UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

OPHTHALMIC DEVICES PANEL

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TUESDAY, JUNE 10, 2008

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The Panel met at 8:00 a.m. in the Grand Ballroom of the Hilton Washington DC North/Gaithersburg, 620 Perry Parkway, Gaithersburg, Maryland, Neil M. Bressler, M.D., Acting Chairperson, presiding.

PRESENT:

NEIL M. BRESSLER, M.D., Acting Chairperson
STEPHEN A. BURNS, Ph.D., Voting Member
TIMOTHY B. EDRINGTON, O.D., Voting Member
JANINE A. SMITH, M.D., Voting Member
DONALD G. AHEARN, Ph.D., Consultant
TIMOTHY T. McMAHON, O.D., Consultant
WILLIAM D. MATHERS, M.D., Consultant
ALICE Y. MATOBA, M.D., Consultant
THOMAS W. RAASCH, O.D.,Ph.D., Consultant
LORETTA B. SZCZOTKA-FLYNN, O.D., M.S., Consultant
RICHARD T. BUNNER, Consumer Representative
BARBARA A. NIKSCH, Industry Representative
KAREN F. WARBURTON, M.H.S., Executive Secretary
MALVINA B. EYDELMAN, M.D., Director, Division of Ophthalmic and Ear, Nose and Throat Devices, FDA

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P-R-O-C-E-E-D-I-N-G-S

8:00 a.m.

DR. BRESSLER: Good morning. I would like to call this meeting of the Ophthalmic Devices Panel to order. I'm Dr. Neil Bressler. I'm the Chairperson of the Panel today. I'm a professor of ophthalmology at Johns Hopkins University and Chief of the Retina Division there. My area of research is in designing and implementing clinical trials in retinal disease.

We will introduce the rest of the Panel Members in a little while. If you haven't already done so, please sign the attendance sheets that are on the tables by the doors. Ms. Warburton, on my right, the Executive Secretary for the Ophthalmic Devices Panel, will now make some introductory remarks.

MS. WARBURTON: Good morning, everyone. I would like to first note that Dr. Bressler is serving as Acting Chair for the

duration of this meeting. I will now read the Conflict of Interest Statement.

FDA Conflict of Interest Disclosure Statement. Particular matters of general applicability. Ophthalmic Devices Panel of the Medical Devices Advisory Committee, date of the meeting June 10, 2008.

The Food and Drug Administration is convening today's meeting of the Ophthalmic Devices Panel of the Medical Devices 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 this panel's compliance with federal ethics and conflict of interest laws covered by, but not limited to, those found at 18

U.S.C. Section 208 and Section 712 of the Federal Food, Drug and Cosmetic Act are being provided to 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 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.

Under Section 712 of the Food, Drug and Cosmetic Act, Congress has authorized FDA to grant waivers to special government employees and regular government employees with potential financial conflicts when necessary to afford the Committee essential expertise.

Related to the discussions of

today's meeting, members and consultants of this panel who are special government employees have been screened for potential financial conflict of interest of their own, as well as those imputed to them, including those of their spouses or minor children and, for the purposes of the 18 U.S.C. Section 208, their employers.

These interests may include investments, consulting, expert witness testimony, contracts, grants or CRADAs, teaching, speaking or writing, patents and royalties, and primary employment.

Today's agenda involves a discussion of general issues concerning the post-market experience with various contact lens care products. The discussion will include recommendations on contact lens care product development topics, such as pre-clinical testing and clinical performance measures and labeling for contact lens and lens care products. This is a particular

matters meeting involving general applicability.

Based on the agenda for today's meeting and all financial interest reported by the panel members and consultants, conflict of interest waivers have been issued in accordance with 18 U.S.C. Section 208(b)(3) and Section 712 of the Food, Drug and Cosmetic Act to Drs. Donald Ahearn, Timothy McMahon and Loretta Szczotka-Flynn.

Dr. Ahearn's waiver addresses several consulting interests with firms at issue. For two consulting interests, he received less than $10,001 for each. For two other consulting interests, he received greater than $50,000 for each.

Dr. McMahon's waiver addresses a consulting interest with a firm at issue for which he received less than $10,001.

Dr. Szczotka-Flynn's waiver addresses a grant for which she and her institution received less than $100,000.

These waivers allow the individuals to participate fully in today's deliberations. FDA's reasons for issuing the waivers are described in the waiver documents which are posted on FDA's website at www.fda.gov/ohrms/dockets/default.htm. Copies of the waivers may also be obtained by submitting a written request to the agency's Freedom of Information Office, Room 630 of the Parklawn Building. A copy of this statement will be available for review at the registration table during this meeting and will be included as part of the official transcript.

Barbara A. Niksch is serving as the industry representative, acting on behalf of all related industry, and is employed by Visiogen, Inc.

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 other participants to advise the panel of any financial relationships that they may have with any firms at issue. Thank you.

Before I turn the meeting back over to Dr. Bressler, I would like to make a few general announcements. Transcripts of today's meeting will be available from Neal Gross & Company, who may be reached at (202) 234-4433. Also, information on purchasing videos of today's meeting can be found on the table outside the meeting room.

I would like to remind everyone that members of the public and the press are not permitted around the panel area, which is the area just beyond the speaker's podium. The press contact for today's meeting is Karen Riley. Karen, there she is waving. And I

would like to request that reporters please wait to speak to FDA officials until after the panel meeting has concluded.

If you are presenting in the open public hearing session today and have not previously provided an electronic copy of your slide presentation to FDA, please arrange to do so with Ann Marie Williams, and Ann Marie is sitting right here in the front.

And finally, please silence your cell phones. Thank you very much. Dr. Bressler?

DR. BRESSLER: Thank you, Karen. Good morning again. At this meeting, the panel will discuss general issues that concern the post-marketing experience with contact lens care products. Before we begin, I would like to ask our panel members and the FDA staff that are seated at the table to introduce themselves, and I thank you for your time.

Please, state your name, your area

of expertise, your position, and your affiliation. And why don't we start with Dr. Eydelman?

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

DR. MATHERS: I am William Mathers, a Professor of Ophthalmology at Oregon Health Sciences University in Portland. And I have a research interest in cornea and external disease, particularly acanthamoeba and confocal microscopy diagnosis.

DR. RAASCH: I'm Tom Raasch. I'm at the Ohio State University College of Optometry. I have research interests in low vision and visual optics and visual performance.

DR. SMITH: I'm Janine Smith, Deputy Clinical Director of the National Eye Institute at NIH, and my areas of research interest are cornea and uveitis.

DR. BURNS: I am Steve Burns. I'm a Professor of Optometry at Indiana University in Bloomington. My area of expertise is in optics, adaptive optics, and retinal imaging.

DR. MATOBA: Alice Matoba. I'm Associate Professor of Ophthalmology at Baylor College of Medicine, and my area of interest is cornea and external disease.

DR. EDRINGTON: Tim Edrington, Cornea and Contact Lens Service, Southern California College of Optometry.

DR. AHEARN: Don Ahearn. I'm at Georgia State University and a Professor of Microbiology an Adjunct at Ophthalmology at Emory University. Areas of expertise include mycotic keratitis and acanthamoebic keratitis.

DR. SZCZOTKA-FLYNN: Loretta Szczotka-Flynn, Associate Professor of Ophthalmology at Case Western Reserve University, Department of Ophthalmology, in Cleveland. And my areas of interest are silicone hydrogel contact lenses,

complications with silicone hydrogels, and epidemiology.

DR. McMAHON: I'm Tim McMahon. I'm a Professor of Ophthalmology at the University of Illinois at Chicago, and my area of interest are contact lenses and corneal topography.

MR. BUNNER: I'm Richard Bunner. I'm the consumer representative. I serve as the Government Affairs Chair for Prevent Blindness America and I'm a retired public health administrator with the Ohio Department of Health.

MS. NIKSCH: I'm Barbara Niksch, and I'm serving as the industry representative. I'm currently Vice President of Regulatory Quality and Clinical Affairs at Visiogen.

DR. BRESSLER: Thank you, everybody. Next, Dr. Malvina Eydelman would like to recognize Dr. William Mathers for his service as Panel Chair. Dr. Eydelman?

