4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-1038]

Over-the-Counter Ophthalmic Drug Products--Emergency Use Eyewash Products; Announcement of Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; request for comments.

The Food and Drug Administration (FDA) is announcing a public hearing to obtain information on the formulation, manufacturing, and labeling of currently marketed over-the-counter (OTC) emergency first aid eyewash drug products, including the components of these products, and the conditions under which such products are safe and effective for their intended uses.

Date and Time: The public hearing will be held on December 4, 2013, from 9 a.m. to 5 p.m. Submit electronic or written requests to make oral presentations and comments by November 13, 2013. Electronic or written comments will be accepted after the hearing until March 4, 2014.

Location: The public hearing will be held at FDA's White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (rm. 1503), Silver Spring, MD 20993-0002. Entrance for the public meeting participants (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information, please refer to

http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.

Contact Persons: Mary C. Gross, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20903, 301-796-3519, FAX: 301-847-8753, mary.gross@fda.hhs.gov; or Elaine Abraham, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20903, 301-796-0843, FAX: 301-796-9899, elaine.abraham@fda.hhs.gov.

Comments: Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

Transcripts: Transcripts of the meeting will be available for review at the Division of Dockets Management (see Comments) and on the Internet at http://www.regulations.gov within 30 days of the public hearing. A transcript also will be available in either hard copy or on CD-ROM after submission of a Freedom of Information request. Written requests are to be sent to the Division of Freedom of Information (ELEM-1029), Office of Management Programs, Food and Drug Administration, 12420 Parklawn Dr., Element Bldg., Rockville, MD 20857.

SUPPLEMENTARY INFORMATION

I. Background

A. Product Overview

OTC emergency first aid eyewash drug products (EE products) are typically water-based solutions used in the workplace to flush or irrigate the eye to reduce the chance of severe injury caused by exposure to acid, alkali, particulate matter, or other hazardous materials. This public

hearing will focus on EE products, including the components of EE products, which are marketed for use in workplace EE stations.

There are two general types of EE products: Large volume and small volume. FDA considers "large volume" EE products those that provide sufficient fluid for 15 minutes of continuous flushing, as needed to satisfy the applicable performance standard for Occupational Safety and Health Administration (OSHA)-compliant eyewash stations (ANSI Standard Z 358.1). It is our current understanding that, within large-volume EE products, there are two general configurations currently marketed:

- Ready-to-use products that include single-use pre-filled, sealed wall-mount or portable eyewash stations and pre-filled, sealed replacement solutions, such as replacement canisters or bags, for refillable eyewash stations. Both sterile and nonsterile products are currently in the marketplace.
- Concentrated solutions and additives intended for mixing with potable water for use in large-volume refillable eyewash stations. The resulting solution is not sterile and is replaced after each use and at regular intervals if not used. Both sterile and nonsterile products are currently in the marketplace.

Small volume EE products (16 fl. oz. to 32 fl. oz.) are marketed in a variety of container and applicator configurations, such as squeeze bottles with built-in eye cups or applicator nozzles. These small volume EEs are often used to deliver immediate flushing fluid prior to use of a large volume EE. We are interested in obtaining information on both the large volume and small volume EE products during this public meeting. Questions posed in this document regarding sterility and formulation are applicable to both types of EE products.

Emergency eyewash stations using direct plumbing will not be considered as part of this public meeting.

B. Regulatory Background

EE products are a type of ophthalmic drug product that FDA is considering for inclusion in the OTC drug monograph system. An OTC drug monograph is a set of FDA regulations that establish conditions of use (such as permitted active ingredients and required labeling) under which products within a given therapeutic category may be marketed without an approved new drug application (NDA) or abbreviated new drug application, based on FDA's determination that products described in the monograph are "generally recognized as safe and effective" when used under the conditions prescribed, recommended, or suggested in the product's labeling.

