



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-0310]

Guidance for Industry on Immunogenicity-Related Considerations for Low Molecular Weight Heparin; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled "Immunogenicity-Related Considerations for Low Molecular Weight Heparin." This guidance discusses how applicants for low molecular weight heparin (LMWH) products should provide information on impurities and their potential impact on immunogenicity.

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-2014-D-0310 for "Immunogenicity-Related Considerations for Low Molecular Weight Heparin." 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: Daniela Verthelyi, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 240-402-7450.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Immunogenicity-Related Considerations for Low Molecular Weight Heparin." It finalizes the draft guidance entitled "Immunogenicity-Related Considerations for the Approval of Low Molecular Weight Heparin for New Drug Applications and Abbreviated New Drug Applications" that published on April 9, 2014 (79 FR 19621). FDA has considered the comments submitted to the public docket and modified statements and added terms for clarity.

This guidance provides recommendations to applicants for new drug applications (NDAs) and abbreviated new drug applications (ANDAs) regarding impurities and their potential effect on immunogenicity for LMWH. This guidance also includes recommendations for ANDA applicants on meeting the requirement for active ingredient sameness, because a demonstration of active ingredient sameness helps to address immunogenicity considerations in this context. In addition, this guidance discusses how to address changes in the source material or other component, or when there are modifications to the manufacturing process after completion of supporting clinical studies, either before or after approval of the application.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). This guidance represents the Agency's current thinking on immunogenicity

considerations for low molecular weight heparin. 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. The Paperwork Reduction Act

This guidance refers to a previously approved collection of information that is subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collection of information in 21 CFR part 314 has been approved under OMB control number 0910-0001.

III. Electronic Access

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

Dated: February 16, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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