DR. EYDELMAN: Dr. Mathers, it gives me a great pleasure to present you with this award. And to start out, I would like to read you a letter of appreciation for your terrific services to Ophthalmic Panel from the Commissioner of the FDA, Dr. von Eschenbach. And it reads:

"I would like to express my deepest appreciation for your efforts and guidance during your term as a member and Chair of the Ophthalmic Devices Panel of the Medical Devices Advisory Committee. The success of this Committee's work reinforces our conviction that responsible regulation of consumer products depends greatly on the experience, knowledge, and varied backgrounds and viewpoints that are represented on the committee. In recognition of your distinguished service to the Food and Drug Administration, I'm pleased to present you with the enclosed plaque."

And the plaque reads: "U.S. Food

and Drug Administration's Advisory Committee Service Award presented to William Mathers, M.D., Chairperson, in recognition of distinguished service Ophthalmic Devices Panel, Medical Devices Advisory Committee from November 2003 to October 2007. Thank you very, very much."

(Applause.)

DR. EYDELMAN: Thank you again.

DR. MATHERS: Thank you very much, and it was a pleasure to serve on the Panel, and I want to say that I have a great deal of respect and regard for the professionals that dedicate their lives to public service in this regard. And thank you for the opportunity of serving.

(Applause.)

DR. BRESSLER: Thank you, Dr. Mathers. Now, we are ready to hear the division updates, so I'll turn over again to Dr. Eydelman.

DR. EYDELMAN: Good morning. I

would like to take this opportunity to update you on our recent personnel changes in the division. Since the last time we provided the panel personnel changes in July of 2006, Division of Ophthalmic and Ear, Nose and Throat Devices had three departures.

As of January 2008, Captain Jim Saviola, Chief of VEDB, has been selected as the Ophthalmic and ENT Matrix Network Leader for a one year detail. This is a new organizational structure for the center to enhance communication and collaborate between various CDRH Offices. Lieutenant Commander Lori Austin- Hansberry was Division's Project Manager and was reassigned to CDC. Mr. Clay Buttemere, Biomedical Engineer, resigned from FDA to pursue missionary work in Macedonia.

While we had three departures, I'm delighted to report that we had 17 outstanding additions to our division's exemplary staff. I would like to take this opportunity to introduce them in chronological order. To all

those present, please stand while you are being introduced.

Dr. Denise Hampton has joined the division in September of 2006. Dr. Hampton received her bachelor's of science degree in biology from the University of North Carolina and her Ph.D. in microbiology from the University of Virginia. Prior to coming to the FDA, Dr. Hampton was a postdoctoral fellow in the Laboratory of Allergic Diseases in the National Institute of Allergy and Infectious Diseases of the NIH. Thank you.

Mr. Andrew Yang joined the division in September of 2006 as a biomedical engineer. He obtained a bachelor's and master's degree in mechanical engineering from The Cooper Union for the Advancement of Science and Art. His studies were focused on research and invention.

Dr. Mridu Virmani graduated from Utah State University with a Ph.D. in biological sciences. She completed post-

doctorates at the University of Illinois, University of Michigan, Georgetown University, and the National Institute of Health. She worked at NIH from 1980 to '84. She joined FDA in '94 in the Division of Radiological, Abdominal, and Reproductive Devices. And we were lucky to have her transfer to our division in October of 2006. Dr. Virmani has expertise in immunology, protein chemistry and toxicology. Thank you.

Mr. Kwame Ulmer became Chief of Diagnostic and Surgical Devices Branch in October of 2006. Mr. Ulmer has earned a B.S. in physics and master's in materials engineering. He also holds a graduate certificate in public management and most recently completed an executive education program through George Washington University. He has nearly 10 years of federal government experience and worked in the areas of technical evaluation, project management, scientific review and regulation of medical

devices.

Dr. Shu-Chen Peng joined the Ear, Nose and Throat Branch of our division in October of 2006 as a scientific reviewer. Dr. Peng received her master's in audiology from the University of Iowa, her Ph.D. in speech and hearing science, and has completed a post-doc in University of Maryland in cochlear implants and psychophysics. Dr. Peng was trained as a clinical audiologist and a speech and hearing scientist. Dr. Peng reviewed submissions related to auditory devices, such as cochlear implants, implantable middle ear devices, and hearing aids.

Dr. Kimberly Brown Smith is a glaucoma-trained ophthalmologist who joined our staff in October of '06. She has a bachelor's degree in chemical engineering from Howard University and a Ph.D. in biomedical engineering from Johns Hopkins University. She worked as an Assistant Professor in the Biological Resources Engineering Department at

the University of Maryland before earning her medical degree from Duke University and completing her ophthalmology residency at the University of Chicago. Prior to joining FDA, she completed a glaucoma fellowship at Johns Hopkins University.

Dr. Anjum Khan is an Otolaryngologist and Head and Neck Surgeon who joined the Ear, Nose and Throat Device Branch in December of 2006 as a medical officer. Dr. Khan completed her otolaryngology residency training in head and neck oncological fellowship from SUNY, Buffalo. Before joining the FDA, Dr. Khan has practiced otolaryngology head and neck surgery in the military, then at George Washington University Hospital, and finally in private sector. During her private practice years, she obtained a Master's of Public Health from Johns Hopkins University. She remains involved in the training of military otolaryngology residents at the National Naval Medical Center and holds an

appointment of Adjunct Clinical Associate Professor of Surgery at the Uniformed Services University of Health Sciences.

In March '07, Ms. Shelley Buchen joined FDA as part of ORISE Program. Ms. Buchen came to us with 30 years of industry experience in medical device evaluation. Twenty-three of these were specific to ophthalmic device research. Her areas of expertise include biocompatibility evaluation of ophthalmic devices, animal model development, and assessment of cleaning and sterilization validation requirements. Ms. Buchen is the U.S. representative to International Standards Organization. In that capacity, she has been instrumental in the development of numerous ISO standards for ophthalmic devices and has served as project leader for ISO 119795 on biocompatibility evaluation of intraocular lenses.

Through ORISE Program in March '07, we were also fortunate to obtain the expertise

of a vitreoretinal surgeon, Dr. Sam Dahr. Dr. Dahr graduated from Stanford University with a B.S. in biological sciences and master's in engineering-economic systems. He completed his medical degree as well as internship in internal medicine at University of Oklahoma College of Medicine. Subsequently, he completed fellowships in uveitis and retina at the National Eye Institute and a surgical fellowship in vitreoretinal diseases.

In April of 2007, Dr. Alex Beylin joined our division. Dr. Beylin received master's in electrical engineering from Moscow Telecommunication Institute and a Ph.D. in biomedical engineering from Technion - Israel Institute of Technology. He worked as a research fellow in Mount Sinai Medical Center, New York, as a research scientist in Instrutech Corporation, and as a Visiting Assistant Professor at Stony Brook University. His areas of expertise are in visual neuroscience, electro-optics and photodynamic

diagnostics.

Ms. Sushma Nair began working for DOD in May 2007. She has assisted us with administrative duties for the office. She obtained a bachelor's degree in human nutrition from University of Houston and is currently pursuing her master's degree in healthcare administration from University of Maryland.

Dr. Daniel Clupper joined the division in May of '07. Dr. Clupper received a bachelor's in material science and engineering from Purdue University. At Clemson University, he earned an M.S. in bioengineering for work involving the surface modification of absorbable glasses. He then obtained a Ph.D. in material science and engineering at the University of Florida.

Dr. Clupper subsequently worked as a postdoctoral research associate in the Tissue Engineering Centre at the Imperial College of London. He also conducted

biomaterials research for Poly-Med, Inc. and taught in the Biomedical Engineering and the Material Science and Engineering Department at Michigan Tech.

In July of '07, Dr. Lee Kramm joined our division as an ophthalmic medical officer. Dr. Kramm earned his bachelor's and master's degrees in biomedical engineering from Tulane University. He subsequently obtained his M.D. from University of Miami and completed ophthalmology residency at the Rocky Mountain Lions Institute at the University of Colorado. Dr. Kramm's training as a biomedical engineer and an ophthalmologist are currently being utilized by the Diagnostic and Surgical Devices Branch.

Dr. Molly Ghosh started with the division in September of '07. Dr. Ghosh holds a Ph.D. in pharmacology and toxicology from University of Louisiana and did a postdoctoral research at Purdue University. She is board-certified in toxicology by the American Board

of Toxicology. Prior to joining FDA, she was the Associate Director of Toxicology at NAMSA. Dr. Ghosh was an Adjunct Associate Professor of pharmacology and toxicology in the College of Pharmacy at University of Toledo. For several years, she has and continues to serve as a United States representative to International Standards Organization TC 194.

