4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-3546]

Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs; Revised Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised draft guidance for industry entitled "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs." This revised draft guidance provides recommendations for the design and conduct of studies to evaluate the in vivo skin irritation and sensitization (I/S) potential of a proposed transdermal or topical delivery system (collectively referred to as TDS). The recommendations in this revised draft guidance relate to studies submitted in support of an abbreviated new drug application (ANDA). The revised draft guidance is intended to clarify FDA's recommendations and expectations related to in vivo skin I/S studies. This guidance revises the October 2018 draft guidance entitled "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs."

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2018-D-3546 for "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for 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 that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Melissa Mannion, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 1611, Silver Spring, MD 20993-0002, 301-796-2747.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs." This guidance revises the draft guidance entitled "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs" that was published in the *Federal Register* on October 10, 2018 (83 FR 50945). FDA received eight comments on the draft guidance, which were considered before publication of this revised draft guidance.

The components and composition of a TDS formulation, including the nature of the drug substance and/or the occlusivity of the TDS materials, in conjunction with other factors such as the environmental humidity or the condition of the skin, may have the potential to irritate the skin or lead to a sensitization reaction. Such reactions can be unpleasant to the patient and may affect patient compliance, skin permeability, and/or adhesion of the TDS to the skin. The collective consequence of these potential effects could create uncertainty about the resulting drug delivery profile and uncertainty about the rate and extent of drug absorption from the TDS. Therefore, when appropriate, applicants should perform a comparative assessment of the test (T) and reference (R) TDS products using an appropriately designed skin I/S study with human subjects to demonstrate that the potential for a skin irritation or sensitization reaction with the T

TDS is no worse than the reaction observed with the R TDS.

This revised draft guidance provides the following updates to the original draft guidance:

(1) Clarifies recommendations for the design and conduct of studies to evaluate the in vivo skin I/S potential of a proposed TDS.

(2) Clarifies when an in vivo study to assess the sensitization potential of a TDS product may not be needed.

(3) Provides guidance to applicants intending to utilize alternative scoring scales or alternative approaches to compare irritation and sensitization between the T and R TDS.

The recommendations in this revised draft guidance relate to studies submitted in support of an ANDA. The Agency is seeking comments on the recommendations reflected in the revised draft guidance announced in this notice. In addition, FDA invites comments on the scoring scales and any alternative approaches, including those recommended by international regulatory agencies, that may have been used for the comparative assessment of the I/S potential for proposed generic TDS products. FDA also specifically invites comments regarding the comparative assessment of sensitization itself, i.e., whether there are clinical scenarios where a comparative sensitization assessment may be uninformative when conducted in addition to a comparative irritation assessment.

This revised 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 "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for 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 revised 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 in 21 CFR part 314 relating to the submission of abbreviated new drug applications have been approved under OMB control number 0910-0001. The collections of information relating to good clinical practice have been approved under OMB control number 0910-0843.

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: April 7, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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