March 17th Ophthalmic Devices Panel and RCAC Planning Meeting Executive Summary

A. Introduction

The safety and effectiveness of peroxide-based contact lens care products when used as directed has been well established for over 30 years. However, the number of adverse event reports related to misuse of these products have been increasing and causing alarm among some consumers. Given the persistence of these adverse events, the Ophthalmic Devices Panel of the Medical Devices Advisory Committee and the Risk Communication Advisory Committee (RCAC) will meet on March 17, 2017 to discuss additional measures to mitigate the potential risk for misuse of these devices.

B. Regulatory History of Contact Lenses and Care Products

The Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act (FDCA) of 1976, afforded the FDA with the legal authority to regulate the marketing of a wide variety of medical devices. With the passage of the Act, contact lenses and care products, which previously had been regulated as drugs, were categorized as class III medical devices, [1,2] As a result of the Safe Medical Devices Act of 1990, daily-wear soft and rigid gas-permeable (RGP) contact lenses were reclassified in 1994 to class II. However, overnight extended-wear contact lenses remained as class III medical devices due to the increased risk of adverse events, such as microbial keratitis. In 1997, all contact lens care products were reclassified to class II. With both reclassifications, the FDA issued guidance documents to industry, which recommended specific preclinical and clinical testing as well as labeling that is considered necessary to regulate these products as class II.[1,2] Submission of a 510(k) is required for most class II devices. As part of the 510(k) process, a manufacturer must demonstrate that a new contact lens care product is substantially equivalent and therefore as safe and effective as a legally marketed predicate device. The Guidance for Industry and Food and Drug Administration Staff - Contact Lens Care Products Labeling describes information to be submitted for review of a 510(k) submission.[8] Recommendations for product labeling, including the carton and bottle, are included in the guidance.

C. Hydrogen Peroxide Contact Lens Care Product History and Usage

Hydrogen peroxide contact lens care products have been marketed for many years. The original approval was obtained by American Optical Corporation in 1983 under PMA P820040 for the SEPTICON" Disinfection System, which consists of LENSEPT® Sterile Disinfection Solution (3% H_20_2), the SEPTICON' Disc, and the SEPTICON' Cups, for use in disinfecting the SOFTCON' (vifilcon A) Contact Lens. Since the first peroxide based contact lens care product entered the market these products were down classified to Class II in 1997 and other peroxide care products were introduced into the marketplace.

Contact lens care products are formulated to clean and disinfect contact lenses by breaking up and removing trapped debris, protein, and lipid deposits. Multipurpose solutions (MPS), which constitute the majority of products on the market, include both a rub-and-rinse step prior to placing the contact lenses in the case containing the MPS for a disinfection cycle. Peroxide care products do not include a rub-and-rinse step because the 3% hydrogen peroxide solution is adequate for loosening debris. Unlike multipurpose solutions, hydrogen peroxide solutions are preservative-free. This makes them especially safe for those who are allergic or sensitive to the preservatives found in multipurpose solutions.

When using hydrogen peroxide, the disinfecting process must be followed with a neutralizer. The neutralizer converts the peroxide into water and oxygen, making it safe to put the lenses back into the eyes.

Neutralization can be either a one-step or two-step process. The one-step process neutralizes lenses during the disinfecting stage, while the two-step process neutralizes lenses after the disinfecting stage. Some storage cases have a neutralizer built-in, making it a simple one-step process. With other cases, a neutralizing tablet must be added. This is the two-step process. Some of these products include the option of a final rinse with saline at the completion of the disinfection cycle. Hydrogen peroxide placed directly into the eyes or on contact lenses at insertion into the eyes can cause severe stinging, burning, and temporary corneal damage. Therefore, it is imperative that contact lenses are not rinsed with hydrogen peroxide care products immediately before insertion into the eyes nor used directly into the eye as a rewetting drop.

D. Hydrogen Peroxide Use and Adverse Events

Consumers have reported adverse events such as severe burning and stinging with the use of hydrogen peroxide products. The reports received to date have one common element --- the packaging is not distinguishable from other lens care products on the shelf resulting in mistaken purchases and subsequently, improper use. Misuse of hydrogen peroxide based contact lens care products has been reported to MedWatch, FDA's Safety Information and Adverse Event Reporting Program.

An analysis of the adverse event reports submitted to FDA and evaluated by the Office of Surveillance and Biometrics can be viewed in Attachment A.

