The Contact Lens Rule and the Evolving Contact Lens Marketplace

Panel II: Contact Lens Health and Safety Issues

RICH CLELAND: Good morning.

Contact lenses are regulated medical devices and it is widely recognized that contact lenses involve some safety risks. The goal of this panel is to examine some of those risks as they relate to the Contact Lens Rule. Before getting into that, I would like to briefly introduce our panel members. There is additional bio information in the program material, so I'm not going to give you everything here.

My name is Richard Cleland. I'm Assistant Director of the Division of Advertising Practices at the Federal Trade Commission. My co-moderator is Andrew Stivers, who is Deputy Director of Consumer Protection in the Bureau of Economics at the FTC. Andrew oversees the provision of economic analysis, and advises the Commission on all consumer protection matters. Andrew joined the Commission in 2014 after serving as Director of the Consumer Public Health and Statistical Analysis research division at the US Food and Drug Administration's Food Center.

Our next panelist is Dr. Jennifer Cope. She is a medical epidemiologist and infectious disease physician at the Waterborne Disease Prevention Branch in the National Center for Emerging and Zoonotic Infectious Diseases. She oversees the CDC's health program, and has published several articles on contact lens wear, behaviors and risk factors associated with infections.

We are also joined by Dr. Malvina Eydelman. She is a board-certified ophthalmologist. For over 20 years, as an Expert Medical Officer, Senior Medical Advisor, Director at the FDA's Division of Ophthalmic, Neurological, and Ear, Nose and Throat Devices, and Director of the FDA's Division of Ophthalmic and Ear, Nose and Throat Devices. Dr. Eydelman has played a key role in assuring the safety and effectiveness of medical devices.

Dr. Michelle Tarver is a medical officer at the Food and Drug Administration in the Center for Disease and Radiological Health. She joined the Food and Drug Administration in 2009, where she works on ensuring that contact lens devices are safe and effective before entering the US marketplace, as well as conducts research that incorporates the patient's voice in the evaluation of such devices.

Also joining us is Dr. Carol Lakkis, who is currently the Clinical Research Fellow, Head of Applied Clinical Services for Johnson & Johnson Vision Care. She has over 100 publications, has lectured extensively, and is recognized as an international expert in Ocular Microbiology and Contact Lens-Related Infection and Inflammation.

Finally, Dr. Edward Chaum is the University of Tennessee Hamilton Eye Institute, inaugural Plough Foundation Professor of Retinal Diseases, and Professor of Pediatrics, Anatomy &

Neurobiology and Biomedical Engineering. Dr. Chaum will become the Margy Ann and J. Donald M. Gass Professor of Ophthalmology at the Vanderbilt Eye Institute in April 2018.

With that, I'd like to turn the program over to Dr. Jennifer Cope from the CDC. Thank you.

JENNIFER COPE: OK, thank you. I just want to check. Can I be heard?

Yes?

Great.

So I just want to say thank you to the planners for this invitation to speak here today, and for this opportunity to present a public health perspective to this issue of contact lens health and safety.

First off, I'll just spend a minute or two-- I often start a lot of my presentations this way-- as to why someone here in the Waterborne Disease Prevention Branch at CDC works on contact lens health.

Next slide, please.

So this goes back to our expertise on organisms called free living amoeba, of which one of them is acanthamoeba. Acanthamoeba is the cause of acanthamoeba keratitis, or AK, which is a serious-- fortunately, rare-- but serious cause of keratitis most often associated with contact lens wear. And so it was our expertise in this disease that started our work in contact lens health. It really goes back to the mid '80s, when our group was called upon to offer advice on increasing numbers of case reports of acanthamoeba keratitis. That led to our first case control study, looking into risk factors for this condition.

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Fast forward about two decades and that brings us to around 2006, when again, we found ourselves in the same position receiving increasing numbers of reports of acanthamoeba keratitis. And this led to another case control study, a large multi-state investigation. It was during this investigation that a specific multi-purpose solution was identified as the primary risk factor and this resulted in the recall of the solution.

However, we also documented a lot of other types of behaviors that were putting people at risk for contact lens-related infections. Even after this recall, we noted that these infections did not go down to the previous levels. So that led to a subsequent case control study conducted in 2011, during which we did not find an association with a specific solution, but again, documented a lot of behaviors that might be putting wearers at risk.

It was at this point where the group I work with at CDC decided, well, we enjoy investigating disease outbreaks. We wanted to put into practice what we had learned, which was there are a lot of behaviors going on, and probably a lack of awareness as to what these behaviors could be doing to contact lens wearers. And so we really took to heart that second part of CDC's name,

which is the Centers for Disease Control and Prevention, and really started to develop our healthy contact lens programs to start to try to prevent these infections, rather than continue investigating outbreaks.

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Our healthy contact lens program has a health promotion and education aspect to it, which I'll get into a little bit later. But another aspect of it is just answering some basic questions that we had as a result of the work we had done. One of those questions was, how much keratitis is there? And while this seems like a straightforward question, there wasn't a straightforward source of data to answer this question.

A lot of the diseases we investigate here at CDC are what we consider nationally notifiable or reportable conditions that have to be reported to a state or local health department. Keratitis is not one of those. So we have to be a little bit creative in how we try to answer this question. We ended up using data from the National Ambulatory Care Emergency Department and insurance claims databases. In using this approach, we estimated that there are 930,000 doctor's office and outpatient clinic visits, and 58,000 emergency department visits annually for keratitis and contact lens disorders. And we are also able to estimate that these cost approximately $175 million in direct health care expenditures on an annual basis.