FDA published a final monograph on OTC ophthalmic drug products in 1988 (the OTC ophthalmic monograph or final monograph, 21 CFR part 349). The final monograph defines an OTC ophthalmic drug as "a drug product, which should be sterile in accordance with [21 CFR] 200.50, to be applied in the eyelid or instilled in the eye" (§ 349.3(a) (21 CFR 349.3(a))). "Eyewash" is defined in the final monograph as "a sterile aqueous solution intended for washing, bathing, or flushing the eye" (id. at § 349.3(f)), and described in § 349.20 as containing purified water as the active ingredient, together with "suitable tonicity agents to establish isotonicity with tears, suitable agents for establishing pH and buffering to achieve the same pH as tears, and a suitable preservative agent" as inactive ingredients.

The reference to sterility in § 349.3(a) and (f) is based on a separate regulation, 21 CFR 200.50, which was adopted in 1975 and is applicable to all drugs intended for ophthalmic use. It states in part that all preparations offered or intended for ophthalmic use, including preparations

for cleansing the eyes, should be sterile, and if they are not sterile may be considered adulterated and misbranded.

The eyewash products that are defined in and marketed under the final OTC ophthalmic monograph are small-volume products for non-emergency use. The final monograph does not currently include conditions of use for EE products because no safety or efficacy data or other information were submitted on these products during the rulemaking process. After the final monograph was published in 1988, FDA received several requests from industry to clarify the regulatory status of EE products. In response, FDA published a request for data and information on these products in 1989 (call for data, 54 FR 50240 (December 5, 1989)). In the 1989 call for data, FDA recognized the need for eyewash products for emergency first aid treatment of chemical burns (including acid and alkali burns). FDA stated in the call for data that these products could potentially be regulated under the OTC ophthalmic drug monograph and invited the submission of data and information to help facilitate the Agency's consideration of whether to amend the monograph to include these products. FDA received comments in response to the call for data.

On February 19, 2003, FDA proposed to amend the final OTC ophthalmic drug monograph to include a section on EE products (the PR, 68 FR 7951). The PR stated FDA's tentative conclusion that medical references support the safety and effectiveness of EE products to remove acid or alkali chemicals and that immediate flushing of the eye with fluid is urgently needed to lessen the impact of the chemical exposure.

The PR defined EE products as "products [that] contain water, agents to achieve the pH within a range of 6.6 and 7.4, and a suitable antimicrobial preservative agent. Additionally, they may contain tonicity agents to establish isotonicity with tears and agents for buffering the pH"

(68 FR 7951 at 7955, proposed 21 CFR 349.22). The proposed indication (intended use/purpose) is "for ["flushing" or "irrigating"] the eye to reduce chances of severe injury caused by acid, alkali, or particulate contamination." The PR included proposed warnings and directions for use for both ready-to-use EE products and EE products that require mixing a concentrate with potable water.

As noted in the PR, FDA may exercise enforcement discretion to permit an affected OTC ophthalmic drug product that is not the subject of an approved NDA to be marketed until the final monograph becomes effective, provided the following conditions are met: (1) The product or similarly formulated products were marketed as OTC drugs on or before December 4, 1975; (2) the product does not constitute a hazard to health; (3) the product is not regarded as a prescription drug within the meaning of section 503(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(b)); and (4) the product is an OTC drug and does not bear claims for serious disease conditions that require the attention and supervision of a licensed practitioner (see 68 FR 7951 at 7954 and 7955).

Like all OTC drug products intended for ophthalmic use, EE products are subject to the general sterility requirements in 21 CFR 200.50, as well as general OTC drug requirements, such as drug facts labeling (21 CFR 201.66) and compliance with current good manufacturing practices (21 CFR 330.1(a) and parts 210 and 211).

II. Scope of the Public Meeting

We have reviewed the information and comments relating to EE products that were submitted in response to the 2003 PR, and have concluded that additional data and information are needed in order to finalize the OTC monograph with respect to EE products.

FDA is holding this public hearing to obtain input from regulated industry, the medical community, consumers, and other interested parties concerning the formulation, manufacturing, and labeling of currently marketed EE drug products, including the components of such, and the conditions under which these products are safe and effective for their intended uses. Input from the public meeting will help FDA to establish final marketing requirements for EE products as part of the OTC ophthalmic drug product monograph, 21 CFR part 349.