In February of this year, Ms. Anna Postell assumed the position of microbiologist in our division. Ms. Postell is a graduate from University of Maryland. Her career has encompassed working at the community hospital level and Walter Reed Army Medical Center. For the last 23 years, Ms. Postell worked in the Department of Microbiology at the National Institute of Health in Laboratory Medicine. She is currently a member of the Intraocular and Corneal Implants Branch.

About two months ago, Ms. Quynh Hoang has rejoined the division as the Acting Chief of Vitreoretinal and Extraocular Branch.

She comes back to the division after five years with the issues management staff in Office of Surveillance and Biometrics where she managed and led the center's assessment and development of solution strategies for numerous post-market medical device problems.

Previously, in her 10 years with our division, she was in the Diagnostic and Surgical Devices Branch and served as an engineering reviewer, team leader, and a refractive surgical devices expert reviewer. She originally came to our division after a three year stint with the Division of Cardiovascular Devices where she reviewed pacing and electrophysiology devices.

Prior to FDA, Ms. Hoang was a research assistant at the Penn State Heart Lab and a co-op engineer at IBM. She holds a master's in bioengineering from Penn State and a bachelor's in electrical engineering with certificate in computer engineering from Georgia Tech.

Finally, last but not least, Mr. Rahul Ram joined us about a week ago as a biomedical engineer. Mr. Ram earned his bachelor of science from Johns Hopkins University in biomedical engineering with a concentration in electrical engineering. He has been involved in several areas of traumatic brain injury and stroke research, including pilot interventional studies, clinical trials, rehabilitation engineering analysis and outcomes research.

I take great pride in my division's outstanding and dedicated staff. The individuals that I just introduced to you are a terrific addition to our already excellent team. Thank you, Chair.

DR. BRESSLER: Thank you for helping us and the public. Next, Dr. Danica Marinac-Dabic will give us the post-approval study program update, and it sounds like we're not going to do that.

DR. EYDELMAN: I would like to ask

Dr. Kesia Alexander to give a branch update.

DR. BRESSLER: Thank you. I appreciate the correction.

DR. ALEXANDER: Good morning. As stated, my name is Kesia Alexander, and I'm the Branch Chief of the Intraocular and Corneal Implants Branch. Since our last meeting in July of 2006, we approved PMA P060011 on May 3, 2007 for Rayner C-Flex Intraocular Lens, Model 570C.

This lens is indicated for primary implantation for the visual correction of aphakia in adults in whom a cataractous lens has been removed by phacoemulsification. The lens is intended to be placed in the capsular bag.

At the last panel meeting in July, we brought before you P050034, which was for VisionCare's Implantable Miniature Telescope. While the April 24th panel meeting intended to reassess this PMA was postponed, we are actively working with the sponsor to address

outstanding issues.

Also at the last panel meeting, I mentioned that we were aware of an influx of Toxic Anterior Segment Syndrome cases being reported. In response to the TASS case issue, which seems to appear sporadically over the years, we have established a TASS proactive program, which is intended to be an inter-center collaborative program.

The goals of the program are to assure relevant reporting of device-related issues; provide trend analysis of TASS occurrences; allow for appropriate testing of suspected devices; offer support for potential compliance action; and facilitate prompt communication with the ophthalmic community. While there is not enough time to address all of the goals, I would like to highlight the last goal centering on communication with the ophthalmic community.

FDA, the American Society of Cataract and Refractive Surgery, and the

American Academy of Ophthalmology have joined resources to create a TASS Communication Task Force. However, it is very important that the Agency is made aware of TASS cases through our MedWatch Reporting System.

Therefore, in an effort to make reporting easier, we have modified the MedWatch instructions to aid in capturing important information related to TASS. To further assist in making reporting easier, both ASCRS and AAO have put a link to our MedWatch form and modified instructions on their websites.

That concludes my updates. Thank you.

DR. BRESSLER: Thank you. Next, we will hear from Kwame Ulmer for Surgical Devices and Diagnostic Branch.

MR. ULMER: Good morning. Since our last Panel meeting, FDA approved the following significant PMAs. In July of 2006, P020050, Supplement 4, WaveLight Allegretto

Wave Excimer Laser System. It was approved for use in conjunction with the WaveLight Allegro Analyzer. The device is indicated for wavefront guided LASIK, for the reduction or elimination of up to 7 diopters of spherical equivalent myopia or myopia with astigmatism with up to 7 diopters of spherical component and up to 3 diopters of astigmatic component at the spectacle plane. It was approved for patients with documentation of stable manifest refraction defined as less than .5 diopters of preoperative spherical equivalent shift over one year prior to surgery.

In August of 2006, P060004, Carl Zeiss MEL 80 Excimer Laser System. The MEL 80 Excimer Laser System is indicated for use in primary LASIK treatments for the reduction or elimination of myopia of less than or equivalent to 7 diopters with or without refractive astigmatism or less than or equal to 3 diopters with a maximum MRSE of 7 diopters in patients with documentation of

stable manifest refraction over the past year, as demonstrated by change in sphere and cylinder of less than .5 diopters.

In October of 2006, P970053, Supplement 9, NIDEK EC-5000 Excimer Laser System. The device is indicated for laser-assisted in-situ keratomileusis (LASIK) for the reduction or elimination of hyperopia refractive errors from .5 to 5 diopters of sphere with or without astigmatic refractive errors from .5 to 2 diopters at the spectacle plane with MRSE of 5 diopters or less. It was indicated in patients with documented stability of manifest refraction over the prior year demonstrated by a change in MRSE no greater than .5 diopters.

In July of 2007, P930016, Supplement 25, VISX STAR S4 IR Excimer Laser System and WaveScan System for monovision. Approval for the STAR S4 IR Excimer Laser System with variable spot scanning and WaveScan Wavefront System, this device is

indicated for wavefront-guided LASIK to achieve monovision by the target retention of myopia -1.25 to -2 diopters in the non-dominant eye, a presbyopic my -- for patients with myopic astigmatism up to -6 diopters MRSE with cylinder up to -3 diopters, and a minimum preoperative myopia in their non-dominant eye at least as great as their targeted myopia, with documented evidence of a change in MRSE of no more than .5 diopters in both cylinder and sphere components for at least one year prior to the date of preoperative examination, and, finally, with a successful preoperative trial of monovision or history of monovision experience.

Post-approval studies. As part of this approval, AMO VISX has agreed to perform a post-approval study for monovision. The objective of the study is to estimate the proportion of monovision LASIK patients who experience visual disturbances that are severe enough to limit activities or adversely affect

the patient's quality of life, especially those associated with monovision.

You will shortly hear from Dr. Danica Marinac-Dabic with more information. Thank you.

DR. BRESSLER: Thank you again. Next, we will hear from Quynh Hoang, the Acting Chief for the Vitreoretinal and Extraocular Devices Branch. Thank you.

MS. HOANG: Panel members, colleagues, ladies and gentlemen, since the last panel update, the Vitreoretinal and Extraocular Devices Branch approved one original pre-market approval application.

In November of 2006, we approved Application P050031 from Paragon Vision Sciences for the Paragon Z CRT (tisilfocon A) Rigid Gas Permeable Contact Lenses for Corneal Refractive Therapy. This device, like other overnight orthokeratology contact lenses, is under a post-market surveillance 522 order to evaluate its use in patients younger than 18.

Dr. Marinac-Dabic, our next speaker, will update you about this post-approval study.

Since our last update, members of this branch have also been at the forefront of FDA's response to two outbreaks of infectious keratitis. These two, the Fusarium and acanthamoeba outbreaks, are also the catalysts for today's panel discussion on contact lens care products.

The members of this branch look forward to hearing your thoughts on our proposals for changes to FDA guidance for these products. We would like to also take this opportunity to thank the CDC, ophthalmic organizations, the individual doctors, and everyone involved in our response to the outbreaks.

And now, Dr. Marinac-Dabic.

DR. MARINAC-DABIC: Good morning, ladies and gentlemen, Dr. Bressler, Dr. Eydelman, distinguished Members of the Panel. My name is Danica Marinac-Dabic. I'm the

Chief of Epidemiology Branch at the Center for Devices and Radiological Health, Office of Surveillance and Biometrics.