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Another basic question we wanted to answer was what epidemiologists are always searching for, which is our denominator. So how many people are at risk for this condition? In this case, this is contact lens wearers. And so one basic question we wanted to answer was, how many contact lens wearers are there in the United States? We know there was a lot of market research data on that, but we wanted to put an estimate out in the scientific literature.

And then the second part of that is what are these contact lens wearers doing? What are their behaviors, how prevalent are these behaviors? So that led to our estimate of 41 million adult contact lens wearers and then the second part of that was surveying about 1,100 wearers, in which we determined about 99%, or almost all of them, reported at least one contact lens hygiene risk behavior. And also part of that survey, nearly one third of them reported having experienced a contact lens-related red or painful eye that required them to seek medical attention.

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So diving in a little bit deeper to that survey of the 1,100 contact lens wearers, this table is showing the most frequently reported behaviors. So the most frequent reported behavior that could put them at risk was napping in contact lenses. 87% reported that, as well as about half reported sleeping overnight in them. I point that out because other work in the literature does show that sleeping and napping in contact lenses to be one of the riskiest things that you can you do to put yourself at risk for contact lens-related infection.

Another common behavior was topping off solutions. This is when you don't completely dump out the old solution in your case, and you just top it off with some new solution. This was done by over half of the respondents as well. About half reported replacing their lenses in an interval longer than what was recommended. And then also, a very large percentage reported replacing their case at an interval longer than recommended.

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I know there's been data already presented on this, but as part of this survey, we also asked where the wearers were purchasing their lenses. Based on this 2014 data, the majority were purchasing them in a provider office. 10% were purchasing them in a retail store without the eye exam. And then nearly 21% were purchasing on the internet.

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And then we did ask this question again in 2016, when we also included adolescents as part of the survey. Numbers don't look terribly different than the 2014 numbers. Again, most are purchasing in the provider office. And then for the internet purchase, you notice that the young adult age group, the 18 to 24-year-old age group, is the one purchasing from the internet most frequently.

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Some additional work we did in collaboration with our FDA colleagues was to use a different data source to kind of, again, get at some of these questions we had about how much keratitis, and what types of the behaviors do our wearers have. This time we again collaborated with FDA to use their medical device report database. As you'll probably hear more about from my FDA colleagues, contact lenses are regulated medical devices, and as such, manufacturers are mandated to report any adverse events occurring with those devices.

In this study, we found just over 1,000 contact lens-related medical device reports that contained the term ulcer or keratitis. And not surprisingly, most of them came from manufacturers, and a smaller percentage were reported by the eye care provider or the patient. And 20% of those described a patient who had a central corneal scar, a decrease in visual acuity, or required a corneal transplant following the event. And we reported this data to show just how serious some of the outcomes are for these events.

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As I mentioned, the other aspect of our healthy program is a health promotion and education aspect. What we were finding is that just a lot of contact lens wearers were not even aware that some of these things they are doing--that they probably just considered harmless shortcuts--could actually be putting them at risk for a contact lens complication.

And so on this slide, we just have a couple examples of some graphics that we've created that can be used on social media. You'll see on the far right, we have our contact lenses are like underwear campaign that's been very popular, and has gotten a lot of attention.

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One of the hallmarks of our healthy contact lens program is contact lens health week, which has been marketed every August, and will be coming up this August for the fifth annual contact lens health week. That's kind of our major push to get a lot of these messages out through social media and through our partners. And this is usually the research that I just presented on estimating the burden of keratitis, and reporting on these behaviors. We publish in our CDC's publication morbidity and mortality weekly report. And so we usually kick off the contact lens health week by putting out whatever our report is that year to garner more attention.

And then next slide.

I'm not sure if we'll be able to get this to work, but this is a video series that we completed last year that featured three patients who had an infection related to their contact lens wear. They are like video testimonials in which they describe what happened, and kind of the lessons learned from that. So if we can get it to play, it's about two and a half minutes. Great.

[VIDEO PLAYBACK]

RON PARIS: My name is Ron Paris. I'm from Madison, Alabama. I'm a junior at the University of Alabama.

I first noticed that my left eye had a problem when we were about to play LSU, and I was getting ready for game day. And I looked at my roommate, and I said hey, is there something wrong with my eye? He said, no, it looks fine, looks fine. But I was having a lot of pain. And after that, my eye started getting more and more shut every day. And I started feeling more and more pain. You know, I just thought it was another scratch, but I didn't know what it was going to turn into.

About a month later, I went to a doctor's office in Birmingham, and she was like, you have acanthamoeba keratitis. I was like, OK, what is that? She told me that some people experience blindness, very sensitive to light. And that basically, it eats away at your cornea to the point where you can either just go completely blind or you have to have a cornea transplant, or you would lose your eye. And so of course, I'm like, OK, well all those sound bad. I'd rather not have to do that.

I was a terrible contact lens user when I was in elementary school. And I got better when I got to middle school, but it still wasn't very good. So I'd just wash them out in tap water, or lake water, or river water, wherever I was. That was just a normal thing for me. I saw my grandfather had hard contacts, and I saw him do that all the time. So I'm like, all right, no big deal. So it was just another thing. I didn't figure anything could come bad from it. It's just water.

