SUMMARY MINUTES

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

OPHTHALMIC DEVICES PANEL

November 10, 2022

9:00 a.m. EST

Attendees:

Chairperson

Neil Bressler, MD
Professor, Ophthalmology Wilmer Eye Institute
Johns Hopkins Hospital — Baltimore, MD

Members

Emily Chew, MD
Director, Division of Epidemiology and Clinical Applications
National Eye Institute, National Institutes of Health — Bethesda, MD

Bennie Jeng, MD
Director, Scheie Eye Institute
University of Pennsylvania School of Medicine — Philadelphia, PA

Jose Pulido, MD
Chair, Translational Ophthalmology
Wills Eye Hospital, Thomas Jefferson University — Philadelphia, PA

Michael Repka, MD, MBA
Vice Chair, Clinical Practice Professor of Ophthalmology
Wilmer Eye Institute — Baltimore, MD

Jayne Weiss, MD
Chair, Department of Ophthalmology
Associate Dean, CMO
Louisiana State University School of Medicine — New Orleans, LA

Consultants

Thomas Freddo, OD, PhD
Vice-Chair for Research, Department of Ophthalmology
Boston University School of Medicine — Boston, MA

David Glasser, MD
Assistant Professor of Ophthalmology, Wilmer Eye Institute
Johns Hopkins — Baltimore, MD

Young Kwon, MD, PhD
Clifford M & Ruth Altermatt Professor Glaucoma Service
Dept of Ophthalmology & Visual Sciences
University of Iowa — Iowa City, IA

Samuel Masket, MD
Clinical Professor, Stein Eye Institute

David Geffen School of Medicine, UCLA — Los Angeles, CA

Industry Representative

Rajesh Rajpal, MD
Chief Medical Officer, Global Head of Clinical and Medical Affairs
Johnson & Johnson Vision — McLean, VA

Consumer Representative

Todd Durham, PhD
Senior Vice President, Clinical & Outcomes Research
Fighting Blindness Foundation — Raleigh, NC

Patient Representative

Jennifer Schwartzott, MS
Founder/Manager, The MitosSantas Program —North Tonawanda, NY

Food and Drug Administration — Silver Spring, MD

Jarrod Collier, MS
Designated Federal Officer
Office of Management, CDRH

Tieuvi Nguyen, PhD
Director, Division of Ophthalmic Devices
Office of Ophthalmic, Anesthesia, Respiratory, ENT & Dental Devices, CDRH

Food and Drug Administration Presenters

Linh Lo, PhD
Regulatory Advisor, Immediate Office, OPEQ, CDRH

Elissa Wong, PhD
Biologist, Division of Ophthalmic Devices, OHT1, OPEQ, CDRH

CALL TO ORDER
INTRODUCTIONS
OPENING REMARKS

Panel Chairperson **Dr. Neil Bressler** called the meeting of the Ophthalmic Devices Panel to order at 9:00 a.m. He noted the presence of a quorum and stated that present members have received training in FDA device law and regulations. He stated the day's agenda: to discuss and make recommendations on the classification of ophthalmic dispensers, which are unclassified preamendment devices to Class I, subject only to general controls, which includes a discussion of the known risks and safety/effectiveness concerns and a general classification recommendation for ophthalmic dispensers.

Chairperson Bressler then asked members of the Committee and FDA participants to introduce themselves.

CONFLICT OF INTEREST STATEMENT

Mr. Jarrod Collier, Designated Federal Officer, announced that no Conflict of Interest Waivers were issued for today's meeting.

He announced the participation of **Dr. Rajpal** of Johnson & Johnson Vision as the Industry Representative. He introduced **Dr. Todd A. Durham** and **Ms. Jennifer A. Schwartzott** as temporary nonvoting members.

OPEN PUBLIC HEARING

There were no requests to speak for the Open Public Hearing, although Genentech made a written submission, from which **Dr. Bressler** read excerpts. Genentech urged FDA to clarify "that the term 'ophthalmic dispensers' is limited to lower-risk, non-invasive, and non-implanted ophthalmic dispensers and will not encompass implantable drug delivery ophthalmic devices or pre-filled ophthalmic syringes that are intended to penetrate the eye."

No other comments or submissions were made at this time.

FDA PRESENTATION — CLASSIFICATION OVERVIEW

Dr. Linh Lo provided an overview of the medical device classification process. Class I devices are only subject to general controls. Class II devices are subject to both general and special controls, and Class III devices are subject to general controls and premarket approval.

Dr. Lo described FDA's process in soliciting feedback on this issue, noting that pre-amendments unclassified devices will be classified once the FDA has taken the following steps. First, FDA will solicit input and a recommendation from the device classification panel, which is the purpose of this meeting. Second, FDA will publish the Panel's recommendation for comment, along with a proposed rule outlining FDA's proposed classification for the device. Finally, after taking into account public comments, the FDA will publish a final rule classifying the device.