And the Epidemiology Branch is the unit that is in charge of the review, monitoring and tracking of the post-approval studies, and also post-market surveillance studies.

My goal for today is to give you a brief update on the recent changes in the Post-Approval Studies Program, and also in Post-Market Surveillance Program, and also to give you an update on the ophthalmic devices post-approval studies, and post-market surveillance studies.

In essence, there are two types of FDA mandated post-market studies, and they are listed on these slides. Those are post-approval studies, and post-market surveillance studies.

On the first glance, they look very similar. Even their acronym looks very

similar, and I know it's going to be very confusing, especially for our colleagues that work outside of the regulatory environment, so I wanted to draw some distinction for you this morning, just to help you understand what type of mandates the FDA has to request the post-market studies that can address specific post-market question.

Of course, taking the second more studied look at those studies, we know that these are distinctive post-market tools for which FDA has specific mandates, and they certainly are different in many ways.

Let's start first with the post-approval studies. And many of you know them also as condition of approval studies. And you will certainly, as Panel Members, very actively participate in giving us a recommendation for those conditions of approval as you deliberate and decide on a recommendation for new PMA applications that we bring to your review and attention.

But the reason why we are asking for those studies is really to ensure the continuing evaluation of the safety and effectiveness of the products that are being marketed. And certainly, there are new questions that are raised when -- arise when the product is moving to a market, dealing primarily with how the product performs under more general conditions of use, under, you know, the use of community types of hospitals and physicians, and outside of the very controlled clinical trial settings.

So these studies are ordered at the time when FDA approves the product. On the other hand, post-market surveillance studies are the ones that give us a little bit more authority to ask for studies when specific post-market questions occurs any time when the device is already being marketed. But certainly, there are conditions under which those studies can be ordered, and they are listed on this slide.

For the device to be candidate to be -- to receive the 522 order, or this type of study order, is that the failure of this device would be reasonably likely to have serious adverse health consequences, and also, the device is intended to be implanted in the human body for more than one year, and the device is intended to be used to support or sustain life, and to be used outside of the user facilities.

And also, the FDA Amendment Act of 2007 added as a condition also that we can ask for this type of studies for any device that is expected to have a significant use in pediatric population.

The new CDRH Post-Approval Study Program encompasses design tracking oversight and review responsibilities for the studies mandated as a condition of approval. This program helps ensure that well-designed post-approval studies are conducted effectively, and efficiently, and in the least burdensome

manner.

During the past couple of years, the CDRH has made significant commitment of resources to enhance the Post-Approval Studies Program with the following major goals: to enhance scientific rigor of post-market/post-approval studies; to establish and maintain accountability for post-approval study commitments; to build post-approval study information management system; to also build bridges between the knowledge we gain post-market with the pre-market device evaluation; and also, to increase the transparency with the public.

So these are the major areas in which had already can reports to you the earlier accomplishments: the areas of oversight, tracking, review process, guidance document, web posting, post-market advisory panel updates, and building public health partnerships.

As many of you know, in 2005, the

Post-Approval Studies Program had been transferred to the Office of Surveillance and Biometrics, and since that time, we have developed and instituted automated striking system for post-approval studies commitments.

I would like also to highlight the major changes in the pre-market review process as it pertains to the post-approval studies. We have added epidemiologist on each PMA review team. That epidemiologist is a part of the team from the very beginning, during the pre-market review process, and it leads the design of post-approval study.

Always with an eye toward what are those post-market questions that may still remain after the reasonable assurance of safety and effectiveness is established pre-market. Our job is to work very interactively with the sponsor, and to help them design the post-approval studies. And the bulk of that work happens pre-market. We study our expectations to the sponsors at that time. We

work with them interactively, and if the presentation -- if the PMA submission goes to the Panel, we also present in Panel meetings.

The goal for both pre-market and the post-market office is that we have at least a good outline of the protocol finalized at the time of the PMA approval, but certainly, we are striving to achieve the goal when all the full development of the post-approval studies protocol will be developed before the product is approved. And we also agreed with the sponsor upon the study timelines.

This is what happened with the post-market review process. Upon the device approval, the epidemiologist assumed the lead responsibility in the review of the interim and final reports, but PMA review team, including our pre-market colleagues, continues to be engaged and informed.

This is accomplished through establishment of the so-called post-market

review team. The concept of epidemiology lead and the post-market team availability is envisioned to couple the epidemiologic expertise in observational studies with the product specific technical expertise from our pre-market colleagues, and also post-market colleagues that we have in our office, to facilitate the knowledge sharing within the center.

We also have issued the guidance document to industry and the FDA staff to clearly spell out our expectations for post-approval studies. This is the link. The device -- this guidance was published in 2006, and also revised in 2007. The guidance also provides very detailed study status definitions that the FDA uses in order to assess the status of the post-approval studies post-market.

And these are our categories for the reporting status: the report can be on time, or overdue -- or overdue and received

after the due date; and also, the final post-approval study report submitted categories listed here as well.

In terms of how we evaluate the progress of the study itself, this slide helps clarify what are the status definitions, and they are very clear. We negotiate, certainly, some modifications, if necessary, with the sponsor as we are trying to listen to their challenges as they conduct studies post-approval, but we certainly try to be very objective in terms of how we define, and how we measure the progress of the studies.

The other important piece that I would like to share with you is, and we are certainly very proud here in OSB and in CDRH, is that we developed the post-approval studies web page that went live on April 6, 2007. And this website provides the reporting schedule status, and the post-approval studies updates for all studies that have initiated -- have been initiated post-2005, and the link is

provided here.

And this is how this web looks like. You can see that there is a basic information about the PMA number, the applicant's name, and the device name. Then we have also the category of medical specialty for easier search for obvious database, the date when PMA was approved, and we also have the summary of the post-approval study commitments.

We also share the time when the protocol was approved, and what is the current status of the studies. We certainly do not share the proprietary information, because we also feel that the information on details of the post-approval studies is proprietary, and we would like to make sure that the study is completed, because -- before this is shared with the public.

This is probably the part that will interest the Panel the most. And I know that many of you contributed very much to giving us

great input in how post-approval studies should be designed, but we found, in the past, we didn't really close the loop and really let you know how those post-approval studies are progressing.

So we instituted two initiatives. We started providing general post-approval studies updates to the Panel. First was presented in November of last year, and at every Panel meeting, we will give you these updates on how the studies are progressing, certainly relevant from your area of expertise.

The other type of updates is so-called specific post-approval studies updates. If there is a specific reason that we would like to ask Panel input on the progress of the post-approval studies, we would invite the sponsor to join us, and we jointly will present to you the progress of the study, what might be our reasons, or specific questions that we would like the Panel to help us

address.

And certainly, these are two examples that we already had, one in January, 2006, an update to Neuro Panel, and in December 14, the update to OB-GYN Panel. We did not have yet the update to the Ophthalmic Panel.

And another piece of our strategy is to engage our stakeholders in this transformation. We have reached out to the clinical community, CROs, industry, all other relevant parties that are interested to help us design the post-approval studies.

We held one conference last year, and we will plan two conferences in 2008 and 2009.

Now, very briefly, I would like to walk you through just to see how our post-approval studies in ophthalmics arena are progressing. As you can see, and I have probably just five minutes to go through all these slides, we have, since 2005, there have

been 15 PMAs or Panel Track Supplements that have been approved, and this is their distribution per year, along with the total number, and four post-approval studies had been requested and ordered at the same time.

This slide presents what are the types of devices for which we had ordered the post-approval study. And certainly, star surgical companies, Visian ICL, we had two studies requested in order for this particular PMA that was approved in 2005. You also heard Paragon CRT rigid gas that was approved in 2006. And the VISX Monovision LASIK that was approved in 2007, they all have post-approval studies.

Again, since this is a general update, I don't want to go into a lot of details with regards to the design and the status of those studies, but I just wanted to include these tables for your reference to see what type of objectives, what type of study design we utilized, and you can also see what

type of study size population we would like to see in these type of studies, and what is the duration of the follow-up.

I would like also to say that there are -- for this particular product, we have ordered two post-approval studies: one that will be the follow-up of the pre-market cohort for five years; and the second study with an objective to estimate the incidence of major adverse events in the post-market environment under conditions of general use, again, as a perspective multi-center study where each subject will be -- each subject's pre-operative status for post-surgical outcomes with a population of 5,000 U.S. patients implanted in order to obtain the complete five year follow-up for 2,000 patients.