Tap water definitely contributed mostly to the whole thing. That week, I ran out of solution, so I just was using tap water. Just a normal thing for me. Right now, I have a giant scar on the middle of my left eye from infection. I cannot see directly in front of me. I can see peripherals pretty good, but I cannot see directly in front of me very well. If I covered up my right eye right now, I could kind of tell what was going on around me, but I couldn't really say specifically who someone is.

We're hoping that surgery or whatever goes well to get that scar away from me, so I can go back to seeing normal and maybe even wearing contacts again.

If I knew more about washing contacts in water back then, I feel like this would have been 100% avoidable.

[END VIDEO PLAYBACK]

JENNIFER COPE: Well, thank you. That's all I have.

RICH CLELAND: Turn it over to you Dr. Eydelman, please.

MALVINA EYDELMAN: Good morning, and thank you for the invitation. As you heard, I work for the Food and Drug Administration and I would like to take a few minutes to share with you what we do at the FDA to assure US regulation for safe use of contact lenses.

I would like to start out by acknowledging the staff members on this slide who have put together this presentation. Most of them are here in the audience, and hopefully, will be available throughout the meeting should any of you have questions.

This as the official definition of a medical device. Medical device is intended to diagnose, cure, or mitigate, treat, or prevent a disease or condition, or intended to affect the structure or function of the body, and does not achieve intended use through chemical action on metabolism. I would like to point out that unlike drugs, there are no generic medical devices.

All of the devices are classified into three classes. Class I being the simple design, the lowest risk. And most of these are exempt from pre-market submissions. Class II are more complex with moderate risk and most of these require pre-market notification to demonstrate substantial equivalence before they are allowed to be marketed. Class III are the most complex, highest risk, and these require PMA or pre-market approval to demonstrate reasonable assurance of safety and effectiveness before these devices reach the US market.

FDA regulates all contact lenses. Lenses are classified as either Class II or Class III. All daily wear lenses, soft, and rigid, gas permeable are Class II. And all of the extended wear lenses are Class III. I would like to emphasize the point that in addition to the refractive error corrections, there are contact lenses that cleared or approved for other indications, specifically to promote corneal healing, bandage contact lenses. For the temporary reduction of myopia, ortho-k contact lenses. To enhance or alter the appearance of the eye, decorative contact lenses.

Again, these are indications which are currently available in the US. But I would like to emphasize that currently we are seeing an explosion of other indications that are being studied, and developed by the manufacturers in the US.

Per our colleagues from CDC, there are approximately 45 million Americans who are wearing contact lenses. 35% wear daily disposable. Over 90% of adult contact wearers use soft contact lenses. Now the next two bullets weren't emphasized sufficiently so far. So I'd like to bring to everybody's attention that about 11 million wearers are between ages 12 and 24. Thus, teens and young adults-- there's a significant public health impact in that population from contact lenses.

The risks from the use of contact lenses are many, and have been addressed by a number of speakers. Some of these, not all, are listed on the slide. These include microbial keratitis, allergies affecting the eye, GPC [giant papillary conjunctivitis], corneal abrasion, contact lens-induced acute red eye, corneal infiltrates, dry eye, and neovascularization.

In a study that looked at all of the emergency room medical record reports from the National Electronic Injury Surveillance Database, it was found that contact lenses accounted for most medical device adverse events compared to all other devices. I bring this fact to emphasize the impact of public health that contact lenses have. Subsequently, FDA has worked very diligently to put a number of safeguards to assure the safety of contact lenses.

We spend significant resources reviewing pre-market submissions. My division has been involved in standards, both on the national and international level for a number of decades. We have guidance, post-market surveillance, such as MedWatch, PAS, and 522 studies. We have conducted our own research and we have spent a significant amount of resources on outreach.

All contact lens pre-market submissions undergo thorough review by the team in my division. We make sure that we review the materials and chemistry, manufacturing, sterility, shelf life, biocompatibility, performance testing, non-clinical, and clinical performance testing. Recommendations for these are described in our guidance and the recognized standards.

The chemistry review of contact lenses is quite unique. Properties unique to each contact lens product that may affect performance are summarized on the slide. These are material composition, physical properties, surface characteristics, packaging solution composition, material and manufacturing residuals, interaction with care product solutions, and lens design.

Evidence supports marketing clearance or approval for each new lens material that reaches the US market. We assess the following: adverse reactions, slit-lamp exams, symptoms, problems, complaints, keratometric changes, visual acuity, average wear times, discontinued eyes, lens replacement, contact lens performance, and lens surface characteristics.

We communicate many of these in our contact lens labeling. The following couple of slides summarize the information in our contact lens labeling that is similar to the prescription elements. Specifically, manufacturer's brand name. This really refers to the entire device, inclusive of the material name, manufacturing process, packaging solution, and other factors which may impact the unique attributes to the lens material. Distinguishing attributes can result

in differences among materials in contact lens fitting, performance, and ultimately, in ocular health.

Base curve affect the alignment of the lens to the topography of the central cornea. Important to point out is that the same base curves for different brands may not be clinically equivalent. Diameter affects the lens centration and once again, same diameter for different brands may not be clinically equivalent. Dioptic power affects strength of the correction. Improper power may result in reduced visual acuity, eyestrain, and headaches.

Currently, there is no regulatory pathway for marketing of generic contact lenses. The current clinical care paradigm does not support substitution of contact lens brands without a clinical evaluation. Additional research and education is needed regarding critical design and material properties to support clinical equivalency between lens brands.

As I mentioned, we at the FDA have worked for a number of decades in creating and recognizing consensus standards. This slide is a summary of those standards, which have been recognized by the FDA. These include both US and international.