FDA PRESENTATION — OPHTHALMIC DISPENSERS (LXQ)

Dr. Elissa Wong provided details on "LXQ"-coded ophthalmic dispensers. She covered device descriptions, indications for use, regulatory history, clinical background, literature review, medical device reports, recall histories, risks to health, and the proposed classification for these devices. Of particular importance:

- Ophthalmic dispensers are intended to deliver ophthalmic liquids to the eye, either to irrigate or to deliver medication, and can include eye cups and eye droppers.
- Indications for use include to hold and place liquids, such as eye was solutions, over the eye to allow the solution to wash out or flush the affected eye; and, to instill ophthalmic medication dropwise to the eye.
- 5 eye cup devices have been cleared under "LXQ" to date.
- There is a lack of literature covering ophthalmic devices to inform these decisions, and only 3 MDRs were obtainable related to "LXQ" devices.
- Inadvertent contamination of the dispenser and self-induced eye trauma were the most widely reported adverse outcomes
- Ophthalmic dispensers are generally low risk.
- Infection, adverse tissue reaction, compromised treatment, and mechanical injury are FDA's identified risks to health.

Thus, FDA proposed ophthalmic dispensers for classification as Class I (general controls), exempt from premarket notification procedures.

PANEL DELIBERATIONS

Dr. Weiss inquired about materials used for the eye cups and whether materials can be variable; **Dr. Nguyen** responded that material alterations would require 510(k) submission and clearance. **Dr. Weiss** also expressed concern about variable drop sizes, whether there is regulation regarding drop size consistency, and whether volume variations are associated with infection risk. **Dr. Nguyen** responded that internal documentations as part of good manufacturing processes are responsible for this type of concern.

Dr. Repka inquired if the good manufacturing practices cover design controls such as sharp edges. **Dr. Nguyen** responded affirmatively.

Dr. Masket wondered if cost-based analyses have been done with individual drop dispensers for dollar cost and carbon footprint; **Dr. Bressler** said literature does not report on this.

Dr. Pulido requested clarification on why such different types of containers can be included under the same classification. **Dr. Nguyen** responded this is due to a combination of similar intended uses and similar technology and similar risks.

Dr. Jeng expressed concern that bottle opacity leads to dosage issues since patients cannot see the quantity of medicine remaining, often causing them to run out of their ophthalmic liquids.

Dr. Kwon wondered if other ophthalmic dispensers exist under other product codes and noted that the Genentech letter points toward a need for a clearer definition of ophthalmic dispensers under code "LXQ". **Dr. Nguyen** responded this is the only code currently present, and everything other than 5 eyecups are currently unclassified. **Dr. Nguyen** also stated that FDA agrees with the points made in Genentech's letter and that devices intended to penetrate the eye to deliver ophthalmic medication, such as syringes and implants, were outside the scope of this classification panel meeting.

Dr. Rajpal wondered if ointments and multiple use, single-bottle, preservative-free containers are in the discussion's purview. **Dr. Nguyen** responded that the Panel should share recommendations on how to create clarification and distinctions here. **Dr. Rajpal** also wondered about sterility requirements, and for this, **Dr. Nguyen** solicited the Panel's feedback and reminded that the 5 eyecups cleared were cleared as non-sterile.

Dr. Durham wondered about post-market surveillance strategies for these devices, to which **Dr. Nguyen** pointed to the MDRs and manufacturer risk analysis reporting.

Dr. Glasser suggested that the word "external" be added to further clarify between these devices and injectable/slow release medications, recommending, perhaps, "controlled external installation." **Dr. Glasser** seconded the notion that single-use, preservative-free dispensers are often used more than once and may have separate risks associated with them due to patient choices.

Dr. Chew echoed Dr. Weiss' concerns about drop size, especially pertaining to pediatric populations. **Dr. Nguyen** expressed this is more of a concern from a drug perspective, not a device perspective.

Dr. Freddo suggested that if a bottle needs to be opaque to protect the liquid, that a strip can be left so the patient can see how much medication they have remaining. **Dr. Nguyen** added that the bottle and the solution are regulated together with all their combined associated risks, and that is a different discussion.

Dr. Kwon brought up membranes and one-way valves as methods of dispensing liquids. **Dr. Nguyen** refocused the conversation on dispensers that are not pre-filled. **Dr. Repka** suggested explicitly adding "empty" or "not pre-filled" to the language of the definition for these devices.

Dr. Masket asserted that different size bottles are in a patient's possession for different periods of time, and larger bottles may be associated with a larger risk of contamination due to this.

Dr. Glasser and **Dr. Weiss** together supported that perhaps different product codes should be associated with eye cups versus other ophthalmic dispensers due to the risk of eye cup contamination and re-use. **Dr. Bressler** found it appropriate to classify them as Class I despite somewhat different risk in this respect, and **Dr. Nguyen** suggested using different product codes under the same Class I regulation to distinguish between the Panel's perceived differences in the devices.

Dr. Rajpal reiterated concerns about regulating sterility.

