DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2023–D–4177]

Quality Considerations for Topical Ophthalmic Drug Products; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Quality Considerations for Topical Ophthalmic Drug Products.'' This draft guidance discusses certain quality considerations for ophthalmic drug products (*i.e.,* solutions, suspensions, emulsions, gels, ointments, and creams) intended for topical delivery in and around the eye. Specifically, this draft guidance discusses approaches to evaluating visible particulate matter, extractables and leachables, and impurities and degradation products; use of in vitro drug release/dissolution testing as an optional quality control strategy for certain ophthalmic dosage forms; recommendations for design and delivery and dispensing features of container closure systems; and recommendations for stability studies. The draft guidance applies to ophthalmic drug products approved under new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biologics license applications (BLAs), as well as to over-the-counter (OTC) monograph drugs.

DATES: Submit either electronic or written comments on the draft guidance by December 12, 2023 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2023–D–4177 for ''Quality Considerations for Topical Ophthalmic Drug Products.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Ranjani Prabhakara, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 6648, Silver Spring, MD 20993–0002, 240–402–4652.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Quality Considerations for Topical Ophthalmic Drug Products.'' This draft guidance provides information regarding quality considerations for ophthalmic drug products consistent with the requirements outlined in section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(B)) and 21 CFR parts 210 and 211 for all drug products, 21 CFR part 601 for biological products, 21 CFR part 4 for combination products, and, for ophthalmic drug products with a United States Pharmacopeia (USP) monograph, the applicable criteria from the USP. The draft guidance also provides recommendations to industry on the documentation that should be submitted in the chemistry, manufacturing, and controls (CMC) section of NDAs,

ANDAs, and BLAs for certain CMC attributes for ophthalmic drug products.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on ''Quality Considerations for Topical Ophthalmic Drug Products.'' It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The collections of information in 21 CFR parts 314 and 601 have been approved under OMB control numbers 0910–0001 and 0910–0338, respectively. The collections of information in 21 CFR parts 210 and 211 have been approved under OMB control number 0910–0139.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, *https://www.fda.gov/regulatory-information/search-fda-guidance-documents,* or *https://www.regulations.gov.*

Dated: October 10, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Screening Framework Guidance for Providers and Users of Synthetic Nucleic Acids

AGENCY: Administration for Strategic Preparedness and Response (ASPR), Department of Health and Human Services (HHS).

ACTION: Notice.

SUMMARY: The Administration for Strategic Preparedness and Response is issuing this screening framework guidance, which sets forth baseline standards for the gene and genome synthesis industry, as well as best practices for all entities involved in the provision, use, and transfer of synthetic nucleic acids, regarding screening orders and recipients and maintaining records. In addition, this guidance seeks to encourage best practices to address biosecurity concerns associated with the potential misuse of synthetic nucleic acids in order to bypass existing regulatory controls and commit unlawful acts.

FOR FURTHER INFORMATION CONTACT: C. Matthew Sharkey, Administration for Strategic Preparedness and Response, Department of Health and Human Services, 400 7th St. SW, Washington, DC 20024; 202–868–9224, *syndnaguidance@hhs.gov.*

SUPPLEMENTARY INFORMATION: A request for public comments on the issues covered in this Notice was published in the **Federal Register** (85 FR 52611 [Aug. 26, 2020]; 85 FR 69630 [Nov. 3, 2020], *Review and Revision of the Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA*) with a comment period of more than 120 days. Following consideration of the comments received in response to this Notice, HHS issued proposed draft revised guidance as a **Federal Register** Notice (87 FR 25495 [Apr. 29, 2022], *Screening Framework Guidance for Providers and Users of Synthetic Oligonucleotides*) and solicited additional comments for a period of 60 days. This *Guidance* was drafted through a deliberative interagency process to address the topics raised in public comments received in response to these prior Notices as well as other considerations. Responses received from these prior Notices and summaries of updates contained in this *Guidance* are available for public review at the following website *https://aspr.hhs.gov/legal/synna.*

Screening Framework Guidance for Providers and Users of Synthetic Nucleic Acids

I. Introduction

Synthetic biology is an interdisciplinary field that focuses on the design and fabrication of novel biological components and systems as well as the redesign and fabrication of existing biological systems. Modern biotechnologies have made the conversion of different types of nucleic acids possible (*e.g.,* RNA to DNA), and longer genomic sequences can now be constructed from very short nucleic acids with higher fidelity. Additionally, synthetic biology is not limited to naturally derived genetic material. Thus, this scientific field has the potential to generate existing or novel components, systems, or organisms directly, using only genetic sequence data.

Advances in nucleic acid synthesis technology and the open-source availability of genetic sequence data have significantly contributed to discovery and innovation in areas such as health and agriculture research and development. However, there are concerns among the scientific community, the nucleic acid synthesis industry, the U.S. government, and the public that individuals with ill intent could exploit biotechnology for harmful purposes. The U.S. government has acted to minimize risks to public health, agriculture, plants, animals, animal or plant products, and the environment due to biological pathogens and toxins. For instance, it has issued the Federal Select Agent Regulations, which regulate a subset of microbial organisms and toxins determined to have the potential to pose a severe threat to public health and safety, animal health, plant health, animal or plant products, or the environment. These regulations are administered jointly by the CDC, Division of Select Agents and Toxins and the Animal and Plant Health Inspection Service, Division of Agricultural Select Agents and Toxins, through the Federal Select Agent Program (FSAP),[1] which sets forth requirements for the possession, use, and transfer of biological select agents and toxins. A second layer of regulation is provided by the Bureau of Industry and Security (BIS) Export Administration Regulations' Commerce Control List (CCL),[2] which identifies agents and genetic sequences that require licenses before export from the United States. However, these regulated pathogens and toxins do not represent the entirety of the potential risks to public health, agriculture, plants, animals, animal or plant products, or the environment that could arise from the misuse of synthetic nucleic acids. Non-regulated pathogens and toxins, as well as other novel types of nucleic acid sequences, may also pose significant risks if they are misused. To minimize these risks, a shift is needed from relying solely on lists of regulated pathogens and toxins to also assessing the risks associated with other nucleic acid sequences that may contribute to pathogenicity or harm if introduced into new genetic frameworks (*i.e.,* Sequences of Concern [SOCs]). Also, modern molecular biological techniques allow the conversion between different types of nucleic acids (*e.g.,* RNA to DNA, and

[1] *https://www.selectagents.gov/sat/list.htm.*

[2] *https://www.bis.doc.gov/index.php/regulations/commerce-control-list-ccl.*