Additionally, we have two current FDA guidances, which describe our interpretation of our policy over regulatory issues, and they talk about labeling, manufacturing, and clinical studies that we would like to see in the submissions.

Post-market, we have a number of ways to collect information to report adverse events, including contact lens related infections. The slide contains the link to the FDA MedWatch and the FDA website specific to report the problems with contact lenses. Additionally, when needed, we have conducted 522 studies, which has a mandated post-market surveillance study.

Given the impact on the US public health, we have taken unprecedented measures and conducted quite extensive research in-house. As a result of our research over the last 10 years, we categorized the numerous silicon hydrogel lenses to address concerns with dimensional stability and toxicity. We evaluated the efficacy of care product solutions in the presence of lenses, i.e., real world evidence, real world testing and we developed acanthamoeba test methodology. The references on the slide summarize some of our articles. Most of these in the eye and contact lenses, and the last one was published just a couple of weeks ago.

To ensure the safety and the transparency of our work, we have held a number of public meetings over the last decade. Most of these are summarized on the slide. As you can see, we have had advisory panel meetings and a workshop to address different aspects of safety of contact lenses.

We have a separate team dedicated to outreach for contact lenses. We have published consumer-focused articles, which were distributed to over 75,000 subscribers. We have very popular websites, two of which are dedicated to contact lenses at FDA; one is to all contact lenses, and one to decorative contact lenses. We're very fortunate to partner with CDC and working on their website as well.

We have conducted Medscape commentaries and interviews. Have put together and a number of videos, including public service videos, which inform the proper way to wear lenses, and recommended getting an eye exam and a valid prescription.

And we have done something very unique for FDA. We have launched a Twitter campaign regarding decorative contact lenses. And as my CDC colleague has mentioned, we also participate in the contact lens health week, and have launched a Google AdWords campaign.

As you can see, we take contact lens safety very seriously, and have dedicated a significant number of resources to assure that the Americans who wear contact lenses remain healthy. Should you have any further questions, I suggest you contact Dr. Angelo Green, who is in the audience. Angelo, if you can wave, he's the acting branch chief overseeing contact lenses at the FDA. Thank you very much.

RICH CLELAND: Thank you. Dr. Lakkis, go ahead.

CAROL LAKKIS: Good morning, everyone. My name is Dr. Carol Lakkis, and I'm representing Johnson & Johnson Vision Care Incorporated. As the head of applied clinical sciences within the contact lens research and development group, I'm responsible for leading exploratory research to support new product development.

In my role at Johnson & Johnson Vision, I bring decades of experience as both an ocular microbiologist, and optometrist, and have spent more than 20 years conducting research on contact lens related infection and inflammation, disinfection and discomfort, and the therapeutic management of ocular disease. In short, I've dedicated my career and my work at Johnson & Johnson Vision to improving patients' overall eye health and the contact lens wearing experience.

Today, I'm pleased to be here to offer my perspective on why it's vital that our vision care regulatory framework continues to preserve the eye doctor-patient relationship to achieve two important goals. First and foremost, to minimize health related risks and complications associated with contact lens wear. And secondly, to bring new and innovative contact lens technologies for physicians and patients.

Over the past three decades, as the contact lens landscape has grown, eye doctors continue to play a critical role, not only in promoting eye health, but also in working with individual patients to find the most appropriate contact lenses to meet their unique and evolving needs.

Ensuring patient access to an eye doctor for a contact lens fitting and evaluation is critical, because contact lenses are applied directly onto the ocular surface, and these complex lens materials interact with the environment, including the patient's cornea, tear film, and eyelids. In clinical practice, I would regularly explain to my patients that finding the appropriate lenses for their eyes doesn't just provide them with overall comfort and enhance their lens wearing experience, but more importantly, it can minimize the negative impact on their eye health, not just over the next year, but over the next 50 years.

That's why wearing any type of contact lens not prescribed by an eye doctor could lead to a variety of complications from mild discomfort to severe adverse events like inflammation and infection. Current research suggests that inflammation and infection are on a continuous spectrum.

So while an issue like inflammation may not sound like a critical health condition, it's important to address as quickly as possible so that it doesn't develop into something more serious, or cause any permanent damage to the eye. In fact, because clinical complications can arise prior to the onset of symptoms, a regular comprehensive exam with an eye doctor is critical to minimizing risks and impacts on eye health, and reducing unnecessary costs to our health care system.

While we know the value of regular patient visits to their eye doctor, one of the most significant challenges that we face stems from the fact that contact lenses have become widely used, and as technology has evolved, doctors and scientists like myself have focused on ways to minimize risks associated with wearing lenses. And we've had great success.

However, these successes also make it easy to underestimate the importance of consistently going to the doctor for a comprehensive eye exam, even when a patient's current contact lens seem to be working, and their eyes seem to be healthy enough to continue to wear their lenses. Furthermore, a patient's eyes are a window to their overall health, and need ongoing care to keep avoidable health risks low.

Importantly, the challenge of reducing contact lens adverse events isn't unique to the US. We have some notable advantages in how our current regulatory system balances access and choice with patient eye health and safety. In fact, when looking at adverse events globally, the research suggests there are higher risks in markets where patients don't need prescriptions for contact lenses or in those markets that don't require a comprehensive eye exam with an eye care professional.

