory.

Here are some of the results, and really, it's just a subset. During the study phase, what percent of the document were they actually reading? Seventy-two percent read completely, 17% just skimmed, and 12% of the document they did not read at all.

Here are some metacognition questions. Now, cognition is the process of knowing what people actually know, and metacognition is what they think they know, and I'll be discussing this more thoroughly. But here are some metacognition questions. We asked people to rate how well they thought they understood the information, could remember it, and had enough information in order to decide whether they would want to use this

product.

And here are the results, and as you can see, the people who saw the enhanced version -- I'll call them the enhanced group -- had higher metacognition scores.

There's one other metacognition question. We said if we asked you questions about information on the leaflet, about what percent do you think you would get correct? This is tapping their self-thoughts about their own knowledge. And so we're plotting their prediction in terms of percent correct, and the enhanced group thought they would do better. And, in fact, they did.

So now let's look and see how people did on testing of actual cognition that they knew. At one point we were studying uses, and we said is this an appropriate use of this product? And we gave them just one possible use, and they said yes or no. So here we are plotting percent yes responses for appropriate uses, and as you can see, the labeling is very effective for knowing that the product can be used to clean, disinfect, and remove protein. Everybody's doing very well. However, for neutralizing, soaking, and storing, the scores go down. Yet, the enhanced version is enabling people to answer this question better.

For inappropriate uses, we made some up, where we gave some that are wrong. Then the percentage of people who said yes did fall, but there was one disturbing one that this product could be used as a saline rinse. I don't know what that means, but they thought it could be.

All right, so we explicitly asked what are the ingredients in this lens solution. And in this free report task, where they're just freely reporting off the top of their head, we can see that hydrogen peroxide was mentioned for half the participants, with a slight edge for the enhanced group, nothing to report harm about particularly. But we had another task. We gave them an explicit question: Is hydrogen peroxide an ingredient in this product? Overall performance went up. That's typical of a recognition procedure versus free report,

but now the difference between the two groups are merging, where the enhanced group is doing better, and for the original group, 20% are denying that there is hydrogen peroxide in this product, despite all of the mentions of it in the labeling.

Now, towards the end of the testing, we repeated the metacognition questions, the same ones as before, and here are the results for post-test, and you can see that now something interesting has happened. Overall predictions and ratings of their understanding, remembering, and ability to decide whether to use the product went down, but now the original people who saw the original labeling are more confident. They just think they're doing better. You may have forgotten about what the pre-test was, so here it is; here's pre-test, post-test, and to have you be able to see better, they're compared on the same screen. And so it's kind of interesting that the enhanced people go down after the testing, that they realized that they did not know as much.

There are two types of studies that can be done. Cognition is what people actually know. Metacognition is what they think they know. Metacognition is not only the type of questions that I showed you here today, but focus groups. Focus groups are really important, and you get people's attitudes, their preferences, their thoughts about what they understand, but it's not the same thing as cognition. There is often a gap. We find a gap between cognition and metacognition in all of our studies, and the basic finding is that people often think that they know more than they do.

Furthermore, those who see the enhanced version have a better understanding of what they know, what they really know. And if you know that you don't know fully enough, you're more likely to go back and look at the box, the bottle, or the labeling to find out if you have a question and you're uncertain what to do. And this occurs not only in the device world but in the drug world. We've also shown this in knowledge of informed consent forms for clinical trials. There's this gap between cognition and metacognition. It's

important to get metacognition data, but without cognition data, it's possible to misinterpret and not have the full picture.

So let's pause from the study a little bit and step back and think about labeling development and revision and how it goes.

After this review of data and determining what safe use might be, we decide what to include and draft the labeling and then what to say and how to say it. As a charter member of the FDA Drug Safety and Risk Management Advisory Committee, we were often called upon to look at possible new warnings and what would we say and how would we say it. There wasn't much discussion after that in the Committee meetings. There was more obviously with FDA. But just to emphasize here, we also have to think about how to display it and for what tasks, what cognitive tasks. And then the real problem comes later when the revision comes up. I've been called in for many Advisory Committee meetings. Well, we like this new warning. Where should we put it? How should we say it? And the tendency is to shove it into what's already there, and I think we always have to step back and see what is the overall display looking like, and where can this go most effectively, and does the display need to be modified?

So the basic problem is that people may not read all the labeling. They may not read it at all, but if it's engaging, they may. There's lots of information there. They only want and need some of it at a given time, and so we have to consider questions of cognitive accessibility. Our job is not done when we've gotten the right warning or the right initial information and we set it in the right way and focus group people tell us they like it. We have to look at these broader questions of cognitive accessibility.

So the questions sometimes are what do they want? Okay, a very important question, and I think CDRH does a wonderful job engaging patients in the discussion on this, what do you want?

We also have to ask what do they need and when do they need it. And when isn't only a point of time but in spatial location into the labeling. Can they get along without some of it, at least some of it? Or is some of it maybe less important, but you could decrease the font or do something? Everything looks like it's the same importance unless it's in red, which I do not recommend, but that's another issue.

All right, so how can we get them to look at the labeling, to engage them, then, in going more deeply into it and help them, so that it will help them find, understand, remember, and use the information, and to be able to use it in real-world situations? We think about the labeling and reading carefully and deeply, and carefully and deeply. But in a real-world situation, oftentimes people only scan. Some of them want to search and find one thing. And when they walk away, do they remember something? What are they going to remember, and how are they going to use it?

So to conclude with some recommendations, and these are very general and preliminary, you've got to start reducing cognitive violations; that is to say, there's normal ways in which cognition works, and some of the labeling, not just for this product, all labeling and all kinds of documents, sometimes they violate clustering principles. Clustering, again, is putting together what goes together, okay? And if you want to repeat it somewhere else because it's important, fine. But when it's the major place where everything goes, put it all together, don't skip to the next thing, the next thing, and then down the page come back to that first thing, all right? That's clustering.

Chunking was once you've clustered the information together, to separate it in some way from the surrounding information; in a video or in an auditory presentation, that would be by letting some time go by, you have a pause in between things, like this.

But spatially in written information, it can be with blank space and titling and other kinds of things.

And then for the coding, that's where you actually put a name on things.

Another recommendation is to try spatial layout techniques, such as those shown today that are content driven, not format driven. I think a lot of the labeling is very format driven, and it takes an *a priori* format, which is good, and it's important to have certain sections and so on. But by just having that format drive how the information is presented, it does a disservice oftentimes to information. But if we turn the operation around, look at the information, this important chunk of information, how can we display it in a spatial way so that people can get it and then use that in the labeling?

Number 3 is to compare, such as the study I showed today, current versus enhanced labeling before it gets out there. Today we've heard questions at the meeting, okay; you change all the packaging, and then have enough years gone by so that we know how it worked out in someone and so forth? Well, we can test up front what comprehension and memory can be. And this way we can learn why people do not understand, why they might refuse. Is it the concept itself, or it's difficult? So it needs to be said in a different way. Or is it the labeling and the way it's been provided?

And finally, to consider tasks such as reading carefully, finding, understanding, remembering, and using.

So cognition does not take place in a vacuum. When we are working to get good comprehension, we still have to get attention. Memory is going to happen whether we like it or not. Is the labeling set up well enough to foster good memory? And there's a lot known about what fosters good memory; and, of course, to be able to solve problems and take appropriate actions.

So I'll repeat one more time: What can patients do with labeling? What can they see at a glance? You know, let me check this, and they only look for 5 seconds. What can you see at a glance? Does everything all look the same, or does anything pop out? Can

they read, understand, remember, search and find, and solve problems?

Thank you very much.

DR. WEISS: Thank you, Dr. Day. We have 5 minutes for questions. I'm going to start off. If it's still saline rinse, it can be used in your eye. Hydrogen peroxide, as we have heard, can't be used in your eye. Was I correct to understand that the enhanced labeling group thought that this was an enhanced saline rinse, a higher chance of it? Because if it was, then that's the one thing you want people not to think --

DR. DAY: Right.

DR. WEISS: -- because that's what's going to give them the complication.

DR. DAY: What I said, okay, so the data show that this is still a problem. There was no special attention given to that in the enhanced group relative to the original group. So as I said, we did not treat everything and boost that. We kept all the content exactly the same as in the labeling. No special attention was given, and there was no chunking and coding for it. And what I showed, I believe, was about 40% of the people still thought that, and there was no difference between the two groups. But I think that the point is that some of that content has to be changed.

So the strategy here is that if you have an original and an enhanced group, you would have to enhance everything in order to test that question specifically. But we were just testing the spatial layout approach at this time. And so this study at present does show that's still a problem; 40% of the people would use it in that way.

DR. WEISS: To me, that's the main thing that's important. The rest of it isn't so important, and that's really critically important. So what is your recommendation for that, if you are going to be using these principles?

DR. DAY: Right. Well, we've just gotten these data very recently, and we have just seen this, and we're just developing that now, so I can't say today. But I would pull it out, I

would pull it out as a separate chunk in the warning, and I would do a bunch of other things with it. But that's something that I have been working on since we saw this. That is definitely a red flag.

DR. WEISS: Thank you.

Dr. Krishnamurthy.

DR. KRISHNAMURTHY: I'm assuming that --

DR. WEISS: If you could identify yourself.

DR. KRISHNAMURTHY: Krishnamurthy from the University of Houston.

The data that you showed has not been subjected to any analysis at this time? There's no statistical analysis of the difference --

DR. DAY: There has been for some of it, and there is enough statistical power to get the results that we've seen for the big effects, and the small ones where I said don't write home about, no. So this is definitely in progress, and I bring it to you in order to show you that there are these contrasts that you can get and to think about this -- two ideas: one, spatial layout, but mostly the cognitive testing to test what people actually do know and to combine that with the metacognition testing.

And I would add that this type of result that -- the results we've gotten here, those two I just mentioned has been subject to statistical testing and review in two review journals on other topics. We've only started the contact lens work within about the last couple of months.

DR. WEISS: Seeing no other questions, I'll ask one, the last one. Do we have any information of what percentage of patients actually read any part of the label, if you go into the population?

DR. DAY: Well, we did not just ask blindly to a general population, are you a contact lens wearer and have you read any of the labeling? But in the context of this study, we

showed it to them and asked them to read it, and then they reported how much of it they read. So I do not know the answer to that question.

DR. WEISS: Yes, a couple of questions. Mr. Pfleger.

MR. PFLEGER: Doing the package insert, did you also do any work with either the bottle label, the point -- which is a point of use, or the carton?

DR. DAY: Some of these are similar, but no, this is the focus on the labeling. That was what I discussed with FDA to present today. Um-hum.

MR. PFLEGER: Okay.

DR. DAY: By the way, some of the labeling and these -- the label is actually shown in some contact lens boxes and in the inside, and sometimes there's an actual insert. I am a contact lens wearer. I don't use the hydrogen peroxide solution, but the multipurpose, and it's printed on the inside of the box. I have to tear open the box and look inside, and it looks just like this.

MR. PFLEGER: And my second question was, in general, do you see a difference in these results between males and females? Because I noticed in this particular study you have actually kind of the inverse of the contact lens population; you have more males than females.

DR. DAY: Right, that's just the way it happened. In all the other studies, we've never found a difference between male and female, older, younger, short or fat or tall, or any of those things. Everybody's a cognitive being and the cognitive processes -- but everybody's a cognitive being and their cognitive processes work in the same way, and so we don't get those demographic differences.

DR. WEISS: Thank you very much, Dr. Day, for your presentation.

Next, I would like to introduce Rollin "Terry" Fairbanks. Dr. Rollin Fairbanks will be presenting Human Factors Engineering: The Science Behind Designing for Human Use.

Dr. Fairbanks, you will have 25 minutes to present, and you can now begin your presentation.

DR. FAIRBANKS: Thank you. So as I was introduced, I'm Terry Fairbanks. What I'm going to do, I'm going to give a quick introduction to my background because it's relevant to what I'm going to step you through, and then I'm going to tell you what I'm going to tell you.

I am a human factors engineer from the industrial systems engineering side and an emergency physician. I did safety engineering before I went into medicine, and I run a human factors engineering center that's embedded in a health system with about 30 human factors and cognitive science folks working alongside clinical folks to do human factors work in healthcare. I have no conflicts of interest with this.

What I'm going to tell you about today, I want to introduce the idea of how safety science impacts these error modes that we're seeing, and as the FDA earlier said, what I would characterize these as are use errors. And for those not familiar with the usability, use errors are characterized as design flaws that facilitate errors by the user, and that's distinct from user errors. So what I want to do is introduce the concepts of the science behind error science, particularly as it pertains to human error. I'm going to give you the science, the principles, and then I'm going to give you some unrelated examples to kind of really demonstrate what I'm talking about with this, and then at the very end, we'll relate it to this.

So I want to start with the big picture, and that is that healthcare is still one of the least safe things you can do, and this is going to connect to my final slide, which I'll tell you now is a picture of Einstein reminding us that when we keep trying to fix the problem the same way and it's not working, that that's what we need to reevaluate. And I think that's the theme of what I'm going to say.

It is much safer to drive to the airport. And remember the old thing -- I'm sorry, to drive to the hospital than it is to enter the hospital, and that's with true data. And remember the old thing about what's the most dangerous part of your flight, the most dangerous phase of your airline trip? By a factor of 100, it's the drive to and from the airport, right? So many factors in how dangerous it is to be in healthcare. And a lot of the principles that make healthcare still such an unsafe environment, we are hearing today and we're seeing in this design.

So the IOM report, and you're all sick of hearing about it, but it's been 17 years now since we really focused on trying to improve safety. And I'll remind you that the title of this report 17 years ago was "To Err is Human." So it's what we've learned from the time we were 2 or 3 from our parents, that one of the first values we learn is everybody makes mistakes. We're not going to be able to train this mistake out of people, and I'm going to give you some very clear science behind that that I think will demonstrate it.

A lot funding, regulations, and everything went in. Where are we are now 17 years later? If we look at the overall data with safety in healthcare, we're at the same place, exactly the same place. And that's because we continue to have discussions, and I'm going to be very frank, like we're hearing today, about how to instead of changing the design, get the people to use the bad design better. And I'll go through that so that I'm making more sense.

We're focusing on individual performance, and a lot of our solutions in healthcare are very inconsistent with safety science. In fact, when I came from the safety science world where I was working in transportation and aviation and I was a pilot, and then I went into healthcare, it was very disturbing because it's such a different approach. So my focal area which I'm going to talk about, human factors engineering, I'm just going to take two slides to tell you what it is because that's what I'm going to walk you through.

Human factors engineering uses data from behavior and cognition, human performance data about abilities and limitations, physical traits -- that's synonymous with ergonomics, so if you design an ergonomically designed chair, you're looking at the physical measurements of the 95th percentile person that you're designing it for, and that's how you do the design. Other characteristics, you apply this design to things that you make for productive, safe, comfortable, effective human use. And safe and comfortable, in the context of today, I just want to make a point: There was an earlier discussion about whether this was an adverse event or not and whether, you know, people went on to have infections or eye-changing events. If anybody in this room thinks that it is not an adverse event to put peroxide in your eye, I invite you to go home and ask a friend, buy one of these products and ask a friend to put it in your eye. This is an adverse event. In my health system, in my health system we would classify this as an adverse event if it happened in one of our hospitals because it is so severely painful and it can be such a traumatic experience for people.

One of the things that human factors engineers do is sometimes we don't even apply safety science; we just go in, and we're the first people that really understand, watch, observe the people at the front line and understand and talk to them, and what we often see is this big gap between work as imagined, the way when we designed the solution, you think things are going to work in the way they work, and the way it's actually done. I'm hearing a lot of work-as-imagined talk today because we're spending a lot of time focusing on how we're going to change the labels.

Now, I want you to go home and talk to your friends, neighbors, aunts, uncles, nieces who have saline -- I mean, who have contact lenses and ask them how often they have ever read the box, the outside, not even the inside of the box, but the outside or the bottle or anything when they buy saline in these products, and think about that and think about

we're spending a lot of time trying to optimize the labeling, and I think that's very valuable for some products but not this product probably.

And another example of this gap, think of the lawnmowers. I'm going to mow -- people in my field 20 years ago would, every weekend, see chopped off fingers from lawnmowers in the summer. That was a very, very common thing because people would go to pull the clumped grass out while the mower was running, right? Well, I don't know if you ever read a lawnmower instruction packet, and it's relevant to this discussion, right, because you've all probably bought a lawnmower at some time in your life, and I want you to -- do you know that on the first page of lawnmower instructions, there's a full-page huge warning that says not to put your hand in there when it's running? Well, that hasn't fixed the problem.

So the industry at the time didn't fix the problem, so it unfortunately had to become a regulation. And what did they do? Well, notice they made the instant cutoff so when you take your hand off the mower, the blade stops immediately. The injuries almost went to zero. Why didn't they go to zero? There are workarounds, right? All of you have seen or heard of somebody that ties it together.

(Laughter.)

DR. FAIRBANKS: So we can't fix everything, but we can fix it in the 99th percentile. This gap is what we want to -- if we want to solve this problem for our consumers, we have to narrow this gap. You get out of the work-as-imagined space into how we're going to fix this.

The last thing I want to say about human factors engineering is that we don't redesign humans. Sometimes people hear human factors, and they think it's about fixing people. It's about studying with really good science how people perform in different environments and then designing around that, particularly safety-critical areas.

So I'm going to give you a couple examples. This is a defibrillator. I work in emergency medicine. We like to pretend everything we do is a big emergency, and it's not, right? But one of the things that is a big emergency is when someone drops dead, right? The medical folks in the room know that when someone drops dead, they're usually in the kind of heart rhythm that if you shock it, you bring them back to life immediately. Pretty miraculous. I mean, they're clinically dead for a minute, and you bring them back to life. The problem is every minute that goes by, there's 10% less chance of resuscitating them. Or 10% more chance of them staying dead. So time is critical, right? So if you have a patient that goes into cardiac arrest, you have a defibrillator right there in front of you, you can grab it and you put it on them and you charge it up with that yellow "Charge" button, and then when you go to shock, you accidentally press that "On" button. Does everyone see the "On" button? I'm going to have a use error trying to use this pointer. Oh, there we go. Okay. See that "On" button? You press that instead of the red "Shock" button.

Now, if I had time, we'd go into the human factors analysis of why it's a normal error to press that button, but what happens on the defibrillator where every second counts to save this person's life and you press the "On" button instead of the "Shock" button? It just turns off. Today, this is the case; it just turns off. And then it takes 3 to 4 minutes to restart it, and it goes through a computer startup, and you have to recharge it. Up to 40% less chance of resuscitating this patient or 40% chance more of them staying dead.

Why is that in this industry that this problem which was first reported in the literature in 2007, why is it that this design persists? And it's relevant to our discussion today. It's because we believe the solution to this problem is to get people to just use it right.

And I want to compare it. In the interest of time I won't do it, but I guarantee, if I walked over to that slide projector right now and I press the "On" button accidentally, what

would happen? It wouldn't just turn off. What would happen? We all know what would happen. It would ask you do you really want to turn me off, and you would get this thing. They all do that, every single brand. Why does it do that? Because the developer of this consumer device said we're going to anticipate a normal human error that might cause an adverse consequence for somebody; it might delay their presentation, not kill them or not burn their eyes, and we're going to put a system fix in place. We aren't going to try to label or train the humans or optimize labeling or show them a video. We are going to fix it with a system solution. We could do that with defibrillators.

So you see where I'm going with this. This is a normal area, and there are lots of studies to show this. We came out with a study in 2008, but then physicians -- I don't know if that's mine. A physician study went back and looked. They did it and found that a certain percent of this happened every time, so it's a normal expected error.

So here's the science behind this. This is a long, deep literature -- there are behavioral scientists in this room that could give this much better than I can right now. But Rasmussen had models of cognitive mode. Jim Reason, who is the father of error science, took that and figured out how that impacts a type of error. I'm not going to go deeply into this, but I want you to understand there are three basic error types, and one of the problems in healthcare is we're always trying to fix one error type with the solutions for other error types that are actually ineffective in the error types we're trying to fix.

And that's relevant in this case because what happens in the bottom one here, what they call skills-based error -- and for the medical professionals in the room, skills-based doesn't mean technical skills. This is psychology, and they weren't thinking of us doing our central lines and intubations. Skills-based error you can think of as automation error. I'll give a great example that you all have done in a minute, and you'll know what I'm talking about, but it's something, a task that you do all the time, you're used to doing, like putting

saline in your eyes, so you're not thinking about the cognitive steps of that test.

Automated routines: Slips and lapses are the error modes in this. And the really interesting thing about this, number one, that's what we're talking about here. This is a slip, is the error mode that we're talking about that's happening to consumers here.

Now, the other two -- in the interest of time I won't go into it, but some of the things we're talking about, video, labeling, good -- Dr. Day's presentation was exceptionally good and really important, usability, what I would call the usability of these instructions, really important in the knowledge base and rule-based area modes.

So it's a huge opportunity for us to fix this if we focus on this automation mode. But here's the thing. These things are not effective, zero effectiveness. When we do studies and we try to fix skills-based error with mindfulness training, vigilance, better labeling, anything, education, it does not change. It can have a blip, but it does not have a persistent change in that frequency. And remember they said this in the year 2000 when they came out with this report "To Err is Human," and we can't change this human error.

So bringing you back to the defibrillator thing, when these studies came out, we had responses from the vendors, and they did some labeling to fix the problem. Now, I want to give you an example to really bring this home to today's discussion, to show you why labeling doesn't work in a skills-based error.

For those of you who are local, this is the exit to the Bethesda Bagels bakery, and one day I was there with my kids, and my wife said, God, the kids were so cranky, and it was crowded. She said just take the kids to the back; I'll get the food, and I'll meet you. So I'm in the back with the kids, and customer after customer after customer comes up to this door, and they pull on it. There is really good labeling. First of all, they came in the door, so they know that it doesn't operate that way, or they would if they were having a mindful moment. Second, it's a public building. The fire code in the U.S. requires that it exits out,

but why do they pull on it? There's a label. I don't know if you can see that. There's a really big "Push" sign right in front of their face. Labeling, instructions. They are in skills-based mode because they have all used a door since they were little.

What is the most powerful display of information to your cognitive mode when you're in automation or skills-based mode? It's the object itself. The object is telling you to pull. The object says I am a pull interface, not a push interface. Now, there's a really elegant design solution for this indoors, right? It's elegant because -- this is the best picture I could find, but it's elegant because not only does the display tell you how to use it, but it's actually also a forcing function because it's really hard to pull on that door. So it has two safety solutions. If the wrong use of the door was safety critical or caused a pain-in-your-eye issue, we would fix doors this way. Fortunately, in most cases it's not safety critical; it's just annoying.

So there is a psychological principle behind this, and it's called affordance, which is what an object suggests to us. And remember, we're talking about skills-based mode, what an object suggests to us when we're not thinking about it, when we're doing a task that we do every day so our mind is not in a conscious mode to think about the steps in that task.

The corollary to that is population stereotype, because affordances are different in different cultures, which is why the CDRH requires, when we do human factors engineering studies in the 510(k) process, that your users have to be from the culture of the intended user group of the device, which makes a lot of sense.

Are those switches on or off? You don't know because there's not really a good public affordance about this. Is that switch on or off? All of you from the U.S. are saying that switch is off. That's an affordance. You don't have to think about that. But if you're from Europe, you'll think that switch is on, right, because they're the opposite in this. It's a great example of an affordance with psychological principle.

There's really good data on different -- sorry, you can't see this, so I'll just overview it, but on different solutions to different kinds of error modes. I think you all can see where I'm going with this. Clearly, what we're talking about in the peroxide error is a skills-based automation error. People with contacts are squirting solution into their eyes all the time, all the time.