Consumer behaviors underlying clinical contact lens complications have been addressed extensively in the literature. The noncompliant habits of many contact lens wearers, especially for reading package inserts, which can be quite lengthy at times, are well known. The literature on compliance and contact lens hygiene shows that many contact lens wearers eliminate steps. Ky et al. (1998) estimated that 80% of contact lens related complications are the result of noncompliance with wear and care regimens.[3] Collins found a noncompliance rate of 74% in adult habitual contact lens wearers who had worn lenses for an average of 2.6 years.[4] This study also found the reasons for noncompliance to be lack of understanding, improper usage of lens care products, and poor hand hygiene. This study population had many symptoms and complaints yet they did not perceive themselves as noncompliant. Likewise, Turner found a noncompliance rate of 91%.[5] Turner's results focused on multipurpose solutions and found that the failure rate was high despite the ease of using MPS. Turner's study emphasizes that even when procedures are simple and minimal, noncompliance can be very high.

Compliance and proper use of care products is of particular concern with hydrogen peroxide based contact lens solutions as they cannot be used without a special case to allow neutralization and specifically, cannot be used to rinse lenses prior to insertion. The special contact lens case, which is equipped with an attached metallic neutralization disc, is provided with each bottle of peroxide based contact lens cleaning and disinfecting solution. Using any other case will not neutralize the peroxide. Direct exposure of the eye to peroxide can be highly toxic to the corneal

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

E. Labeling of Hydrogen Peroxide Based Contact Lens Care Products

FDA recommends that lay language be used in patient labeling to adequately present potential adverse events and the risks and benefits of the device.[6,7, 8, 9] Patient labeling, if possible, should not exceed the eighth grade reading comprehension level. FDA further recommends that eye care professionals review care product labeling with patients and that companies provide this labeling on their websites.

The 2010 Guidance for Industry and Food and Drug Administration Staff - Contact Lens Care Products Labelingstates, "Patient information labeling includes information contained on the outside packaging, package insert and primary container and is directed to the contact lens wearer.[10] The patient labeling should instruct the patient on product care to ensure lenses are used safely and effectively, potential risks and benefits, and what to expect when they use these care products. When translating information from professional terminology into lay language, the manufacturer should not alter the intent of the indications, contraindications, warnings and precautions. The labeling should contain sufficient information to describe the device, its intended use, and specific descriptions of the patients for whom the product would not be a good choice (e.g., allergy to specific components of the product(s))."

In 2009, a signal regarding adverse events associated with misuse of hydrogen peroxide contact lens care products was raised. To address these issues, FDA convened experts across the Center of Devices and Radiologic Health to evaluate the problems and strategize a resolution to the problem. Significant modifications to the carton and bottle labeling were recommended to industry, which were assessed through structured focus groups. Here are examples of the modified current labeling and instructions for use specific to the issues of misuse:

- The phrase "NO RUB" has been removed so that it would not be confused with other products portraying the "No Rub" label.
- The addition of a red cap and a red tip to identify it as different from other care products.
- Carton and bottle both state the following in enhanced text and red boxes to alert the user:
    - Use only the lens case provided
    - Only use the special case for disinfection and neutralization.
    - DO NOT use flat lens case.
    - Hydrogen Peroxide (Brand X) only works with the special lens case provided.
- IMPORTANT: Failure to follow directions for use will result in burning and stinging

F. Summary

- Consumers believe that the packaging is too similar to other contact lens care products resulting in misuse of the product. Consumers do not read the packaging.
- Consumers have reported numerous adverse events – severe burning and stinging to FDA. Consumers do not always read the labeling instructions.

- Despite updated and enhanced labeling instructions, use errors resulting in adverse events continue.
- Consequent restructuring of the labeling has not addressed the problem of misuse of the products.

This joint advisory committee meeting will discuss and identify steps to mitigate the potential risks of misuse of peroxide-based contact lens products. Specific questions to be discussed are included in Attachment B.

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ATTACHMENT A

POSTMARKET DATA: MEDICAL DEVICE REPORTS (MDRs)

Overview of the MDR Database

Each year, the United States Food and Drug Administration (FDA) receives several hundred thousand MDRs of suspected device-associated deaths, serious injuries, and malfunctions. The database houses MDRs submitted to the FDA by mandatory reporters (manufacturers, importers, and device user facilities) and voluntary reporters such as health care professionals, patients, and consumers. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. MDR reports can be used effectively to:

- Establish a qualitative snapshot of adverse events for a specific device or device type
- Detect actual or potential device problems used in a "real world" setting, including
    - rare, serious, or unexpected adverse events
    - adverse events that occur during long-term device use
    - adverse events associated with vulnerable populations
    - use error

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about frequency of device use. Because of this, MDRs comprise only one of the FDA's several important postmarket surveillance data sources.