And again, primary endpoints for this study are cataract information, retinal detachment, corneal decompensation, chronic uveitis, persistent elevated IOP, secondary surgical interventions, and duration, again,

five years, and the follow-up visits are listed here.

Now, the study that Quynh just alluded to a minute ago is a -- has a relatively unique regulatory past, because this is how the -- our 522 section, or post-market surveillance studies and post-approval studies program kind of cross paths this way. And we have the study that is currently under the 522 order, but -- whose results will be sufficient for us to satisfy the company's need for the post-approval study, as well.

So the objective of this study is to compare incidence of microbial keratitis in pediatric patients in adult patients that are wearing corneal reshaping lenses. And again, this is the controlled, multi-center, retrospective, cohort study, randomly selected, stratified by practice volume. We also -- the population would involve 1,000 pediatric patients and 1,000 adult patients with sufficient follow-up to provide 1,000

patient years of exposure in each group. And they are randomly selected from lens orders of selected practitioners. And again, the primary study endpoints are listed here.

And also, the objective, okay, the data collection would include the practitioner's survey, would be conducted to determine if patient is still wearing lenses, patient's last visit, absence of, presence of MK, and also if patients had keratitis during the duration of the study.

And finally, one study that I would like to draw your attention to, primarily because of the study design, and of views of the quality of life questionnaires that we started utilizing that we are very proud of is the study of monovision LASIK post-approval study, with an objective to estimate proportion of CustomVue Monovision LASIK patients with visual disturbances and diplopia.

And again, the study will be multi-

center, single arm prospective study, again, with each subject serving as its control. Population would be 522 out of 15 U.S. clinical sites, out of which two would be academic sites, six corporate, seven private practices. And the vision-related quality of life of subjects would be the primary study endpoints.

And so I just wanted to, again, because of the time constraints, I would like to just show you what type of quality of life questionnaires we are using. NEI Refractive Quality of Life (RQL), and also NEI-Visual Function Quality of Life (VFQ), and also invalidated diplopia questionnaire. Again, this is very important piece in the way how we improve the study designs in the post-approval setting.

I think it comes as no surprise that most of the studies, all studies are observational. And this is how the reporting status of the post-approval study currently

is. We have two studies for which report is pending, and one study for which report is on time, and one study for which report is overdue, but received.

We also have these categories of the progress status. Two of the studies, again, are pending, because of the fact that their reporting due date is still not due. And we have one study on time, one study is overdue.

Now, this is our vision for the Post-Approval Studies Program. Again, we would like to make sure that important post-market questions are addressed; that studies are realistic, and founded on good science, and not led by the scientific curiosity of the FDA staff, but really, the studies that will have specific questions that the sponsor can address. And we also would like to keep stakeholders apprised, and to collaborate with pre-market and post-market colleagues.

I would like also just to say that

the post-approval studies transformation, vision and goals certainly represent higher expectations by the CDRH, and those heightened expectations often bring heightened concerns about burdens, about work load, perceived fairness, and added value. And it is up to us and our stakeholders to discuss them openly, responsibly, and collaboratively.

We understand the concerns, but we have to put them into large context of asking and answering the right post-market questions. We welcome an exchange of ideas on diverse methodologies that may be cost-effective, innovative, and productive. We value all analytical approaches and data sources, and will give us high -- that will give us high quality answers to the right post-market questions.

So any input that you would like to give us as Panel Members is very welcome. We will continue moving these answers toward the transformation of the Post-Approval Studies

Program to ensure that this transformation is a lasting one. Thank you.

DR. BRESSLER: Very nice. Thank you for that update. We are now going to proceed with the open public hearing portion of the meeting. Public attendees are given an opportunity to address the Panel to present data, information or views that are relevant to the meeting agenda.

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 such 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.

Now, as we have a number of public speakers today, I would like to go over the process to ensure a smooth transition from one speaker to another. Ann Marie Williams will direct you to the podium right next to the podium here.

When you begin to speak, the green light will appear, and a yellow light will

appear when you have one minute remaining. That's when you should be wrapping up. At the end of the 10 minutes that each speaker has, a red light will appear, and your presentation should be completed as soon as that red light appears. If not, unfortunately, we will have to turn the microphone off to give everyone a chance to be able to present.

So since we have a large number of speakers throughout the entire morning, it's very important to adhere to the 10 minutes.

The Panel will be given an opportunity to ask questions of the public presenters at the conclusion of the open public hearing. If recognized by a Panel Member, we would ask the public presenters to approach a podium to answer the questions.

I'd like to remind public observers at this meeting that public attendees may not participate, except at the specific request of myself, as the Chair.

So the first speaker will be Mr.

Thomas Moore. Mr. Moore, if you could come forward to the microphone? And we would ask each speaker, including yourself, to please speak clearly to allow the transcriptionist to provide an accurate transcription of the proceedings of this meeting. Thank you. Mr. Moore?

MR. MOORE: Thank you very much, doctor. Good morning. My name is Thomas Moore, and here is my financial disclosure. My law firm currently represents a large number of Americans from across the country who contracted devastating corneal infections associated with their use of ineffective multi-purpose contact lens care solutions.

Every single one of my clients wishes that they could be here today. They have waited a long time to see critical public health issues surrounding contact lens care products taken up by FDA in what is a truly public forum with both industry and non-industry voices being heard.

I'm simply a messenger, probably an inadequate one, attempting to relate to you the thoughts and concerns of the many individuals whose lives have been forever changed by their use of this product, and the hopes that future infections can be reduced, or prevented entirely.

I can't more aptly describe the latest outbreak of acanthamoeba infections as prominent ophthalmologist, Dwight Cavanagh, did recently when he called it a train wreck in slow motion. Indeed, the train started to wreck many years ago in the 1990s when multi-purpose solutions began to replace proven disinfection techniques, such as heat and hydrogen-peroxide systems.

My clients are hard pressed, as lay people, to understand why manufacturers designed multi-purpose solutions that relied on PHMB in concentrations that they knew full well were ineffective against acanthamoeba. My clients are understandably angered when

they learn that FDA never required testing against acanthamoeba.

They also find the International Standardization Organization's justification for omitting acanthamoeba as a challenge organism in efficacy testing as nothing less than bizarre. The ISO, an organization that at least appears to be largely controlled or influenced by industry, has consistently maintained that there is a lack of consensus as to how acanthamoeba testing should be conducted.

ISO and FDA have thus reasoned that such testing should not be required, even if it means that products ineffective against this devastating disease will be cleared for marketing.

The great irony is that at the same -- the same manufacturers who lobbied against acanthamoeba testing as a regulatory hurdle nevertheless conducted, and in many cases published, the very tests that they said could

not be done in a scientifically valid manner.

Paradoxically, some would say outrageously, manufacturers such as Advanced Medical Optics and others, are even now using such internal testing as the basis for advertising claims that their current PHMB-based products provide enhanced effectiveness against acanthamoeba strains.

If the testing is valid, it should have been required as a regulatory matter. If it isn't, it should not be allowed as a basis for marketing claims. It's as simple as that.

In 1998, one of your colleagues, Debra Schonberg, and her colleagues were prescient in their article entitled "The Epidemic of Acanthamoeba Keratitis: Where Do We Stand?" When they opined that the risk of acanthamoeba keratitis was likely underestimated, even after the 1980s outbreak, and that a major risk factor was, quote, the continued existence of ineffective lens disinfection systems, indeed, it was

apparently known early in the marketing of PHMB-based solutions that these products showed great variability in their effectiveness against acanthamoeba trophozoites, and little or no effect against acanthamoeba cysts.

It should have, therefore, come as no surprise when starting in 2003, the same year that Complete Moisture Plus was launched in this country, ophthalmology centers started to see increasing cases of AK at their institutions.

These outbreaks, which were reported at numerous U.S. and international ophthalmology meetings, should have been a wake-up call, but several years later, and after two major lens solution recalls, testing and labeling standards have not changed.

My clients wholeheartedly applaud FDA for convening this meeting. However, I must tell you that there is an element of mistrust as to the motives and objectives of

FDA and the contact lens branch, in particular. This has largely emanated from a lack of transparency on the part of FDA insofar as the general public is concerned.

