4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-D-0142]

Nonclinical Safety Evaluation of Reformulated Drug Products and Products Intended for Administration by an Alternate Route; Guidance for Industry and Review Staff; 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 guidance for industry and review staff entitled "Nonclinical Safety Evaluation of Reformulated Drug Products and Products Intended for Administration by an Alternate Route." The guidance provides recommendations concerning the evaluation of the nonclinical safety of reformulated drug products or products being used by an alternate route. It is intended for use by interested individuals in industry and reviewers within the Center for Drug Evaluation and Research (CDER). The goals of this guidance are to foster and expedite the development of reformulated drug products or the use of previously approved drugs by alternate routes, communicate to industry current CDER thoughts pertaining to safety data needed to support these drug products, and increase uniformity within CDER on expectations for the nonclinical development

of reformulated drug products or products being used by an alternate route. This guidance finalizes the draft guidance of the same name published on March 7, 2008.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to http://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 http://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): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, 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-2008-D-0142 for "Nonclinical Safety Evaluation of Reformulated Drug Products and Products Intended for Administration by an Alternate Route; Guidance for Industry and Review Staff." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at http://www.regulations.gov or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- 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 http://www.regulations.gov. Submit both copies to the Division of

Dockets Management. 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: http://www.fda.gov/regulatoryinformation/dockets/default.htm.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to http://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 Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of this 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 guidance document.

FOR FURTHER INFORMATION CONTACT: Paul C. Brown, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg., 22, rm. 6472, Silver Spring, MD 20993-0002, 301-796-0856.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry and review staff entitled "Nonclinical Safety Evaluation of Reformulated Drug Products and Products Intended for Administration by an Alternate Route." This guidance provides recommendations regarding the nonclinical evaluation of a new formulation containing a previously approved drug substance and of a product proposed for use by an alternate route of administration for which the product was not previously approved.

Generally, nonclinical data support use of a drug product by a particular route and also reflect the planned duration of use. Much of the available nonclinical information used to support approval of the initial formulation can be used to support the safety of additional formulations assuming all legal rights to the information are met. Information used to support an initial formulation, however, may not always be sufficient to support such additional approvals because changes in the formulation could produce a new toxicity. This is particularly true if the drug product's route of administration is different or the duration of use changes markedly. Therefore, additional nonclinical studies might be recommended to ensure that the toxicity of a new formulation is fully characterized.

This guidance provides general nonclinical considerations for all reformulations or new routes of use and several route-specific considerations. The considerations in this guidance can also be applied to routes not specifically mentioned in the guidance.

This guidance finalizes the draft guidance of the same name published on March 7, 2008. Changes to the guidance include the addition of a recommendation that toxicology studies be conducted under good laboratory practices, clarification that histopathology can be

limited in some cases to locally exposed tissues, the addition of a reference to the International Conference on Harmonisation guidance for industry entitled "S10 Photosafety Evaluation of Pharmaceuticals," and other clarifications to the studies recommended for specific routes such as dermal, ocular, and intranasal.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on nonclinical safety evaluation of reformulated drug products and products intended for administration by an alternate route. 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. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: October 21, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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