A related thing, heparin: You know, probably a very famous case because Dennis Quaid's kids had -- the heparin on the left is 10 times the concentration of the heparin on the right. They're in the same exact bottle, and there is some color. The one on the right is given day in and day out by nurses, all day long, directly into the vein. The one on the left, if you happen to give it directly into the vein by accident, it kills the patient. Right? Would they do that in aviation? Would they make them look exactly the same, come in the same bottle? Now, what's interesting, this says "Indiana: 5 nurses." That was a year before Dennis Quaid's children experienced this error, and all five nurses were blamed, not by the hospital; the hospital handled it really well. There was a design change that cost more money, but it was very smart, but there was no recall. So this problem persists. And remember, they were trying education, they were trying to tell the nurses to check, do their "five rights" rather than looking at the design in this skills-based error.

These two medicines look exactly the same. One goes into the vein; the other is a shampoo used before neurosurgery to get the bacteria out of the hair.

So aviation got this. So the nuclear industry figured this out in the '70s. Aviation figured it out in the early '80s. We haven't had a large aviation accident in the U.S. in a major carrier in over a decade, from a U.S. air carrier. They're doing it this way. We, in healthcare, have to transition to this, and we can start with this product. This is an opportunity.

In aviation, there used to be this problem after they'd land. Instead of putting the

flaps up, which they should do, they'd pull their landing gear up. It's not good. And it turns out the flaps and the landing gear handles were next to each other in planes, and what do you do when you first land? You don't look down; you look at the runway so you don't run off the runway at 110 miles an hour. So what did they do? I don't know if you can see this, but they changed the design -- here's a better picture -- so that -- I'm just going to tell you because I can't find it. The handle for the flaps felt like a flap and was on one side, and the handle for the landing gear feels like wheels, and it's on the other side so that you can feel it, and you're not going to have this skills-based error when you're looking down. So that mistake almost completely went away.

So now let's bring it all home, right? Part of what we do in this gap, narrowing the gap between work as imagined and work as performed, so we think about the environment, right? People go in, and they'll often be doing their contacts in a dark bathroom. They're not looking clearly. They're used to picking up the bottle and squirting saline in their eyes to get it -- before they get it in or out, their eyes are dry. It's a very common use environment and use case. And you can't have two bottles that look exactly the same, when one goes into the eye regularly all the time directly and the other one practically kills you when it goes into the eye. And I understand that -- we've established that. But it's a very, very bad, nasty adverse event.

I don't know why we have to talk about this because I know we work with people in the industry; I know industry cares about their consumers. They care about this. They don't want their consumers to have this kind of event. It's actually surprising to me that there's so much resistance to changing the design. This is basic. You take somebody out of a Human Factors 101 class, and they can tell you the solution to this, and it's not education and it's not labeling.

So you get this red cap that looks very different indeed, but once the cap's off -- and

often people leave their caps off -- it looks different.

So I previewed this slide. We're trying to do this for a long time with labeling, and it's not working. Let's do it the right way with a design change to fix this skills-based error. And I'd be happy to entertain questions if we have time.

DR. WEISS: Thank you very much.

Dr. Berube.

DR. BERUBE: Thank you very much. This is really useful. I work with UX Lab, so I use user experience all the time. And so I've got a page of notes of graduate students' use of research here. But what happened in this field is, in order for a new product to enter the field, they used design similarity in order to break into the field, and what ended up happening is they needed to use design dissimilarity to prevent this problem from occurring. And so we need to try to figure out what's the best way to introduce design dissimilarity into this product line without causing the product to collapse upon itself. And I mean, I've done a lot of consulting in the business world, but not in this world, and I mean we talk about de-routinizing behavior, and we talk about distribution dissimilarity. There are a lot of ways to produce dissimilarity here.

For example, if you're using the contact lens, why don't you have a service that provides the fluid via mail so the association between the fluid that you use in one system is completely different from the other?

And so when we're talking about how do we de-routinize this stuff, it's not often a gigantic thing. It's often incredibly simple and very small things, but it's a whole area which I found missing when I was doing my work in preparing for this meeting. This meeting was not about design, and the reality was that's the problem. The problem is this is a design issue. This is --

DR. FAIRBANKS: Right.

DR. BERUBE: -- a design issue more than it's any other issue.

DR. WEISS: Dr. Krishnamurthy.

DR. KRISHNAMURTHY: First, I want to thank you for a very insightful presentation, and like Dr. Berube mentioned, you have clearly brought the focus on the world of human interaction with the device, or the drug for that matter. I do want to kind of make a friendly suggestion that, as interesting and sexy, the interesting slide was that healthcare is the most risky -- and I would then encourage everybody to take a look at the possibility of severe selection bias. People who go to bungee jumping are not sick. People who go to hospitals are sick, and therefore they're more prone to die.

DR. FAIRBANKS: So this is a question -- since it's a question session, if the Chair is okay, I'd like to respond because that has been very well vetted, and we could do a session on that; it is very good data, and it really is a very risky environment. And we're not talking about deaths because of risks from being sick. We're talking about deaths from unintended and unnecessary adverse events from errors that occur in the healthcare environment process.

DR. WEISS: So this is Dr. Weiss.

So if you were king, what recommendations would you make for this specific device to change things?

DR. FAIRBANKS: So those in affordance or a population stereotype, in our culture, the bottles would squirt with a little thin -- you know, a little ripple-looking top device that has a squirt thing, but it looked like a saline bottle, but they're meant to go directly into the eyes. So the solution is that the delivery container cannot be that kind of a device. Now, there are lots of ways of -- I actually find functionally -- I use this product. I have found functionally that they are really thin streams, and it takes forever to fill up that cup, which is like 10 cc or so. It doesn't make sense to me. Why am I wasting my time filling it up with

this thin stream?

So it's not even a good design functionally. I have to guess that it has to do with standardization of cost of container. So I understand, and I'm sympathetic to the fact that it might be hard to change this. But my colleague from ISMP showed -- you know, those mouthwash containers where you squirt it up into a big cap and then you pour it in, that kind of thing would work, but we'd have the same affordance problem; we don't want people to drink this. So I'm not suggesting that.

(Laughter.)

DR. FAIRBANKS: But what we need to find is a very different container that functionally has a faster pour and does not look like something that delivers fluids into a body in some way.

DR. WEISS: Dr. Dillard.

DR. DILLARD: James Dillard.

And what you said is that the solution might be just to make the hole in the top of the bottle a little bit bigger, and that might be enough?

DR. FAIRBANKS: Sorry, good clarification. I was talking about two separate problems. One is the user interface design of the container needs people, when they're in skills-based mode, to believe it can go directly into the eyes. That's problem number one. The second one is functionally it's not even a good design because people need to pour fast. But we can't fix one without the other because if you made it a faster pour, it would make the adverse event worse, right, if we put it in the eye. So you're right, I was pulling both out, and I apologize.

The second thing about the speed of the pour rate isn't as relevant to my topic, but I guess what I'm trying to say is you could fix both problems with an elegant redesign. And a good redesign, the reason I can't answer your questions, Madam Chair, is because a good

redesign with user-centered design, I would have to go do some prototypes, try it with user groups, come back, and redesign it. So we can't know immediately what the answer is.

MS. ELLIS: Annie Ellis.

And as we're thinking about this, I would just like to remind the Panel and industry that it needs to be portable as well, for people who travel or, you know, need to take smaller amounts.

DR. WEISS: Dr. Berube.

DR. BERUBE: I guess I want to make -- this is Dr. David Berube. I just want to make sure that when we start thinking about this, don't just focus on redesigning the package. Also focus on redesigning the distribution, right? There are two whole redesigns here. You talked about redesigning distribution, and you talked about how pharmacists might provide more information, and that's a simple way of doing it. But there are two worlds of design here. One might be will it cost the -- for the industry? It may not. And the other one is control distribution or control the product. You have two design routes, and I think if you go along both routes, you might find it to be much more efficacious than just choosing one over the other.

DR. WEISS: I don't know if the least burdensome would apply here, but basically, we also want to -- we want to recommend something that is good for the consumer and also practical for industry.

MR. PFLEGER: Yes, Michael Pfleger.

So just to throw -- there are a few other things that are just fact things here. So the big, large bottles of saline that everybody keeps saying put that in your eye, that's actually labeled to not put in your eye, because years ago when there were issues where people were taking that in slippery hands -- a big heavy bottle and there were issues. So those are not actually supposed to be used in the eye.

The second aspect of this is you have to think of it when it comes to the actual microbiology. So there's a rinsing step that goes along with squirting the solution over your lenses, pouring the solution over your lenses without a dramatic impact upon the micro-efficacy of that step. So it's a multi-factorial thing. It's not just so simple as saying, well, let's change one individual thing. It cascades, and we have to look at everything whenever you make a change to a system.

DR. WEISS: Dr. Yin.

DR. YIN: Shonna Yin from NYU.

I understand how the human factors approach could address the issue of the confusion between the two different kinds of bottles. I wondered about some of the other causes of misuse and how you imagine human factors coming into play. For example, the erroneous purchase issue and the failure to follow the neutralization methods, do you have also some design suggestions, or do you think some of that is also involved in labeling changes?

DR. FAIRBANKS: I think the purchase -- I think we heard some good ideas with the purchase problem. I would have to look at it. My observational kind of context is that the manufacturers have done a relatively good job of making the boxes look different enough for the purchase that we may have already maximized that problem. I hope this doesn't sound like a copout because it's very sincere, is that I think without looking at it and without seeing why, asking the question of why people are mixing it up in the purchase, which I haven't done, it would be hard for me to give good insight.

DR. WEISS: Dr. Lee. You have 2 minutes before our break.

DR. LEE: I have a quick question. So I completely agree with you that this is a reflex behavior around grabbing the bottle on the counter. I actually went to CVS yesterday and looked at the packaging on the shelving, and I thought I saw a pattern of green versus

purple, and then I found a multipurpose solution that was purple. So that pattern wasn't actually there.

DR. FAIRBANKS: Um-hum.

DR. LEE: And I was thinking about what I'm actually used to, and I'm used to actually seeing the peroxide bottle as being brown, and if there was a brown bottle and a white bottle, that would be an automatic difference between the two. Do you see any problem with brown bottles being used?

DR. FAIRBANKS: I don't think I have enough insight into the implications of using brown bottles, but I want to really capitalize on one of your good insights, that I think you were also saying -- because I think it's an important point, is that it might require standardization, and often in the context of FDA, we do hear we benefit from industry's innovation all the time. And so to be able to allow industry to innovate is critical. And sometimes we hear industry say standardization will inhibit innovation. I would argue that very basic standardization does not and particularly when it's safety critical.

And I'll give the example of probably the most -- one of the most innovative things we all know is a Tesla vehicle, and Teslas still have the accelerator to the right of the brake pedal, right? Every car you get in, no matter how innovative and different it is, the accelerator is to the right of the brake pedal. Safety critical human factors, affordance, population stereotype that is safety critical is standardized, and no one has said that that's going to inhibit innovation. So I think if you're very selective -- and I hope this doesn't have to be from regulation; I hope it's standardization that the industry comes up with themselves -- I think we can solve that kind of problem.

DR. WEISS: Thank you very much.

We are going to now take a 10-minute break. We will resume at 10:15. Panel members, please do not discuss the meeting topic during the break amongst yourselves or

with any member of the audience. Thank you.

(Off the record at 10:05 a.m.)

(On the record at 10:15 a.m.)

DR. WEISS: We're going to now proceed with presentations from the manufacturers of the hydrogen peroxide. If you could please take your seats. If you could please take your seats. We'll now proceed with presentations from the manufacturers of hydrogen peroxide care products. First, I would like to invite Dr. Mohinder Merchea from Alcon to approach the podium.

I will remind public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific request of the Panel Chair.

Dr. Merchea, you will have 15 minutes to present. You may now begin your presentation.

DR. MERCHEA: Good morning, thank you. My name is Dr. Mohinder Merchea. I represent Alcon, a division of Novartis, and my role there is the Head of Medical Affairs for the Vision Care business in North America. I am an optometrist, a clinical researcher, and a cornea contact lens expert. I have been in the area working for over 18 years.

At Alcon, our top priority is the patient, and we're committed to providing the best experience to those patients and consumers using our hydrogen peroxide solutions, Clear Care and Clear Care Plus.

As with any medical device, there is the potential for misuse, whether intentional or unintentional, and Alcon has worked with the FDA over the years to evolve packaging, labeling, and consumer education materials to advance the proper and continued use of hydrogen peroxide systems, and we welcome the discussion today, the opportunity to present at the Panel, and look forward to working with this group to find an effective way

to continue to improve the safety and efficacy of these products.

Three percent hydrogen peroxide systems that are used in ophthalmic solutions are safe and effective and have been safely marketed in the U.S. for over 30 years. They offer unique and important benefits to ECPs and to their patients, eye care practitioners and their patients. And these benefits have really led to a very high level of satisfaction among patients, and we'll share some of that information with you. In fact, the Clear Care family of products is used by over six million patients in a given year in the U.S. alone.

Presented here on the right of the slide, in fact, is an example of the unique lens case that we provide with each package of peroxide solution. At the bottom of that package is the platinum neutralizing disc that changes the 3% peroxide into a gentle saline over the neutralization process.

One improvement that we at Alcon have made over the years is that we include this new lens case with every package of peroxide that is sold, and that's important because it does promote better compliance with lens care replacement, and we know that that can have an impact on infection rates.

Additionally, Alcon has also evaluated the potential design changes related to lens case technology. Such an example is a redesign that would involve the docking of the bottle and the lens case to control the flow or distribution of the peroxide solution. Now, this connected case-lens type of technology was obviously a very complex type of technology, but it also led to significant technical issues such as leakage and concerns for contamination -- contamination of the bottle, contamination of the case as well. And certainly if the peroxide leaks, that in itself is an inadvertent exposure that could lead to stinging and burning complaints.

Overall, we know that these types of changes that, you know, we're interested in evaluating, we certainly have evaluated in the past. Those types of changes also involve

significant cost. It's important to recognize that that cost gets applied to the majority -- well, in fact, all consumers, the majority of whom don't have these issues related with sting/burn, as we'll share with you some data.

With respect to the market share of peroxides in the overall lens category, it's important to remember there are two distinct methods for lens disinfection and cleaning. These are multipurpose solutions and hydrogen peroxide systems. Alcon happens to be the market leader in both of these categories.

With respect to peroxides, as you heard from the FDA presentation this morning, peroxides are growing in their overall use of the marketplace. Our data, which is from Nielsen, shows that they currently represent, in 2016, about 22% of the market, and that's the top blue line. That's 22% of all lens care ounces that are used in the U.S.

The Clear Care family of products represents about 18.5% of all lens care disinfection that's utilized in the U.S. That translates to Alcon having about 84% market share within the U.S.

You can see in this slide, that there are a variety of products available for hydrogen peroxide systems. The boxes on the top represent Alcon's products. You can see in Alcon's products that we have a red cap and a red tip and extensive red labeling on the branded label on the bottle, as well as the package insert that's in the box. There is differentiation among the products, as you can see. In the retail setting, there might be some visibility of the red differences amongst these products.

When you look at these grouped together, it's important to remember that we talked about placement on shelf. Retailers are the ones that ultimately make the determination of where these products sit on shelf. We at Alcon encourage retailers to group peroxides together and distinguish them from multipurpose solution sections, but the retailer is the one that finally decides how they're positioned.

We believe that restricting peroxide dispensing, for example, behind the counter in a pharmacy or simply by restricting it to eye care professional dispensing would negatively affect patient access on these products. And that really comes to mind when you think about the fact that there's roughly 20 million bottles that are dispensed per year. The impact that that would have on patients trying to obtain these solutions would be quite significant, let alone the significance in the delays that it could lead to within pharmacies or eye care practitioners and the reduced ability of patients to access these. And we know that any impediment that we put in front of the patient to access and ease of use of these products may lead to further noncompliance.

One other key element to remember is that restriction of distribution in any way also does not address one of the leading causes of misuse that was identified in the FDA summary, and that was accidental use.

Some additional benefits of peroxides: We know that they provide exceptional disinfection, though that's against standard organisms, clinical isolates like *Acanthamoeba* or biofilms. We also know that when these peroxides are neutralized, they end up as a gentle saline. And we heard even from some of the previous presenters that's incredibly important because not all patients are able to use multipurpose solutions. They may have sensitivities to the preservative agents that are used in multipurpose solutions. We also know that preservatives can be taken up into contact lenses, and this can affect the biocidal efficacy of the product over time, as shown by some of the work in the past by the FDA.

In terms of patients that are actually using Clear Care, this is some data that we're excited to share in terms of this is a sample of over 9,000 patients that have used the product, and we know that these products have benefits that we detailed in previous slides. They also have benefits associated with compliance. We can see that, through this data, we were able to document that they're four times less likely to reuse solution or top off old

used solution in the case. They are more generally going to use fresh solution. They're seven times more likely to replace their lens case as recommended. And they return more frequently for routine eye care follow-up, which is important in contact lens wearers.

Clear Care is also one of the best recognized hydrogen peroxide systems and has a high level of loyalty amongst users.

We also have opportunities to educate patients on behalf of Alcon, through practitioners as well as through direct-to-consumer tactics. What I'm sharing with you here on this slide is some of the tools that we at Alcon supply eye care practitioners to better educate patients on the differences and the directions for use that are distinct to hydrogen peroxide systems versus multipurpose solutions.

On the left you can see that there is a fitting mat. On that fitting mat, that's typically where the staff or eye care practitioner will sit down with a patient and educate them on the wear and care of a contact lens. And clearly, we show the differences in Alcon's portfolio, in particular, with the purple side of the mat showing the hydrogen peroxide systems and the distinct directions for use, and the green side of the mat showing the Opti-Free family or the multipurpose solutions that Alcon markets and, again, with its distinct directions for use.

We also provide consumer brochures or patient brochures that detail, not just in text but in some graphical format, the directions for use, as well as the key warning areas and the fact that you have to use a unique case with this type of care system.

Through our direct-to-consumer education tools, we utilize websites that Alcon manages, so the Clear Care website, for example -- again, another example of where we're using clear visuals and moving beyond simply boxes of text to try and convey the proper use and care of contact lenses with peroxide systems. We also provide videos on how to use the product and how not to use the product in an appropriate way.

Social media is another important vehicle that we've started to utilize to communicate to patients more effectively. Clear Care itself has over 160,000 followers on Facebook, for example. We utilize that with some of the images shown to reach these patients and remind them of those key warning areas that call their attention to making sure they safely use these products.

We wanted to take an opportunity to also go through the timeline of some changes that we've implemented in where these products were packaged previously. So we're looking at back in the 2010 time frame, 2009 time frame to where they currently are with this packaging.

So some of this work has definitely been with collaboration with FDA, as you've heard this morning. On the slide here, obviously you saw from a previous image that I showed, not every private label manufacturer of hydrogen peroxide utilizes the same red cap and red tip format that Alcon uses. So we obviously use this to clearly signify to the patient, do not put this directly into the eye, the hydrogen peroxide solution directly into the eye.

Here we're presenting to you the labeling that's actually on the bottle, and the Panel has access to both the box and a copy of the label that is applied to the box so it's a little easier to see.

The labeling clearly highlights the important warnings and instructions for use in these red areas and highlighted areas with graphics. One important area made on the labeling is we've also highlighted areas related to social media, where patients that may not be comfortable reading through this text or may not necessarily understand the infographics that we placed on there to simplify the directions for use can go to see a video to help guide them on the appropriate use of the product.

The top red banner, as was noted in a prior presentation that replaced the

removable collar, is now permanently affixed on this label and calls out those key areas, that misuse will clearly lead to stinging and burning, use only with the lens case provided, never rinse lenses prior to insertion, and do not put peroxide in the eye. So, again, a clear example of clustering the appropriate and important warnings for a patient and highlighting those in red in a permanent place on the bottle.

We reinforced those warnings from the top banner and now add graphical icons in another section of the labeling. And additionally, we provide recommendations about what to do if peroxide is inadvertently introduced to the eye. Flush the eyes, rinse them, contact an eye care practitioner immediately for follow-up care.

And a third area of reinforcing directions for use, in particular, now identifying the appropriate soak times for complete neutralization is also presented.

With respect to the box -- and, again, you have a copy of the box packaging in front of you, for the Panel members. You can see that as the consumer opens the box, they're immediately presented with a graphical representation indicating the appropriate lens case to use, and in this case we are clearly showing them, in a graphical format, not to use the typical flat case that is packaged for the multipurpose solution versus the barrel case here for the peroxide solution with a neutralizing disc.

And again, the box duplicates the directions for use and the appropriate warnings and the graphical formats over its entire structure.

You did see similar package inserts presented earlier. Obviously, this is the package insert that is on the inside of the box. The package insert, again, clearly highlights in red the relevant warnings, but it does contain all of the required regulatory language about the products that we need to include in package inserts. It's important to recognize, however, though, that those key areas related to warnings and directions for use are on the outside of the box and all over the bottle to clearly indicate to the patient how to safely and

effectively use these products.

We also wanted to share with you Alcon's complaint rates, and what we're presenting here on this slide are complaint rates associated with our Clear Care family of solutions. What we're presenting here are complaint rates per million bottles sold of the Clear Care family of products. The rates are low in general, both over time in our database, as presented here, as well as in the database that you saw from the FDA, only 370 cases in total for all peroxides globally over a 10-year period.

It's important to recognize this data that I'm presenting here in context of the market size as well. You know, we recognize that this is an important event if it occurs for a patient, and traumatic, but it is relatively rare. We can look at these rates and recognize that we have about five million users in the U.S. using the Clear Care family of products alone and additional peroxide users in some of the other brands.

So taking these into context, you know, the complaint rate related with misuse is less than 0.01%, meaning that 99.9% of patients are not having these complaints or reporting these complaints.

So as part of Alcon, we're committed to patient safety, and we're committed to patient satisfaction. We want every patient that uses Clear Care or Clear Care Plus to have a great experience with those products. As part of that commitment, we are committed to evaluating and working with the Panel and with the FDA on any recommendations that it has to improve labeling and further reduce these low complaint rates related to misuse and stinging and burning.

In particular, if there are opportunities to further minimize the text -- some of Dr. Day's presentation was very fascinating, that there are different ways to present it, those are all areas that we're open to. Having graphical representation, video representation, we think those are opportunities to further educate patients and guide

them on the appropriate use of these products.

We'll carefully consider the recommendations of the Panel. You know, we obviously want to make sure that we are testing any recommendations and applying changes that we know and have confidence will lead to improvements in the usage of these products for patients.

So with that, I'll thank you for your attention, and I'll be happy to answer any questions.

DR. WEISS: Thank you, Dr. Merchea. So we have 5 minutes for questions.

Dr. Wolf.

DR. WOLF: So I'll be quick. So first off, I'm not a contact user, but I do appreciate the comments of other Panel members, and it is an adverse event if you do it once, and the repeated behavior I get. And for whatever reason, if you don't have a lot people reporting these events to you or that these just don't capture, I completely get that these numbers, I think, as Dr. Dillard had mentioned, are just probably underreporting. So we have to appreciate that the problem is still there, even if it's for less than 0.1%, as you're saying.

You know, I do think, though, that there is a lot of value beyond the label here that -- you know, there's a little bit of an irony here that, based on the way people are talking about how a lot of these errors occurred in terms of consumer behavior, that it's like you're likely to be having this event maybe at the point of use and in a moment when you are compromised because you do not have the corrective lens to guide you through. I mean, there's just kind of an element there. So I think a lot of these human factors issues really do -- beyond the color of a cap, I do like that idea from Dr. Fairbanks that there really needs to be a lot more explanation there just to really kind of help people when they're going to make these mistakes very unintentionally.

Some specific comments about -- that I'm just kind of confused about in terms of the

value of some of the labeling that I've seen on these images, in particular, the collar label. That wraparound text is very problematic to me and it's also fairly dense, especially going back to Dr. Day's. So I'm just curious how you kind of came up with that and if that's -- and even kind of making it a more permanent part of the label, I think, is it still possible that you could do things better, even again if it's a point-of-use problem, a larger font, simpler message, to just kind of make people stop momentarily? I just was curious about that.