It is a perception based partly on statements by industry and FDA officials that at least appear to place much of the blame for these infections on so-called consumer noncompliance, as opposed to the lack of solution efficacy.

I will tell, you ladies and gentlemen, that the vast majority of my many clients were very diligent in their use and care of contact lenses. They did not sleep in their lenses, or reuse or top off solutions, or rinse their cases with tap water. Some rubbed, and some didn't. And on that score, they weren't any more confused by AMO's no rub marketing claims than their optometrists were.

The minority who AMO and others would likely consider as noncompliant patients wonder why a company would market a solution

with such a slim margin of safety, and without any indication on the label of the risk of acanthamoeba infections.

In addition to feeling that they are being blamed for their infections, my clients are concerned that industry's role on these outbreaks has not been sufficiently scrutinized in a fair, objective, and public forum, while FDA maintains a close working relationship with manufacturers.

It has been unwilling, until today, to allow the public access to important data about these products, or a voice in the debate on these critical public health issues.

By way of example, my clients made a series of Freedom of Information Act requests over a year ago seeking access to documents concerning the evolution of testing standards, the clearance of the AMO Complete Moisture Plus product for marketing, and events leading up to the recall of that product.

Most of these requests have not been complied with. An appeal by my clients to the Department of Health and Human Services designed to expedite access to these materials was denied on the grounds that there was, quote, no showing of an immediate threat to the public health.

In addition, FDA has, at least thus far, deemed confidential all briefing documents submitted by it and the solution manufacturers to this Advisory Committee. Perhaps that will change in the coming days.

FDA's conduct in this regard is inconsistent with my long experience in dealing with other divisions and branches. Similar information, including safety and efficacy data in new drug applications, for example, is routinely furnished to the public by the drug branches in a timely manner, and with few redactions.

So there is no question in my mind that FDA has the discretion to release these

records, and I hope they will do so soon. Inevitably, a lack of transparency necessarily leads to rumors. The notion that FDA has delayed changes to testing standards because most marketed multi-purpose solutions would not pass those tests is a common perception; that FDA delayed calling this Committee meeting for months or years at the request of manufacturers is another.

Still another is that FDA and CDC disagreed vehemently with each other as to whether the recall of the AMO product should be voluntary or subject to FDA Class I Recall Protocols. Now, these perceptions may be accurate or inaccurate. But without transparency in the regulation of the contact lens care products industry, victims of corneal infections related to solutions may see the Agency's relationship with industry as collusive, rather than cooperative.

FDA often talks in terms of acting in the interest of stakeholders. We should

all hope that FDA considers its most important stakeholders to be consumers who use the products the Agency regulates.

There is an enormous opportunity that presents itself today which goes far beyond politics, corporate profits, or lawsuit recoveries. There is an opportunity for FDA to change the direction of the contact lens care industry, and by so doing, make contact lens wear substantially safer for millions of Americans.

This can only be achieved by adding to the diversity of voices FDA listens to, starting with this Committee, and by instituting a transparent process in which testing and labeling issues are carefully considered, and resolved in a way that best protects the public health.

My clients and I thank you for this opportunity to speak, and simply ask that FDA and the Advisory Committee make the health of consumers their number one priority. Thank

you.

DR. BRESSLER: Thank you, Mr. Moore. Our next speaker will be Dr. William Ehlers.

DR. EHLERS: Thank you. Thank you, Dr. Bressler, members of the Ophthalmic Devices Panel, I'm Dr. William Ehlers. I'm a corneal specialist at the University of Connecticut Health Center, and retro-refractive surfaces at that institution. I am past president of CLAO, Contact Lens Association of Ophthalmologists, and I have a special interest in contact lens safety, and I have personally conducted research on this, and written and lectured extensively on the subject.

I am particularly pleased to be here today to address this Panel, and I congratulate the FDA on attempting to address this very difficult problem. I am here today representing the American Academy of Ophthalmology, the Contact Lens Association of

Ophthalmologists, the Cornea Society, and the American Society of Cataract and Refractive Surgery.

The significance of this representation is that, over the last several months, representatives from all of these organizations have been working together to develop guidelines, some of which are recommendations to the industry and the FDA, and some of which are recommendations to consumers.

I will be addressing the recommendations that we have developed for consumers. And this is the first time in at least a decade that four large ophthalmic organizations have come together to develop recommendations with regard to contact lens care.

I have no financial interest to disclose, and will proceed to the recommendations.

First of all, we recommend that

consumers observe proper personal hygiene. Before handling contact lenses, wash your hands with soap and water, rinse and then dry them with a lint-free towel. This seems slef-obvious, but it is often omitted.

We recommend that wearers avoid contact with water. This includes removing contact lenses before swimming or using a hot tub. All the water that we get in recreationally is contaminated. Contact lenses similarly should not be rinsed or stored in water, either tap water or supposedly sterile water.

Lens cases, likewise, should be rinsed with lens care solution, not with tap water, then allowed to air dry before using again. You should always use appropriate solutions. Never put your lenses in your mouth to wet them. This always gets a shudder from people, but it does happen, believe it or not. Saliva, obviously, is not a sterile solution.

Do not use saline solution or re-wetting drops as a disinfectant. They are not disinfectants. They are re-wetting drops and saline, and it is important that consumers understand that difference. We recommend that all contact lens wearers follow the schedule prescribed by their eye care professional.

Wear and replacement schedules are developed for specific products and solutions, and should be followed by all contact lens wearers. The specific contact lens cleaning and storage guidelines should be made clear by the eye care professional, and by the manufacturers of care systems.

We recommend that patients rub their lenses during the cleaning process. We feel that this little bit of mechanical stimulation results in additional cleaning, and that we then recommend they be rinsed with the lens solution before soaking them. The rub and rinse method is considered superior to simply using the no-rub solutions as a no-rub

approach.

We also recommend that careful attention be paid to case care and replacement. Contact lens cases should be rinsed with solution and allowed to air dry before they are reused. The empty case should be left face down to dry. We recommend that contact lenses be replaced regularly. I recommend that my patients replace them at the time they replace their solutions, and that that be at least every three months.

Also, if your case is damaged, it should be replaced. Also, the case should be cleaned regularly. I see my patients sometimes pull a case out of their pocket or purse that makes me cringe, and I tell them that putting a clean contact lens into that case is like putting freshly cooked food on the plates from last night's dinner, and that usually makes the point.

We recommend that solutions be handled with care. You should never reuse old

solutions or top-off the solutions in the case. Do not transfer contact lens care solutions to smaller travel size containers. Any time you transfer a solution, there is a risk of contamination, and that can lead to eye infection.

Never allow the tip of the solution bottle to touch any surface. Keep the bottle tightly closed when not in use. If you are going to store your lenses for an extended period of time, you need to consult the instructions that came with the lens care product to see how long they can be stored before they need to be re-disinfected prior to using.

In no case should lenses be stored more than 30 days without re-disinfection.

Lens selection is also an important aspect of safe lens care. Consumers should know that single use daily disposable contact lenses are the safest type of soft contact lens in terms of reducing infections with

applications, and that rigid gas permeable lenses are a safer alternative than any type of soft contact lens.

It is important that consumers understand the risk of extended wear. Extended wear lenses may be an appropriate choice for some consumers, but they should understand they are selecting a modality that does carry with it increased risk of infections.

You should only wear lenses approved for this lens wear modality, and only with the approval of their eye care professional. The lenses that are used for orthokeratology for overnight use are likewise subject to increased risk.

If you have an eye infection, use good common sense. See your ophthalmologist immediately. Ophthalmologists are trained medically and surgically to treat eye infections, injuries and diseases without delay.

Regular appointments with an ophthalmologist or an eye care professional are also necessary, but it is important that patients know what the symptoms of lens problems are, that, if they experience redness, pain, tearing, increased sensitivity, that they should remove their lenses, and see their ophthalmologist. If they smoke, they should stop smoking. Several studies have shown that to be a risk factor.

The importance of regular examinations with their eye care professional cannot be over-emphasized. We recommend at least yearly, more often if needed.

Contact lenses are a prescription item that do expire, typically within one year. You should see your eye care professional yearly to ensure that you have an accurate and appropriate prescription. Regular examinations are also an important means of reinforcing proper lens care.