FDA is requesting public feedback on the following questions:

1. What ingredients are necessary in EE formulations besides water? What are the functions of these other ingredients? What is the minimum and maximum quantity that should be allowed for these other ingredients?
2. Are there any potential safety concerns or suitability issues with the use of ingredients other than water? What data are available to support the safety and suitability of EE ingredients other than water?
3. What evidence supports the safety and effectiveness/suitability of antimicrobial preservatives when mixed with potable water to limit the presence of certain pathogenic microorganisms (such as Acanthamoeba, bacteria, or fungi)? For example, FDA is aware of published reports of Acanthamoeba having contaminated reservoir EE stations and been a source of infection in people who used these types of EE products (Refs. 1 and 2).
4. Is there evidence that solutions made from EE products mixed with potable water are safer or more effective than potable water used alone? If not, what data would be needed to make that determination?

5. What EE products or types of products are not currently manufactured and distributed as sterile? Are there EE products for which sterility is not necessary for safety? Why or why not?
6. What directions for use are appropriate to ensure the safety and effectiveness of EE products for OTC use?

III. Attendance at and/or Participation in the Public Hearing

If you wish to attend the hearing or make an oral presentation during the hearing, you must register by submitting an electronic request to: CDEREYEWASHMEETING@fda.hhs.gov by close of business on November 13, 2013. Those without email access may register by contacting Mary Gross or Elaine Abraham (see Contact Persons). You must provide your name, title, business affiliation (if applicable), address, email address, telephone and fax numbers, and type of organization you represent (e.g., industry, consumer organization) and a brief summary of comments, including the discussion topic(s) that will be addressed and the approximate time requested for your presentation.

FDA will try to accommodate all persons who wish to make a presentation; however, the duration of each speaker's testimony may be limited by time constraints. FDA will notify registered presenters of their scheduled presentation times. Persons registered to make an oral presentation should check in before the hearing and are encouraged to arrive early to ensure their designated order of presentation. Participants who are not present when called risk forfeiting their scheduled time. An agenda of the meeting and other background material will be made available at least 3 days before the meeting at: http://www.fda.gov/Drugs/NewsEvents/ucm356526.htm.

The public meeting is free and seating will be on a first-come, first-served basis. Early registration is recommended for those wishing to attend the meeting as observers or to provide testimony because seating is limited. FDA may limit the numbers of participants from individual organizations as well as total number of attendees based on space limitations. Registrants will receive confirmation once they have been accepted to attend the hearing. For those unable to attend in person, FDA will provide a Webcast to the meeting. Additional information about the Webcast location will be posted on the Web page, http://www.fda.gov/Drugs/NewsEvents/ucm356526.htm, prior to December 4, 2013.

Any person requiring special accommodations to attend the hearing should direct those needs to the contact persons (see Contact Persons) at least 7 days in advance.

IV. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by FDA senior management from the Center for Drug Evaluation and Research.

Under § 15.30(f), the hearing is informal and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation. Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (21 CFR part 10, subpart C). Under 21 CFR 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b) (see

section III of this document for more details). To the extent that the conditions for the hearing as described in this document conflict with any provisions set out in part 15, this notice acts as a waiver of those provisions as specified in § 15.30(h).

V. Request for Comments

Regardless of attendance at the public hearing, interested persons may submit either electronic comments to http://www.regulations.gov or written comments to the Division of Dockets Management (see Comments). Persons who wish to provide additional materials for consideration should file these materials with the Division of Dockets Management by March 4, 2014. You should annotate and organize your comments to identify the specific questions identified by the topic to which they refer. It is only necessary to send one set of comments. All comment submissions should be marked with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

VI. References

The following references have been placed on display in the Division of Dockets Management (see Comments) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at http://www.regulations.gov.

1. U.S. Environmental Protection Agency, "Health Effects Support Document for Acanthamoeba," 2003.

2. Bowman, E. K., A. A. Vass, R. Mackowski, et al., "Quantitation of Free-Living Amoebae and Bacterial Populations in Eyewash Stations Relative to Flushing

Frequency," American Industrial Hygiene Association Journal, vol. 57, pp. 626-633, 1996.

Dated: September 12, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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