And the last thing, again, on these issues -- and again, I do a lot of my work more on medications, whether it be on OTCs or oftentimes on prescriptions. You know, obviously, there's a very limited value to what often most people do is throw away. So if it's redundancy or if it's to inform point-of-purchase decision making, I get the need for how you do this, especially on the front of a label to kind of distinguish products, but you know, a lot of this is just stuff that I think has very, very limited utility to most consumers who are not probably as activated and engaged in wanting to learn. So I'll stop there.

DR. MERCHEA: Thank you. I'll start with saying, from an Alcon perspective, I think, as I mentioned, we're very open to working with any recommendations from the Panel in terms of simplifying, reducing text, find easier, better, more effective ways at communicating the appropriate warnings to patients for use, particularly at that point of use. So we welcome the opportunity to have that dialogue and to review and to test any recommendations that are made from the Panel.

With respect to the comment that you made regarding the box, I think we would agree with you that the warnings are there at the point of purchase. We recognize that the box is typically thrown away, but that's why the warnings are also replicated on the bottle.

DR. WEISS: I would just ask some -- we only have two other questions. I would just ask the Panel to limit your comments to clarifying questions as opposed to further thoughts. We'll have time in discussion for that.

Dr. Dillard.

(Off microphone response.)

DR. WEISS: Dr. Dahr.

DR. DAHR: Sam Dahr.

Is it, from a practical or cost perspective, prohibitive to change the color of the underlying white bottle or the white container? Is it possible to make it a different color?

DR. MERCHEA: So there's obviously -- with any change, there is cost involved. Now, you know, the question becomes what does the color change lead to, and will it make a benefit or a change in behavior of patient use at that point of use, when the patient is perhaps not having their contact lenses in? I think that's something that, you know, obviously needs evaluation, and we can then determine whether it's the appropriate action to follow.

There is cost associated with it, there is cost associated with it because, as was said earlier in the Panel meeting, any type of change isn't a change in isolation. Those changes cascade, and when you start thinking about manufacturing and biocompatibility, sterility, all of those factors ultimately will add up.

DR. WEISS: Ms. Witczak.

MS. WITCZAK: I have a question, two in fact. In terms of going to the retailer, I know you guys don't really control that, but has -- I mean, maybe some of the FDA -- but do you ever go -- obviously, there's a huge incentive with 84% of the market share, but in terms of working together to get them to see like kind of almost hydrogen peroxide all in one section and multiuse in the other, because when I've gone into my research for this, going to Target, Walmart, all of them, it's kind of just one big, you know, scattered mess, and I don't know if it's something that can be done, and obviously, that would be in itself something at a point of purchase, in addition before we even get into packaging and the

bottles itself.

DR. MERCHEA: Sure, I'm happy to answer on behalf of Alcon. I'll let FDA respond with regards to regulated activity. On behalf of Alcon, what we do is we do work closely with retailers. We present to them our entire lens care portfolio, multipurpose solution as well as our hydrogen peroxide systems. We clearly try and differentiate them within our own portfolio. But when we go to retailers, we spend a lot of time emphasizing that peroxides are different, they perform very differently, and they work very differently. The use of them is very different. We educate the retailers on that. Some retailers take that education and have made decisions to put all peroxides together on a shelf and separate from multipurpose solutions and then create signage that creates that distinction. But we, as Alcon, can't control what any individual retailer is going to do, but we provide that -- we have that dialogue with every retailer, and we provide instructions and recommendations on doing that. It's up to the individual retailer whether they adopt that recommendation.

DR. WEISS: Ms. Ellis, do you have a brief question? And then we'll finish up there.

MS. ELLIS: Yeah, just very briefly. On the erroneous purchase, I have really appreciated how the color helps signal that this is different, and I have been a recipient of erroneous purchases by my sister. But I was wondering if a similar color on the top of the cartons may help signal that these products are different from the others, you know, peroxide or whatever, as just, you know, that population of misuse. It might help.

DR. MERCHEA: And again, you know, I think on the outside of the carton, point of purchase -- you know, keeping in mind that in the FDA dataset we were talking about, roughly 40 instances of erroneous purchase over a 10-year period with roughly 6 million users of peroxide in each of those years, so it's a very small number. Still an important question. What we want to validate is what is the appropriate way of showing that differentiation on external packaging, the same way we would on any internal packaging.

So we'd be happy to review and evaluate any recommendations from the Panel to improve that type of labeling.

DR. WEISS: Mr. Merchea, I'd like to thank you for your presentation.

We're now going to invite Dr. Chris Smejkal from CooperVision to approach the podium. Dr. Smejkal, you will have 15 minutes to present.

DR. SMEJKAL: Good morning, everyone. I'm Christopher Smejkal, the regulation affairs director from CooperVision. Thank you to the FDA and to the Panel for inviting CooperVision to present on our peroxide system.

Okay. So the objectives for today are to give an overview of the CooperVision system, to talk briefly about the characteristics and the efficacy of the product, and then user issues, which we've all discussed quite extensively already this morning. We'll touch on some of the past product changes that we've implemented and also to give an overview of our proposed future changes and improvements to the product, particularly centered around labeling because they're the things we can fix pretty quickly, and also some of the initiatives that CooperVision is developing in terms of improving education, so compliance education programs and a proposal that we're developing internally to improve that.

Product shelf segregation in retail locations is an important discussion that we've had with retailers that we work with. The other, looking forward, we'll touch on some of the proposed technologies that we can adopt in terms of the labeling. An example would be quick response technology codes on the labeling which link to websites and other information. And then we'll touch on some -- you know, a bit more of the blue sky concepts around information sharing technologies with Apple and others who have already developed.

So to give an overview of the peroxide system, it was approved by Sauflon Pharmaceuticals, which was a UK lens care manufacturer back in 2001. It's been marketed

as a product in the USA through several retail outlets, and some of those outlets have been mentioned already.

Just for an information point, Sauflon was acquired by CooperVision in 2014. So lens care, in itself, is quite a new product portfolio for CooperVision as an organization.

So just to touch on -- and this has been described also already this morning, but the one-step peroxide system is essentially known as the gold standard for disinfection efficacy, particularly against a broad range of ocular pathogens and also obviously meets the 14729 panel of microorganisms as indicated to disinfect and clean and store lenses. It contains hydrogen peroxide as the active ingredient at 3%. And recall, an element of the system is the case, which neutralizes the peroxide over a period of 6 hours, and the key feature, obviously, of that case is the catalytic disc which neutralizes the peroxide.

Known user issues, which we've touched on and know very well when we see them: You know, we know that patients rinse the lenses directly and with peroxide and then obviously put the peroxide directly into the eye, which causes the discomfort and stinging and sometimes redness as well.

I think one of the things we also see is that patients don't use the correct case. For various reasons, they discard the cases in the box and use a novelty case or something different. So, therefore, the peroxide will remain unneutralized. And then the key one is that they don't leave the lenses soak for the desired 6 hours obviously. And then when they put the lenses into the eye, it causes stinging.

So some past product changes that have been implemented is the use of the bright red cap which distinguishes the product from the white cap which is on the MPS, the multipurpose solution. Some other things we turned up are specific links and information with a link to the FDA guidance on our website with clear patient user guides. And our labeling also fulfills the latest guidance from the FDA. We do know that there are retailers

where we -- you know, we're working and engaging with them actively to ensure that their labeling also meets the latest guidance.

So what else can we do? We know that we can do a lot more. So some of the things, you know, we've touched on today quite extensively as well as around the labeling. We acknowledge that it's very, very busy. There's a lot of information on the instructions for use leaflet. It's very small text; it's quite hard to read. So obviously we need to look at ways to make that a little larger for patients to make it clearer, and also to really focus on the primary instruction that the patient really needs to focus on.

And we say the key six or key -- sorry, the six key rules of success, but that could be four, five, six or even ten rules to key success and to add that information to the labeling. The key areas are really around indicating against the areas of misuse. So the obvious things:

- Do not put the contents of the bottle directly into the eye.
- Do not put the contents of the bottle directly onto your lenses, which you then insert into your eye.
- Do not wear the lenses unless you have allowed them to soak for the desired 6 hours.
- Ensure that you use only the neutralization lens case provided with the product.
- And clear directions for the patient to follow the detailed instructions for use.
- And then, really, the only -- eye care professionals is really to make sure that they follow the eye care professional's instruction.

Some areas also which members have already presented on is really, how do we put some kind of clearer message on the product, on the primary packaging, to direct the patient not to put the contents of the bottle directly into the eye? And here are some

suggestions. We feel that really we need to really explain that the bottle contains hydrogen peroxide and direct the patient to not put that into their eye.

We also already have been employing the use of universal diagrams and symbols, and that also makes the product more practical in the European Union, where we have to translate all language requirements and text as well anyway.

So as I touched on at the start, another area that we really believe we need to enhance and focus on is around educating both the ECP and the patient. So we're developing a compliance education program which really the objective is to ensure that patients experience a safe, comfortable, and satisfying contact lens-wearing experience from start to finish, and that really is our objective and focus.

Some of the elements of this program will be to improve lens care compliance generally, not just for peroxide; take a proactive position so we don't just passively give the information, but take a proactive stance in educating our ECPs, retailers, and end users on the importance of lens care product selection and also following the lens care instruction.

We would like to also partner with the ECPs in the provision of the materials and the tools and get those developed, fully developed, particularly around ECPs that are prescribing FRP lenses in practice.

We've mentioned today shelf segregation, and we think we can probably work a lot more with our retailers to ensure that the positioning of the product is delineated on the shelf, and we know that our retailers are open to that sort of discussion based on obviously any recommendations that come out of today.

Just to touch on some technology, we believe that we can move into the 21st century, so to speak, and align ourselves with possible use of apps and the quick response coding which we can put onto the labeling and which will link to an informative video for patients to use.

And then some other possible technologies that could be considered are things like near-field communication, so when the patient walks into the store and the Bluetooth technology will communicate from a position on the retail shelf to the phone, which gives information around the product. There's a technology, iBeacons, that Apple has already developed, so it is in use and something that we could potentially consider into the future.

Other examples are things like Google Goggles where a patient can take a photograph of the product, and instantaneously there will be an informative description around the product and what it does and any information or user information which they can follow.

SNAP-tag is really something where we could turn our brand logo also into a potentially informative way to share information and promote the product and/or give a clear message around noncompliance and to use the product appropriately.

So I think generally, overall, our commitment at CooperVision is to ensure that we fully engage, and we are committed to fully engaging with any initiatives for the discussions and certainly partnering with the FDA on improving the lens care wearing experience for our patients.

Any questions? Thank you.

DR. WEISS: Thank you very much for your presentation.

I would ask if anyone has, the Panel, any clarifying questions, not comments, but any clarifying questions to the speaker?

(No response.)

DR. WEISS: Seeing none, thank you very much.

DR. SMEJKAL: Okay, thank you.

DR. WEISS: We are now going to continue on to presentations from professional organizations. First, I'd like to invite Dr. Michael Cohen from the Institute for Safe

Medication Practices to approach the podium.

I will remind the public observers at this meeting, while the meeting is open for public observation, public attendees may not participate except at the specific request of the Chair.

Dr. Cohen, you have 10 minutes to present, and you may now begin.

DR. COHEN: Thank you very much. Thank you for having me. And happy St. Patrick's Day to everybody from Michael Cohen.

(Laughter.)

DR. COHEN: Actually, our organization is a nonprofit. We're not a professional organization, and we don't have members or anything. We've operated the national Medication Error Reporting Program for many years. We're recognized by the federal government as a patient safety organization, and we have an MOU with FDA, and all of our reports go to the Agency, and I believe they are contained -- we were the organization that sent out the signal case back in 2009, and since then we've had 115 additional reports. But I can tell you, it doesn't even touch what's actually happening out there. You already have seen, and this is no accident, we had two people on this Panel say that they've had this happen to themselves.

And I can tell you, I teach a class in medication safety at Temple University at the School of Pharmacy. I am a pharmacist, and year after year I've shown this Clear Care since '09, and I don't even screen people to say do you wear lenses or do you wear contact lenses? I just ask the whole group, we have about 120 in the room, to raise your hand if you've had this happen, and I will consistently get three or four people raising their hand. Sometimes it's more and sometimes a little less. I did it at FDA a year ago; exactly the same thing happened. In my office we have 30 people; I've had 5 people that have done this, in the office. We have nurses, pharmacists; we have a medical director that's a physician. So

it's not a minor thing. My only daughter has done this as well. And the word, the working word is "excruciating," and we heard that already, and it is very, very painful.

And let me just move forward. I'm going to try to get through this in 10 minutes.

This is typical. We get a lot of narrative information, and we have the ability to communicate with the reporter directly. We have a consumer website, and that may be part of the answer as to why there are -- you know, the reports have spiked, etc., because we use social media. It was on NBC, and there was a Health Canada alert on this. There are other reasons for a possible spike a couple of years ago. This is a typical comment that we get. And usually, people are so much in pain that they will actually send us pictures of what happened to them.

We have three new priority programs actually, including Vaccine Error and Consumer Error Reporting in addition to Medication Error Reporting Program. We have an Excel spreadsheet. The information, the identities are redacted. If anybody's interested in research, I'm more than happy to have you contact me, and we can, you know, interact with you and get you the material that you need.

This is a typical thing: "Our four-year-old son had sand in his eyes and started screaming. I immediately attempted to flush out his eye with the solution I had picked up from the store earlier that morning. I used about two drops...only to find out, after further screaming, that I hurt his eye more." And later on she says, "I honestly thought the color of the bottle was simply for design purposes." So this thing with the red cap, I can tell you, that is about useless. It doesn't mean anything. There are other ophthalmics that have red caps. There are other materials that have a red cap.

Also, the warnings are not really placed where they're always going to be useful. You probably learned in psychology about inattentional blindness where nothing's wrong with your eyesight, but unless something is conspicuous enough, it's pretty easy to miss

important information. In this case with the Clear Care, what you see is the lens. This is a recently purchased bottle with the carton, and really, you need to turn it four times in order to see the warnings, if you turn it to the left. So I think that's important to note.

That "Warning" probably should be headed "Danger," and it probably should be on the front label panel, and I think that would bring more attention to it, if labeling is all that you are going to do.

As mentioned before, there have been other iterations of this label. They used to have a disc, a little piece of cardboard disc that was on the top of the container; it would fall off or get wet, etc. So that wasn't of much value.

I did want to point out one thing. I just realized that do you see where it says, "Never rinse lens with product prior to insertion?" If you just turn that just slightly on a round surface like that, it will actually say, "Rinse lens prior to insertion." So this is not a well-designed label, a well-designed warning or placement, and so information could easily be missed readily.

I did want to point out that not all -- and somebody did already, one of the manufacturers, that not all of the products do have a red cap. So this is one that I purchased from -- I spend a lot of money on this, by the way, buying containers.

(Laughter.)

DR. COHEN: This is one that does not have a red cap, so it really doesn't have a lot of value. I'm sorry, I hit one too fast. There we go. We'll talk about that later.

I wanted to point something else out, too. This labeling is not an insert that comes out of the carton. It's literally the inside of the carton, as was mentioned by one of the manufacturers. So a lot of people don't even recognize that that's there, let alone read it. And it's very difficult to read, as Dr. Day pointed out a little bit earlier. Again, this information does not shout out with you, and it needs to be simplified if we're going to just

rely on the labeling, and I don't think that's enough. I really think we do need to do something with the packaging, and I'll explain that in just a second.

So, I'm sorry, that's the actual label, and you can see how difficult -- I ripped the carton open.

And so you know most of the safety issues. I'm not going to go through all of these, but just recognize that it does cause people to miss school, miss work. They wind up in the emergency department very, very often. So there's a cost to this. It's not just, you know, something happens, and they're hurt, and you know, it goes away in a little while. That's not what happens. Too often, many people tell us that they went to the emergency room and there has been harm, as you know from the reports that you've seen, about half of which are ours, the voluntary reports anyway.

So I told you about the audience. People won't have their contact lenses in sometimes when they're working with this bottle, and they don't necessarily see the label. They've taken their lenses out. Some of these have been 6-year-old kids that are on a sleepover at their girlfriend's house. All the labeling that you want and all the training that you want is for naught because these are kids that were never taught to use it. They're using what they see as a contact lens, and they squirt it in their eye sometimes. They think it's saline. It's not like they even use it all the time with a lens case. We've seen that. There has been a lot of publicity given to this.

As far as storage, that has been mentioned a couple of times. It is stored with all the others. I also agree that I don't think it is a good idea to put this behind the pharmacy counter. This is a very, very well-liked solution, and it does its job, and people like it. It is in supermarkets; it's all over the place. I don't think you could restrict it, and if you do, in fact, normally there are some things that we would recommend be behind the counter. I don't think this works for that situation.

As far as prevention, I do think you need to communicate with health professionals, pharmacists, and ophthalmologists in particular. I asked a lot of pharmacists about this. They don't know anything about it, and they're selling it. Well, not really, because if the lens is sold, it's taken off the shelf. I think, if anything, if a pharmacist wanted to put it behind the counter so that they -- and they put a sign out where the other solutions are, you know, to direct them to come to the pharmacy and the pharmacist was willing to do education, that might be a help. So any of that kind of thing, a message like that from a company or FDA might be helpful.

Advise lens wearers who begin use of lenses. Improve warnings on the container, and we talked about that. I think the word "severe" should be in there. It's not in the labeling; it just says "may cause burning." I think placement of the warning on panel four should be on the primary display panel. I think signal words like "danger" would be helpful if you're going to rely on warnings. I think simplifying the warnings we heard from Dr. Day and redesigning the container.

I did bring a container. I was disappointed to hear that there may be some leakage, and I just wanted to show this as a little experiment. This is the mouthwash that Dr. Fairbanks mentioned, and I know you did, and I could see how the cap could have the metal ring and the basket and that when you screwed it on, it would push this rod down so only then you could push the solution up into the container like that. So now you have that in place, and I think that would work.

So I would urge them to continue looking at the packaging and things like this that I think are, as Dr. Fairbanks would say, you know, much higher-level strategies for prevention than the labeling itself. It's just not going to work. We're always going to have this problem.

Thank you very much.

DR. WEISS: Thank you very much. And we wouldn't have imagined you were Irish, but that's good.

(Laughter.)

DR. WEISS: So does the Panel have any clarifying questions?

(No response.)

DR. WEISS: Thank you, Dr. Cohen.

We are going to now invite Dr. Susan Gromacki from the American Academy of Optometry to approach the podium.

I will remind public observers again that they may not participate except at the specific request of the Panel Chair.

And, Dr. Gromacki, you have 10 minutes to present.

DR. GROMACKI: Thank you very much. My name is Dr. Susan Gromacki, and I'm speaking on behalf of the AAO. And as the director of the contact lens service at the Washington Eye Physicians and Surgeons, I see contact lens patients all day, every day. I fit soft, gas permeable, and hybrid contact lenses, and I prescribe hydrogen peroxide, multipurpose, and multi-step care systems for these lenses.

To begin, a primer on some of the categories of contact lens solutions: You heard a little bit about this, this morning from Dr. Lepri. But just to get some of you who are not eye doctors up to speed here, I'm going to categorize them in a few ways.

First, multipurpose solutions contain cleaning, rinsing, and disinfecting agents all in one bottle. In most cases, the preservative also serves as the active ingredient of disinfecting agent.

Multi-step care systems utilize separate solutions for cleaning, rinsing, and disinfection. They are primarily used in this day and age of gas permeable lenses.

We talked a lot about hydrogen peroxide, and we'll continue to do that, but I will say

that all hydrogen peroxide systems are approved for soft contact lenses. They're not all approved, however, for gas permeable lenses. And they can either be categorized as no rub or, in some cases for gas permeable lenses, the lens does need to be rubbed even using the system.

Enzymatic cleaners remove protein.

So my question to the Panel is which of these solutions should not be placed directly into the eye? Here's your answer. So let's talk about some of these different systems out there.

Optimum by Lobob conveys three separate solutions: ESC, CDS, and WRW. CDS is a soaking solution. It contains some potent anti-infectives. It cannot be placed directly into the eye, and the patient must rinse it off profusely after storing it in the solution before putting it in his or her eye.

Progent by Menicon is part of a larger system which contains a multipurpose solution but then uses an A solution and B solution for disinfection. Is everyone familiar with what the A and the B contain? The A is sodium hypochlorite. The B is potassium bromide. As most of you know, sodium hypochlorite is bleach. So this too must be rinsed before placing the lens into the eye.

Hydrogen peroxide, of course, we're going to talk about in a minute.

Enzymatic cleaners also are made to be rinsed profusely before the patient is able to wear their lens.

Here is a patient that I actually saw a couple weeks ago. After I was invited to present here, I happened to see a patient, a gas permeable lens wearer. She wears scleral lenses and needs them for her keratoconus, and she has been disinfecting her lenses appropriately with Optimum CDS every night, and one morning she just forgot to rinse. She was tired. She put her lens in her eye, and Day 1 is what the cornea looked like. As you can

see, she quickly developed a white keratitis which stained with sodium fluorescein. After artificial tear use for 2 days, her cornea cleared up completely. That's the image on the right, Day 3.

And I want the Panel to note, of course, we all know what patients are doing, and that's a given. I think we've proven that this morning.

This type of keratitis, though superficial and temporary in her case, in most cases no long-term consequences. And again, this is similar to what I've seen very infrequently over the years also with hydrogen peroxide systems, is your image on the left there.

So now let's discuss hydrogen peroxide. Three percent hydrogen peroxide is an efficacious microbial disinfectant, and it's an essential product for many types of contact lenses. It has been a mainstay on the market for 3 decades. Over the years, the contact lens industry has simplified the use of this type of care system, increasing safety while maintaining efficacy. They've also improved the labeling and color coding on the product. Still, the potential for noncompliance remains.

As we know, the FDA has received some medical device reports directly from consumers. From the February 2016 report on the FDA website, FDA wrote, "most often because consumers fail to read and follow directions for use."

So now I'm going to present the potential avenues for noncompliance with this vital disinfectant and the frequency that I've seen in my 23 years of practice.

First of all, an existing hydrogen peroxide patient -- that's my patient in the image -- inadvertently applies solution to his or her contact lens or directly into the eye. I see contact lens patients all day, every day, and I've only seen one patient, the one I showed you, in the last year who has done this. I asked one of our respected cornea specialists at our practice, who is another person in our practice that this type of patient would see with an emergency complication, and he said that he has seen none in the past year. So, again, a

pretty rare thing, but it does happen, and we all know that.

The next area is an MPS patient borrows hydrogen peroxide from a friend or family member and uses his/her own flat case rather than the basket-type case used with hydrogen peroxide. This too is quite rare; I have rarely seen it in practice, but I have. I must admit we do see this occasionally.

Next, an MPS patient inadvertently purchases hydrogen peroxide and uses it with a flat case. This too has come up this morning. This also is rare. And the way I look at it is this; we haven't mentioned this, the hydrogen peroxide is much more expensive to purchase for the patient than an MPS. So it is much less common for a patient to go ahead and purchase that and have to pay more. They're going to choose what they have rather than choose the more expensive one by mistake.

We haven't really talked a whole lot about neutralization, but I think it's an important topic. It could be that the hydrogen peroxide is incompletely neutralized after the 6-hour cycle, but with the current products on the market, this is rare. I'm sure everyone on the Panel knows about the one particular product that was recalled. So before the advent of this product and after its recall, it has been quite rare. A couple of reasons for this: One is there's a new case with a brand new disc right in the case that comes with each new solution purchase.

One study shows that residual hydrogen peroxide after neutralization with current products is about 15 plus or minus 8 parts per million. Another paper states that the patient really needs to have greater than about 100 parts per million to get a stinging response. And levels as high as 800 parts per million do not disrupt the cornea or conjunctival epithelial surface.

So some patients do have a slight sensitivity to that 15 parts per million. The thing that they end up doing is using a rinsing solution prior to insertion. I've never personally

seen, in 23 years, a damaging keratitis from this.