For example, in many Asian countries, patients don't need prescriptions for contact lenses, and as a result, higher infection rates are reported. In addition, contact lenses can be the leading cause of corneal infections in unregulated markets, such as in Taiwan, which is not always the case in studies from regulated markets such as the US and Australia, where ocular surface trauma and diseases are common causes of infection.

It's extremely important to balance source of supply with an eye doctor's guidance and supervision to make sure lenses have fitted correctly, and maintain biocompatibility with the patient's eyes.

So in closing, at Johnson & Johnson Vision, we take our role as a leader in eye health seriously. It provides us with a platform to advocate for better standards of care for all patients. As part of this commitment, we support the eye doctor-patient relationship, and continued patient access to innovative lenses, which best addressed that evolving eye health needs.

I'd like to thank the Commission for this opportunity to share my comments here today and I'm happy to address any questions during the panel discussion. Thank you.

RICH CLELAND: Thank you. Dr. Chaum.

EDWARD CHAUM: Thank you. I'd like to bring just a slightly different perspective to the conversation this morning. I think you've heard some really important data about the potential risks of contact lens wear if they're not managed properly, and proper hygiene isn't used in their daily care. I think it's very clear, and I certainly agree that all patients who wear contact lenses should have an appropriate contact lens fitting by an eye care professional. I don't think there's any there's any question about that.

But, a lot of the health issues around the availability of contact lenses for consumers has focused on the need for an annual eye exam that, in some way, it's critical, as Dr. Lakkis says, feels it's critical for there to be an annual eye examination for the patient, for the patient's health. And the America Optometric Association has a preferred practice pattern, and they recommend an annual eye examination and I certainly respect the perspective of that Academy. And obviously its members are going to follow the recommendations of their professional association.

I'm an ophthalmologist, a physician, and surgeon and my professional academy, the American Academy of Ophthamology has a different recommendation. And I think it's important for the FTC and consumers to understand that there's a difference of opinion about what is required to maintain proper eye health.

So my academy issues what's called a preferred practice pattern. It's their recommendations of how we should manage patients. And the Academy's preferred practice pattern for patients between the ages of 18 and 40 is that those patients need a periodic eye examination to maintain good health and that examination should occur anywhere between five and 10 years. That's the recommendation of AAO, not mine. That's the recommendation of the AAO.

Patients under the age of 40 should have a good complete examination every five to 10 years. Patients above the age of 40 and less than 55 should have an examination every two to four years. So I think there's a legitimate difference of opinion between the professional societies as to what is required in terms of a periodic eye exam to maintain good health.

Now clearly, the risk of developing conditions like keratitis in contact lens wearers is known. Dr. Cope has presented a good example of that. It's not an infrequent occurrence. You've seen the numbers there. But Dr. Cope's data also shows that the vast majority of those patients are cured within one visit of the physician. She's published that data.

And it's not clear, actually, that seeing a physician or an optometrist on an annual basis has any impact at all on the incidence or prevalence of keratitis. There's actually no data in the published peer-reviewed literature that shows any beneficial relationship between a normal eye examination and the incidence of keratitis.

As a matter of fact, there's one page paper in the literature that actually addresses that association. It was published by Morgan in 2006 and it showed that for case controlled patients who had an episode of keratitis, the patients who had documented a normal healthy eye exam within six months of developing that keratitis were at a two-fold increased risk of developing

keratitis. In other words, the normal eye examination documentation was associated with a higher risk in that case control study.

So it’s not that there's something about the eye exam per se, that puts that patient at risk. Maybe that patient's behavior changed. But it's clear from the publications across the world for the last 25 years that the risk factors associated with the development of keratitis and contact lens wear are behavioral and hygiene-related risk factors. It is sleeping in your lenses. It is napping in your lenses. It's not changing the solutions.

And we've seen this dramatic decrease in the incidence of keratitis over the last few years that you've heard about in parallel with the onset of the adoption of daily wear lenses. And it's that change in technology that's making contact lens wear safer for patients and reducing the risk of keratitis.

And so really, in terms of sort of helping the FTC decide how should patients get their lenses, who should provide them, the data clearly shows that open access through channels of large retailers online really has no impact at all on the incidence of keratitis, and complications. It's all about the patient's behavior.

And again, Dr. Cope showed some data earlier this morning that show that the incidence of keratitis in patients was unchanged. Two-thirds of those patients had a close relationship with their prescriber, and had gotten their lenses from their prescriber. And one-third of them had gotten them online. There is no relationship between documenting a normal exam in an asymptomatic patient and the risk of keratitis.

So, I don't think there's any question that we all want to provide good health care. The question is how do we provide that in a way that is convenient for the patient, that meets their personal needs, and meets their financial needs, that addresses appropriate management of health care risk, and provides an open forum for patients to participate and for the physicians to help them wear their contact lenses safely. Thank you.

RICH CLELAND: Thank you.

I would like to start up actually kicking off a couple of things that you said, Dr. Eydelman, and talk a little bit first about the interchangeability of lenses, and the characteristic of lenses that suggest that they may not be interchangeable. And you had a couple of slides here in your presentation about what's unique about contact lenses as well as some labeling-- a slide relating to labeling-- where you mentioned base curve diameter and dioptic power. I wonder if you could comment on what the relationship is between these elements and the risk to the eye. The material may be different. How does that relate to safety?

MALVINA EYDELMAN: And I was hoping-- I don't know if there's a way to project the slides back, but I was trying to go back and highlight the specific aspects of prescriptions.

No, I have it. Just the notes so the audience can see it again. Basically, my groups spent a bit of time to try to be very objective, and clearly stated what are factual.