Ophthalmologists remain concerned

about the process of passive verification, where third-party sellers notify eye care professionals if a customer requests for a refill. Eye care professionals then have a limited amount of time, typically eight business hours, to either verify, or say, no, this is not an appropriate prescription.

If they are not contacted, some sellers presume the prescription is correct, and then complete the sale.

I recently had a patient come into my office who has been getting her prescriptions refilled from an office which has not existed for eight years. I know, because I was with that office. Passive prescription verification can lead to fulfillment of inappropriate prescriptions and complications.

It is important to recognize that, as we all share goals, we share responsibilities. The contact lens industry, researchers, the FDA and eye care

professionals must work together to ensure safe contact lens wear. Eye care professionals, in particular, must educate their patients with regard to the best contact lens practices.

But just knowing the risk factors and knowing the proper thing to do is not enough. Studies have shown up to 79 percent of patients are noncompliant with at least some aspect of their lens wear, care, or replacement schedules.

The partnership of lens wearers and eye care professionals is vital in that, often, there is a slow drift away from good practices. If there is no immediate consequence, this slow drift continues. If there is immediate consequence, it's a learning experience. I say putting unneutralized peroxide in your eye is a learning experience. If the results are not immediate, it takes longer.

Lastly, this slide is intended to

represent the complex interplay of all of these elements that contribute to safe lens wear. I would like to point out that, in this particular case, only the patient has full control of their wearing schedule, their replacement schedule, their lens care regimen, and treatment of pre-existing conditions such as dry eyes, or blepharitis.

So the importance of the relationship between the eye care professional and the patient cannot be overstated. I thank you for your attention.

DR. BRESSLER: Thank you, Dr. Ehlers. Our next speaker will be Dr. Elmer Tu.

DR. TU: Good morning, Dr. Bressler, and members of the Ophthalmic Devices Panel. I appreciate this opportunity to address you concerning contact lens disinfection systems, and our recommendations for preclinical testing and development.

My name is Elmer Tu. I am an

Associate Professor of Clinical Ophthalmology at the University of Illinois at Chicago, Eye and Ear Infirmary. I'm currently a practicing cornea specialist, and was the primary clinician involved in describing the ongoing outbreak of acanthamoeba keratitis in Illinois, cited in the CDC's investigative time line released in May of 2007.

I am here representing a consortium of four groups: The American Academy of Ophthalmology, The American Society of Cataract and Refractive Surgery, Contact Lens Association of Ophthalmologists, and The Cornea Society.

As far as disclosures, I have received honoraria and travel expenses from both Allergan and Alcon for educational activities which are unrelated to my testimony today. Our related research, personal research, has been funded by private nonprofit groups, as well as federal grants.

My role this morning is to discuss

the two recent outbreaks of rare contact lens-related corneal infections, and their implications for the development and preclinical testing of contact lens products. Before we address contact lens solutions, however, it should be acknowledged that experts agree that the estimated rates of microbial keratitis, in general, have not substantially declined, despite the evolution of contact lens disinfection systems over the past two decades. And in fact, this has been proven in studies from 1989 to 1999, and there is very little evidence today that that has changed.

Beyond that, research shows that the disinfection regimen is but one element of the risk of infection. Other factors include the extended wear of lenses, reduced tear exchange under the lens with current designs, various environmental factors, as well as poor consumer hygiene. And we feel that, in addition to the contact lens disinfection

systems, that additional research is required into all of the factors involved.

In regards to currently approved contact lens disinfection systems, we have a few issues that we would like to have recommendations on. One is a discard date on lens care products, in addition to their established expiration dates, with special attention to disinfection efficacy once those products are opened, as well as the possibility of secondary contamination.

Further, on extended storage of lenses, the FDA should encourage industry to conduct additional research to verify the duration of the safe extended storage of lenses after a single disinfection cycle.

With regards to labeling of contact lens solutions for use with specific lens types, our feeling is that, although corneal staining with certain combinations of disinfection products and specific types of contact lens types has been reported,

available evidence is very preliminary.

Furthermore, it has not yet been demonstrated what the long-term consequences are, if any, for ocular surface health, or the risk of microbial keratitis. But because this exists, I think additional information should be gathered regarding biocompatibility of solutions and lenses. This is particularly important as new materials and lenses are developed and introduced.

The last two years have seen the recall of two contact lens disinfection systems, the uses of which were associated with a significantly higher risk of contracting two different rare, but potentially devastating, corneal infections with Fusarium and Acanthamoeba.

Although the root causes are still not fully understood, each has potentially taught us different lessons concerning the role of contact lens infection in protecting lens wearers.

The international outbreak of Fusarium corneal infections in 2005 and 2006 were strongly associated with the use of a single solution, ReNu with MositureLoc. The evidence for this was strong. There was broad agreement between studies in Singapore, Hong Kong, and with the CDC demonstrating a strong association here in the United States.

Relatively rapidly, a steep decrease in the number of cases of contact lens-related Fusarium keratitis followed the recall of this particular solution from the market, reinforcing the strong association of the solution with this particular outbreak.

This is pertinent because it is my understanding that the solution performed well in current and required preclinical testing, and particularly well against Fusarium in comparison to solution systems that were not implicated in this particular outbreak.

The work of Dr. Ahearn, among others, Dr. Saltene, suggests that, while the

solution remains highly effective in optimal use, that non-disinfectant additives, combined with not uncommonly practiced consumer noncompliance could result in promotion of Fusarium growth.

Because of this, we make the following recommendations: that preclinical testing should include more rigorous, standardized, real-world scenarios that more accurately replicate the conditions and environment that contact lens products will be exposed to when used by consumers.

These include effectiveness while in the contact lens case, effectiveness when exposure time is less than recommended to the solution, and also effectiveness when the solution evaporates in the case.

Further, given the complexity of the interaction of contact lens disinfectants, additives, and the environment with which -- within which they are expected to work, each change in product formulation, however minor,

should be subject to similarly rigorous regimens of testing.

Acanthamoeba keratitis is strongly associated with contact lens wear, with greater than 90 percent of cases occurring in contact lens wearers. An analysis of a nationwide survey conducted by the CDC and the Ocular Microbiology and Immunology Group during an outbreak in the 1980s suggested an outbreak incidence of approximately two cases per million contact lens wearers per year in the U.S., thought related at that time primarily to the widespread use of non-sterile water in the care of contact lenses.

While the ongoing Acanthamoeba outbreak was similarly associated primarily with a single contact lens disinfection system in two independent studies at the University of Illinois Eye and Ear Infirmary and the CDC, respectively, with highly complimentary results, there are significant differences between the two outbreaks.

Despite the positive association with AMO Complete MoisturePlus in both cohorts, only about 50 percent of cases in both studies used this product. One should not lose sight of the fact that, with simple exclusion of those cases among AMO Complete MoisturePlus users, that the remaining 50 percent not using the implicated solution would still be considered an increase over previous estimates.

In the Chicago Metropolitan Area, for example, the number of non-AMO cases alone would suggest at least a five times greater rate than was calculated during this outbreak of the mid-1980s.

This indicates that other factors may be involved other than changes in the detection of acanthamoeba keratitis, or recent contact lens hygiene practices. Further, data presented by our group at the March ASCRS 2008 meeting, and an informal canvas, at that time, of other academic centers, indicated that the

recall of AMO Complete MoisturePlus has not resulted in an appreciable decline in the number of cases of acanthamoeba keratitis seen at those institutions.

Examined in context, this suggests that the underlying factors for the persistence of acanthamoeba keratitis remains unknown, but most previous outbreaks of this magnitude have been related to water involved in lens hygiene, and not individual exposure, as Dr. Mathers and others has previously demonstrated.

For this reason, we feel that acanthamoeba may represent an ongoing challenge for contact lens disinfection systems and contact lens wearers. Because of this, we make the following recommendations:

That besides testing for acanthamoeba, the testing requirements should be updated to ensure products are effective against a more diverse and representative set of infectious organisms. At the same time,

tests currently required should be continued, because of their historic use, and for comparison purposes for efficacy.

Further, we understand that preclinical testing of efficacy against organisms is complex and challenging. The testing protocol should be standardized, and validated by the FDA to ensure all products are meeting current, and hopefully, future microbial challenges. This should include a spectrum of clinical ocular isolates selected for their virulence, and maintained in such a way as to maintain a wild type capacity for disease.