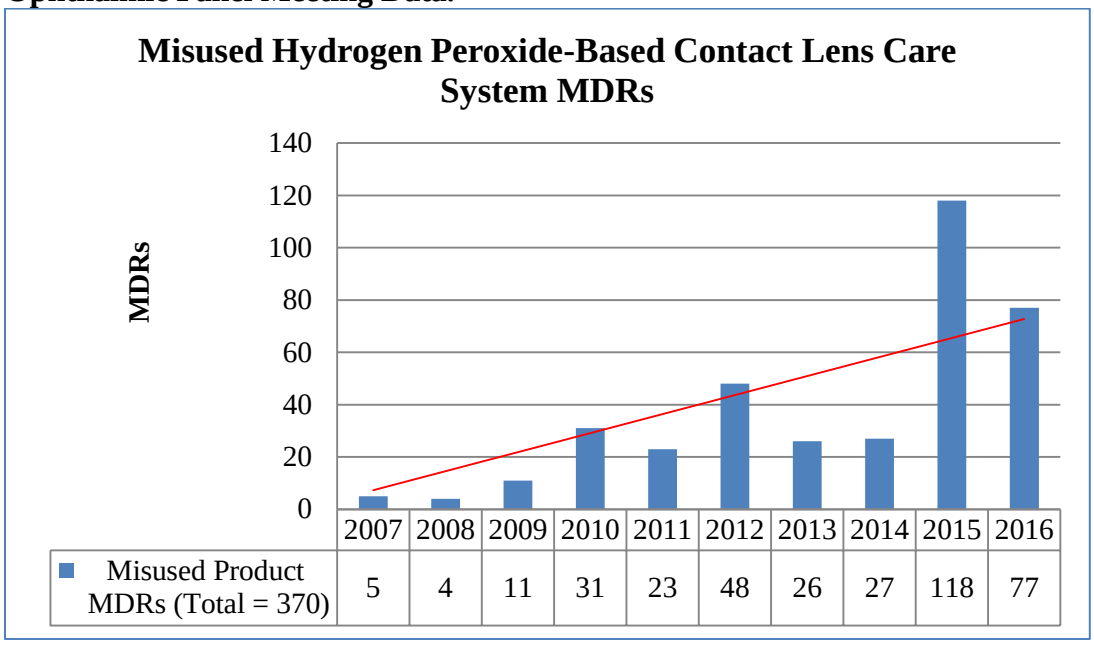
- MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time, or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices.
- Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified or if the device in question has not been directly evaluated.
- MDR data is subjected to reporting bias, attributable to potential causes such as reporting practice, increased media attention, and/or other agency regulatory actions.
- MDR data does not represent all known safety information for a reported medical device and should be interpreted in the context of other available information when making device-related or treatment decisions.

MDRs Associated with Misuse of Hydrogen Peroxide-Based Contact Lens Care System Products

The Agency searched the FDA's MDR database to identify reports associated with misuse of hydrogen peroxide-based contact lens care system products in a ten-year period entered December 14, 2006 to December 14, 2016. An MDR was associated with product misuse when the narrative mentioned that the product's instructions for use were not followed. The searches resulted in the identification of 370 unique MDRs. For the purposes of this MDR analysis, these 370 MDRs will be referred to as the "2017 Ophthalmic Panel Meeting Data."

The number of MDRs for the 2017 Ophthalmic Panel Meeting data is presented in Figure 1, where a significant increase in the number of reports received is noted for 2015. This spike may be attributed to an advocacy group submission of 74 reports on behalf of consumers during that calendar year.

Figure 1. The Number of Medical Device Reports (MDRs) Per Year for the 2017 Ophthalmic Panel Meeting Data.



There were 58.38% (N=216) voluntary reports and 41.62% (N=154) reports submitted by manufacturers. The FDA did not receive any reports from user facilities or healthcare providers.

Patient gender information was reported in 289 of the MDRs of which 228 were female and 61 were male. The median age was 42.5 years based on the information provided in 110 MDRs.

The event types are presented in Table 1. The MDRs were mostly reported as injuries (N=357) with a small number of reports submitted as malfunctions (N=13). There were no death reports associated with misuse of these products.

Table 1. Medical Device Report (MDR) Event Types Included in the 2017 Ophthalmic Panel Meeting Data.