First of all, what we put in the labeling-- only factual information, as you can imagine. We spend a lot of time reviewing the submissions, and then communicate that information in the labeling. And the point we wanted to make-- and I'm going to just essentially accentuate the same-- that the manufacturer's brand name refers to the entire device. And distinguishing attributes within that manufacturer's brand name can result in differences among materials and contact lens fitting, which will have impact on performance and ocular health.

RICH CLELAND: Right. And I'm trying to distinguish between what part of that relates to comfort, and what part of that relates to safety.

MALVINA EYDELMAN: So sometimes, comfort has to do with fitting and if it doesn't fit right, first you're uncomfortable. And then at some point, you start getting irritation and subsequent inflammation and I would like Dr. Tarver to pipe in.

MICHELLE TARVER: So the factors that Dr/ Eydelman already described in her slide about the different materials-- there are other aspects, such as the stiffness of the material, how the lens edge, and how it interacts with the ocular surface that potentially could put the patient at a higher risk of infections. And so some of those factors are not the same, even though it may be the same material, or the same base curve, or the same diameter. They may not fit exactly the same from patient to patient, or within the same patient.

RICH CLELAND: And there is no way to determine that without an actual fitting? I mean, we got 41 million contact lens wearers. Obviously, some of those could wear any type of lens, or most types of lenses that are popular.

MALVINA EYDELMAN: And so unfortunately, at the current time, the same diameter of different brands is not identical. The same base curve, the same number, if it's a different brand, doesn't mean the same thing. So ultimately, you still need to fit in order to prescribe the appropriate contact lens.

EDWARD CHAUM: There may be a movement towards a more generic fit. There was a publication in Contact Lens Spectrum last year by Ngo that showed that if you look at the contact lenses that are available by brands, they're really becoming commodities. There's one diameter for most brands, and one or two base curves. And Ngo's paper showed that 90% of patients had a good and comfortable fit with just selecting one of those base curves, and 98% of those patients were comfortably fit if you checked both.

So the changes in the way the lenses are made, the thinness, the nature of the wear with the lenses is becoming, at least according to this author, much less dependent upon the specific fit, and much more of a generic type of fit.

CAROL LAKKIS: I was just going to add that while there are many different features to lenses that can impact the way that they fit, what we do know and from the research data is that if, for example, a lens is tightly fitting on the eye, then the risk of having an inflammatory or infectious event increases. And sometimes, those things can't be detected just at the fitting visit. It requires evaluation after the lens has been worn for some time, and that is necessary during follow up

visits, and examinations at different times of the day. So there are specific ways that different properties of the lenses can actually impact fit that have a distinct impact on comfort, but also on actual eye health.

MALVINA EYDELMAN: To come back to your point, we at the FDA think it would be wonderful if one day the base curve would mean exactly the same thing for all brands. Unfortunately, we're not there today.

RICH CLELAND: I have one more follow up question on this topic, and then we'll move on. But in your slide presentation, you had the statement that additional research and education is needed regarding critical design and material properties to support clinical equivalency between lens brands. Given the current regulatory and market structure, is there actually incentive out there to conduct that type of research?

MALVINA EYDELMAN: So maybe this workshop will be the incentive. But in the current regulatory paradigm, that's not needed in order to get new product on the market, new contact lenses approved and sold in the United States. But there are many other impetus and perhaps, again, this workshop will be such.

RICH CLELAND: Thank you. Andrew.

ANDREW STIVERS: Thanks. I want to spend a little bit of time focusing on the role of the examination itself and Dr. Chaum talked a little bit about the fact that there doesn't seem to be any data linking eye health to examinations. And I want to unpack that a little bit. I think there's been some discussion of maybe a distinction between an initial visit, and ongoing visit but I want to give folks an opportunity to talk-- is there additional data that might be out there that would link these things? And the thing that we always want to see with data is what's the mechanism by which we would think there would be a link and also examine the empirical data for that mechanism. So I would open this to any of the panel members to talk a little bit about what the mechanism for reducing risk factors associated with contact lens use by the examination, either initial examination, or ongoing examinations.

EDWARD CHAUM: A correction. My point wasn't that an eye examination was not indicated or required, it's really about how often do you need to reassess the patient. So obviously, every patient deserves and needs an appropriate eye examination, and an appropriate contact lens fitting. It's very clear that an initial fitting is important. And it's the unregulated use of contact lenses, people who don't get fit, buy them over the counter, at a flea market or wherever, who have significant complications we hear a lot about.

The issue then really becomes what is effective management for that patient, and how often does that patient need to be seen. I would assert that patients who wear contact lenses, when they have difficulty with those lenses, they become uncomfortable. Their wear time goes down. Maybe they get a little bit of redness. They become symptomatic from the use of those contact lenses. And we heard, actually, today about how patients drop out of contact lens wear because they develop these issues.

And I think it's part of our education as eye care physicians to inform those patients that if you have a problem, if you're having difficulty with your lenses, if you're having difficulty with your wear time, then you should come back for an examination. It's not about keeping the patient away from the eye care professional. It's about trying to find a balance between what is an appropriate periodic re-evaluation of a patient who is asymptomatic, who doesn't have clinical symptoms, who has good vision.