Okay, this is the one that I've seen most often: inadvertent purchase of private label or generic hydrogen peroxide by private label MPS users. This is my opinion. A most primary weakness of the entire hydrogen peroxide conversation is the labeling of generic hydrogen peroxide. As we noted this morning, so far, some of these products do not have a red cap at the moment on the outside. They all do have a red tip, however. And the instructions regarding the cases and package labeling are not clear enough. Generic sellers are allowed to sell products with labels that are too similar, bottom line. And this, in my opinion, is a global labeling issue that affects all generic products, not just hydrogen peroxide. And this is a better issue for the FDA to address.

All patients do not understand that multipurpose solutions are different from one to the next. They are. They contain different preservatives, buffers, and wetting agents. If their doctor understands that they may be sensitive to one preservative and switches them to a different solution and then the patient goes to the store and picks up a generic bottle, this can be deleterious to the patient.

A few years ago I wrote a column in *Contact Lens Spectrum* on this topic. Anyone familiar with the Meijer store in the Midwest? It's an awesome big box store. I love it. At Meijer, the same exact formulation, the same exact ingredients, was packaged in different packages which contained different colors, and these packages were sitting next to the name brand products that contained the same color. So the patient really doesn't know what's in the bottle. The bottom line is because these retailers entertain bids for these generic products every 18 months or so, what's in that bottle can change, and the label can stay the same.

So here at Meijer, I was looking at the shelf in preparation for my article, and I saw a sign that said, "If you like Opti-Free, try me." And like Opti-Free, it was sitting in a green

box, but the problem is this formulation inside that bottle had absolutely nothing in common with Opti-Free.

So solutions, no pun intended. Practitioners, or their staff, need to completely understand the features of all care systems, prescribe the one optimal for their patient. And I do use the word "prescribe." It's not a medicine, but I think it's very important for the practitioner to know the differences between these solutions and to choose one that works best for that patient's lens modality, that patient's tear chemistry, that patient's potential dry eye, that patient's potential allergic sensitivities. So to me, it's prescribing. And to say this -- and I tell this to my patients, and I have my technician do the same, instruct them not to deviate from what we have given you. We give them a handout with the solution name on it. We give them a sample care kit and tell them to go to the store and purchase the one that I have chosen specifically to be used in conjunction with your lens and your eye health, no generics. Some patients do just fine on generics, the older formulations, and they work well for many, many patients. But if the doctor sees --

DR. WEISS: Please begin wrapping up because you're over time at this point.

DR. GROMACKI: Oh, sure. So, again, communication is important, but also collaboration is extremely important. So more specific labeling by the contact lens industry, particularly if they're private label products.

Improve practitioner and staff education on the product's mechanism of action and how to best communicate its use, and this can come from either FDA or industry; FDA vigilance to ensure the proper use of hydrogen peroxide and all contact lens care products; and lastly, full patient compliance with the practitioner and label instructions and guidelines.

So, in conclusion, hydrogen peroxide is a safe, effective contact lens disinfectant, perhaps the most effective on the market, and the benefits of its sterile disinfection and

preservative-free composition far outweigh the rare complications associated with the system.

Thank you.

DR. WEISS: Thank you.

Does anyone on the Panel have clarifying questions? I have one question for you. How would you differentiate between the rare occurrence of a patient having an adverse event versus the rare occurrence of a patient having an adverse event requiring seeing a doctor because I don't know that those -- I don't think those are the same.

DR. GROMACKI: That is a really, really good question because I would assume the majority of these patients that do get it in their eye and experience that burning don't give me a call because I have seen so few of them over the years. But also the facts are that I have seen so few of them over the years. When this patient that I illustrated here called a couple weeks ago and told me about this, I said please come in; we need to take a look at this because I want to ensure that it's not going to be a complication that can lead to something worse, other than just to ensure that it's a superficial punctate keratitis and be able to help her heal that.

DR. WEISS: So I guess the point that I'm making in terms of the person using the hydrogen peroxide in their eye inadvertently, while it might be rare to consult you for that, it might not be rare. We don't know.

DR. GROMACKI: Well, we don't know how many are actually are doing it.

DR. WEISS: Right, right.

DR. GROMACKI: But we do know how few of them actually come in to our offices, and that's like very, very few.

DR. WEISS: So I think those are two different things.

Ms. Ellis.

MS. ELLIS: Right. And when you were explaining your experiences with the rare visits, and I think you mentioned you and one of your practitioners, has your association been surveyed as far as the whole association's experience with seeing these cases?

DR. GROMACKI: You mean survey every doctor within the association?

MS. ELLIS: I see that you're representing the association. I was just wondering if you're representing your personal --

DR. GROMACKI: Right. These are my personal opinions.

MS. ELLIS: Okay. And your personal experience?

DR. GROMACKI: Exactly, my experience. I can't speak for everyone, but since I see contact lens patients exclusively, I do see a lot of them probably compared to most optometrists.

DR. WEISS: Thank you very much.

We are now going to invite Dr. Jeffrey Sonsino, Chairman of the American Optometric Association Contact Lens and Cornea Section to approach the podium.

Dr. Sonsino, you will have 10 minutes to present.

DR. SONSINO: Thank you. I'm Jeffrey Sonsino. I represent the contact lens section and cornea section of the American Optometric Association.

By way of disclosures, I am a full-time private practitioner with a specialty contact lens practice in Nashville, Tennessee. Prior to that, for 12 years I was faculty at Vanderbilt Medical Center, where I directed the contact lens service. Pertinent to this, I am a consultant for Alcon, and the nature of that consultancy is a 2-hour advisory board this year and a travel lecture grant to students, supported by a travel grant through the American Academy of Optometry.

The American Optometric Association represents 33,000 doctors of optometry and optometry students. We are the voice of the nation's eye care providers and a resource for

vision care, healthcare needs, and patient safety.

The American Optometric Association actually has a policy statement directing our members to educate the public about the use of contact lens solutions, and we're very interested to work with the FDA to resolve the matters that we've heard about today.

I want to give some perspective on the problem that we see based on our membership. And we know there's been literature that peroxide solutions are by far the best lens care solutions on the market for killing bacterial, amoebal, and fungal causes of infection. And make no mistake, I mean, these infections do cause blindness. So bacterial infections, amoebal infections, and fungal infections are a big problem in our industry.

In fact, you can see the picture on the bottom right here. This is a case that came in to my practice. This is a patient who had been buying their contact lenses online without seeking a doctor's opinion for 3 years, had a little bit of eye irritation, went to see a local ophthalmologist, was sent directly to a cornea specialist, and in the cornea specialist's office perforated and had to be taken in for an emergency penetrating keratoplasty or a corneal transplant.

And so the main thing I want to get across is we have to make sure that patients are following their doctor's recommendations. So when I prescribe a peroxide solution, we need to make sure that that patient is going to the pharmacy and picking up a peroxide solution and not a multipurpose solution. And so we want to make sure that there are no barriers to them following through with that recommendation. You know, barriers could include pharmacist control. The barriers could include increased cost or really any inconvenience to the patient.

Also for a perspective, I want to show the difference between -- you know, sometimes this is referred to as a chemical burn, and the picture here is a true alkali chemical burn, which is devastating to vision, and it leaves permanent damage.

In contrast, here we have peroxide toxicity, images of peroxide toxicity, which are self-limited and usually resolve with no treatment. Sometimes these patients do present to our offices, and sometimes we prescribe, you know, an antibiotic or a combination antibiotic-steroid. But as you can see from the picture, we have a little bit of conjunctival or the white part of the eye injection, a little bit of chemosis or swelling, and the picture here shows no damage to the cornea. A little bit of pouring of fluorescein in the bottom. Sometimes they can stain, indicating a keratitis, as Dr. Gromacki showed you. But in all cases, this doesn't lead to permanent vision loss.

So what can we do about this? Well, we want to make sure to continue to educate the population. The most important thing, as I mentioned, is physician oversight. We need to make sure that patients are coming to see their doctors, where they can be educated about the proper type of solution that they should be using for their contact lenses. We can also leverage existing partnerships. The American Optometric Association works with the CDC to put on a Contact Lens Health Week where we can educate patients about peroxide solutions. And then we can also make some recommendations about product packaging changes. And my recommendations would be very similar to the ones you've already heard.

When patients look at the box or the case in front of them and they are unable to see all of that tiny writing, it serves no purpose whatsoever. So tiny writing on the case -- these are already contact lens patients who need some kind of correction for their vision, so how are they going to see this? So my recommendation would be to relax the requirements for whatever the manufacturers have to put on the case or the box and use huge infographics. I mean massive. A big red circle with a line through it saying not in the eye. And if that's on the bottle itself, we're going to see a lot less of this problem.

Thank you.

DR. WEISS: Thank you.

Does any Panel member have any questions, clarifying questions?

(No response.)

DR. WEISS: Thank you.

Our next speaker is Dr. Deborah Jacobs from the Contact Lens Association of Ophthalmologists, who will have 10 minutes to present.

DR. JACOBS: Thank you for the opportunity to address these combined panels. I'm here as a representative of the Contact Lens Association of Ophthalmologists, where I'm the immediate past president. And I also serve as medical director at BostonSight. We're a nonprofit in Needham, Massachusetts, taking care of patients with complex corneal disease, and almost every instance patients wear a contact lens or a therapeutic lens for the treatment of disease. I also serve as faculty at Massachusetts Eye and Ear Infirmary and at Harvard Medical School.

CLAO has a mission, which is to advance quality of medical eye care for the public by providing comprehensive ophthalmologists and other eye care professionals with education and training in contact lenses and related eye care science. We're an educational society, as it says in our logo. We have a journal called the *Eye and Contact Lens* that's published now by LWW Wolters Kluwer.

I'd like to talk for a bit about the impact of misuse of peroxide care systems. As we've heard today from panelists personally, and from our presenters, insult to the cornea surface is painful. Peroxide causes shedding of the epithelial surface layers, and that's why we have pain. That's because the cornea has the highest density of nociceptors or pain detectors in the body. The picture to the lower right shows these little fibers penetrating up through the cellular layer of the cornea. And just for comparison, the density of the fibers is 20 to 40 times greater than dental pulp and 300 to 600 times greater than skin. So the cornea is super sensitive, and nobody trivializes an insult there.

When patients come in with corneal pain, or their family members try to tell me how miserable they are, I tell them I understand. I tell them, and I don't have data on this, that cornea pain is among the top three pain conditions. The most top three are kidney stone, childbirth, and corneal abrasion, in no particular order. And when there's an insult to the cornea such that you're sloughing epithelium, that's the equivalent of an abrasion.

I like that there's the Faces diagram system for identifying pain in hospitals, and I work with Charles Schulz's adaptation, he was way ahead of the curve with this, and I've seen people put corneal pain up there at 10 when there's direct peroxide exposure. We have heard a little bit about the burning and stinging, and that comes from a different mode of misuse with incomplete neutralization. And I think the reporting data confounds the two, so the numbers include both people who have stinging, like say after incomplete neutralization, and they'll be in the 4 and 5 category, but misuse that's from direct application into the eye or from no neutralization at all, that definitely would be a 10.

So despite this being a problem in the moment for the individuals who have misused the solution, we find, though, that the impact of misuse is this, that there are no long-term problems associated with peroxide insult exposure, if you wish to use that word "burn." There are none in the literature, and I did a pretty big search through peer-reviewed journals, textbooks, and there's no peroxide exposure disease in the medical ophthalmic literature.

And I, in my 25 years of practice, both in comprehensive care and at the specialty academic practice where we care for patients who need lenses medically, including patients with sick corneas, and their own peroxide systems, including patients who have suffered inadvertent exposure, because I've seen cases in my practice, none of them have a long-term problem related to that exposure.

So I'm pleased that Dr. Sonsino mentioned, and I agree, that peroxide insult to the

cornea is a self-remitted process. And I continue digging, and actually, like George Washington, I cannot tell a lie. Yesterday I found one report, it's from a paper of 1994, cases of marked punctate staining, but I couldn't dig up the entire -- to find out if there was any long-term consequence. So if some scholar in the audience wants to tell me there is one report, yes, I found it. That's it, again only one case with a corneal ulcer. So the implication of misuse is terrible pain, yes, but it's a self-remitted problem.

Now, the medical merits of peroxide systems have also been outlined here, and I'll just go through it quickly. They have the lowest rate of microbial keratitis but have the lowest tendency for *Pseudomonas*, which is one of the bad guy bacteria for binding to the cornea. They have the highest microbicidal activity.

And this is a fairly recent study. It's from January. And so the products depicted and the peroxide products on the left and the multipurpose on the right show much higher microbicidal activity for the peroxide products compared to the MPSes.

And most importantly, the peroxide systems have the highest microbicidal activity against what we call the really bad guys, and they're depicted below, *Acanthamoeba* and fungal isolates. These are things that do cause blindness, particularly in contact lens wearers. And this product is very important in reducing the likelihood of these things from happening.

It's also true, and that's been mentioned by others here, that the peroxide products have the lowest rate of toxic staining and corneal inflammation. There are people who are sensitive to the MPSes, and they're depicted with the flat case on the left, and who did very well, 4 decades, with peroxide systems depicted with the red tip and the special barrel cage on the right. So I think that we can distinguish them just by their profiles, and this is from the CDC website, and truly, as follows, sensitivities and such, the peroxide systems are better.

I would also like to say that the peroxide systems are the preferred disinfection method for patients who wear lenses on a medically necessary, as opposed to cosmetic, basis. Now, they don't drive the market per se, but they are an important part of -- an important part of the public, so by these products, by the solutions, and by the FDA. These are patients who can't get -- can't see at all without a special contact lens for medical purposes. And I give examples of these eyes. The lower left, that eye has ocular surface -- Stevens-Johnson syndrome and needs the lens to support the cornea. And another eye with keratoconus, fairly common, coexisting with eczema, and that patient is very sensitive to all kinds of solutions. These patients need access to peroxide systems, and they're critical for their quality of life.

So as far as a recommendation, we have a problem. Peroxide systems are critical to the health and well-being of contact lens wearers who need them on a medically necessary basis. The problem is that there's no method to weigh the advantages to those who need peroxide systems against the disadvantage of misuse among cosmetic wearers. I chose this image that shows blind justice, but we know she's not blind from misuse of solutions.

(Laughter.)

DR. JACOBS: So some recommendations here. I personally think, and this is my personal opinion, it is not of the membership of CLAO, that red labels and the red tips and red collars are useful in distinguishing peroxide solutions from the multipurpose solutions. And perhaps this should be pursued further for the -- I'm not going to use the word "right," but that, you know, the picture of the sink with the two bottles is a perfect description of when and how things go wrong, and I think we need to think about maybe how that type of inadvertent misuse can be avoided.

I had the comment, who reads instructions? And that's my opinion on the detailed labeling.

And I think that the provision of neutralization cases with every bottle does encourage adherence, and I think that's been a good industry move.

And I think we may want to focus more on the linkage of the case to the red bottle in some way, or to the red marker in some way, so that people understand the two must be used together and can only be used together and should not be individually. So as I said, red labeling, red tips, red collars.

In conclusion, regulators should not place undue burden on the providers or manufacturers that might limit availability and utilization of the superior approach to contact lens care.

Thank you. And I'm from Boston. Boston is more Irish than any other city in the country, and although my name is Debbie Jacobs and I'm 100% Jewish, happy St. Patrick's Day to everyone here from Boston.

(Laughter.)

DR. JACOBS: Thank you.

DR. WEISS: So I guess that message is unanimous here. So thank you very much for your presentation.

Does anyone from the Panel have any clarifying questions?

(No response.)

DR. WEISS: So I have one question based on the previous speaker and the skills-based errors that people make with two bottles next to each other or generic bottles looking the same. Is that a concern of yours, or that is just what it is and it's not something that you think would have to get addressed?

DR. JACOBS: It is a concern, and I think the size and shape and color of the bottles are one way to address that. And I think there might be cost and practicality issues, but those should be pursued. Someone from the Panel asked about brown bottles. We have

patients who use what we call brown bottle peroxide, and they rinse. We follow our patients closely. We prescribe a very deviant, I would call it, pattern. But I don't recommend brown bottle use generally, and it's certainly not a society recommendation, and I don't think confounding contact lens solution with brown bottle solution is a good idea. But there might be something in the shape, color of peroxide systems that separates them, other than a brown bottle system. That might work. And I think the brown bottle question was raised asking why these solutions couldn't be brown. I don't think they should be brown, but I think we might think about some bottling system separate from the dispensing system that would allow distinguishing.

DR. WEISS: Thank you. Any other questions?

Yes, Dr. Sneed.

DR. SNEED: I'm not sure if this is for Dr. Jacobs. It might actually be for FDA. This is very, very dense. How much of this information is required versus optional? And how much of it is a regulation that would be very difficult and time consuming to change versus what can FDA change?

DR. EYDELMAN: So, as was brought up in the earlier presentation by the FDA staff, we have guidance that has recommendations for labeling. This is not regulation; it's a guidance.

DR. SNEED: So that means it could be changed by FDA fairly readily?

DR. EYDELMAN: It could be changed.

(Laughter.)

DR. SNEED: There's nothing fairly readily about the government, right?

DR. WEISS: But there is fairly readily ability for starting our lunch break, which will start now. It's 11:35, and we will meet back here in 1 hour. I would ask Committee members to not discuss the meeting topic during lunch among yourselves or any other

member of the audience, and I ask that all Committee members return on time. And audience members, please remember to take any personal belongings with you at this time. The room will be secured by FDA staff during the lunch break. You will not be allowed back into the room until we reconvene at 12:36.

(Whereupon, at 11:35 a.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(12:36 p.m.)

DR. WEISS: Will everyone take their seat, please? Please take your seat.

So we are now going to proceed with the Open Public Hearing portion of the meeting. Public attendees are given the opportunity to address the Panel to present data, information, or views relevant to the meeting agenda.

Ms. Aden Asefa will now read the Open Public Hearing disclosure process statement.

MS. ASEFA: Good afternoon.

Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company's or a group's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting. Likewise, FDA encourages you, at the beginning of your statement, to advise the Committee if you do not have any financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

DR. WEISS: There are two formal requests to speak. The first speaker, Samantha Watters, will be speaking on behalf of the National Center for Health Research in Washington. Is Ms. Watters here?

(No response.)

DR. WEISS: So we will proceed to the next speaker. Glenn Moro will be speaking on

behalf of NovaBay Pharmaceuticals.

Mr. Moro, you have 5 minutes.

MR. MORO: Good afternoon. I'd like to thank the Panel for inviting us to present today. And I do have a financial obligation with the company NovaBay because I am their vice president of marketing.

I'd like to talk about a different take on how to look at this compliance problem with peroxide. And we know from this morning that there are a lot of problems with compliance, and most of the remedies have been about, you know, changing directions of use or basically trying to do things we've done in the past. We've taken a little different tack.

Now, the peroxide system hasn't changed since its introduction. The case for the peroxide system has not changed. And we like to think of that as it's a done case. Once you put the solution into it, it doesn't provide any more information. And we said, well, what can we do technologically to make it a better case?

So the first thing we did is try to find a variable between peroxide systems that we can measure, and what we found is that every combination of peroxide and disc has a distinctive heat signature, and it's very reproducible. And as an example, here's an example of a case over a series of cycles, where you can see that the heat index is very, very predictable over time, and you can see the cycles that we ran the case and solution through. As you might expect, at the beginning of the first cycle we would have a higher heat index, and it declines as the catalyst loses its effectiveness.

So once we knew that, we took that heat sensor, and we put it to work. We took that heat result. So we designed a case that's intuitive, okay, and allows you to track that neutralization process for the patient. And what we have is a simple case, and I'm going to just let you guys -- the case doesn't look any different than a normal case, but the

difference is it has heat sensors, and it has a chip that actually measures this process of neutralization of the peroxide.

Now, we made it really simple; we set it up like a stop light. It has three blinking lights: red, yellow, and green. Now, if the light blinks red on the top of the case, that tells the user that the initial peroxide concentration was too low or that the catalyst was deleted; it no longer is providing neutralization to the peroxide. Also, that red light will pick up if the patient tries to put saline into the case; it will blink red and say no, this isn't the right solution. All right.

It will also pick up -- somebody mentioned brown bottles. We have enterprising patients who try to use store-bought brown bottle peroxide as their system. This case will differentiate that and tell the patient you've got the wrong solution in here; this isn't the solution that's matched with the case. And the same thing with multipurpose, so if you tried to put multipurpose in here, it will blink red, okay?

So if the solution matches the catalyst, then you'll get a yellow blinking light. What that tells the patient is, hey, it's disinfecting, it's going through the process. And finally, when you see the green light, it says okay, it's done with the neutralization, your lenses are clean, it's ready to put in.

And the interesting thing about this is you can actually program the chip so it will not go beyond the length of the bottle or the number of cycles as per the manufacturer.

So this product, it's FDA cleared, and we got a clearance for it April 29th, 2015, and it can function with any of the commercial systems that are out there. So it will work with Clear Care or any other product on the marketplace.

Now, the flexibility of the programming means that you can program every chip to whatever system. But once it's gone through the manufacturing process, it's impossible for the patient or the doctor to change the programming on the chip.

Now, that's just step one. Now, we have two other additions to this we think will really help. The next thing we've developed -- and again, these are patent pending. We have a tip that can be placed on a regular bottle of peroxide and prevent that bottle from pouring out unless it's matched with the case. So, you know, you talk about that that is one of the big problems; your patients grab the wrong bottle and whoop, in your eye, they burn themselves. This system will allow this to prevent that from happening, all right, this new tip.

The other thing we found is if you can maintain a higher concentration of heat, that's a representation of better activity of the peroxide. So we've also got a case that's insulated to increase the heat level.

So all three of the -- the one product is already cleared. The other two products are patent pending. So we think this is a novel approach to addressing this compliance issue with peroxides.

And I want to thank you for your attention.

DR. WEISS: We can just do one or two brief questions.

Yes, Dr. Rimal.

DR. RIMAL: Hi, Rajiv Rimal.

My question is what is the source of power for this? Is this battery operated and how? And what would you expect the price range to be for something like this?

MR. MORO: Well, we did an initial run just to test it for clearance, and we ran about 250 or 300 of these. These cost about $1.50 a unit, okay? Yes, there's a battery in here with the chip.

DR. WEISS: Thank you very much.

MR. MORO: Thank you.

DR. WEISS: Is Samantha Watters in the audience as of yet?

(No response.)

DR. WEISS: If not, we'll proceed. Does anyone else in attendance wish to address the Panel? If so, you will be granted 5 minutes.

(No response.)

DR. WEISS: Okay. We may be able to have Ms. Watters address us later, if she comes.

Then we will close the open public speaker session for right now. Because we have a little bit of extra time, did anyone else have any questions for the last speaker?

Yes, Mr. Delost, you could address those questions for the last speaker.

MR. DELOST: Kort Delost.

I have a question. Is this design a standalone purchase, or are you planning on having this developed with the manufacturers?

MR. MORO: We are not in the peroxide business. Okay, we just have a tool, we think, that would make compliance better. We would like to partner with one of the larger companies with our product.

MR. DELOST: Thank you.

DR. WEISS: Yes, Dr. Dillard.

DR. DILLARD: James Dillard.

Can you tell me about the lifespan of the unit and how long it will last?

MR. MORO: Yeah, the lifespan, you know, it's designed for 30 or 60 days, depending on the size of the bottle. But we know that there's at least 4 or 5 months of life in the unit. In fact, the unit will start blinking red before it actually loses power. So we've tried to match the unit with the compliance directions of the manufacturer.

DR. DILLARD: Okay.

DR. WEISS: Are there any other questions?

(No response.)

DR. WEISS: Thank you very much.

MR. MORO: Thank you.

DR. WEISS: We will now enter the Panel deliberation and FDA questions portion of the day. I want to open the floor to the experts around the table to begin deliberating on any issues that you may have with any data you have heard today, either in the Panel presentations, the discussions with the FDA, or material you've read in your Panel packs.

Although this portion is open to public observers, public attendees may not participate except at the specific request of the Panel Chair.

Additionally, we request that all persons who are asked to speak identify themselves each time. This helps the transcriptionist identify the speakers.