Event Type	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total	%
Injury	5	4	6	23	23	48	26	27	118	77	**357**	**96.49%**
Malfunction			5	8							**13**	**3.51%**
MDRs Total	**5**	**4**	**11**	**31**	**23**	**48**	**26**	**27**	**118**	**77**	**370**	**100%**

The number of MDRs based on reporter country of origin for the 2017 Ophthalmic Panel Meeting data is presented in Table 2. The majority of the MDRs come from unknown or unreported countries of origin (N=179). There were 161 reports received from the United Stated (US) and 30 reports from outside of the US (OUS).

Table 2. The Number of US[1] and OUS[2] Medical Device Reports (MDRs) for the 2017 Ophthalmic Panel Meeting Data.

Reporter Country	Count of MDRs	%
UNKNOWN/UNREPORTED	179	**48.38%**
US[1]	161	**43.51%**
OUS[2]	30	**8.11 %**
Total	**370**	**100%**

[1] US – the United States
[2] OUS – Outside of the United States

The number of MDRs by year and manufacturer is presented in Table 3. The manufacturer with the most MDRs identifying misuse was Alcon (N=248), followed by Abbott Medical Optics (AMO) (N=64), Bausch + Lomb (N=37), and CooperVision (N=20). There was one report which did not specify the manufacturer/brand name.

Table 3. Number of Medical Device Reports (MDRs) for the 2017 Ophthalmic Panel Meeting Data by Manufacturer.**

Manufacturers	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total	%
Alcon	5	2	5	21	13	32	15	18	105	32	**248**	**67.03%**
Abbott Medical Optics		2	6	10	8	11	9	6	4	8	**64**	**17.30%**
Bausch + Lomb									2	35	**37**	**10.00%**
CooperVision					2	5	2	3	6	2	**20**	**5.40 %**
Unspecified Manufacturer									1		**1**	**0.27%**
Total MDRs	**5**	**4**	**11**	**31**	**23**	**48**	**26**	**27**	**118**	**77**	**370**	**100%**

**Important Note: Number of MDRs may be impacted by factors such as market share or number of products sold.

The breakdown of MDRs by specific manufacturer and brand name is presented in Table 4. The top five most reported brand names associated with misuse of hydrogen peroxide-based contact lens care system products were Alcon's Clear Care (N=226), Bausch + Lomb's Peroxiclear (N=37), AMO's Oxysept (N=27), AMO's CONSEPT (N=25), and Alcon's AOSEPT (N=16).

Table 4. Number of Medical Device Reports (MDRs) for the 2017 Ophthalmic Panel Meeting Data by Manufacturer and Brand.

Manufacturer and Brand	Number of MDRs**	%

Alcon	**248**	
Clear Care	226	**61.08%**
AOSEPT	16	**4.32%**
AOSEPT/Clear Care	6	**1.62%**
Abbott Medical Optics (AMO)	**64**	
Oxysept	27	**7.30%**
CONSEPT	25	**6.76%**
Goretex	8	**2.16%**
Hydramat	2	**0.54%**
Omnicare	1	**0.27%**
Unspecified AMO Brand	1	**0.27%**
Bausch + Lomb (B + L)	**37**	
Peroxiclear	37	**10.00%**
CooperVision Inc. (CVI)	**20**	
CVSHealth	10	**2.70%**
EQUALINE	4	**1.08%**
Sauflon	3	**0.81%**
Best Choice	1	**0.27%**
TopCare	1	**0.27%**
Walmart equate	1	**0.27%**
Unspecified Manufacturer	**1**	
Unspecified Brand	1	**0.27%**
Total	**370**	**100 %**

**Important Note: Number of MDRs may be impacted by factors such as market share or number of products sold.

Outcomes of Clinical Interest

Tables 5 to 10 depict specific outcomes of clinical interest, where information was obtained by individual review and analysis of the MDRs. The following parameters were used to identify specific instances of **misuse**, **reported eye problems**, and **personal burden**.

***A. Misuse*:** Individual MDRs which contained information suggesting that the product instructions were not followed and the contact lens care product was used inappropriately were grouped into the following categories:

- Accidental use - This category included claims of accidental/inadvertent use of peroxide solution regardless of how the product was misused, use of fingers contaminated with peroxide when the lens was inserted, accidental splash to the eye, accidental ingestion, applying hydrogen peroxide-based solution directly to the eye, rinsing the contact lens with hydrogen peroxide-based solution prior to insertion, and mistaking/confusing/using the hydrogen peroxide-based contact lens solution like saline or multipurpose solution.