While we understand that expanded and strengthened testing of contact lens solutions does not guarantee that the next outbreak of eye infections will be able to be prevented or predicted, however, it will increase the overall safety for contact lens wearers, especially against those organisms most commonly responsible for contact lens

related infections.

Further, some mechanism for monitoring contact lens infections, and the frequency in distribution of the organisms causing those infections could prove beneficial in both validating preclinical testing regimens, as well as protecting the public from eye infections.

Thank you for your attention.

DR. BRESSLER: Thank you, Dr. Tu. Next, Thomas Henteleff will be the speaker.

MR. HENTELEFF: Thank you, and good morning. This will be very short, and I hope sweet and noncontroversial. I'm counsel to the Contact Lens Institute, which is an association of research-oriented manufacturers of contact lenses and lens care products.

The Contact Lens Institute will be making a presentation, and that will be delivered by Dr. Glenn Davies, who's sitting behind me, who is with Bausch & Lomb, and is also Chairperson of the Regulatory Affairs

Committee of the Contact Lens Institute.

I requested the opportunity to make a presentation solely for purposes of being available to respond to questions at a later date if deemed necessary or useful either by Glenn Davies or the Panel. So with that said, I actually can save a lot of time, and turn the podium over to Dr. Glenn Davies. Thank you.

DR. BRESSLER: Thank you very much. So the next speaker will be Dr. Glenn Davies.

DR. DAVIES: Good morning. I'm Glenn Davies. For the purposes of financial disclosure, I'm an employee of Bausch & Lomb. Today, I'm here to represent The Contact Lens Institute. The Contact Lens Institute is an association of research-oriented manufacturers of contact lenses, and lens care products.

Its membership consists of Alcon Laboratories, AMO, Bausch & Lomb, CIBA Vision, CooperVision, Johnson & Johnson Vision Care.

CLI supports enhancements to the

testing requirements for lens care products that provide increased assurance of the safe and effective use of these products. CLI has a long history of working cooperatively with the Agency in the development of guidance and other test methods.

Lens care products are classified as Class II Medical Devices, and have an associated Class II special controls guidance that identifies the testing requirements for these products. The Agency recently made available an informal paper to discuss their current thinking for enhanced testing requirements in labeling.

Some of these concepts will likely be discussed this morning by FDA. CLI agrees with many of the ideas presented in the concept paper. CLI opposes the collection of data in the absence of sound scientific methods and appropriate acceptance criteria.

These recommendations represent a significant change to the existing Class II

special controls for these products, and warrant public participation and scrutiny as described in the FDA Good Guidance Practice Policy.

We look forward to working cooperatively with FDA in this process. In addition to my comments provided this morning, CLI will carefully consider the comments and recommendations expressed during today's proceedings, and where necessary and appropriate, file written comments.

This morning, I'll review CLI's ongoing efforts regarding lens care products, our thoughts on acanthamoeba testing, grouping of silicone hydrogel lens materials, labeling for lens care products, and new initiatives imposed market surveillance.

CLI has developed, with the participation of FDA, a testing protocol that assesses the disinfecting efficacy of multi-purpose solutions as a system. This method evaluates the efficacy in the presence of the

lens and lens case, parameters that are not addressed in the current FDA special controls applicable to the lens care products. This method has been introduced as a work item at ANSI, the American National Standards Institute, and ISO, the International Standards Organization, and is being evaluated in a ring test with five separate laboratories.

Once the method has been validated, and its feasibility confirmed, the method will be advanced in the formal ISO standard development process, and acceptance criteria established.

CLI is also working with ANSI and ISO to develop a new series of standards, and improvements to existing standards that address disinfecting efficacy, preparation of test samples for cytotoxicity evaluation, the kinetics of preservative uptake and release by lenses, and the standard for lens storage cases.

The acceptance criteria of all the preclinical and clinical evaluations for these products must be evaluated as a whole. There is a delicate balance between efficacy and toxicity, with an over-arching concern for compliance and reliability.

CLI agrees that acanthamoeba testing is an appropriate addition to the safety and efficacy evaluation for these products. As we all know, to require testing without standardized validated methods would provide marginally useful information. We believe that developing a test method for acanthamoeba should be given the highest priority, and we will pursue that belief with both ANSI and ISO working groups in which we participate.

The standard needs to clearly delineate the test procedure, test organisms and their forms, and the evaluation criteria. These are substantial unresolved technical issues.

The minimization of risk through enhancements and labeling is also important, and achievable in a shorter time frame. CLI members have already eliminated water from all care regimens for soft contact lens, and the labeling for contact lenses remind practitioners to advise their patients about water-related activities.

Although similar in many ways, CLI agrees that lens care compatibility of silicone hydrogel lens varies, and may differ from conventional hydrogel lenses. Therefore, testing of silicone hydrogel lenses with lens care products is warranted. We realize the need for a scientifically sound grouping system to simplify testing. But no single proposal to date provides all the answers for this rapidly evolving technology.

Any proposal for testing silicone hydrogel lenses should consider both existing materials, and be able to accommodate materials as they evolve. Although we are

still in the information gathering period, in the interim, we believe there are four groups of silicone hydrogel lenses based on current manufacturing technologies.

Here are the proposed interim groupings. Again, the groupings are based on manufacturing technology, which just happens to align with the manufacturers at this time. The grouping system goes beyond FDA's proposal by adding a fourth group reflecting the different properties of these materials.

CLI is developing a concise, user-friendly caution statement to clearly communicate the importance of patient compliance. CLI recommends that the statement appear prominently on the outer packaging of these products, and be standardized to minimize consumer confusion.

An expanded caution statement reiterating the importance of total patient compliance will be recommended for the package insert. Both statements will be presented to

FDA for their consideration and industry-wide implementation. Implementing class labeling for use of these products could mandate steps that are not necessary for their safe and effective use and, indeed, could be counterproductive.

Contact lenses and lens care products are subject to ongoing innovation, which should not be impeded by class labeling limitations. CLI members have either de-emphasized the no-rub directions on their packaging, or moved exclusively to a rub and rinse regimen.

All products currently labeled with directions for a no-rub regimen also provide directions for use as a rub regimen. As part of the 510k clearance process, manufacturers of rub and no-rub products submitted valid scientific evidence in support of the safe and effectiveness of the recommended regimen.

CLI supports FDA's efforts to develop Sightnet, which is part of the FDA

Medical Product Safety Network Initiative, MedSun. In an effort to identify and understand and correct problems with medical devices earlier, MedSun has recently recruited health care facilities to report adverse events on-line.

Manufacturers of medical devices are also required to report serious injuries through medical device reporting, and sponsors of clinical trials must report adverse events under the IDE process.

In closing, I want to emphasize CLI's willingness to participate in a cooperative public process to develop enhancements to the current Class II special controls that govern lens care products. It is CLI's position that any test requirements for labeling mandates should be based on evidence and sound science, and should be administered uniformly.

Again, if warranted, CLI will be submitting additional, more detailed written

comments to FDA. My CLI colleagues and I thank you for your consideration.

DR. BRESSLER: Thank you, Dr. Davies. Now, our next speaker will be Dr. Art Epstein.

DR. EPSTEIN: Thank you, Dr. Bressler, and thank you for the Panel for the opportunity to address you. My name is Dr. Arthur Epstein. I'm a private practitioner with a practice specializing in contact lenses and anterior segment complications of contact lens wear for the past 30 years. I currently reside in Phoenix, Arizona.

I am a past chair of the American Optometric Association, Contact Lens and Cornea Section, and served as the spokesperson for the AOA during the Fusarium outbreak. I am the Chief Medical Editor of Optometric Physician, the Executive Editor of Review of Cornea and Contact Lenses. I do an extensive amount of consulting, and have consulted at one time or another for most of the industry.

I receive honoraria for speaking and research funding. I am currently a consultant for Alcon Laboratories.

And I again thank you for your -- allowing me to present this perspective. And I think you will find it to be, hopefully, a unique perspective, although I will, without doubt, second some of the very excellent recommendations that have already been made.

I think one of the most important things that we have to do is not lose sight of the realities of what we deal with. We are here to make patients safer, and I think that's something that we all share in common.

Contact lenses are medical devices. We sometimes see them as refractive devices, and sometimes underestimate the fact that, like all medical devices, contact lenses bear some element of risk, which most always is justified by the benefit that it brings to our patients.

I'm not going to rehash the