To start, do any of the Panel members have a question or comment for the FDA?

(No response.)

DR. WEISS: And I think I may just go around the table and -- because at this point, I think I've created fear of anyone saying anything, which is good in the earlier session, but now you're actually supposed to speak. So if there are no questions, we will then just go, and we'll go around the table so everyone has an opportunity to speak on the specific FDA question.

So the first question is the following, and is there a way to project these? Okay, Question No. 1: Please discuss the currently used labeling for peroxide-based contact lens care products with respect to the adequacy of specific warnings and clarity of instructions for use. Does the panel have any recommendations for modifying this label? During your deliberations, please address the following examples of current labeling and instructions for use specific to the issues of misuse in your discussion:

First, the phrase "NO RUB" has been removed so that it would not be confused with

other products portraying the "No Rub" label.

Second, the addition of a red cap and a red tip to identify it as different from other care products. Carton and bottle both state the following in enhanced text and red boxes to alert the user:

- Use only the lens case provided.
- Use only the special case for disinfection and neutralization.
- DO NOT use a flat lens case.
- Hydrogen Peroxide X only works with the special lens case provided.
- And finally, failure to follow directions for use will result in burning and stinging.

So, basically, sort of summarizing this, we're going to go around and ask you what is your opinion of the currently used labeling provisions; is there anything else you would suggest? And the examples that were just given are what we have currently; is that sufficient or not?

So why don't we start with the Industry Representative first. Do you have any thoughts from what you've heard beyond what is being presently done?

MR. PFLEGER: Yes, so a couple of thoughts. One is, you know, since the no rub's already gone, I don't know if there's a lot of need to discuss it. So the rest of it, in terms of the red tip and red cap, the difference that I saw is some products have a red tip and a red cap. I think the original discussions with the Agency was to have a red tip, so a red cap, again, trying to have some level of consistency, there's clearly some advantages to that. Same thing with the others. I think there were some statements that we're not totally sure what all of the products, including the generic products, have for labeling. So I think anything that can be done from an industry perspective to have a level of consistency would probably be a good thing for the warnings and precautions.

DR. WEISS: Ms. Witczak.

MS. WITCZAK: Kim Witczak.

I would say the current, when I look at some of this, I do like -- I think we do need to have consistency, but I'm not really sure that I would say the burning and stinging is really strong enough for -- you know, I like the idea of adding "severe" because I think it is pretty severe, whether that it's all in context, if that's a -- you know, I mean, even when you saw that little -- whoever had that pain indicator, I think that would be the consistency. I like the idea, the recommendation of having -- I think it was somebody earlier in the audience presentation with an icon or the infographic. That was a little bit clearer and bigger and probably at the front of the box and almost on every part of the box, because I think the consumer just rips the box, so I also would see it on the bottle as well.

DR. WEISS: Ms. Ellis.

MS. ELLIS: Yes, Annie Ellis.

I think that, as a consumer, the labeling has greatly improved. I love the red tip and the red cap as well as the collar. I'd love to see that extended to the carton, if possible, to create a signal. And I agree with the severity needing to be added and just keep it as simple as possible. I don't think longtime users, once you start using the product, are really taking the time to read anything further, even if it's very simple.

DR. WEISS: Thank you.

We're going to pause right now and go back to the public session because I'm told that Samantha Watters is now present and she can give her 5-minute presentation. Can you come up to the podium, please? And if you have any conflicts, it is helpful if you express those, if you're willing to.

MS. WATTERS: Hi. I'm sorry to interrupt you guys. I definitely did not realize the schedule had changed; otherwise, I would've been here. But it's just a couple minutes I just

wanted to take of your time, and I don't really have any visual aids or anything like that, so just a few things I'd like to say.

So thank you for the opportunity to speak. My name is Samantha Watters, and I'm the Director of Communications and Outreach for the National Center for Health Research. What our center does is we conduct and scrutinize medical research and health information, and then we try to translate that information into plain language so that patients, consumers, media, and policy makers will understand it.

As today's meeting makes clear, even when the information that consumers need is on the package, they may not read it or understand it. This is especially difficult in a product such as contact lens solution, where consumers may assume that they know everything about this product without reading any of the particular directions. This meeting reflects the fact that FDA knows it's not enough to require that the risks are listed, but it's essential that they're clearly explained both why and how a product should be used and, in this case, how it's different from other solutions.

There are many forms of communication that have little to do with words, as you guys were just discussing. FDA is considering many ways to make the overall look of the product packaging different when a solution contains hydrogen peroxide. We, at our center, do not think that necessarily changing just the color or adding a logo or making the box significantly different will necessarily be enough.

Where the products are placed on shelves in relation to other lens solutions might help, but it also might not. I mean personally, I've used contacts on a regular basis in the past, and I didn't even know that some solutions had peroxide in them. So it was completely new to me, and this lack of awareness could definitely be a problem because consumers might not even realize they should be looking carefully enough for different types of lens solutions to figure out the kind that they want.

Unfortunately, most people don't take the time to read the information on the box or the bottle or even the label that carefully. In addition, many people have limited reading skills, which is why you guys know that communicating this information at a fifth or eighth grade level is really important, but having warnings that are large and impossible to ignore is also very important.

The only way that our center saw to completely protect consumers is to restrict lens solutions so that they're available behind a counter, requiring an explanation from some sort of staff member. This behind-the-counter arrangement works for things like Sudafed, and it's a little different because obviously it's not about how much you're buying; it's more giving that additional moment to educate the person who is buying this product. And it would definitely eliminate erroneous purchases because if it's something that needs to be -- you know, you need to go to the counter, somebody who is looking for just a multipurpose solution isn't going to mistakenly pick it up.

We also suggest that in terms of the warning bullets and things that are on the packages, that they're a little bit stronger, which I heard you guys discussing a little bit as well. So the sample bullets that I read in the background material, we felt like they weren't super clear, and they were also kind of repetitious, so we thought something like this product contains hydrogen peroxide; it will burn your eyes unless you use the special lens case provided. You must use the special lens case provided; it will disinfect your lenses in a way that will make them safe for your eyes and won't hurt them. Something stronger could be very beneficial.

So that's really all I had to say. Thank you so much for taking the time to listen, and again, I'm sorry to interrupt.

DR. WEISS: Does anyone have any questions?

(No response.)

DR. WEISS: So I have one question.

MS. WATTERS: Sure.

DR. WEISS: I don't know if you were here for the earlier presentation on hydrogen peroxide being efficacious to prevent some of the infectious keratitis that patients have.

MS. WATTERS: Um-hum.

DR. WEISS: Would you have any concern that raising the barrier to obtain these solutions might dissuade some patients from buying hydrogen peroxide with the downside of getting more infectious keratitis?

MS. WATTERS: So I think, at least from my perspective, again, I think that's definitely an education issue. If it's something that -- and perhaps that teaching moment is when you're actually at the doctor getting your contact solution or your contact lenses and having someone explain to you the differences, and maybe that's something, again, that FDA -- I know you guys have a lot of great information on your website that people are not necessarily getting to, so trying to get that information out to people.

And yes, obviously it does create a little bit of a barrier because you can't just pick it up and take it to the checkout. But in my opinion, I think having something like that behind the counter just makes it clear that there is some level of risk that's not there with the other solution, something that they need to be aware of. So that's my personal perspective, but obviously, you know, you guys are the experts.

DR. WEISS: Thank you very much.

We're going to now go back to our Panel deliberations. I think, Dr. Dahr, you were next to ask -- to comment on the labeling of these solutions.

DR. DAHR: Sam Dahr.

The only point that I would make is looking at the four bullet points under 1b, it strikes me that bullet points 1 and 2 are almost redundant, and I'm one always for simplicity

and using as simple language as possible. I don't know if one could combine bullet points 1 and 2 such that it was "Use only the lens case provided for disinfection and neutralization," and that would put two lines into one without really making it difficult to read or interpret, just for the sake of simplicity.

DR. WEISS: Thank you.

Dr. Dillard.

DR. DILLARD: James Dillard.

If I could comment on this generally, but specifically using examples from two of the earlier presenters, the Alcon representative and the CooperVision representative, with regard to the Alcon message, which some of us have here in front of us, there are some improvements that could be made to that message, in particular, the addition of reasons. The fourth point there says do not remove lenses from the lens cap, the lens case, for at least 6 hours; the solution needs time to neutralize. That's an example, a really good, clear warning message that has those two important parts; there's an action, and there's a reason given for it.

The next one up says do not use a flat lens case; use only Clear Care Plus with the special lens case provided. That's an example of a bad piece of a risk communication message. It says don't do it, there's an action; it doesn't say why you shouldn't do it. When I looked at that, without knowledge of how contact -- these contact lenses work with a peroxide system, it sounds to me like you're saying you can't drink wine out of a coffee mug; you can't use this container. There's no reason. But what I've learned today, the type of container really is important. So if it were to say because it won't neutralize, that would be a reason.

If I could then turn to the CooperVision message, it had six bullet points, the first three of which were "Do" something and the last three of which were "Don't"; that's a good

design. "Do" behaviors are governed by a different part of the brain than "Don't" behaviors, so it makes a lot of sense to group those together. The need for improvement on that message, I think, is that the "Don't" behaviors were all very specific behaviors. The "Do" behaviors varied a lot in terms of level of abstraction and a target of action. They weren't parallel in terms of the hierarchy of which behavior you're delivered. So I thought there was some room for improvement there.

DR. WEISS: Dr. Kreps.

DR. KREPS: Yeah, I find the labeling to be way too small, way too busy, and very difficult for people to read, especially people who have challenges with their vision. I like the idea that one of the presenters gave of putting in a large graphic warning on the bottle, "Do not apply to eye," with kind of a skull and crossbones or something on there that would get people's attention. You know, I like what Jim was saying about more reason, but I think that will add to the complexity of the message, and I think it's really critical to give people very simple, very straightforward, and very powerful messages with the label. And so my recommendation is to make it very clear, make it very strong, and make it very easy to recognize.

DR. WEISS: Dr. Sneed.

DR. SNEED: Jeannie Sneed.

I agree with everything that the other people have already said. Somehow we've got to boil it down to what are the three or four most important things that people need to know and make sure that those are very prominent because it does get so cluttered that you can't sort through it. And the older I get, the more sympathetic I am with people who can't see the fine print, so making it big enough so that it's readable and also getting rid of any duplicity that might be there. So that's all I have to add.

DR. WEISS: Dr. Wolf.

DR. WOLF: Just in general, I think the solution has to match the problem, and a lot of what we've been talking about is almost around product identification and making sure, very first and foremost, that at least again, if I believe what I've been hearing a lot about in terms of the nature of the -- the causes of a lot of these adverse events are associated with mixing up the product. I think, first and foremost, the label, whether it be on the box, package, as well as on the actual bottle, that does much more clearly -- and we've had these issues with OTCs as well. Identify hydrogen peroxide.

I do think that the follow-up message, that's really an important point that was already stated by my colleague, is this notion that you need also an explanation of what the risk entails, so not just to say do not do something or to do something without explaining the why. The challenge is going to be how to say that in a very parsimonious way so people will read it.

My other just quick comment I made was a lot of the labeling I'm concerned about, especially around the wraparound text, that allows for maybe a misinterpretation. There are some improvements that could be made there as well.

DR. WEISS: Dr. Yin.

DR. YIN: Shonna Yin from NYU.

I agree with and echo the comments of the others here. In terms of the red cap and the red tip, I think it's a step in the right direction, but I think more definitely needs to be done to -- because it doesn't seem sufficient to prevent those mix-ups from happening. And then also, I'm thinking about the standardization that, you know, all products would use the same strategy so that there is consistency and people can better be able to distinguish things, products with the hydrogen peroxide and without.

In terms of the labeling, I agree that it's important to focus on the box as well as what's on the bottle, and I agree with more clearer wording, and even on this product, you

know, where it's like rinse lens prior to insertion or direct use, words like neutralize, those are hard words, and being more clear in the wording on the more prominent warnings, I think, would be important and especially having user testing being part of the picture.

DR. WEISS: Dr. Owsley.

DR. OWSLEY: So I don't want to be redundant. This is Cynthia Owsley. I don't want to be redundant, but I agree with the previous comments by the panelists. The font is too small. The critical safety information needs to be prioritized. The information is highly salient in terms of the safety of the product, and how you can use it safely should be prominent both on the box and the labeling.

In addition, I think we learned today that there is an increasingly active and growing area of science that is developing evidence-based information on how to design patient information such as labels and information on packages. And ultimately, I think this evidence-based research should be used to guide labeling by FDA and by -- well, their guidelines and by the manufacturers.

And then the last comment I have has to do with the burning and stinging issue. Fortunately, I have not been subjected to this product in my eye, so I don't have any personal experiences, but many of the speakers referred to this as excruciating burning and stinging, and as a consumer, when I think of burning and stinging -- this is what they tell you when they put dilating drops in your eyes or when you get a blood draw, and it's not excruciating; it's yeah, you notice it, but it's not devastating. So I'm just wondering if we need some adjectives in front of burning and stinging. Thank you.

DR. WEISS: One thing I would question is the -- putting the information on the inside of the box rather than your traditional insert. But I will say that I am skeptical that you can make all the efforts in the world and many people, and I don't know what percentage, aren't going to read anything you put in there. And this will get to another question in

terms of the skill-based things because I do really think industry is making an attempt to make this clear, but if people don't read it, that would be an issue. It has been said already, front and center, big letters, of what the main issues are so it doesn't get lost in the 5,000 other things.

Mr. Delost.

MR. DELOST: Kort Delost.

I've done some -- those icons we've talked about, I see on other products there's a big stop sign on some of them, so I thought, you know, the graphic of a big stop sign could be used to describe this and put an example of "Stop: This product contains hydrogen peroxide, and it cannot be used to rinse or wet contact lenses. This product is for disinfection and storage only," something in that regard.

Another "Stop" below that: "Use only the enclosed contact lens case for disinfection and storage. Using other cases will not" -- in big bold -- "properly neutralize the peroxide-based solution."

And then one more "stop," sorry. "Improper use of this product may, quote -- I have a couple of terminologies. May "damage the eye, may cause burns to the eye, or cause harm to the eye." The more severe type of consequence to the -- to what you do when you put them directly in the eye.

One thing I didn't notice on any of the packaging at all, and I don't think it's even possible, but what happens when a person comes off a bender at 2 o'clock in the morning, throws their contact lenses in, and has to get up for work at 6:00? What do they do to fix that, make sure that's properly neutralized? I haven't heard an answer yet or seen an answer. So we need to address that as well.

MR. PFLEGER: So what's typically -- you recommended every time I've gone into --

DR. WEISS: Can you identify yourself first?

MR. PFLEGER: Michael Pfleger.

So you're supposed to have a pair of glasses for people who wear contact lenses. I mean, if you're on -- if you do that on a regular basis, you probably might not want to wear contact lenses at all because you're probably going to fall asleep with them in instead of taking them out and putting them in if you're coming in at 3:00 in the morning.

DR. DILLARD: A real-world scenario, there are lots of people that can't afford both, so they pick one or the other.

DR. WEISS: And those are the ones who come in with infectious keratitis.

DR. DILLARD: I think those are the ones that are probably the higher risk.

DR. WEISS: Did you have anything else to say, Mr. Delost?

MR. DELOST: Let's see. Oh, I think it's a great idea to put social media-type connections and have a social media connection to the FDA as well as the manufacturer, especially those connections to the videos; that's a great idea. Oh, less is more. Get rid of a lot of the labeling; just concentrate on those big bullet points.

DR. WEISS: Dr. Rimal.

DR. RIMAL: I really want to go back to Terry Fairbanks's presentation earlier today. And it made me think when I rent a car, the car rental agency never tells me, hey, don't put diesel in this car because it's a petrol car, right? And the reason is that if I go to a gas station, I actually can't put the diesel nozzle in there because it's too big. So all the driver education is eliminated by technology, technological solution.

And so I feel like framing the question in terms of how do we re-label seems like we're asking the wrong question, and I wonder if small things like make it tactilely different so the peroxide bottle would feel very different in your hands because maybe it's got a rougher surface or something like that so that even in the dark when you're not seeing what you're pouring into --

DR. WEISS: Actually, for this question it's just labeling, and we will go on to these other things.

DR. RIMAL: Okay. I'll stop.

DR. WEISS: So these other things will be addressed, but just for the specific question of labeling that's identified there, do you have any other suggestions in terms of the red cap, the red tip, anything else for modifying the labeling?

DR. RIMAL: I think, in that case, I would just support what Drs. Dillard and Kreps have already noted. Thank you.

DR. WEISS: Dr. Lee.

DR. LEE: Yeah. And as with others, I believe that the labeling itself is not going to prevent a lot of the issues that have been raised, but that doesn't mean that it couldn't benefit from some improvements. One suggestion, not to copy anybody else, but that I have is that if you're creating a warning that you want to stand out, like this red box, and the first thing you say is if non-neutralized Clear Care Plus -- I mean, you're starting out with a concept of non-neutralized, and most people may not know what that means, and I try to find where it's non-neutralized, and it's actually on the other side in this little box. So this warning box should actually stand by itself, and if you're going to use a term like non-neutralize, you should define what that means for the consumer.

DR. WEISS: Dr. Krishnamurthy.

DR. KRISHNAMURTHY: So I was looking at this box. I have some suggestions for the design itself that I will talk about later. In a box like this, real estate is very valuable. And I was looking at where the people open the box for the first time or something, there is a flap here, at least, which is a lot of white space, and you could put that infographic that many people have mentioned here, like the "Do not use directly on the eye," so this is at a place where people can -- they have to open the box one way or the other, like -- you know, so

we have something inside, say a packaging insert for information, and we really can't see the insert. So I think it kind of needs to be moved. But you do have to illustrate on the flap so people -- where people first encounter the product when they open it, where you can put that infographic.

And the second thing was this was done by CooperVision, I think, and it can be a standard practice, even if it's not regulated, that is to put a QR code somewhere that if people want to know how to use them, just simply scan it, and you can see the video of how to use the product, and that again goes to the point of use, which is more useful for people to actually work on.

So these are the two parts that I have. One is to make use of the flaps where people actually open, to put some warnings or infographics or whatever and then possibly put a QR code that will show people how to use it rather than write it out.

DR. WEISS: Dr. Berube.

DR. BERUBE: Yeah, I think -- this is David Berube. I think there's a three-prong approach to this, and this is just one of the prongs. I think education and design is part of the other prongs. The thing I know about labels, having lectured about it for decades it seems, is consumers expect labels, so you've got to give them labels. The absence of a label is kind of frightening; you know, what does this mean? That's why those cereal boxes that are all white don't sell very well. We need to have an awareness campaign so people know what to expect out of the labels, but that's more of an education thing that comes up later.

But the second thing is it has to be written in -- and the term is registry. There are different registries we write in. I used to work for *USA Today*. I mean, when you wrote for that newspaper, you wrote in a different registry than I write when I'm writing for the *Journal of Nanoparticle Research*, right? There's a whole different registry. And it doesn't seem as if this has caught on in the industrial world. We used to have folks trying to make it

simpler. There are professionals who know how to do this, how to take really complex language and turn it into stuff that's understandable.

I also teach persuasion, and we have a huge literacy problem. We have an innumeracy problem in this country that you just -- you can't even estimate how large it is. Also, the public has self-selected themselves out of reading labels in a lot of instances. I honestly think that the people who are causing the most damage to themselves may be the ones who will never read labels. You know, I can't prove it to you yet; I could if given enough time to research. I know there's a language tradeoff in label theory. I know there's a density tradeoff in label theory. I know there's a fear tradeoff, that if you produce high levels of fear, you will affect whether people will use the item or not, right? That's going to be also true.

The third thing I know is -- I have a grant on visualizations. Infographics, probably the best you can do is cross-cultural. It also deals with language issues. And it's the one thing that uniformly is able to cross different educational backgrounds, right, that one infographic works at multiple educational backgrounds when you don't have control over registry as much as you would like.

DR. WEISS: Thank you.

Dr. Blalock.

DR. BLALOCK: Sue Blalock.

And I also agree with much of what's been said thus far. One thing that I would like to sort of emphasize is the importance of the first thing that appears on the label, and I see here at the top, at least with the red -- I'm looking at the Clear Care, I guess this is what actually goes on the package. It says, "Important: Misuse will result in burning and stinging," and I absolutely agree that the word "burning and stinging" don't convey the severity of what I've heard here that we're trying to avoid.

And from my perspective, as a behavioral scientist, I agree that many people will never read this, you know, but you can approach it from the perspective of what would motivate people to read it. And to motivate people to read it, there needs to be a perception that they will benefit from spending their time when looking at this information. When I see the word "misuse," I don't really think of the things that I heard here today, that there were two anecdotal incidents where you wander into the bathroom at night and accidentally use something. I think of some of the asthma products that are, you know, snorted by adolescents when I see misuse.

So I know that we were given a specific definition of misuse in the context of this meeting, but I don't think that's how a typical consumer would read that. So if I think I were reading this, misuse, well, I'm not going to misuse this, and you don't think about accidental things. So I think, if anything, because it's the first thing, because that first phrase is so important in terms of providing the motivation that might make someone, you know, read more, that both that word "misuse" and then not capturing the severity of what's trying to be avoided are big issues. And I absolutely agree with the suggestion for the reason for doing that because you can tell people to do things and put it in very simple plain language, but helping people understand what's in it for me, why do I need to do this and why is this important are just crucial, and if it takes a few extra words, you know, it takes a few extra words, get rid of something else that's less important.

And I think that the other thing -- and I've never used, worn contact lenses, so I really don't understand sort of the user experience, but I don't really quite get the red cap, and I know that you said you liked it as a user. But I see, you know, a problem with some of the things I've look at more, like some of the icons that are used on prescription bottles, and people typically don't understand that. You know, there's something like you avoid the sun. Well, am I supposed to avoid the sun when I take the medication or I keep the bottle

out of the sun? So what is this red cap all about? I don't quite get it. So I think that's all that I had to add.

DR. WEISS: Thank you.

Dr. Jeng.

DR. JENG: Bennie Jeng.

So as a cornea specialist, along with my esteemed colleagues here, we see contact lens-related corneal problems including infections all the time, and then knowing the literature, which has already been alluded to today, this population of contact lens wearers is notoriously noncompliant; we know this. And so getting them to read something like this with very small print is going to be extraordinarily unrealistic. I think that the information is good; I honestly have never read it in totality, but the information is good, but it has to be much simpler, it needs to be bigger, there needs to be more diagrams. That's for one.

The second thing is I also understand why the insert is not there, and it's easier just to have a box, but there are people who open letters with a letter opener, like my wife, and there are people who rip open the envelope. So I actually tried to be very careful about opening this box, and part of my words are on this side and the box is ripped over here, so you need to think about that when you're constructing a box, how to deconstruct it so it doesn't fall apart.

And since we're sticking just to this topic and not about design things, if we're going to talk just about the red cap thing, whether we like it or not, it needs to be consistent and, you know, to be able to have companies that can make it without, you know, being consistent is a problem because the inconsistency will lead to, you know, people misusing it.

DR. WEISS: Dr. Huang.

DR. HUANG: I concur with Dr. Jeng's opinion in the sense I need this in risk

communications, and I thought I took everything for granted, but now I listen to the Panel as far as the deliberation earlier today, and I all of a sudden realized, you know, I mean, to err is human, that we commonly can make mistakes. But then I think about deeper, I think the problem is really that maybe that it was a lack of standardization, you know. If everything is the same, just like I was taught to go to a bathroom and this and that, you know, I would know exactly where to go and I would probably rarely confuse the bathroom with some other facility, you know.

But the problem was that the product itself is made by a different company, and they have a different warning, so I thought about that, and actually, I was very impressed by the concerted effort between FDA and the industry in promoting the so-called safety of the medical devices as well as the consumer product. But I think even though this product is not perfect, but I think if FDA can provide some guideline to standardize the product, such as, you know, unify the color so people know, you know, that this type of color, you know, I'm not making any -- say a purple color or whatever type of color, whether it's green or blue color for the multiple purpose solution, you know, that would contrast the difference between the safety of the two various products.