We used to think that every patient needed a general medical examination every year. I'm incentivized by my health care plan to go see my internal physician every year. My health care costs are less if I do that. But it's very clear from the Cochrane collective publications and from other sources that an annual examination, an annual physical examination, for someone like me, who is asymptomatic, has no benefit to the patient. It adds health care costs to the system, it has no benefit. And the US Preventive Health Care Task Force, which is an independent agency that assesses health care utilization, came out in 2012, 2013, and recommended against routine annual physical examinations for people like me.

Same thing happened with glaucoma. In 2015, the task force said, patients don't need to be screened for glaucoma on a yearly basis. I think that's a terrible idea for certain patients-- for patients who are at risk. But the routine screening of patients to look for glaucoma was determined by the preventive task force as having no value in preventing disease, and improving health care.

ANDREW STIVERS: Dr. Lakkis, seems like you want to respond to that.

CAROL LAKKIS: Yes, I'd first like to make a comment that there are a number of things that can occur when you are wearing contact lenses that do not actually first start with symptoms. So one thing that we often see as a complication in contact lens wear is asymptomatic infiltrates.

So sometimes, the first time that these are discovered is actually during an eye exam where you may see a scar. And a scar in the cornea, depending on its location, may impact vision. But more importantly, as I mentioned previously, something like that indicates an inflammatory process is occurring.

Now when inflammation gets bad, then yes, you might notice symptoms. And like we saw in the video from Jennifer Cope, the footballer who noticed that his eye was getting more and more uncomfortable. But a lot of these early changes to the tear film, changes to the corneal integrity, looking under the eyelid, and looking for early signs of inflammation in that area as well, these things can occur without symptoms. And as a practitioner, you have a better chance of success intervening earlier if you're able to actually do that rather than waiting until things actually progressed. And in the field of inflammation, what we understand, particularly with CIEs, is once you've had your first corneal inflammatory event, your chance of having another is then increased by 50% for the following year.

So there is a definite need to have a comprehensive evaluation of every contact lens wearer for health and safety purposes, but then also, as an opportunity for re-education. So we also heard a lot this morning about the opportunities for modifying behavior, and there is lots of research, and

lots of evidence that shows that when you do actually receive education, your behaviors can change. But it's not a long lasting and permanent thing. It requires a lot of periodic re-education to keep the actual information for patients relevant, and focused on their specific needs, and their lifestyles, and their scenarios themselves.

ANDREW STIVERS: Apparently, that's a really that's a very popular view.

CAROL LAKKIS: Yes, clearly. Thank you, everyone.

ANDREW STIVERS: One brief clarification question for Dr. Chaum. Does the American Academy of Ophthalmologists have a specific recommendation for the frequency of visits for contact lens wearers in particular?

EDWARD CHAUM: Not that I have seen. Not in their preferred practice plan.

ANDREW STIVERS: Thanks. So the final question I want to address sort of in this area of examinations in particular is, there was mention of other countries that have different practices. Is there specific data that relates to the frequency of visits in some of the other areas that have different rules, versus how the US practices?

EDWARD CHAUM: I think the data is actually pretty informative. So outside of the United States, although it is recommended that patients have periodic exams, depending on the country, every two or three years, for all intents and purposes, contact lenses are more of a commodity. You can buy contact lenses in any vending machine in any train station in Europe.

And yet, if you look at excluding the Asian data, if you look at the data of the incidence and prevalence of keratitis in regulated areas like Australia and in Europe, what you see is that the incidence and prevalence of keratitis is exactly the same as it is here in the United States. The risk factors are behavioral, modifiable risk factors that relate to duration of use, hygiene-- sleeping with lens and so forth-- the exact same risk factors. So in countries in which FDA regulations do not exist, and they are less regulated, the incidence is the same.

The one thing that is, I think, important to point out is that things have changed here since the original FCLCA a ruling in 2004. And so the concern at that time, as I go back and read the notes on it, was that we would see an increase in the incidence and prevalence of keratitis associated with contact lens wear if the markets were opened up to online vendors and non-eye care professionals selling contact lenses. That was a very significant concern. And what we've seen since that time is that there's been absolutely no change in the incidence and prevalence of keratitis in this country after the initiation of the Contact Lens Rule.

So I think it's very clear that the vast majority of the risk relates to behavioral use of lenses. And I think the biggest and most important thing that we can do for our patients is to educate them properly, and continue to educate them on how to wear their contact lenses properly.

ANDREW STIVERS: Are there any other-- yeah, please.

MICHELLE TARVER: I know that there is literature out of France that looked at the different dispensing patterns of contact lenses with opticians, optometrists, ophthalmologists, and found that when the patients did not undergo an eye exam, their risk for microbial keratitis was exponentially higher. So there is data out there about the harms that can happen with contact lens use without the eye exam.

I would want to offer one other statement, which is that a lot of the literature that we're citing are case control studies about the impact of the visit. And what we really need is a prospectively done study, where we are not biased by recall bias of patients who are harmed, recalling when they go to see their doctor. And to do that, we would need a registry or some other mechanism to collect data in an unbiased way on the patient population that's using contact lenses.

So one of the challenges with a lot of the inferences that are made is that the data doesn't really support a causal inference and so we have to be very careful in interpreting the literature.

RICH CLELAND: I'm going to intervene here just second. We've got about 10 minutes left on this panel, and we still have a couple of questions that we want to get out there and discuss. So if the audience could hold their applause in between the speakers, that would save us some time. Thank you.

So we were going to move into actual identification of the risks from use of contact lenses, but I think that's already been covered in a number of the presentations. So we don't have to spend much time on that. I have one question I would like to ask, and probably, I'll start with you Dr. Lakkis, on this question.