- Failure to follow neutralization method - This category included claims of using a flat lens case, forgetting to add the neutralizing solution/tablet, forgetting the neutralization procedure, inadequate neutralization time, not using the provided lens case, reusing previously neutralized solution, shaking the lens case, lens case not placed on a flat surface during neutralization process, and storing the contact lens more than recommended storage time/in a very cold environment.
- Erroneous purchase - This category included claims of mistaking hydrogen peroxide-based contact lens care products as multipurpose/saline solutions and product placement on store shelf with non-hydrogen peroxide-based contact lens care products leading to erroneous purchase in which the consumer assumed he/she was buying multipurpose/saline contact lens care solution.
- Unspecified detail of misuse - This category included reports in which limited information of misuse was provided.
- Use of expired product - This category included claims of using the product beyond the expiration date.
- Improper care of lens case - This category included claims of using tap water for cleaning the lens case and lens case not cleaned properly.
- Healthcare provider error - This category included claims of error on the part of the healthcare provider such as soaking lenses inappropriately, inadequate health teaching, wrong instruction given, and error in dispensing.

The different types of hydrogen peroxide-based contact lens care product misuse are presented in Table 5. The top three categories of product misuse were “Accidental use” (N=168), “Failure to follow neutralization method” (N=107), and “Erroneous purchase” (N=40).

Table 5. Medical Device Reports (MDRs) of Product Misuse for the 2017 Ophthalmic Panel Meeting Data.

Types of Misuse	Count of MDRs**	%
Accidental use	168	**45.41%**
Failure to follow neutralization method	107	**28.92%**
Erroneous purchase	40	**10.81%**
Unspecified detail of misuse	19	**5.14%**
Use of expired product	15	**4.05%**
Improper care of lens case	12	**3.24%**
Healthcare provider error	9	**2.43%**
Total	**370**	**100%**

**Misuse-associated MDRs were categorized based on one type of misuse that mostly reflects the manner how the product was misused.

Accidental use (N=168):

This is the most common type of misuse. Any consumer complaints that used the terms "accidental" or "inadvertent" were considered as "Accidental use" regardless of how the product was misused.

Accidental use reports described in the narratives include splashing of peroxide solution into the eyes while disposing of the solution and fingers being contaminated with peroxide during lens insertion. This also includes consumer mistaking or confusing the hydrogen peroxide solution with saline or multipurpose solution. According to the MDRs, the primary reason for why this product was used incorrectly was that the consumer either did not read or did not understand the labeling or instructions for use for the product.

The MDR narratives indicated consumer confusion regarding the terms "cleaning", "disinfecting", and "no rub" in the labeling. The text terms were associated with the use of saline or multipurpose solutions where the box packaging may convey the same information as the hydrogen peroxide-based contact lens care solutions. Other complaints were included in this category due to similarities between the hydrogen peroxide-based solutions and the saline or multipurpose solutions. These similarities include the color, size, and shape of the bottles in which consumers described in narrative events having a difficult time distinguishing between the different types of solutions if they were placed in close proximity.

Consumers also describe rinsing the contact lens with hydrogen peroxide solution just prior to lens insertion or the hydrogen peroxide being applied directly to the eye.

Additionally, there appeared to be confusion regarding the travel size of the hydrogen peroxide products. In one report, the consumer did not realize that the hydrogen peroxide-based solutions came in travel size and mistook it as saline/multipurpose solution.

There was one report of accidental use citing ingestion by a child; however, the caller disconnected the phone call with the Poison Control Center before any further information could be obtained.

Failure to follow neutralization method (N=107):
Based on the review of the narrative event descriptions, this appears to be the most frequent type of misuse and is frequently attributed to consumers not using the special lens case that comes with the product or using an inadequate neutralization time. These steps are written on the carton and in the package insert for the products distributed in the US market. The result of the failure to follow these required steps is that the lack of neutralization of hydrogen peroxide prior to insertion of the contact lens into the eye may cause eye injury.

Erroneous purchase (N=40):
These were narrative reports, both from voluntary reporters and manufacturers, describing the consumer's erroneous purchase of hydrogen peroxide-based contact lens care system products. According to the reports, this was primarily attributed to the store's product shelf placement of the hydrogen peroxide based solution in close proximity to other contact lens care solutions. The narratives also indicate that the text labels "Clean/Disinfect/No Rub" on the hydrogen peroxide-

based contact lens products led consumers to purchase these solutions thinking that this was the same as the saline/multipurpose solutions.