And also I think, you know, just that this is a multimedia state, you know, that consumer wants to know something, but, you know, I don't think we have the time to read the so-called premium product. So if we can, you know, have some sort of, like presented by the CooperVision, you know, just like today, this time was the first time I used my iPhone to access my room without using any of the -- I didn't even have to check in, I didn't have to check out, and then basically just iPhone. So ideally, if I can just use my iPhone to scan some of the code here and find out all the product, you know, ingredient and that's a -- frequency type of technology or the QR code type of situation. So I think that will also improve the standardization.

And lastly, I think what we haven't talked about much is the educational part. I think we all depend on the patient to read this, but truthfully, even though I read this today very carefully, I think 3 weeks from now I won't remember the detail. And then especially for those people, you know, occasional contact lens use, they're only used on the weekend or something, they put a contact lens in the store solution, they probably don't remember to rinse or anything. So I was thinking how do we improve the compliance, either again using the same type of recent technology or simply just bring out some of those warnings, you know, in the sticker and then patient can stick onto their medicine cabinet or stick on their bathroom door or something. So in that regards, you know, that would remind them, hey, anytime I use this kind of contact lens solution, I need to be careful, and I think it all boils down to the standardization. Thank you.

DR. WEISS: Thank you.

Dr. McLeod.

DR. McLEOD: Great, I get to go last after a roomful of experts have spoken. Thank you very much.

(Laughter.)

DR. McLEOD: So, you know, I think that if we're going to just focus on the labeling piece, I guess the difficulty I'm having is that we seem to be commingling a number of different functions all under labeling. So there's the very important alert function, and then there's the education function, and then there's a reminder function. But as I look through the data represented to us, it seems as if probably -- and, you know, it would be interesting to see if there's a different perspective on this, is that really one of the foremost issues is really the alert function. It's the I'm making -- you know, I bought this for a reason, but I'm reaching for the wrong one, or I know which one I want to buy, but I'm buying the wrong one. So it seems as if really making sure that the labeling problem we're trying to solve

actually addresses the alert part of the equation is really important.

As far as the education goes, one would think that it's, you know, when the individual is in their optometrist's office or they go to their physician's office, that's when they would have the most part of the education. I didn't see from the data that there are a lot of people that seem to be naive users who went to the store and decided they were going to switch from one method to another method, picked up this new method and didn't use it properly. But that, of course, would be an education function, assuming that's not as much of the issue. And I think I'm speaking to Andrew's point. There are people who have been educated at a provider's office but now need a reminder, that's a different function. I think that, you know, spending a lot of time on parsing how big the text is and how small the text is and what's in it and what's not in it really seems to be placing a lot of emphasis on the education and -- I would say that it probably makes more sense to focus on the alert piece.

Just one last thing and, you know, sitting through this is almost like sort of sitting through a hearing on, you know, middle school education; everybody has an opinion. And as a one-time user of these products, I can just imagine going into the store and quite simply just having a little bit of trouble finding on the box where it is, hydrogen peroxide. Saying that it will cause, you know, stinging and burning as opposed to horrible pain, again, seems to be more of an education function than just I know I don't want to put this in my eye, which is the one that has peroxide in it, and it's very small print, and there's no contrast, and the only red thing on this box says, "Voted product of the year." So I think that that's one place, again, where an emphasis on alert would be really helpful.

DR. WEISS: Dr. Eydelman and Ms. Duckhorn, is that sufficient? Has the Panel sufficiently answered that for you?

DR. EYDELMAN: Yes. Thank you very much.

DR. WEISS: We're going to go on to Question No. 2. And I don't want to put anyone under pressure, particularly if you're the last one who is being asked the question, so if you have nothing to add to this, that's also a completely acceptable response.

What strategies should be considered to reduce the risks of mistaken purchases of peroxide based contact lens products? Please include the following propositions in your discussions and recommendations including potential benefits/additional risks these strategies may impose.

So this is the situation where the consumer grabs the wrong box.

a) Redesigning the carton label so that it is distinctly different than other contact lens care products
b) Placement of hydrogen peroxide care products separate from other contact lens care products
c) For sale only at offices of contact lens practitioners or
d) Other strategies

So why don't we start with you, Dr. McLeod? Would you prefer any or all of these or something else?

DR. McLEOD: I have to say that I actually was very much convinced by Dr. Fairbanks's presentation. And so, you know, coming in it seemed to be the most rational place to spend -- to expend efforts, and I do think that the physical tactile, whether it's shape, whether it's size, clearly, again, consistent with another avenue of -- I'll persist with it -- alert, I do think this is really where the emphasis should be laid.

DR. WEISS: Dr. Huang.

DR. HUANG: Andrew Huang.

I concur with the statement. You know, I think going back to the earlier presentation or comment by Dr. Berube that design dissimilarity is the key thing of this type of problem.

So I think that if you can have a different color, different shape, and then we have a proven product, having a proven type of concept -- I mean, in ophthalmology, you know, we design medications for glaucoma, you know, various type of glaucoma medication, which is different color, the cap. You know, there's a bar code; we use the yellow and so on and so forth. And then topical corticosteroid to suppress the inflammation which has some side effect, we make it into pink, you know. And then the dilating drops we make into red. I think, you know, that is the standard practice.

So, as a result, the patient rarely has confusion. Of course, occasionally there is some confusion, you know, low-vision patient, they cannot distinguish the red from pink. But for the most part, you know, that is very standardized, so as a result, the patient acceptance and the compliance is very good. So I think that would be one of the things, you know, to consider, that, you know, I think standardize or do we assign a color or do we design a shape or, you know, the texture of the bottle would be idea.

I'm just going to give an anecdote. You know, I have a patient come to me multiple times, you know, always put rubbing alcohol into her eyes, and I was wondering how come it's always rubbing alcohol, not something else. She doesn't use the contact lens, so there's no contact lens issue, so I ask her how come you don't put your mouthwash into your eye; it's always the rubbing alcohol? She said, oh, the rubbing alcohol is red, just like the standard saline solution that I had, and then the mouthwash is a square bottle. So, you know, I touch the square bottle, I know it's wrong. So that's, you know, the concept. Thank you.

DR. WEISS: For clarity of aiding in terms of us taking notes, with this one we are just really talking about when you grab it off the shelf. So I think it would be helpful, to me as well, if you identify if you're going with (a), basically redesigning the carton label or maybe the shape of the carton, whatever, or you endorse at all (b), placement of the products

separate from other contact lens products, or (c) sale at offices of contact lens practitioners, because this is one of the questions the FDA has for us. So from what I understand from both of Dr. McLeod's and Dr. Huang's response, neither of you are endorsing (b) or (c); you're endorsing making the shape of this or the color of this or something different but not putting it somewhere else.

Steve.

DR. McLEOD: I think that (b) is neither practical nor enforceable. I think that (c) reduces the patient access, and there's very strong evidence in support of the continued ready access to peroxide products, and I think that other strategies are, by and large, going to be subordinated to the first.

DR. WEISS: So that's sort of where I want this conversation going, is do you at all believe that they should be separate, or you believe they should be restricted to certain -- behind the pharmacist or the eye care practitioner, or is your interest more in making it look different or some other novel idea that you may have?

Dr. Jeng.

DR. JENG: Bennie Jeng.

So with that clarification, it makes my discussion very short because I completely agree with Dr. McLeod that (b) is not enforceable, especially since people take things off the shelf and put them in the wrong place, and if you just rely on that, you just grab it by accident. (c) is not practical. And so I think that if we're going to answer this question, I think we talked about it already, focusing our time and efforts on redesigning, yes, but making it consistent. I think consistency is very, very important. It's just like the color caps for glaucoma and stuff, but there has to be some sort of uniform way to be able to identify quickly if you're in a rush.

DR. WEISS: Dr. Blalock.

DR. BLALOCK: This is Sue Blalock.

I think I'll just agree with that.

DR. WEISS: Dr. Berube.

DR. BERUBE: Yeah, I think (b) and (c) are both impractical and ineffectual. I don't think we're going to get anywhere there. I completely agree that we need to redesign the carton, and we need to redesign the bottle.

DR. WEISS: Dr. Krishnamurthy.

DR. KRISHNAMURTHY: I think this question sort of is moot because the problem is not the people buying the wrong thing; it's more of them using the wrong thing like more, so it is -- you can buy whatever you want, but the question is if you use it wrongly, that's where the problem is. And like others have mentioned, redesigning the carton maybe is not that easy. I mean, there is a lot of trademark stuff that we have to go through. You cannot change the color of the packaging just like that and lose so much of the market branding that has been accumulated over the years. So I don't think like that there is a solution that needs to be speaking to a problem that is not a problem in the first place. I think it's more in the use rather than the purchase.

DR. WEISS: Dr. Lee.

DR. LEE: Yeah. And I think the industry is already doing some of this differentiation with a purple box and a green box; it's just that it's not consistent across different manufacturers, and sometimes that's causing more confusion. So as long as there's some consistency with the purple and green, I think that addresses (a).

DR. WEISS: Dr. Rimal.

DR. RIMAL: I agree. I agree. I think standardizing the container in some way, whether it's color or feel or shape or something, will go a long way.

DR. WEISS: Mr. Delost.

MR. DELOST: Kort Delost.

I agree with the rest of them, that (a) is the way to go. I just want to comment on the (b) part since I run a pharmacy and know how, you know, the products are placed. There is continued -- continuing to use the voluntary industry -- talking about planograms, things like that, I think it's got an importance to still work together, but it does not have the effects. As soon as someone orders -- hands on, it's all over.

DR. WEISS: This is Jayne Weiss.

I would agree that (b) and (c) are not practical. I would also agree that it would be nice if we could make the color or something unique about the hydrogen peroxide carton uniform among all companies selling this, but I don't know that that's possible because I would assume that the companies want to distinguish the colors from each other. But if they were all black or some unusual color which you could spot them, that would make it easier for the consumer.

Dr. Owsley.

DR. OWSLEY: I agree with everything previous, and I'd like to add that on (a), from my perspective, if I was a contact lens user and I went to the shelf and I wanted to make sure that I was either not buying a hydrogen peroxide product or I was buying one, I think that that labeling on the package needs to be much more prominent than it is in current product -- current packaging, at least the ones I've seen recently.

And then with respect to (c), it not only would be particularly burdensome if it was the case that it was only sold at contact lens practitioners, but it would just be devastating. For example, I live in a state with about 20, 25% percent of the counties having no optometrists and no ophthalmologists, so it would just be a huge barrier.

DR. WEISS: Dr. Yin.

DR. YIN: Shonna Yin from NYU.

I agree with others that it would be important to have some sort of -- I mean, to create -- if we could have some sort of uniformity in the color so you could really distinguish between the hydrogen peroxide products and others, and also to have the word "hydrogen peroxide" be much more prominent on labeling.

As for (b), I mean, I understand that it would be difficult to enforce this, but if we could even recommend that if people had the power to do this, that they could do it, that might go a long way in people changing some of their practices and making things safer for patients.

DR. WEISS: Dr. Wolf.

DR. WOLF: Just to be quick. I agree, just absolutely underscore (b) and (c) being impractical and not to fit what needs to be, and I agree with (a) without getting into the thick of it.

DR. WEISS: Dr. Sneed.

DR. SNEED: The only thing that I would add would be maybe change and put the hydrogen peroxide information at the top so that it gets a little bit more visibility because it is kind of small. And I know they're focusing on Clear Care, as that being their trade name or whatever, but if they could emphasize the hydrogen peroxide system, that might be less confusing.

DR. WEISS: So what you're saying is maybe if a certain font was suggested so that it would be front and center for all manufacturers if you had hydrogen peroxide?

DR. SNEED: Right. And maybe if it's at the top of the box, you know, it's a little bit bigger, but it's at the top of the box, so that's the first thing you see, rather than, you know, it kind of blends in a little bit more when it's separate.

DR. WEISS: Dr. Kreps.

DR. KREPS: I'm going to break the rules. I think that (a) is a good idea, but I don't

think it's sufficient. I want to do (a) and (d). We haven't talked about (d) yet, and (d) is that I think we need to come up with a multiple communication strategy for alerting people. And so I think health education is a critical piece here, so I'm going to recommend the first one, with (a) I think we need to say hydrogen peroxide in big letters, just as Shonna was saying, so people are alerted, but that's not going to be enough. I think we need to do a multi-channel communication, warning people about the nature of the product, warnings about the product, and educate them, particularly at point of purchase.

And I want to recommend two different ways, but that's assuming not all of them. One way is that I think we need to train optometrists or ophthalmologists and others to educate their patients when they refer them for these products and tell them clearly and powerfully about the risks and strategies and warnings about what to choose and how to use it.

And then I think you need to utilize multimedia. I'd love to see, as I suggested earlier, videos that would be available to patients at the point of referral so they can get more information and then make that information available to them through social media so they can get them when they want them and refer back to it over time. And maybe even send them regular warnings and recommendations about products and to make sure that they are on track and keep the information. But I don't think you can put this all into one channel, and labeling is not going to do it by itself.

DR. WEISS: Dr. Dillard.

DR. DILLARD: Thank you. I'll join with the table here in seeing options (b) and (c) as impractical, although like Gary, I'm open to (d) because it's what's in the unopened box. As for (a), if I were king, I would make all the bottles brown, I'd make them square, and I'd make them tippled so that they are different on every possible dimension from the other lens care products. I think that that solves part of the problem of this Question No. 2 that's

in front of us here, but it also goes some distance towards solving the next question that we're up against.

DR. WEISS: Dr. Dahr.

DR. DAHR: Sam Dahr.

I think I echo everyone else's comments on color. I've been looking, over the past hour, online at some of the different contact lens solutions available. It's interesting that Alcon makes their multipurpose solutions green and the peroxide solutions blue, but then when you look at other brands and other types of solutions, you'll see multipurpose solutions that are blue cartons, you'll see saline solutions that are blue cartons, and the cartons are very confusing. And so if we could give some guidance to industry with regards to some color standardization, not even just for multipurpose versus peroxide, but even including saline solution bottles, including rewetting bottles, some sort of color coding, I think that would be useful across the whole contact lens care solution spectrum.

With regards to (b), I think it's haphazard and difficult; it seems like industry is making some efforts on their own. It seems like it's going to be hard to guide or regulate in terms of (b).

With regards to (c) and (d), I agree with most of the rest of the Panel. Again, I think anything that makes it harder to get the solutions will actually result in noncompliance, reuse of old solution, and not replacing bottles in a timely way, so we don't want to restrict the ability of consumers to get these products because that would just encourage noncompliance.

DR. WEISS: Ms. Ellis.

MS. ELLIS: Annie Ellis.

I'm going to get back to this red strip again, because as a user of peroxide disinfection for over 20 years and seeing the changes that have come along, having the red

tip and this red thing on top has been helpful, and you know, I've got two chances to see that this product is different from my regular saline solution. If we can extend that to the carton and everyone can keep whatever colors they like when they, you know -- whatever scheme they like to sell it, but add a red strip on top. I'm going to borrow your warning, I'm going to borrow from the FDA's literature that I went online to look at and have something like a warning, "Contains hydrogen peroxide," and then these exact words: "To avoid injury, follow all instructions." And if that could be standardized across the industry with all the products, maybe, you know, placement on a shelf might not be as important, and it's kind of hard to enforce.

As far as (b), good luck; (c) and (d), sitting here and as someone who has experienced accidental use, I mean straight in the eye, I was reaching for saline, but seeing that the benefit of avoiding bacteria that could cause blindness, which is not reversible, versus short-term extreme excruciating pain, I don't want any barriers to my having to access something that's going to contribute to my eye health. I don't want to wait in line, I don't want to show my ID like I do with Sudafed and feel like a criminal every time I have allergies.

(Laughter.)

MS. ELLIS: And as far as, you know, I've traveled this whole week. You know, if it's only available at a practitioner's office, how am I going to have 24-hour access, you know, when the stores are closed or I had to leave it at TSA because they took it out of my bag or I just ran out and I didn't plan. I'm buying for two in my house. Are they going to take that into account as well, if these kinds of things are implemented? So as a Patient Representative, I am against any access -- any barriers to my access.

DR. WEISS: Ms. Witczak.

MS. WITCZAK: Kim Witczak.

I would say, for me, I agree with the red line or some kind of identification on the box, and then we'll get into the bottle the next, and also hydrogen peroxide being up in the prominent. But I would also -- and then that warning, just to keep it all consistent and everybody kind of -- across whatever brand. Generics as well. But I would also, because as someone who does work with a lot of stores in the marketing area, I don't know if you've ever actually invited the Walmarts, the Kmarts, and the Walgreens into these meetings and not have to rely on industry to do some of that work on planogram. You know, we do -- it would be interesting to hear from, not just a letter, but to hear why it's needed or, you know, even if it's -- just even everybody can do it their own way within the different brands, whether Walmart, whatnot, but they're always looking at new ways, and it's important to them for their own consumers.

So I think I would encourage the FDA to help the industry on this one and not leave it to them because, of course, they're going to see it as just wanting to get better placement on the shelves. But there's a consumer need for this, and I do think there is a way to organize it, hydrogen peroxide, and I think by having some kind of identification on the box, that might just naturally do it because it will just look better visually. And as much I would love the idea of Sudafed, it's annoying for me to have to go as a consumer, and I hear that all the time, so I think -- and I do think that's just something to think about.

DR. WEISS: Mr. Pfleger.

MR. PFLEGER: So I think it's reasonable to ask the industry to work with the Agency about what can be done to flag at the shelf that this is hydrogen peroxide. So I think there are things that can be done, and you've heard from some of the companies that they're willing to do that, so I think one can be done. Changing the color scheme of the product. I think you're going to have a difficult time getting all companies to agree to become generic in a non-generic category. But something to make it clear to people, if they're reading

anything, which is a big "if" on some of the complaints we've seen, I think that's a doable thing.

So number two will be here. I think continuing to ask the manufacturers, say look, do what you can to work with the planogram systems to try and group the hydrogen peroxides together. That's not an unreasonable thing for industry to keep trying to do, recognizing that we don't control that final decision; that's up to the individual pharmacy and companies that sell it.

(c)'s a non-starter. Even from a practical standpoint, it isn't -- you know, which doctors' offices has, you know, a loading dock for cartons and cartons and cartons of hydrogen peroxide, where are they going to put it, how are they going to handle the volume, recognizing the fact that there are -- you know, it's oftentimes not convenient at all. And unless doctors want to stay open 24 hours, 7 days a week like Walmart, you're going to have people who are going to have problems with compliance because they won't be able to access.

DR. WEISS: So Dr. Booker (ph.) or Dr. Eydelman and Ms. Duckhorn, with regard to Question 2, the Panel generally and completely believes that option (c), for sale only at offices of contact lens practitioners, was not advisable. There was a minority that thought the placement of hydrogen peroxide care products separate from other contact lens products would be advisable, and I think the majority felt that redesigning the carton label so that there will be a larger warning label, it would be front and center, there would be a larger font saying hydrogen peroxide, and optimally, to have the same color carton or some uniformity between all hydrogen peroxides seemed to be endorsed by the majority.

Was there anything else that you would like us to address on Question No. 2?

MS. DUCKHORN: No, thank you.

DR. WEISS: Question No. 3.

(Off microphone comments.)

DR. WEISS: Sorry, Dr. Sneed. Please.

DR. SNEED: That's okay, thank you. Jeannie Sneed.

As I was listening to the discussion, it apparently -- and the ophthalmologists can -- but apparently, this is the most effective cleaning mechanism or a highly recommended one. What I want to make sure is that when we think about the recommendations and when FDA thinks about them, that we don't get so warning heavy that people don't balance out the fact that it's a really good product. And so to me, knowing how I value my eyesight, if I picked up this box and the very first thing I saw was a warning, then I might think, oh, well, maybe I better look at something else. So I just want to make sure that we keep that in perspective and make sure that that balance of efficacy and potential risk is understood.

DR. WEISS: Dr. Krishnamurthy, please.

DR. KRISHNAMURTHY: I heard that a lot of us want to distinguish the hydrogen peroxide somehow without necessarily changing the bottle color or the color of the carton. One way that could be done would be to have a brown kind of box with the hydrogen peroxide label that is used across all hydrogen peroxide cleaning products, likewise a different one for saline, and another one for the multipurpose. That way there will be some uniformity; even if their boxes get mixed up, people will be able to distinguish them in the aisle.

DR. WEISS: So I think what we've just heard from industry is it's not going to happen. Was my interpretation correct on that?

MR. PFLEGER: Correct. And also just as we go down, because I've heard the brown thing a number of times, we do not want to encourage people to go in and buy standard cleaning hydrogen peroxide and use it in any of these systems. That will cause problems.

DR. WEISS: And the whole idea of having, let's say, saline boxes one color where it's

a different label from different manufacturers and hydrogen peroxide bottle -- cartons, excuse me, cartons another color with distinct labels from different manufacturers, is that something that you think could happen in industry, or that's remote?

MR. PFLEGER: I think it's remote, and it's not just the industry; it's also the individual -- the Walmarts and Kmarts and Targets, they have their brands, and they have their own brand schemes that they use color-wise, etc., for their products. So it's going to be difficult to get all those people to agree on any one thing. You know, think about going to the cereal aisle, telling everybody who sells Raisin Bran that it's got to look exactly the same; that's going to be extremely difficult to do.

DR. WEISS: So for the FDA -- oh, Dr. McLeod and then Dr. Berube.

DR. McLEOD: So I guess just as an analogy, you know, and there's the no GMO label, you know, just sort of one box that has a logo that is identifiable across different brands, do you think there would be objection to a logo that's a peroxide logo?

MR. PFLEGER: So my point, and that's -- I was thinking that that would be one of the things we can talk about from the industry perspective with the Agency, is there something we can come up with that would say use -- doctors would be able to say instead of what -- today is hopefully, you know, go for this color box. It would be you have to use the product that has this across the label; something like that would be something I think we could work on.

DR. WEISS: Dr. Berube.

DR. BERUBE: Yeah, two comments. The first comment is there's a lot of waste to do creative packaging. I mean, this is overly simplistic that we just change the color. I mean, there are a lot of things you can do. I mean, I've watched people put odorants in packages, right? I mean, you can make the package smell differently if you want to. There's real creative ways of packaging, and it's not overly complex to do this stuff, and I mean, I don't

see, you know, why this -- that this becomes such a thorny problem. I mean, we do all -- you talked about the cereal aisles. You think you can smell all those cereals; you think you actually smell the cereal that's in a hermetically sealed package? Of course you're not. You smell the packaging. That's what you smell, right? And if they can do it, why can't we do it, you know, in something as easy as this? So there's a lot of really creative ways of doing this, and I think we're just -- we just got to get out of this '50s, '60s, '70s mindset about how we used to market stuff because it's just changed dramatically.

DR. WEISS: FDA, are you good with our final answers on Question No. 2?

DR. EYDELMAN: Yes, 3, yes. Thank you.

UNIDENTIFIED SPEAKER: No, 2.

DR. WEISS: And now we're going on to Question No. 3: What are the panel's recommendations for reducing the risks of misuse of peroxide based contact lens care products once purchased? Please consider the following in your discussions.

And some of us have mentioned this, but we'll use this as a way to summarize.

a) Redesigning the bottle size, shape and color to alert the consumer that it is not the same as saline or other contact lens products.

b) Redesigning the case and bottle to be functionally dependent (the peroxide cannot be released unless directly and physically connected to the special neutralization case).

Just to be a little bit creative, we'll start with Dr. Owsley, go on that side, and then start here and go on back.

DR. OWSLEY: Okay, Cynthia Owsley.

On (a), I'm in agreement with a lot of other comments on this in the earlier sessions, that making the bottle itself distinct would be useful. In particular, what I didn't really learn this morning, and I'm not a contact lens user, so I don't know whether this is true, to what

extent are the bottles for hydrogen peroxide products different than the multi-use products? It seems like that's where the huge distinction needs to be, but I didn't see examples, so I don't know, well, maybe they are really different already. So that would just be one issue that I think would somehow need to be analyzed.