Ms. Jismi Johnson of FDA commented that if intended use and risks to health are similar, one regulation can be used, and products can be further separated out by product code. She requested clarification from the Panel on what the additional risks they perceive for eye cups are. **Dr. Weiss** responded that patient expectations regarding sterility are different, and **Dr. Glasser** concurred. **Dr. Bressler** added that there is not literature to support that infection rates are higher for the different products. **Ms. Schwartzott** reported that as a patient, she has experienced multiple mysterious infections and finds sterility to be a prime concern in the use of any ophthalmic dispenser. **Dr. Masket** added that in sterility considerations, it must be defined exactly what part of the dispenser is expected to be sterile.

Dr. Kwon requested clarification on whether combination products, such as multiuse dropper bottles, are under consideration here; **Dr. Nguyen** responded affirmatively.

Dr. Weiss wondered whether lack of manufacturing expertise on the Panel was problematic for this sterility discussion and wondered whether the Panel should be concerned about patients filling up single-use containers for re-use.

Dr. James Bertram of FDA weighed in that the sterility discussion will vary greatly depending on product, and manufacturers undertake the burden of proving sterility when it poses significant risk. He added that the re-use component should be considered, but labeling can mitigate that health risk by informing consumers not to re-use.

Dr. Angelo Green of FDA added that what consumers do with a product cannot be controlled but that FDA does take into consideration the sizes of the bottle as it pertains to likelihood of re-use.

Dr. Rajpal checked with Johnson and Johnson Vision on their current practices and heard back that: "From the FDA guidance on contact lens care solutions, we are putting the following warnings: to avoid contamination, do not touch tip of container. Replace cap after using. To avoid contaminating, do not transfer to other bottles or containers." **Dr. Green** confirmed that this is typical to most manufacturers.

Dr. Pulido asked if, with the way the system is now, non-sterile eyecups can be placed on an eye for irrigation. **Dr. Green** responded yes, and **Dr. Nguyen** asked the Panel to contribute their thoughts towards mitigating the sterility issue. **Dr. Wong** weighed in with additional clarifications from the executive summary.

Dr. Freddo wondered if the specifications for eye drop containers would also extend to nose and ear drop containers, and **Dr. Nguyen** responded that those are different intended uses, so the situations do not parallel.

Dr. Jeng and **Dr. Kwon** contributed final concerns about sterility and re-use.

Before concluding the Panel Deliberations, **Dr. Bressler** added that, despite infection not being particularly present in MDRs and literature reviews, clinicians know that this is a definite risk for patients.

PANEL Q&A

Question One

FDA has identified the following risks to health for ophthalmic dispensers: infection, adverse tissue reaction, compromised treatment, and mechanical injury. Please comment on whether you agree with the inclusion of all the risks in the overall risk assessment of ophthalmic dispensers under product code "LXQ." In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these ophthalmic dispensers.

Dr. Repka and **Dr. Glasser** concurred that the risks have been appropriately identified and seem low in prevalence. **Dr. Pulido** added that there is a risk the patient may mistake bottles of other shapes and sizes for the ophthalmic dispenser and referred to a case study in which this occurred with super glue. **Dr. Freddo** brought up that variability of drop volume may pose a risk, particularly to pediatric patients.

Dr. Bressler summarized the Panel's attitude that the Panel agrees with the identified risks and believes such risks should be low in likelihood and frequency.

Question Two

Please discuss whether you agree with FDA's proposed classification of Class I for ophthalmic dispensers under the product code "LXQ." If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification. This concludes the panel questions.

Dr. Weiss supports Class I classification, suggested further categorizing eyedrops separately from droptainers, and suggested that indications for sterility and single/multiple use should be incorporated based on the device.

Dr. Rajpal, on behalf of industry, supports Class I. He advocated for clarity in FDA's definition to include "topical" and "unfilled".

Dr. Repka finds Class I sufficient and suggested that "empty" be added as clarifying language, as well.

Dr. Bressler summarized the Panel's attitude by saying that the Panel generally believes that Class I is appropriate, with consideration for product code distinctions between droptainers/eyecups and labeling considerations for topical/external use, clarification pertaining unfilled nature of containers, and labeling considerations for preservative free/preservative-containing and single/multi-use.

FDA SUMMATION

Dr. Nguyen thanked the panelists, the industry, patient, and consumer representatives, and the FDA team for their extensive research into the topic. She stated that the Panel's feedback will be taken into account while drafting the final classification rule.

ADJOURNMENT

Dr. Bressler thanked the participants for the discussion and adjourned the meeting at 11:33 a.m.

I approve the minutes of the meeting
as recorded in this summary.

Neil M. Bressler, MD

Digitally signed by Neil M. Bressler, MD
DN: cn=Neil M. Bressler, MD, o=Editor in Chief, JAMA Ophthalmology, ou=Johns Hopkins University School of Medicine, email=nbressler@jhmi.edu, c=US
Date: 2022.12.09 11:06:19 -05'00'

Neil Bressler, MD
Chairperson

Summary Prepared By:

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November 18, 2022

I certify that I attended this meeting on November,
10, 2022 and that these minutes accurately
reflect what transpired.

Jarrod W. Collier -S

Digitally signed by Jarrod W. Collier -S
Date: 2022.12.13 08:21:40 -05'00'

Jarrod Collier, MS
Designated Federal Officer