4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-D-1864]

Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in Abbreviated New Drug Applications; Draft Guidance for Industry, Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs." This draft guidance is intended to assist applicants who submit abbreviated new drug applications (ANDAs) for liquid-based and/or other semisolid products applied to the skin, including integumentary and mucosal (e.g., vaginal) membranes (referred to as "topical products"). This draft guidance document provides recommendations for physicochemical and structural (collectively, "Q3") characterizations that can be used to identify the dosage form of a proposed generic (test) topical product, and to describe properties of the drug product that may be critical to its performance (to support a demonstration of bioequivalence (BE)).

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2022-D-1864 for "Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs." 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 the office in processing your requests. See the

SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Susan Levine, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 1674, Silver Spring, MD 20993-0002, 240-402-7936.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs." This draft guidance is intended to assist applicants who submit ANDAs for liquid-based and/or other semisolid products applied to the skin, including integumentary and mucosal (e.g., vaginal) membranes. This draft guidance document provides recommendations for physicochemical and structural (collectively, "Q3") characterizations that can be used: (1) to identify the dosage form of a proposed generic (test) topical product and (2) to describe properties of the drug product that may be critical to its performance (to support a demonstration of BE). This draft guidance does not address Q3 characterization of topical products for purposes of product quality control.

Basic Q3 characterization of a topical product can be used to describe its dosage form (e.g., an emulsion). The nomenclature used to describe the dosage form of topical products (e.g., solutions, suspensions, gels, lotions, creams, shampoos, ointments, pastes, etc.) is not precisely defined by a systematic classification of the compositional, physicochemical, or structural attributes of the drug product. Consequently, for topical products, it may not be possible to infer the Q3 attributes of a particular dosage form based upon the dosage form nomenclature.

Comprehensive Q3 characterization of a topical product can be used to establish a detailed profile of Q3 attributes that specifically describes the nature of that product and identifies a collection of attributes that describe the arrangement of matter (e.g., the polymorphic

form(s) of the active ingredient(s) and/or the pH of the drug product) that may modulate the systemic or local availability of the active ingredient(s) from the product. Because Q3 characterization describes essential attributes of a drug product that may be critical to its performance, differences in Q3 attributes between a test product and the reference standard selected by FDA can indicate a risk that the differences may impact the respective bioavailability and/or BE of the two products. Conversely, a demonstration that there are no differences in Q3 attributes between a test and reference standard substantially mitigates the risk of potential failure modes for BE that may otherwise arise from any differences in Q3 attributes.

This draft guidance provides recommendations on the types of characterizations that constitute a basic and comprehensive Q3 characterization. This draft guidance also describes the concepts of "sameness," "similarity," and "difference" in comparing Q3 characterizations of two topical products, and how a showing of "Q3 sameness," "Q3 similarity," or "Q3 difference" between a test topical product and the reference standard may impact what additional evidence may be recommended to demonstrate BE, as part of a comparative product characterization-based approach.

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 "Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs." 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 draft guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to

review by OMB under the PRA. The collections of information for the submission of ANDAs have been approved under OMB control number 0910-0001. Applicant submission of controlled correspondence related to generic drug development and FDA approval is approved under OMB control number 0910-0797. The collections of information that support Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies have been approved under OMB control number 0910-0119. The collections of information in 21 CFR part 320 for "Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans" have been approved under OMB control number 0910-0014. The recordkeeping requirement for Current Good Manufacturing Practice (CGMP) sample retention in 21 CFR 211.170 has 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 18, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022-23016 Filed: 10/21/2022 8:45 am; Publication Date: 10/24/2022]