And then secondly, redesigning the case and bottle to be functionally dependent sounds like a great idea, but not being an expert in the design of a product such as that it's hard for me to weigh in. What I would not want is a very costly solution which is then passed on to the consumer because, as we said earlier and I think everyone agrees, these hydrogen peroxide products are preferred products for many consumers, so we don't want to discourage their use.

DR. WEISS: Dr. Yin.

DR. YIN: This is Shonna Yin.

I absolutely agree with what Dr. Owsley just said about -- I think it would be very helpful to make the bottle very distinctly different for the hydrogen peroxide versus other products, and I agree that I wouldn't want the cost to be a barrier to access.

DR. WEISS: Dr. Wolf.

DR. WOLF: Agree with (a) and how to get there. I think there should be innovation around that. (b), again, yeah, I think I would completely agree that I would not want a product that is so widely available and in need and in demand to -- I would imagine that that would -- that just seems like it would be yet another barrier, so I would probably vote no to (b).

DR. WEISS: Dr. Sneed.

DR. SNEED: I don't really have anything to add. Thank you.

DR. WEISS: Dr. Kreps.

DR. KREPS: Gary Kreps.

I was very influenced by Terry Fairbanks's presentation, and as what Jim mentioned earlier, I really think we need to design a bottle that cannot be -- a peroxide solution that cannot be used and applied to the eye so we don't have to kind of convince people other than just you can't do it. And in the same vein, I like the idea of (b), of redesigning the bottle so that it will be used appropriately with the right receptacle.

DR. WEISS: Dr. Dillard.

DR. DILLARD: I want to also endorse the design solution. (b) is a specific case of that, but there might be many other ways in which bottles could be created, as Dr. Fairbanks suggested, that would prevent people from being able to do it, and if they -- even if there isn't an ability issue, there are certainly ways to design bottles like this one. I never look at this, this hole and think, oh, I should pour that in my eye. So even just a big hole might signal to people that it's not for that purpose.

DR. WEISS: Dr. Dahr.

DR. DAHR: I'll make a comment on (b) and then skip to (a), if that's okay. With regards to (b), I think it's conceptually very attractive, but again, as has been mentioned, would it be cost efficient? These are cost-sensitive products, and so we really don't want to add to their cost. Also, if we had any type of product where there's a special hookup between the bottle of solution and the case, could that in any way penalize people with a disability or with a tremor or with low dexterity? So it might be tough from a practical point of view to implement.

With regards to (a), I just have a few comments. Number one, it's been discussed about smartphone solutions and scanning QR codes and such, and I think there is a portion of the population that uses those tools very well, but there's a large proportion of the population that either doesn't want to use those tools or can't use them very well, and so I would favor more low-technology approaches.

With regards to usability and color coding and such, I think those are options that should be explored. We had a very nice talk in the morning about usability. I'm not the usability expert, but if there are ways to change the tactile feel of the bottle or change the way that the bottle pours in a way that signifies that bottle is not a squirt bottle, it's a bottle where the solution is meant to be poured into the case, those are all usability design considerations that should be looked at.

In Question No. 2, we looked at colors for the carton, and I would just make the point that if some sort of color coding is encouraged for the carton, I would recommend that that color coding also be carried on to the bottles inside the carton and even to the cases. So, for example, we've talked about red tips for the peroxide bottle; maybe the case of the neutralization cassette could be red as well, so that they match. Maybe if green is chosen for multipurpose solutions, maybe we could encourage that flat contact lens cases have a green top or some sort of green dot on them, some sort of consistency both going from the carton to the bottles and cases inside the cartons.

And then lastly, anything I think can be done to -- we've talked about the busyness of the text inside this case, and anything that can be done from a regulatory or guidance point of view to reduce the small font text and maybe allow two or three infographics that are cross-cultural, cross-language, I think that's helpful as well.

DR. WEISS: Ms. Ellis.

MS. ELLIS: Yes, I'm Annie Ellis.

Just very quickly, over the 20 years that I've used these products, there is no difference in the bottles. I mean, they all look so much the same that from a layperson, like I would think you're getting them all from the same place. But I think it's really important that they look different somehow because with accidental misuse, we're talking about people at their most vulnerable and their most tired. It's first thing in the morning or last

thing at night when people may not be alert or thinking clearly or inebriated or, you know, whatever. So making it easy to distinguish between the products would be very helpful. I don't know what that answer is.

And also, as we're thinking about this, that travel sizes and portability need to, you know, have that same signals or, you know, the same formats that come out of this. And if we go on to (b) and that's considered, it does need to be easy to use for the consumer.

DR. WEISS: Ms. Witczak.

MS. WITCZAK: I'm going to reiterate some of the same points. As somebody who's worn them for 20-some years, I happen to be -- I did start out with the system, and I moved to the multipurpose. But I'm going to say that the bottles are the same, and if it's -- and I liked the presentation, and I also liked that example of the act is really simple. It might be something for the industry, and it's a challenge to them, but, you know, maybe it's as simple as the top, so it's not a whole -- you know, from an expense standpoint. So that's a manufacturing thing.

But I do also think that color should be -- if we're going to do whatever it is on the box, it has to be on the inside because people aren't going to see it. The same with the type and a lot of the same comments I made earlier about what's on the box. But I do think it would be nice because in the morning they feel the same; you go to someone's house, they look the same. And so that would be my comments.

MR. PFLEGER: So Michael Pfleger.

So just a thought in terms of, you know, consistency has its virtue, and simple is also a virtue. Would someone come to something that's being adopted already, which is red cap, red tip means don't put it in your eye. And, you know, I don't think perhaps the message has gotten out to all contact lens wearers that that's what red means. You know, we do in the ophthalmology side with drugs, individual colored caps mean specific things

for this industry. You know, something as simple as a red cap, red tip means don't put that in your eye. That's something that's already been agreed to and is being done. So perhaps, you know, rather than thinking of, well, let's try and come up with other things that may do the same thing, one consistent message would be a lot better and much more efficient and quite frankly less costly. So I think if you ask everybody to change their bottle to some other shape beyond round, you're going to come up with a bunch of other bottle shapes, and you won't have achieved anything. So, again, I would emphasize if we can just spread the message that red means stop, don't put it in your eye, you know, hopefully we have the opportunity then to influence behavior.

The second thing is on (b), you know, it's not that industry hasn't thought of these kinds of things. There have been projects over the years by multiple companies, and there are projects today by companies, as you heard today, to try and figure out -- if you have an idiot-proof way of using hydrogen peroxide. The problem is it's not simple. Something like that is nice and attractive, but all it does is gurgle some product up that you dump into a cup. That's not what this product does. It's a medical device. It has to clean and disinfect those contact lenses that are in that case. So it's not just a matter of getting the juice into there and leaving it alone; there are other aspects of it as well. Everything you do has an impact on all of that.

And so I just want to throw a little cold water on the idea that there's a simple solution. Millions of dollars have been spent trying to come up with one, and it hasn't been achieved yet. Someone who does will gain a large market share.

DR. WEISS: We're going to go on with (a) and (b) before we come back. I appreciate you pouring some cold water on it because it's not going to be beneficial to the FDA for us to come up with a wonderful idea that's not going to be able to take place.

What I see is that there are three different problems, and I don't know that there's

one solution for the three different problems. One is grabbing the wrong bottle, even if you're informed, but grabbing the wrong bottle. The second one is using the wrong case. The third one is using the right case and the right bottle, but taking it out too soon. None of the things that I know of that we're talking about right now address all three of them. I think there are three different things that we need. I would endorse a rectangular bottle, but I know it's not going to happen, so I would endorse something very distinctly different, but that's not going to happen, so I'm not going to give you anything that's beneficial. With that in mind, I'm willing to listen to Lost. Maybe he will.

MR. DELOST: No such luck. No, anyway, I do like the idea of what we talked about earlier, the gentleman this morning that had all the great ideas about, you know, the gas pump, things that have to fit, but it has to be technology that's driven by the manufacturer, that it's cost effective, that it doesn't drive the cost up to the consumer. If you guys can achieve that, more power to you.

DR. WEISS: Dr. Rimal.

DR. RIMAL: I think I keep coming back to the idea someone mentioned about, you know, we're finding solutions for people who are visually impaired or challenged, and relying on something that's overtly visual seems kind of not quite the right approach. So I was thinking, you know, maybe there's some way of -- even if you put little bars on the bottle so that when you hold it, you can feel the grooves, and over time you come to be socialized to know that, ah, okay, so that's this product. And it may not be, you know, here's the expensive thing to do, but something like that, I would be biased towards a solution something like that.

DR. WEISS: Dr. Lee.

DR. LEE: Yeah, I think if we're going -- they have to be really obviously different, so whether you're tired or drunk or whatever, that tactilely it feels different, you know.

(Laughter.)

DR. LEE: And regarding number (b), I think it's going to add cost, but at the same time, I think whatever innovation surfaces from the industry should be standardized and not just for one company to take advantage.

DR. WEISS: Dr. Krishnamurthy.

DR. KRISHNAMURTHY: I'm going to heat up the water a little bit here. So I agree that by the cost and completely because hydrogen peroxide is more expensive and people are buying it, so -- but I do think it is important to find some way of marketing the red cap idea because if that is what the industry is gravitating to, then there is some way, shape, or form that the consumers can be advised that it means you don't put it in because it's already been adopted, and I think that is certainly something to consider.

And also, one other thing that I was thinking, and I don't know how practical this is, is to have a bottle that cannot dispense straight into the eyes through gravity or something like that, some kind of a side spout rather than straight down. I do not know; I'm not a design specialist, and I did -- there are professional designers who can kind of come up with different solutions.

But I do think, as a principle at least, industry must embrace some idea that, you know, the bottle has to be different if it is going to create a very painful sensation for the consumer if it is going to be used in a context that is similar to another product that's just not distinct.

DR. WEISS: We're going to have everyone have their first chance to speak, and then we can have comments after that.

Dr. Blalock.

DR. BERUBE: No, it's my turn.

DR. WEISS: Oh. Sorry, Dr. Berube.

DR. BERUBE: I'm the design guy here.

(Laughter.)

DR. BERUBE: Yeah, I listened to Fairbanks and Cohen and Moro closely, and I mean, I know how the design world works, and we have a college of design, and I work with them, and one of the variables we put in the formula is cost. So when we have design camp and we throw a project at a bunch of grad students, we don't tell them make something that's incredibly -- we don't care about the cost. We tell them this is what you're dealing with, this is what has to be done, and let's see what happens.

And I think there are approaches we can take here. I think if the importance of this subject of safety for these consumers is significant enough, then we should make some effort to go beyond the traditional, oh, I'm not sure, this might be costly, because that's how we got stuck with the internal combustion engine, right? I think we can do better here.

I think what I would do is I would take this project, I would throw it at a design camp, and I would say find a way to attach this case to this bottle, find a way to make it efficacious and cost effective, and see what happens. I would take your best people, and I would bring in some really smart students, and have them go. I direct an international genetically engineered machine competition, and I can't tell you what these kids will come up with, right? These are very smart folks; they can come up with ways of doing this. Then I would tell them make sure you get a TSA version so you have both ends covered. And make sure, you know, it's sufficient with this, sufficient efficacy so people who have impaired mobility can use it. These are things these students do; these are things that designers do for a living. I mean, the stuff that comes out of design, it is costly at some level, but there often are benefits in the long term that I think we have to consider.

The second problem of design often is not physical, right? The second problem of

design is you need to de-routinize the process by which people use this product. What happened is the product was designed to parallel what was already on the market, and in the process of doing this, it fed a whole bunch of misunderstanding. Now, that's just a bunch of people sitting in a room with focus groups going, how can we change the routine here? How can we adjust the routine in such a way that the routine is sufficiently unique so you don't confuse it with another routine? And that is not big money; that's just brain power.

And I think when we look at the solution to this problem -- I said it was multi-pronged -- I think the first prong, one of the prongs was labels, I grant you that. I think another prong is design, and I think you need to do at least both those.

DR. WEISS: Dr. Blalock.

DR. BLALOCK: Sue Blalock.

You know, I pretty much agree with that. I certainly share the concerns about we don't want to price this -- you know, pass these prices on to consumers in a way that makes the product, you know, less accessible. And I know that we don't live in a world where there are infinite resources, but I would actually say, yeah, I know that we were asked to link, you know, these various questions. But I would actually argue against spending a lot more money on figuring how to make the label better and focus those resources on how to make the product so the use of the products are more distinguishable.

And, you know, someone else said anything -- part of the reason why the red cap doesn't do much for me, in the experience of just everyday life, I come across different things that I see, and I say I know this means something to someone, but I don't know the message that it was meant to convey to me, and that's why I'm just not sure how well that red cap is understood universally.

And, in addition, things that -- you know, if you're reaching for something when

you're tired -- I'm not going to say drunk.

(Laughter.)

DR. BLALOCK: When you're tired, when the bathroom is dark, you don't want to -- you want it to feel different. You don't want it to look different; you want it to feel different, and you want to say, oh, that's not my multipurpose solution, that's my dog, you know. But you really want it to be --

(Laughter.)

DR. BLALOCK: You want it to, you know, alert you instead of -- and it kicks you out of automatic pilot. So I definitely -- you know, I really believe that if we're going to make -- I think we've already probably gained as much as we can by improving the label, and that if there's more to be spent, it should be spent more on number three.

DR. WEISS: Dr. Jeng.

DR. JENG: Bennie Jeng.

So, many years ago, I think we all know, asthmatics used to carry around their agonists and their steroids in the MDIs, and you'd shake it, you'd put it in water to see if it floated, and you're never sure how many of those 120 actuations are left in there. And people would say why wouldn't there just be a counter? And so now they all come with counters, and at some point there was an investment, a one-time investment to make it work, and now it's been long-term dividends. So I'm sure it saved lives because why would you have a rescue medicine not have a counter on it?

Okay. So I think this is one of those situations where, yes, there's going to be cost, but it's going to have long-term positive ramifications, and it doesn't have to be expensive. I think that, you know, we're talking about tactile feel, shape, keeping the bottle and not having it square. I mean, it's as simple as just having a different maneuver to the top. I mean, I know that there are issues with like the material or the bottle and whether it

leaches out, you know the active ingredients or not. And so there's a lot of R&D that has to go into that. But if you're just talking about the top, you know, whether it's a squirt bottle but it looks like the tip of an eye dropper versus, you know, you see one of those carafes at a cafe where you turn the top and it releases, opens up a little bit and then you have to pour it, I mean, it could be simply one of those things where the top is you just twist it a little bit and you decant it, but it's not a big decant like you drink water out of it but something simple like that, widespread and consistent, a one-time literal investment, and long-term it won't cost very much, but it will be beneficial.

DR. WEISS: Dr. Huang.

DR. HUANG: Yeah, I'm a little bit philosophical. And this is Andrew Huang.

What happened is, you know, I mean, the root of the problem is that we use the contact lens. So if we don't use the contact lens without this problem, right, so then why don't we just use the disposable contact lens? But you know it's not going to happen. Some people cannot, you know, afford it. Some people have various ocular serious conditions, so they cannot use. So this problem is going to stick with us.

So I concur with Dr. Jeng, you know, in a sense there's an investment, and what happened is -- happened in the contact lens. Many years ago we only have a glass, you know, the original contact lens was glass using 17, 18 centuries. That was the way to improve the cosmetic or improve the vision, and over the years people improved the material -- and then reached gas permeable and then soft lenses, then the corneal arterial, and then so on, so forth. So every little improvement led to now, you know, you can have this device.

So I think, you know, that even though it may be some spray, a dry stick or maybe not even so dry stick, you know, it's a big investment. I still think it's worth pursuing because, you know, the bonus or the benefit down the road, you know, it may not be

foreseeable. And I still agree with, you know, Dr. Dahr's opinion that it may have to be high tech because, you know, you can put computer chips, and it's going to break the bank of the industry; I don't think anybody wants that.

But on the other hand, we may think about, hey, why don't we put, you know, food coloring or some sort of a color indicator in the solution to alert the consumers? Whether it addresses all the three points Dr. Weiss mentioned, you know, in terms of the safety, you can still buy the wrong solution; you can still put in the wrong solution. But it's, I mean, an increment improvement. But in the long run, I think, you know, I mean down the road, I think we're going to realize, you know, that if the safety is our ultimate goal, you know, I think the investment down the road is going to be paid off.

And especially, I hate to say this, but hydrogen peroxide is so cheap, okay, I mean, the Boy Scouts, sometimes they run out of hydrogen peroxide solution, they use the brown bottle to dilute, you know, they use them. It is 10% versus 3%, yeah. And then that on the market, at this moment, hydrogen peroxide product is much more expensive than the multipurpose solution, and I just don't see why the industry cannot spare, you know, a few more dollars and cents, you know, to improve the safety if this is going to be the product that we're going to use in the long run.

DR. WEISS: Dr. McLeod.

DR. McLEOD: So I think we've been gravitating to (a), and I would have to say that I'm just not convinced that the red cap has been successful or that this problem will be solved just by education, and I think we've heard a lot about why that might be. So I do think there is something else that should be done, but of course, everything within reason. And I'm sure that with clever design, as has been brought up today, that there's something in the realm of 3a that will work.

I think 3b is really just a subset of 3a, to some extent. I would caution against

prescribing a particular route in a forum like this, particularly with that particular approach, which is a contact approach. One of the big problems that we have with contact lens infection is the microbiome that will develop inside a contact lens case. It turns out that peroxide systems are actually far better than the alternatives in terms of protecting against these microbiome films. But even in the peroxide systems, you know, there are some studies that have found that between the platinum disc and the base of the case, you can on occasion recover bacteria from people, organisms from people who are particularly badly behaved about their management.

So, by definition, any contact device, there's a non-zero probability of contamination that could get back into the solution, so I would just caution that we might not go down the route of prescribing that particular solution, but something creative, I think, is opportunity.

DR. WEISS: Were there any members who wanted to make an additional comment?

Yes, Ms. Duckhorn.

MS. DUCKHORN: So my question is for our Industry Rep. I realize you said that it isn't as simple as just kind of getting the juice, as you called it, into the top, and maybe I'm oversimplifying, and again, forgetting this top piece, but if this piece just goes into here, is it just not that simple?

MR. PFLEGER: No.

MS. DUCKHORN: Okay.

MR. PFLEGER: If it was that simple, it would have been done years ago. So you've got to remember what this product does, right? So it's cleaning and disinfecting. So anyone who has cleaned dishes at home knows that when you spray the spray portion of your nozzle, right, versus the just single stream, big heavy stream, you remove a lot more debris from the pan. So think about the same thing. When you're spraying the contact lens with the bottle when it's in that case, before you put it in the solution, you're doing part of the

cleaning step. Part of the cleaning step also adds to the micro-efficacy of the product.

So as I said, if it was simple, we'd already have a good solution. There are people who are working and spending money on projects because, as we all know, technical innovation leaps lead to huge market share gains. And so I think, from the standpoint of the suggestion that industry should spend money, I think industry is spending money. No one has gotten there yet, but will some? I think in most things, eventually you get a good, technologically acceptable solution. What you don't want to do is decrease the efficacy of the peroxide, which is the major benefit of having that product available today, to try and help a small number of patients at the cost of efficacy for millions of patients. So it's a balance that we have to look at for every kind of change that we try and do as an industry.

MS. DUCKHORN: So I guess I want to be clear that I'm asking the right question. So not just sticking this in here, the act of squeezing it up and having it sort of swish around as if it -- depending on where I guess it comes from, that doesn't count as sort of the spray part of it?

MR. PFLEGER: It's not going to be anywhere near as efficient.

MS. DUCKHORN: As spraying.

MR. PFLEGER: Yes.

MS. DUCKHORN: Okay. Thank you.

DR. WEISS: Dr. Kreps and then Dr. Krishnamurthy.

DR. KREPS: And I forgot to mention that I like the product that was demonstrated with the smart bottle with a warning system as a way of providing information to guide our decision making. If it can be implemented easily and inexpensively, I think that can be a really good source of health information for guiding good decision making of the use of these products.

DR. WEISS: And just a personal comment on that. I think that sort of elucidates the

different issues of the no disc, the using it for an insufficient amount of time and using the wrong bottle, it could address some but not all of the issues.

Dr. Krishnamurthy.

DR. KRISHNAMURTHY: Yes, I am very much in tune with the industry's concerns that we don't want the costs to go up. Or also, Dr. Dahr was talking about the importance of when you redesign something, you cannot make it difficult for people to use it. So these limitations and these concerns taken into account, it is really not true that everything that can be done has been done and therefore there is nothing further than can be done.

And I like Dr. Berube's idea that throw this to a design school and see what people can come up with. And I would think that there are always ways of doing things better than what is being done right now, but also, we do keep in mind the idea that hydrogen peroxide is the best, most efficacious method, and Dr. Weiss mentioned earlier on, and Dr. Berube mentioned it as well, that we don't want the labeling to be so stark and so dark that it causes people to not use the product in the first place, which would be a bad tradeoff to have. So keeping all these things in mind, I do think it is possible to look at simple labeling solutions and perhaps slightly different design solutions that you alert people to inadvertent use of a product that is very helpful to the consumer.

DR. WEISS: Do any members of the Panel have any other comments?

Yes, Mr. Delost.

MR. DELOST: Kort Delost.

I'd just like to direct this to Michael Pfleger, is it?

MR. PFLEGER: Yes.

MR. DELOST: Okay. I love the fact that when you make design changes and do innovation, it's always done voluntarily with industry versus having it mandated by a government agency. So if we can get maybe a commitment to have you guys at least look

at design changes down the road and --

MR. PFLEGER: So I think you heard from some people or from the industry side today. People are doing projects today.

MR. DELOST: And then lead as focus groups and standardizing across the industry.

MR. PFLEGER: So I think anytime you say standardization, when you go to, you know, iPhone and tell Apple they have to provide their innovation that just made them very successful to another company --

MR. DELOST: I'm just talking the bottle shape.

MR. PFLEGER: Again, there are lawsuits with Apple's shape of their case. So I think you just have to be realistic about what's doable in an area where there are lots of different players, and there are lots of different people who have different views of what marketing should and shouldn't be.

MR. DELOST: Okay. So keep trying.

DR. WEISS: Any other members of the Panel with comments on this question?

Dr. McLeod.

DR. McLEOD: I just wanted to just put up one word of caution in terms of the concept of -- which is very interesting, of de-routinization of the process, which, you know, contact lens wearers are an interesting group. Even that small change of going from rub it three times to you don't have to rub your lens at all, it's amazing just how transformational people thought that they -- you know, not having to rub their contact lenses anymore because people really hate, you know, just doing it for a few seconds. And so, you know, unfortunately, compliance does tend to fall off with any addition of a break in routine or anything that seems that it adds a little bit, and so I think that has to be borne in mind, and of course, that's something that does play out in the testing process.

DR. WEISS: Mr. Berube. Dr. Berube. Sorry.

DR. BERUBE: Yeah, that's not in the literature. That's not just the literature, I'm sorry. The routinization techniques that you can use to establish due protocol, especially with the industry, we discovered in many applications, and there's good literature out there that when you do routinize, you actually increase compliance. And I think it has to do with the age of the user as well. I mean, if you have a reluctant -- user, you can expect them to be much more unlikely to adopt a change in routine, but younger populations tend to accept routine changes quite easily.

DR. WEISS: Yeah, I would also probably second what Dr. McLeod says. In terms of the contact lens users that I've taken care of, people want things simple, quick, simple. One step is better than two; three-step isn't going to get done. So anything that will add to complexity will lower compliance, and I think that's part of our issue.

I was kind; you don't think I'm being kind, but I was kind. I didn't query the Panel as far as how many of us read labels. I see some smiles, so you can take that for what that is. How many of us have put hydrogen peroxide in -- how many of us who have used hydrogen peroxide systems have done this at one point?

