Classification of Ophthalmic Dispensers Under Product Code "LXQ"

Presenter:
Elissa Wong, PhD
Division of Ophthalmic Devices
Office of Health Technology 1- Office of Ophthalmic, Anesthesia, Respiratory, ENT, and Dental Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health
US Food and Drug Administration

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Device Description

- Ophthalmic dispensers are intended to deliver ophthalmic liquids to the eye, either to irrigate or to deliver medication. There are many different types of ophthalmic dispensers.
- Eye cups are cup shaped devices used to temporarily hold liquids such as saline, eye wash solution, or other ophthalmic medication. An eye cup is fitted and inverted over the eye to allow the solution to irrigate, wash out, or flush the affected eye.
- Droppers are manual devices that are intended to instill ophthalmic medication dropwise into the eye.

http://shop.apothecaryproducts.com/products/flents-plastic-eye-wash-cup

http://www.berlinpackaging.com/glass-boston-round-bottles-w-dropper-cap/

http://www.pccarx.com/products/Bottle,-DROPTAINER,-15-ML-WHITE-OPAQUE/35-2177/DEVICES

Indications for Use

Representative Indications for Use statements for ophthalmic dispensers include the following:

- Intended to hold and place liquids, such as eye wash solutions, over the eye to allow the solution to wash out or flush the affected eye.
- Intended for instilling ophthalmic medication dropwise to the eye.

Regulatory History

- Ophthalmic dispensers such as eye cups and droppers are pre-amendment devices, marketed prior to May 1976.
- Ophthalmic dispensers are unclassified.
- Since these devices are unclassified, there is no regulation associated with the LXQ product code.
- To date, FDA has cleared 5 eye cups under the LXQ product code via the 510(k) pathway.

Clinical Background

- Wide variety of ocular symptoms and conditions that are treated using ophthalmic dispensers.
- Dispensers are used to administer liquids as drops or in larger volumes.
  - Drops accommodate extremely limited volume capacity of the ocular surface, particularly the tear film (approximately 3 µL).
  - Maximizes the concentration of the liquid in the eye.
  - Minimizes exposing the rest of the body to the liquid.
  - Larger volumes can be used to flush debris or foreign material off the ocular surface, whose presence may cause ocular pain or discomfort.

Literature Review- Methods

- Articles only in English
- Databases searched – PubMed, Embase
- Time period – Between January 1, 1976 and May 11, 2022
- Search terms – “Eye cup, eyecup, “droptainer,” “eyedropper,” “eye dropper,” “eye drop dispenser,” and other similar terms
- Excluded – Non-clinical studies, case reports on ≤9 people, economic and cost-effectiveness analyses, narrative reviews, conference abstracts/proceedings, commentaries, and editorials
- Initial yield was 185 articles; after review, 15 articles determined relevant

Literature Review – Adverse Events

- Bacterial keratitis – 11 cases, 3 articles (Alfonso et al 1987; Schein et al 1987; Templeton et al 1982)
  - Associated with bacterial contamination of the ophthalmic dispenser used by affected patients.
  - Droptainer tips +/- caps were found to be contaminated with the same bacteria cultured from corneal scrapings.
  - Some patients had prior ocular trauma (e.g., with mascara brush).
  - Serious sequelae included significant corneal scarring, corneal transplant, enucleation, intractable ocular pain requiring retrobulbar alcohol injection.

Literature Review – Adverse Events (cont'd)

- Microbial contamination of ophthalmic dispensers – 6 studies
  - Culturing droptainers used by patients (5 studies) or directly inoculating eye droppers and droptainers (1 study).
  - Range of clinical settings (clinics, home, long-term care facilities).
  - Contamination found in 8% - 28% of droptainers.
  - Geyer et al. 1995 – Testing of 194 droptainers found contamination in 40% in droptainers open for >9 weeks (17/42) vs. 19-20% of those open ≤ 8 weeks (29/152); difference statistically significant; p=0.0045.
  - Coad et al. 1984 – Tips of eyedroppers and droptainers containing Fluress® inoculated with Pseudomonas aeruginosa.
    - Swabbings from eyedropper caps showed no growth within minutes after inoculation, but swabbings from droptainer caps consistently yielded bacteria for 24 hours.
    - Design of dispenser may play a role in the contamination.

Literature Review – Adverse Events (cont'd)

- Conjunctival inflammation – Case series by Solomon et al. 2003 (N=12)
  - Unintentional touch of dropper tip to eye caused conjunctival trauma
  - All 12 had baseline corneal conditions (e.g., herpetic keratitis) or were s/p anterior segment surgery (cataract extraction, penetrating keratoplasty, laser in-situ keratomileusis)
  - Presentation: Sudden onset of painful, red eye
  - On exam: Corneal epithelial erosion in the lower bulbar conjunctiva with surrounding hyperemia and conjunctival edema
  - Self-induced injury from inappropriate use of the ophthalmic dispenser
  - Patients unaware of the possibility that their injuries were self-induced

Literature Review – Adverse Events (cont'd)

- Inadvertent touch of droptainer tip to eye – 5 studies evaluated the use of eye drop guides in conjunction with droptainers
  - Healthy adults (Brand et al., N=26; Gomes et al. N=23), glaucoma patients (Sanchez et al., N=50; Sakiyalak et al., N=59), patients with rheumatoid arthritis + dry eye (Averns et al., N=29)
  - Inadvertent tip contact with the eye was common – 22% to 76% of participants

Literature Review- Summation

- Very little literature available specifically about ophthalmic dispensers.
- There was no literature identified for eye cups.
- Inadvertent contamination of the dispenser and associated infection possible, as well as inadvertent self-induced trauma to the eye.
- Secondary infection is uncommon.
- There are no large clinical studies prospectively examining the rate of infection secondary to dispenser contamination.
- It may be concluded that ophthalmic dispensers are generally low in risk.