When I looked through the research-- and a lot of the research is articles that you provided to me-- there are a number of studies that focus on microbial-- I got it right-- keratitis. And then there are some other studies, particularly I think the Clay study recently, that look at more than just keratitis. What's your view the appropriate risks that should be looked at in this?

CAROL LAKKIS: So as we've heard about today, fortunately, microbial keratitis rates are fairly low relative to inflammatory event rates. So in microbial keratitis, we're looking at analyzed incidence rates between four and 20 per 10,000. But for inflammatory events, we're seeing rates anywhere between 5% and 25% of contact lens wearers per year.

And Dr. Eydelman and Dr. Tarver can comment more than I can, but for understanding health benefits and risks for eye health in terms of inflammatory and infectious events, we can use corneal inflammatory events as a surrogate for MK, for microbial keratitis. And what we do often see is a lot of the similar risk factors between both. And as I mentioned earlier, inflammation and infection are now, the research tells us, on a continuous spectrum. So what might start off as what appears to be an inflammatory event could actually be a potentially infectious event.

And luckily, for ourselves here in the US, and other countries like Australia, and the UK, the standard of care is that if you see one of these inflammatory events in a contact lens wearer, you

treat it as if it is microbial keratitis, so that you don't take the risk that it will actually progress. So that that's where the data is differing. But the risk factors tend to be very similar for both.

ANDREW STIVERS: So I want to ask a fairly specific question in terms of what the role of point of sale might be in determining some of these risk factors. And in particular, is there data? If there isn't data, what the mechanism, associated with, linking risk with point of sale might be. And then a brief comment about what factors might influence that mechanism, and how that might be changed. And again, open this up to anybody on the panel that might want to comment.

CAROL LAKKIS: I could start. So there's actually some recent evidence that suggests that internet purchase may result in a five times higher risk of infection compared to purchasing through a more traditional channel. But there are other studies that don't show internet purchases being a significant risk factor. So I think we do need more evidence in that area.

Going back to a previous point, more critical, I think, is ensuring that when a contact lens is fitted and prescribed that patients are actually obtaining that actual prescribed and fitted contact lens. That they're obtaining what the eye doctor has determined is the best for their eye health, their eye anatomy, their lifestyle choices, and needs. And so ensuring that that happens, I think, is a factor that plays a role in some of these epidemiology studies.

It's also been suggested in those studies that there could be a lack of relationship with the eye doctor, and knowing when to go back, and see the eye doctor could be what is underlying that increased risk. So it's not the purchase process itself, but the possible education around that. Further research is needed.

EDWARD CHAUM: Yeah, so there really isn't a lot of data that suggests that there's any relationship between the development and incidence of keratitis and the point of purchase. There was a study back in 2004-05 Stapleton's a group in Australia, which has done a lot of work in this area, that suggested that there might be an association. And that study was repeated and was published back in 2016, and showed that there was no association of point of purchase related to that development of keratitis.

The study that Dr. Lakkis is referring to is a recent study by Sorbara, which is, in my view, a fairly weak study. In the data that suggests that there's a five-fold increased risk of developing keratitis from purchase online has to be balanced with the fact that the other findings in that paper were that there was a three and a half fold increased risk if my mother purchased it for me. And there was a three and a half fold increased risk if the young person lived on their own as opposed to having a roommate.

So these sort of weak associations really are, I think, statistical noise, and really don't add to the literature in a meaningful way. We just don't know. But what we do know is that for the many, many, many studies of case controlled keratitis that have been published over the last 25 years, there is no real strong evidence that there's any relationship between point of purchase and the development of keratitis.

CAROL LAKKIS: Can I just clarify, I was actually referring to the Stapleton's studies for the five time increased risk. And the more recent Stapleton publication is looking specifically at daily disposables, where point of purchase was not a significant risk factor in reuseable wear as it was.

RICH CLELAND: The reuseable one-- please, you know this better than I do-- I thought the reuseable one with the total was the 2008 study. So it's an older set of data, it's older than 10 years at this point. And the while the 2017 study didn't show a relationship for a specific type of lens-- that's kind of, you don't know what you would do if you had looked at all lenses there at this point.

CAROL LAKKIS: I think it's important to look at the body of evidence overall. We don't look at any one individual study, as Michelle was also saying. You need to actually look at everything-- the information that's coming from all different countries, as well as different types of studies that are conducted, and interpret that overall, rather than just honing in on one particular outcome.

RICH CLELAND: I have one last question, because we're out of time. But I need to at least touch on this for a second. And if somebody has a one minute response, I will take it.

Cosmetic contact lenses. How is that affecting some of these studies? Is the sale of those types of lenses OTC reached such a proportion that they're affecting the results of the data that we're seeing at this point?

MICHELLE TARVER: So a lot of the studies have incorporated or collected information about decorative lenses, and we do see a higher risk with decorative lenses. We've seen patterns within our NDR database also with decorative contact lens wearers having higher impacts on their vision. The challenge, as I already alluded to, is that we don't have a good denominator, and we don't really know the true incidence rate associated with the different types of devices, because we haven't systematically studied it. And I'll make a plug once again for a registry for contact lenses so that we can have some answers to these questions that we're all trying to understand.

RICH CLELAND: OK, thank you.

All right. We are going to break now. I want to thank all of my panelists for an excellent discussion, and I apologize for all my mispronunciations. But thank you again.

ANDREW STIVERS: And we will reconvene at 11:15.