So I think people move quickly nowadays. They don't read. They want the message in 3 seconds, maybe less than that, and I think that's part of what we're dealing with, which is why we're trying to come up with these other modes of doing it.

Any other comments on this question?

(No response.)

DR. WEISS: So for Dr. Booker, Dr. Eydelman, and Ms. Duckhorn, the Panel on Question 3 seems to endorse making a change in either the bottle, texture of the bottle, shape, and the bottle size. It seemed that there were many on the Panel who are less impressed whether the red top really was understood by the patients, and there was some interest in redesigning the case and the bottle to be function-dependent if that was not

cost-prohibitive and it was possible to do. Yet, at the same time, I think we heard from industry that many of these things are not likely to happen.

On that note, we can take a 10-minute break. It's 2:33. We'll meet back here at 2:43. I did want to make an announcement to members of the Panel who ate in the restaurant, and maybe some of the others who ate in the restaurant: Check to see if you took your credit card with you because they have some extra credit cards there.

(Laughter.)

MS. ASEFA: Also, if you need transportation, please see AnnMarie Williams at the registration desk. Thank you.

(Off the record at 2:33 p.m.)

(On the record at 2:46 p.m.)

DR. WEISS: We're going to go on to our last question, Question 4. What are the panel's recommendations for how we can better engage contact lens consumers, advocacy groups, professional organizations, and industry to promote improved compliance with instructions for use for contact lens regimens?

Mr. Pfleger, can I start with you? I think your microphone may be off.

MR. PFLEGER: I'm sorry.

DR. WEISS: If you could just give your name.

MR. PFLEGER: Michael Pfleger.

So I think, you know, industry -- the speakers today in general, I know, have expressed willingness to listen to any ideas about what can be done better for communication. I think there are a lot of things being done, but there's a clear willingness to do more, so we will listen attentively.

DR. WEISS: Ms. Witczak.

MS. WITCZAK: Kim Witczak.

So I had suggested earlier that idea of retailers, you know, and I don't know if that's the FDA, and I know this is very public, that you guys are already having this meeting, but maybe it's something that the retailers can -- or the industry can meet with the retailers and have FDA representatives to help understand what the problem is so that they can come up with solutions and how they want to display it. So that would be one idea, just for that piece.

I would say you have a lot of different consumer -- *Consumer Reports*, I know, does a very good job in educating the public with all the different -- whether it's online, the magazines, some of the organizations that are here that have large consumer populations that they represent. And then there's obviously the social media and things like that that FDA can continue to do, but the reality is I think it's going to have to be a joint effort because a lot of people don't necessarily go on the FDA's panel.

And I think also, going back to just using the eye doctors and the doctors that we go to, because there isn't a lot of communication, I don't -- I mean, I go every year, and a lot of people go every year to get their prescriptions checked, and there isn't a whole lot of conversation about the solution set themselves, so I would say to utilize some of that in the communication piece.

DR. WEISS: Ms. Ellis.

MS. ELLIS: Annie Ellis.

Before this meeting, I didn't realize how noncompliant I was in a lot of different areas and not just about an accidental, you know, experience that happened. I have various cups and, you know, disinfecting, neutralize. I think I have, I counted maybe 14 or 15 in our drawer. And that comes from -- you know, you're buying for two people, you get one or two in each box, and every time you travel you get one in the box and all along, things have changed, you know, the rules have changed. It used to be 90 days at one point; now it's 60

or 30. And so there is a need for awareness, especially for people who have been using this for a while and the product and the literature may have changed. You know, there was an opportunity every time you get your eyes checked, but what that should look like. I mean, I normally go in; what do you use? If I use multipurpose or a peroxide, I get a little bag, maybe a sample, some coupons, but I don't think I've ever been checked in, do you have, you know, any questions about using this, are you using this properly, and I don't know where the responsibility lies. I do know, from preparing for this meeting, that October is Contact Lens Safety Awareness Month, and maybe that might be an opportunity to get out there in the public PSAs, life-size cutouts, you know, the contact lens supplies. I don't know, but I know that noncompliance is a problem and awareness is a problem, and it depends on whether you're a new user or you've been using this so long that you don't even look at what you're grabbing.

DR. WEISS: Dr. Dahr.

DR. DAHR: My main point on number 4 would be we had a talk earlier in the morning about the use of focus groups and such, and I think focus groups would be helpful in terms of engaging consumers and figuring out what works for consumers once some decisions are made with regards to different labeling, different color, or different packages, etc. So I would encourage the use of focus groups.

And just a general point, I thought it was fascinating that, with regards to the MDRs, the average age was 42. You know, a 42-year-old wearing contact lenses has probably been wearing contact lenses for 20 years and is not a novice at wearing them, and at the same time is probably relatively healthy. And so it's interesting that that was sort of where the average age ended up for the MDRs. It might be a reporting issue in the sense that the 20-year-old who has had a few beers and been out celebrating St. Patrick's Day and put some peroxide in their eye doesn't fill out an MDR. But still, it is interesting, and again, I

think it's important to use the appropriate focus groups. Thank you.

DR. DILLARD: James Dillard.

When I reflect on my -- on a little bit of experience and the mistake that I made in 2014, it occurs to me that I might have benefited from simply knowing that there was more than one kind of system. I didn't know that at the time, and had I known and that one of those kinds might have done me harm, I think I would've been more cognizant of the product that I was using. That information probably should have come to me from my eye doctor and presumably could.

DR. WEISS: Dr. Kreps.

DR. KREPS: Gary Kreps.

I'm willing to build on what Sam said. I think that there is a very nice earlier presentation by Katie O'Callaghan about the recent reinvolvement programs, and I think that we should engage those kinds of programs to try to reach out. And I think there are three different ways that I would want to do it, and there's maybe four. You know, as a social scientist, I'm always big on data gathering, and I'd love to see some kind of data collection, so I mentioned focus groups, but maybe even a broader survey, maybe an online survey will save cost, to kind of get a sense of what people know and what they don't know about this issue.

And then that would drive the development of a campaign that you could develop, utilizing a variety of different media to educate people, even a public service campaign, television-based, social media-based, print-based to try and educate people about these issues, as well as reaching out to different advocacy groups, corporations, and associations to participate actively. Maybe these would end up being -- you know, hosting some kind of a consensus meeting or event where you bring in stakeholders from these different organizations to talk about the issues and collaborate on developing programs for raising

awareness and influencing behavior.

DR. WEISS: Dr. Sneed.

DR. SNEED: Jeannie Sneed.

Changing consumer behavior is very difficult. You were talking about -- Dr. Dahr was talking about if they're 42, they've probably been wearing contact lenses 20, 25 years, and so they already perceive that they know what to do and what's correct and that sort of thing. My area is food safety, and if you talk about -- with consumers, about, you know, do they take temperatures, how do they know when something is done if they don't take temperatures, well, they just know because they've been doing it for so many years. So it's really difficult to change behavior, and so you have to figure out what would motivate them to do that, what would motivate them to make a change.

Just some ideas: And I didn't know there was a contact lens month. You mentioned PSAs, but maybe that could be a time when FDA and maybe FDA along with CDC could do, you know, a big push to get some information in the popular press, magazines, e-magazines. When I go to just my regular doctor, there's usually a medical TV show that's on video in the office, so some little clip in that that would get people's attention. Maybe focusing on health class in high schools or science classes, those kinds of things, could be useful in helping people learn about the issues.

DR. WEISS: Dr. Wolf.

DR. WOLF: Michael Wolf.

You know, I think from hearing today -- again, I don't use contacts. And in fact, this is not even my subject area in terms of the work I typically do. I'm more focused on medications, and so this has been more learning. I think that I'm convinced that a lot of this issue is probably, yeah, we'll have minimal benefit by improving labeling, but you can always do that because the issue -- you know, there are lots of pieces. Some patients are

going to want to know more, and that's one of the reasons for the errors. But if a lot of it is designed, if it is just the fact that a lot -- you know, that this is an issue of people making a one-time or, you know, isolated incidents of making a mistake because -- again, we keep talking about the drunk example, but this Friday and St. Pattie's, but they -- I kind of feel like maybe -- and if there's not long-term damage, that I thought I heard that, you know, this is not something where even case finding necessarily would be that important. So the underreporting of what likely happens to a lot of people despite the numbers makes me feel like a lot of the involvement to this question really is less on trying to do these very isolated -- and I personally just don't feel -- we've tried this a lot, trying to educate professionals to talk more to their patients, and we still have stagnancy in medications around high-risk drugs that have REMS and so forth, dealing with trying to educate one-off, kind of large diffuse campaigns.

I feel there's maybe a low impact over time, but really, getting patients involved in working with industry, you know, to provide feasibility, acceptability of design solutions, I think that actually, to me, feels the way best to use and motivate to bring -- you know, bring together, if that's not already happening. I kind of feel like you're hearing that there's a lot of innovation under study, it's not an easy problem, the investment is one to be made, and you have a fairly motivated community.

DR. WEISS: Dr. Yin.

DR. YIN: Shonna Yin.

You know, I think that if we are going to have an educational campaign, that it really doesn't need to be very organized and cohesive involving the range of stakeholders making sure that we're having simple messaging for the providers and patients, doing some sort of focus group testing to figure out what the key messages that we want to get out there is and then standardizing. I mean, we talk about standardizing bottles, but I think we need to

standardize the messages also that we're providing and really taking a systematic approach to an educational campaign if we're going to do one.

DR. WEISS: Dr. Owsley.

DR. OWSLEY: Okay, so who's responsible for education? I think it's kind of several -- several agencies or organizations or parts of society are. I think certainly the professional organizations in this area have an obligation to make sure that the providers are educated, and I know they work on this, and they do this. Also, the nonprofit advocacy agencies, for example, one I'm familiar with is Prevent Blindness, it's an advocacy organization that's been involved in advocacy for patients in the eye health area since the beginning of the 1900s, they can play a role. I also think industry has a very significant role since they're developing the products, selling the products, and it's in their best interest to make sure the patients know how to use the products.

The challenge in eye health education is not in just designing eye health education and implementing it. There's actually a science of health education, and I would encourage that we concentrate on evidence-based approaches in education in this area. The challenge there, and I've worked in the area of eye health education not related to contact lens use, is who's going to pay for it. Everybody thinks, well, it can't be that expensive, it's not bench research, but eye health educational evaluation is actually a very expensive enterprise.

And so the problem is that the agencies I'm familiar with in Health and Human Services really -- like the National Eye Institute, Centers for Disease Control, really aren't prepared in terms of the programmatic priorities nor their budgets to support development of evidence-based approaches, although there are small pockets in these areas, people who have been funded by those agencies. I don't know about FDA. I suspect that it's probably not a major area, but that's just my hunch.

So it may be falling to industry to make sure that however they propose and they

implement educational programs for their products, that they make sure that they actually evaluate those -- whether those programs and messages are efficacious. So thank you.

DR. WEISS: So I think we're all advising education programs, but then it hits the reality of who's going to make that happen, as we just heard. I can just tell you from my personal experience, the level of ignorance on contact lens care is staggering. Physicians don't know how to take care of their lenses, ophthalmology residents often don't know how to take care of their lenses, and if those individuals don't know how to take care of their lenses, then what are we going to expect from the public? I think it's all trivialized, and one of the reasons it's trivialized is that you can perhaps get away with breaking the proper regimen for a certain number of times, and then you don't.

And inevitably, every contact lens corneal ulcer patient I see who isn't following the contact lens regimen, and I point it out to them, they always say, well, that's what I've always done and I say, well, it's like running across the street in traffic. Most of the time you might not get hit by a car until you do. So here, who's going to invest the money to put out those public statements? Is it going to be the organizations here, is it going to be industry? But they're certainly needed.

Mr. Delost.

MR. DELOST: Kort Delost.

I think, because we've adopted the red cap, for better or worse, it's there, and we ought to utilize that through PSAs, emphasizing if you see red, stop, read the label. And then work with advocacy groups and the industry and professional organizations through education. I know that industry has come into my store before to talk about certain products and safe ways to use them, something we can learn through ophthalmology, optometry, pharmacy. The advocacy groups could actually be the spokesman on behalf and maybe with a little bit of funding for the PSAs from the industry as well. So I think to take a

cohesive group approach to do it, and I think if we emphasize the red cap situation, I think -- and make sure it's done across the industries, including generics. I think at least it's a starting point for education.

DR. WEISS: Dr. Rimal.

DR. RIMAL: I think in terms of consumer engagement, you know, I was struck this morning by the MDR study that found 374 or something cases, and we really don't know what the denominator is, so that 374 is 374 out of what? And part of the problem, of course, is that it's a very passive system, and we don't know -- I mean, we got anecdotal evidence that there are probably many, many more cases that go unreported. So I think if there are resources to be spent on sort of understanding the consumer, I would say those resources probably need to be spent on a more active as opposed to a more passive -- a more active data generation process so that we have systems on place for adverse event reporting and maybe even asking the industry to keep those kinds of numbers and report those kinds of numbers.

DR. WEISS: Dr. Lee.

DR. LEE: It sounds like changing package design is going to be a little bit of a challenge, and we're stuck with a red cap. And I really like Dr. Kreps's ideas about having video, multimedia access via QR code. I was thinking of how we could break the patient's routine of just opening the bottle and actually making them stop and think. And then how do we then engage them and point them in the right direction. So I was thinking if we have a red cap, that's one of those push-lock ones where you got to squeeze to open, and at the top of the bottle we have something like why is this bottle locked, scan this QR code to find out. And then that links to a video demonstration of the importance and why this is different than, you know, the bottle. It would be a relatively simple implementation, and I think that could be carried out.

DR. WEISS: Dr. Krishnamurthy.

DR. KRISHNAMURTHY: So the question in front of us is how to engage more of the patients, and a couple of the Panel members already mentioned this. This is a hard one to tackle, I think in part because it is not that the contact lens customers, or any customer of any product for that matter, is waiting to be engaged -- whether somebody engages or not. If it rises to the problem point where they feel that they need some help, they will kind of express themselves. But at the same time, it is clear, at least there are two people who mentioned here in this Panel that we're not confident at 317, that they had a significant amount of underreporting.

So the only way this is going to change is if the advocacy groups that stand for the consumers can actively reach out to consumers, create databases or panels from which they can collect data. I'm not sure -- in the industry can be asked to do or share data. I have no expectation that anything will change in that regard. So, in fact, I'm not sure that if the problem is at the level where it is, which is if you accidentally put it, you're going to kind of have some pain for a couple of days and then it's going to resolve itself, the consumers will necessarily come out and engage a whole lot; that is, I'm sort of like a little bit negative about the prospect of engaging more than what has already been, like getting panel members together, industry experts together, consumer representatives together, and they have highlighted this. I think this is the best that one can expect at this point in time.

DR. WEISS: Thank you.

Dr. Berube.

DR. BERUBE: I want to underline, I think, the importance of using some sort of evidence-based approach to this issue. I read about cholera last night, and I was reading about how -- it was only when it was decided that mapping the water distribution sites throughout London that they were able to get a handle on this. And prior to this, oh, doctor

after doctor were talking about well, you know, it's what floats in the air, what falls in the air, it's what I inhale, it's the phase of the moon, there were all these positions. What Dr. Kreps argues is that, you know, this is a hard field to be into because we have no benchmarks, we just have no benchmarks at all to compare a standard, a patient's feelings and understanding about all of this so we can compare what we're doing.

And so every time you adopt changes, you're adopting changes in a fog, you really are, because you just have no idea what to compare it to. And years -- not years ago, a few years ago I wrote an article that said the weird thing about patients is they're not the normal public. Something happens when you become a patient. You become something different than just the standard public. There are all these different motivations and concerns that get involved there, and I don't think we know enough about this group, and I think anything we can do to get better information would be great. I'm a big fan of using new media, teaching a doctor a program with digital media, and you know, the 40-somethings now are into new media. So I mean, it is something we're going to have to deal with, and it's something that works.

And I do remember one thing when I was contacting -- I do workshops and nanosites, and I was contacting people in the public, trying to figure out what chemical formulas -- one thing we were able -- we really taught everybody what H_2O means. They got it universally. People know what H_2O is, and I think you need a big campaign that H_2O is not H_2O_2. I think you just have to get a campaign going on this. And then you have a lot of opportunities there. And I agree with Gary's comments, and he's the specialist and health god, is that you really do need to use multiple approaches to this, not just one approach. Furthering education has to be on many, many different levels. But before we do this, we should get some benchmarks.

DR. WEISS: Dr. Blalock.

DR. BLALOCK: It's Sue Blalock.

Let me just enter the prophecy in this. I'm interpreting this question very broadly as to improve compliance with contact lens care products, you know, very generally, not just the hydrogen peroxide products, but the compliance issues here more generally. And I definitely agree with Dr. Wolf that, you know, it's hard to get physicians to, you know, provide much patient education.

But on the other hand, you know, patients do tend to listen to what their doctors say, and the first step to behavior changes are tending to the message. The patients may not do what their doctor said, but they at least hear it, and so I think -- and this also, you know, goes along with some of the things other folks have said, that I think if we better understood what kind of patient education people were currently getting, probably primarily from their eye care provider, that we would, you know, be a step closer to activating folks, and because it's -- we're facing a very different issue if you did a study and you gathered information. Say you take the office visits and found out that, well, everybody, you know, is being counseled, you know, just the way that we would prescribe in following the best guidelines. Then it would lead you to wonder -- it would lead you in a different direction.

But on the other hand, if you take those patient encounters and find out that this is not being discussed, it would lead you in a different direction. So I guess this is, to some extent, arguing for, you know, some baseline information on what's currently being done to enhance patient compliance, and I would actually start with the physician's office or the optometrist's office.

DR. WEISS: Dr. Jeng.

DR. JENG: So I'll start by saying I don't know the answer, but I think that if we are answering the question, I would better engage contact lens consumers. You know, we've

talked a lot today about underreporting, and people not necessarily saying anything. I think part of getting people to speak up is, you know, them not feeling that they're going to be heard, and what's the difference anyway? And so we, as professional organizations, advocacy groups, industry, need to promote that we want to hear, and we want to help and to open up a dialogue somehow via multimedia or whatever it is to get people to speak up, and questions will be answered, and the more dialogue that happens, the more we'll continue and we'll be able to dispense information in that manner hopefully.

DR. WEISS: Dr. Huang.

DR. HUANG: Sorry, I'm a little bit holistic and idealistic about this. Actually, the way I look at this problem is I think, you know, we are as a group -- you know, consumer advocacy and professional organization as well as the industry is doing a good job, you know. If you look at -- we don't know the common denominator of this problem, but assuming there were six million contact lens user and we can only identify 374 that reported, okay, and if you magnify this a hundred times, okay, say one in a hundred reports, you only have 5% of complications, and these are minor complications. This is not truly blinding complications. It's not a true infection. We're not talking about it.

So, you know, I mean -- so I'm a little understanding that engaging is that -- I mean, the necessity is the driver for invention, you know, but I'm not sure that we need to really spend enormous amount of effort to reinvent this wheel in terms of the so-called contact lens care at this moment with the current product, whether it's hydrogen peroxide or anything, because, I mean, who knows? I'm just making it up. In 5 years, in 10 years, if we have this super solution, whether it's antibiotics or anything, maybe we will then notice. At that time we have another different scope of the problem. It's not just a chemical or conjunctivitis or keratitis issue.

So, you know, I mean -- and we don't know at that time. If we're going to create

another, you know, reality, then -- create another, you know, I mean, enormous monster, we don't know. So, you know, I'm thinking the problem is going to continue to evolve, just like many years ago everybody worried about, oh, you have a computer, now you're going to pollute the environment. So everything, you know, we have to be very careful, and we have to recycle. But now, you know, I mean, hardly anybody has a really big computer, and then those things become of less of important issue.

So I just feel that, yes, we need to continue to exercise our diligence in terms of educating our patient and educating our profession to know what's the advantage and the disadvantage of this system. And, you know, I think a little bit imperfection is actually a driver for a better product in the future or better idea to reinvent the wheel, yeah. Thank you.

DR. WEISS: Dr. McLeod.

DR. McLEOD: So I think I'm going to follow up on, I think, the theme that Dr. Blalock raised, which is I think it is important to identify whether or not what we're talking about is marketing or educating the population at large on the universe of issues important in contact lens wear, or are we actually focusing on this rather specific issue? And, you know, to Ms. Ellis' point, it seems as if none of us can really remember any contact lens education campaign of note, and in the grand scheme of things, honestly, if you step outside of this room, it would be a very difficult justification of very large resources for a mass marketing campaign for the universe of contact lens education to be focused on peroxide.

And if you look at what causes blindness associated with contact lenses and not occasionally but significantly, it is, you know, simple things like people not realizing, kids not realizing that they shouldn't wear their friends' cosmetic contact lens or that they shouldn't sleep in them at night if they're not overnight lenses or they actually do have to clean them and not leave them in, you know, the peroxide that sat out there and, you know, and has

turned into water ages ago.

So it just seems that, you know, we really should decide on this question what actually are we trying to accomplish, and in that context, really what is the cost-benefit. I certainly would not advocate pulling out peroxide issues and devoting, you know, the universe's first educational campaign to that issue in light of the other things that would be money better spent.

DR. WEISS: Thank you.

DR. KREPS: May I follow up on that?

DR. WEISS: Yes, Dr. Kreps.

DR. KREPS: I'd really like to -- maybe what we need to do is to think about a more -- a broadly framed health education campaign about eye safety and contact lenses, not just about the peroxide issue. The peroxide issue would come up as one of them. But it appears that there needs to be a lot of different issues raised and so, you know, I think we can think about this more broadly and achieve more with the kind of health education programs we desire.

DR. WEISS: Thank you.

For FDA, I think the Panel's recommendations are to look at where the education is -- what's going on presently, where is it lacking, where would be the sources for finances, financial support of this, and to have a more broad-based campaign, if this was undertaken, to discuss the whole contact lens care education instead of carving out hydrogen peroxide issues by themselves.

Does the Consumer Rep have any additional comments at this point?

MS. WITCZAK: No, but I do like it being more of a general contact lens or just eye care because I don't think we even understand that for someone who's worn them to your point forever, we don't really learn about it; you don't even ever hear about it unless

there's like the latest contact solution or a lens that comes in from your eye doctor when they actually want to recommend that, but not so much on the care side, so I do think it would be beneficial. But I think peroxide, I think that does have to be a part of the conversation.

DR. WEISS: And does our Industry Rep have any additional comments?

MR. PFLEGER: I'd just like to say thank you to the Panel for a lot of very thoughtful discussion, and if anyone's got really good ideas, I know the industry is always willing to listen.

DR. WEISS: And does our Consumer Rep [sic] have any additional comments?

MS. ELLIS: Yeah, I appreciate the opportunity to participate in this meeting. It seemed to me that a lot of the labeling is focused on increasing compliance and hearing these things; I don't know how much labeling would prevent accidental misuse. And what was missing for me were metrics to balance and determine what was acceptable risk versus long-term benefits, and I don't know that that's been really quantified. We've seen pictures of ugly eyes and things like that, but as far as, you know, in other drug industries you know your threshold is, you know, 1.5% or whatever, but we even have no idea what the actual -- you know, what's not being reported. We don't know what we don't know, and so how do we know what's acceptable?

DR. WEISS: I would like to thank the Panel and the FDA for their contributions, as well as our presenters today.

Dr. Eydelman, do you have any final remarks?

DR. EYDELMAN: Just to thank all of the Panel members for their very interesting and unique contributions on this challenging topic.

DR. WEISS: Thank you.

I now pronounce the March 17th, 2017 Ophthalmic Devices Panel for Medical

Devices Advisory Committee and Risk Communication Advisory Committee adjourned.

Safe travels.

(Whereupon, at 3:30 p.m., the meeting was adjourned.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

OPHTHALMIC DEVICES PANEL AND RISK COMMUNICATION ADVISORY COMMITTEE

March 17, 2017

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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Official Reporter

Free State Reporting, Inc.
1378 Cape St. Claire Road
Annapolis, MD 21409
(410) 974-0947