Medical Device Reports

- Medical Device Reporting (MDR): the mechanism for the FDA to receive significant medical device adverse events from:

  - Mandatory reporters (manufacturers, importers and user facilities)

  - Voluntary reports (health care professionals, patients, consumers)

Medical Device Reports

- 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/environment, including:
    - Rare, serious, or unexpected adverse events
    - Adverse events that occur during long-term device use
    - Adverse events associated with vulnerable populations
    - Off-label use
    - User error

Medical Device Reports

- Limitations
  - Under reporting of events
  - Potential submission of incomplete, inaccurate, untimely, unverified, or biased data.
  - Incidence or prevalence of an event cannot be determined from this reporting system alone.
  - Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report.
  - MAUDE data does not represent all known safety information for a reported medical device.

Medical Device Reports

- The Agency searched the medical device reports databases using general terms for ophthalmic dispensers including eye cup, eye dropper, droptainer, dropper, eye dispenser and other similar terms.
- Search range: No start date through August 15, 2022.
- 3 relevant MDRs were identified. These 3 MDRs were voluntary reports from the United States related to difficulties experienced by patients using different ophthalmic dispensers to self-administer ophthalmic medication.

Medical Device Reports

- MDR (February 2015):
  - Voluntary report from patient using “glaucoma and tissue rejection drugs” expressed general concern that “plastic squeeze dropper bottles” posed risks to patients if they are “opaque” because he could not see whether he needed to obtain replacement supply before the bottle is empty. This “is an issue involving the entire pharmaceutical industry that uses plastic squeeze dropper bottles.”
- MDR (March 2021):
  - Voluntary report from patient that there were “sharp plastic corners on either side of the dropper, which makes it very hard to maneuver” and she “feels the dropper is hard to use.”
- MDR (July 2022):
  - Voluntary report from pharmacist on behalf of patient who was prescribed a biologic for neurotrophic keratoconjunctivitis of the right eye. The dispenser is a “pipette” with a plunger that is designed to connect to the vial top, uptake the medication from the inverted vial, detach from the vial to top, and deliver the eye drop to the eye when the plunger is pressed. The patient complaint was that when he pushes the plunger, “the medicine squirts out” and that “it’s very difficult to control how much medicine gets into the eye.”

Recall History

- The Medical Device Recall database contains Medical Device Recalls classified since November 2002.
- Since January 2017, it may also include correction of removal actions initiated by a firm prior to review by FDA.
- The status is updated if the FDA identifies a violation and classifies the action as a recall and again when the recall is terminated.
- FDA recall classification (resulting in the posting date) may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall.

Recall History

- A review of the medical device recalls database was performed with no start date and end date of August 15, 2022.
- General search terms were used such as eye cup, eyecup, eye dropper, eyedropper, eye drop, eyedrop, droptainer, eye dispenser, ophthalmic dispenser, ophthalmic, and other similar terms.
- The search did not identify any relevant recalls regarding ophthalmic dispensers, including eye cups, eye droppers, or droptainers.

Risks to Health

Identified Risk	Description/Examples
Infection	• This can result from a new device that has microbial contamination as packaged or a device that becomes microbially contaminated because it is improperly cleaned and re-used. • This can result from the microbial contamination of the ophthalmic dispenser and ophthalmic medication because the dispenser tip has touched the eye or touched another unintended surface.
Adverse tissue reaction	• This can result from the use of device materials that are not biocompatible. • This can result from the interaction between the device and ophthalmic medication (for example, chemicals from the device leach into the ophthalmic medication).
Compromised treatment	• This can result from a damaged device or defective device. • This can result from inadequate instructions and the device not being used as intended. • Design of dispenser may cause incorrect dosage of medication to be dispensed to the patient.
Mechanical Injury	• This can result from unintended direct physical contact of the eye with the device

We believe general controls are sufficient to mitigate these risks.

Proposed Classification

886.5880 Ophthalmic Dispensers.

(a) Identification.

Ophthalmic dispensers are manual devices that are intended to irrigate the eye or provide controlled instillation of ophthalmic medication.

(b) Classification.

Class I (general controls). Exempt from premarket notification procedures in subpart E of part 807 of this chapter, subject to the limitations in § 886.9.

Thank you

Questions to Panel - LXQ

Question 1 to Panel

FDA has identified the following risks to health for ophthalmic dispensers:

- Infection
- Adverse tissue reaction
- Compromised treatment
- 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.

Question 2 to Panel

Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

- insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, AND

- if, the device is purported or represented to be for use in supporting or sustaining human life, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, AND

- there is sufficient information to establish special controls to provide such assurance

Question 2 to Panel (cont'd)

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, OR
- insufficient information exists to:
  - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness, OR
  - establish special controls to provide such assurance, BUT
    I. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
    II. does not present a potential unreasonable risk of illness or injury

Question 2 to Panel (cont'd)

FDA does not believe that special controls will be required for ophthalmic dispensers under product code "LXQ" and that general controls will be sufficient to provide a reasonable assurance of the safety and effectiveness for ophthalmic dispensers. As such, FDA believes that Class I is the appropriate classification for ophthalmic dispensers under product code "LXQ."

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.

End of Panel Questions for Product Code "LXQ"