Healthcare provider error (N=9):
There were nine reports in which the healthcare providers placed the contact lens in hydrogen peroxide-based solution and then had the patient reinsert the lens (n=3), dispensed hydrogen peroxide-based solution without including neutralizing tablets (n=1), and failed to provide adequate instructions to patients (n=5).

Other types of misuse:
Additional types of misuse include consumers failing to provide proper care of the lens case (N=12) in which consumers used tap water to rinse the case or the consumer used a dirty lens case. Expired solutions were also used (N=15).

There were 19 reports that did not provide a description of the type of misuse or the manufacturer was not able to confirm the type of misuse.

B. Reported eye problems – These are clinical outcomes of hydrogen peroxide-based contact lens care system product misuse. The following are the reported eye problems of clinical interest identified:

- Serious eye injuries (not including infection or inflammation): refers to any serious injury to the eye region (e.g., corneal ulcer, corneal damage, vision loss/blindness)
- Visual issues: refers to subjective complaints of effects on vision or visual acuity (e.g., impaired vision, blurred vision, visual disturbance)
- Eye infection/inflammation: refers to an eye disease that is caused by a pathogenic microorganism and/or localized eye protective response elicited by an injurious agent (e.g., conjunctivitis, keratitis)
- Ocular signs and symptoms: refers to reports received concerning clinical signs (e.g., epithelial loss, chemical eye burn) and patient reported symptoms (e.g., burning sensation)

The four sub-categories on reported clinical events of eye problems: **serious eye injuries**, **visual issues**, **eye infection/inflammation,** and **ocular signs and symptoms** are presented in Tables 6 to 9, respectively.

B.1. Serious eye injuries (not including infection or inflammation): The two serious eye injuries experienced by consumers allegedly due to misuse of the hydrogen peroxide-based contact lens care products are presented in Table 6.

Table 6. Serious Eye Injuries (Not Including Infection/Inflammation) for the 2017 Ophthalmic Panel Meeting Data.

Serious Eye Injuries	Count**
Corneal ulcer	11
Corneal damage - nonspecific	9
Vision loss/blindness	2

**The total number of serious eye injury events does not equal the total number of Medical Device Reports. Each Medical Device Report may have multiple serious eye injuries.

Corneal ulcer (N=11):
Based on narrative description, these ten manufacturer and one voluntary report described ulceration of the cornea. Within these 11 events, the ten manufacturer reports described consumers seeking medical care. There were four reports that described recovery. The remaining seven reports did not provide recovery information.

Corneal damage – nonspecific (N=9):
There were nine events which claimed nonspecific corneal damage. The two voluntary and seven manufacturer reports did not specify the extent of corneal damage. One voluntary and one manufacturer report did not provide information on the medical care sought, whereas, the other seven reports described seeking medical attention. There were only two reports that described recovery. Limited information was provided on recovery for the other seven reports.

Vision loss/blindness (N=2):
There were two events of loss of vision or blindness. In one of the events, the manufacturer reported a past medical history of “uveitis” and “intermittent compromised cornea” prior to product misuse. The other event from a voluntary report did not provide additional information on recovery status. Due to the limited information provided on the recovery status, it cannot be determined if these issues were permanent or if they were caused by product misuse.

B.2. Visual issues: The various visual issues adversely experienced by consumers allegedly due to misuse of the hydrogen peroxide-based contact lens care products are presented in Table 7.

Table 7. Visual Issues for the 2017 Ophthalmic Panel Meeting Data.

Visual Issues	Count**
Blurred vision	41
Temporary vision loss	7
Partial vision loss	2

**The total number of visual issue events does not equal the total number of Medical Device Reports. Each Medical Device Report may have multiple visual issues.

Blurred vision (N=41):
Based on the narrative descriptions, events of blurry vision following exposure to the hydrogen peroxide solution were the most frequent complaints related to visual issues. These include visual acuity concerns, deteriorating vision and unspecified visual problems described by

consumers. Of these 41 reports, 18 stated recovery from blurred vision, 15 reports had no information on recovery, and eight reports claimed continuing blurred vision at the time the report was filed.

Temporary vision loss (N=7):
There were seven complaints of temporary loss of vision in which consumers claimed eventual recovery. Limited information was provided indicating which eye was affected or the level of or time to recovery.

Partial vision loss (N=2):
The two events of partial vision loss did not provide recovery information.

B.3. Eye infection/inflammation: The reports of eye infection/inflammation experienced by consumers are presented in Table 8.

Table 8. Eye Infection/Inflammation for the 2017 Ophthalmic Panel Meeting Data.

Eye Infection/Inflammation	Count**
Chemical conjunctivitis	12
Chemical keratitis	9
Eye inflammation – nonspecific	8
Eye infection – nonspecific	7
Bacterial eye infection	3
Conjunctival inflammation	3
Keratoconjunctivitis	2
Blepharoconjunctivitis	1
Fungal keratitis	1

**The total number of eye infection/inflammation events does not equal the total number of Medical Device Reports. Each Medical Device Report may have multiple eye infection/inflammation.

The most frequently reported eye infection/inflammation event was chemical conjunctivitis (N=12), followed by chemical keratitis (N=9), and nonspecific eye inflammation (N=8). Additionally, there were events of nonspecific eye infection (N=7). In the nonspecific eye infection events, there was one report which stated that the infection was due to incorrect lens care instruction given by the eye care practitioner.

Limited information on the infectious organisms causing the eye infections was provided. There were three events which mentioned bacteria as the source of the infection without specifying the organisms and were allegedly caused by poor lens care; another report was allegedly associated with reusing a previously neutralized solution. There was one event of fungal keratitis which mentioned fungus as the source of infection due to improper care of the lens case.

B.4. Ocular Signs and Symptoms*:* The various ocular signs and symptoms adversely experienced by consumers allegedly due to misuse of the hydrogen peroxide-based contact lens care products are presented in Table 9.

Table 9. Ocular Signs and Symptoms for the 2017 Ophthalmic Panel Meeting Data.

Ocular Signs and Symptoms	Count**
Burning sensation	210
Chemical eye burn	186
Corneal abrasion	33
Conjunctival hyperemia	18
Superficial punctate keratitis	11
Ocular injection	9
Corneal epithelial erosion	7
Conjunctival hemorrhage	6
Epithelial defect – nonspecific	2
Superficial punctate epitheliopathy	1
Superficial punctate keratopathy	1

**The total number of ocular sign and symptom events does not equal the total number of Medical Device Reports. Each Medical Device Report may have multiple ocular signs and symptoms and the same sign or symptom may have been reported using multiple different terms.

The most reported serious eye symptom was burning sensation (N=210). These reports described consumer subjective complaints as a result of immediate eye exposure to hydrogen peroxide solution. There were also reports of chemical burn to the eye region which included corneal burns (N=186), and reports of corneal abrasion (N=33).

C. Personal Burden Outcomes: These are different types of burden outcomes personally experienced by consumers as a result of hydrogen peroxide-based contact lens care system product misuse. For this categorization, personal burden is described utilizing a qualitative measure. The following are the different subtypes of personal burden outcomes identified and presented in Table 10:

- Medical practitioner consult (e.g., visit to emergency room/urgent care/clinic/specialist, in-patient admission to hospital, call to poison control)
- Did not report personal burden (i.e., limited information provided)
- Missed work/school (e.g., unable to go to work, unable to attend school)
- Difficulty driving (e.g., complaints of struggling to drive)
- Difficulty in providing family care (e.g., having trouble fulfilling parental duties)

Table 10. Medical Device Reports (MDRs) of Personal Burden Outcome for the 2017 Ophthalmic Panel Meeting Data.

Personal Burden Outcome**	MDR Count	%
Medical practitioner consult	193	**52.16%**
Did not report personal burden	162	**43.78%**
Missing work/school	8	**2.16%**
Difficulty driving	4	**1.08%**
Difficulty in providing family care	3	**0.81%**
Total	**370**	**100%***

**Burden outcome-associated MDRs were categorized based on one type of burden outcome that mostly reflects personal burden experienced by consumer.

The outcomes of personal burden consisted primarily of the consumer seeking a "medical practitioner consult" (N=193) which included visits to the emergency room, urgent care, eye clinic, or eye care practitioner, hospital admission and calls to poison control. These medical consults were allegedly needed as a result of the consumer eye injuries sustained from chemical exposure to hydrogen peroxide solution. Medical interventions to treat the consumer included the application of eye patches, medications dispensed to relieve eye pain, eye irrigation, and treatment with topical antibiotics. Consumers were also advised to seek additional follow up with their eye care practitioners. Limited information was provided on five reports which stated that inpatient hospitalizations were required.

There were 162 reports which did not report personal burden.

Reports of Recovery Data

Reports of Recovery: The outcome reports of recovery from hydrogen peroxide-based contact lens care system product misuse were obtained from the narrative event description section of the MDRs. Reports of recovery or event abated were based on the most recent information received. The following are the identified outcome reports of recovery:

- No further information on recovery status – no outcome provided
- Recovered from eye injury – return to prior condition; in the process of recovering
- Continuing eye issues – eye complaints still ongoing; no recovery
- No eye injury – no untoward outcome

The reports of recovery from eye problems are presented in Table 11.

Table 11. Medical Device Reports (MDRs) of Recovery Outcome for the 2017 Ophthalmic Panel Meeting Data.

Recovery Status**	MDR Count	%
No further information on recovery status	243	**65.68%**
Recovered from eye injury	83	**22.43%**
Continuing eye issues	30	**8.11%**
No eye injury	14	**3.78%**
Total	**370**	**100%**

**Recovery status-associated MDRs were categorized based on one type of recovery status outcome that mostly reflects status post recovery from reported eye problem experienced by consumer.

The recovery status post injury was not reported in 243 MDRs. Among those where recovery status was reported, 83 MDRs stated that the consumer recovered, while 14 stated that the consumer did not suffer an eye injury.

There were 30 reports which described "continuing eye issues." Based on the most current information received, the most frequent "continuing eye issue" described in the narrative description was chemical eye burn (N=21). No additional information was provided on the recovery status.

MDR Conclusions

- There were 370 MDRs which identify the misuse of hydrogen peroxide-based contact lens care system products from December 14, 2006 to December 14, 2016.

- More than half of the MDRs submitted to the FDA related to misuse of hydrogen peroxide-based contact lens care system products (58.38%) were voluntary reports.

- Based on the associated narrative event descriptions on misuse of hydrogen peroxide-based contact lens care product, burning sensation and chemical eye burn were the most frequently reported adverse events described.

- Two reports describe loss of vision/blindness. Due to the limited information provided status post injury, it cannot be determined if these issues were permanent or if they were caused by misuse.

- Based on the narrative descriptions, it appears that some consumers may have assumed that all contact lens care solutions (i.e., saline, multipurpose, and hydrogen peroxide-based solutions) are the same and safe to be applied directly to the eyes or for use with contact lens cleaning/disinfecting. The narrative descriptions also indicate that consumers believe this confusion may be due to the similarity of the packages, the close proximity of the different types of solution on the store shelves and inadequate labeling on the packaging and/or bottles.

- Included in the narratives were consumer suggestions on how to avoid possible misuse. Some suggestions were: making the product appearance less similar to the saline or multipurpose solution, having the hydrogen peroxide based solutions dispensed by the pharmacist, and creating separate areas on the store shelves for the different products so that there is less confusion between the different types of products.

ATTACHMENT B
QUESTIONS

1. Please discuss the currently used labeling for peroxide based contact lens care products with respect to the adequacy of specific warnings and clarity of instructions for use. Does the panel have any recommendations for modifying this labeling? During your deliberations, please address the following examples of the current labeling and instructions for use specific to the issues of misuse in your discussion:

    a. The phrase "NO RUB" has been removed so that it would not be confused with other products portraying the "No Rub" label.
    b. The addition of a red cap and a red tip to identify it as different from other care products. Carton and Bottle both state the following in enhanced text and red boxes to alert the user:

        - Use only the lens case provided
        - Only use the special case for disinfection and neutralization.
        - DO NOT use flat lens case.
        - Hydrogen Peroxide (Brand X) only works with the special lens case provided.

    c. IMPORTANT: Failure to follow directions for use will result in burning and stinging

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

    a. Redesigning the carton label (color, font sizes, etc.) so that it is distinctly different than other contact lens care products
    b. Placement on store shelves separate from other contact lens care products
    c. Implementation of the use of a purchase card that when brought to the pharmacy counter to obtain the product, the pharmacy staff can alert the consumer to the fact that they are purchasing a peroxide product and that there are specific directions that must be followed for safe use.
    d. For sale only at offices of contact lens practitioners (optometrists, ophthalmologists)

3. What are the panel's recommendations for reducing the risks of misuse of peroxide based contact lens care products once purchased? Please consider the following in your discussions:

    a. Redesigning the bottle size, shape and color to alert the consumer that it is not the same as saline or other contact lens products

b. Redesigning the case and bottle to be functionally dependent (the peroxide cannot be released unless directly and physically connected to the special neutralization case)

4. What are the panel's recommendations for how we can better engage contact lens consumers, advocacy groups, professional organizations, and industry to promote improved compliance with instructions for use for contact lens care regimens?