DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2012–D–0083]

Guidance for Industry on Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality; 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 ''Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality.'' This guidance was initially published as a draft guidance on February 13, 2012. The draft was revised to clarify FDA's expectations and recommendations and to include references to a recently-developed assay for detecting ruminant contamination of crude heparin.

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

ADDRESSES: 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, 10903 New Hampshire Ave., Bldg. 51, Rm. 2201, 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.

Submit electronic comments on the guidance to *http://www.regulations.gov.* Submit written comments to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Frank W. Perrella, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 4257, Silver Spring, MD 20993–0002, 301–796–3265; or Dennis M. Bensley, Jr., Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–276–8268; or Scott McNamee, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3416, Silver Spring, MD 20993–0002, 301–796–5523.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality.'' This guidance provides recommendations that will help active pharmaceutical ingredient (API) manufacturers, pharmaceutical and medical device manufacturers of finished products, and others, to prevent the use of crude heparin that might contain oversulfated chondroitin sulfate (OSCS) or non-porcine material (especially ruminant material) contaminants. This guidance on crude heparin recommends strategies to test for contamination and should be used in addition to the United States Pharmacopeia (USP) monograph testing required for other forms of heparin to detect the presence of OSCS.

Following reports of serious adverse events (including deaths) among patients injected with heparin sodium in 2008, FDA identified the contaminant OSCS in crude heparin sourced from China. FDA is also concerned about the potential for contamination of heparin with ruminant materials. The control of the quality of crude heparin is important to ensure the safety of drugs and devices and to protect public health. FDA developed this guidance to alert manufacturers to the risks of crude heparin contaminants and to recommend strategies to ensure that the heparin supply chain is not contaminated with OSCS or any non-porcine ruminant material (unless specifically approved as part of drug or medical device application).

The guidance recommends that manufacturers test and confirm the species origin of crude heparin in each lot of every shipment before use in the manufacture or preparation of a drug or medical device containing heparin. The test method should be qualified for use in testing crude heparin and for the identification of species origin. The method should be based on good scientific principles (e.g., sufficient accuracy and specificity) and possess a level of sensitivity commensurate with the current state of scientific knowledge and risk. FDA has posted a method entitled ''Heparin Multiplex Real-Time PCR Assay (hMRTA),'' on the Internet at *http://www.fda.gov/AnimalVeterinary/ScienceResearch/ToolsResources/ucm350289.htm.* This method will be updated occasionally and persons performing the assay should visit the Web site regularly to ensure they are using the most current version.

The guidance also recommends that manufacturers test for OSCS in crude heparin in each lot of every shipment before use, using a qualified test method that is suitable for detecting low levels of OSCS concentrations and is based on good scientific principles. FDA has also made an HPLC method for testing for the presence of OSCS in crude heparin available on the Internet at *http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM206230.pdf.* Users of this method should also review the Web site occasionally to ensure they are employing the most current version.

In addition to testing crude heparin for species of origin and the presence of OSCS in crude heparin, manufacturers should reject for use any crude heparin found to contain any amount of OSCS, or to be derived from, in any amount, ruminant mucosa (unless approved in the drug or device application). If imported into the United States, any such crude heparin or heparin products in which it was used should be controlled, and manufacturers should notify FDA of any such finding. The guidance also recommends that manufacturers identify and audit crude heparin suppliers and heparin API suppliers to ensure conformance to appropriate quality standards. Manufacturers should employ the controls described in the guidance for industry entitled ''Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients'' and comply with the quality system regulations (as applicable).

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

III. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). In the guidance, FDA advises drug and medical device manufacturers who receive and use crude heparin to manufacture drugs and medical devices to notify the Agency of crude heparin found to contain any amount of OSCS, or to be derived from, in any amount, ruminant mucosa (unless approved in the drug or device application) (for human drugs, 21 CFR 314.81(b)(1)(ii); for animal drugs, 21 CFR 514.80(b); for medical devices, 21 CFR 803.50). The collections of information in 21 CFR 314.81(b)(1)(ii) have been approved under OMB control number 0910–0001; in 21 CFR 514.80(b) under OMB control number 0910–0284; and in 21 CFR 803.50 under OMB control number 0910–0437.

IV. 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: June 19, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–N–0001]

Tobacco Products Scientific Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Tobacco Products Scientific Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the Agency on FDA's regulatory issues.

Date and Time: The meeting will be held on August 16, 2013, from 8:30 a.m. to 3 p.m.

Location: Sheraton Silver Spring Hotel, 8777 Georgia Ave., Silver Spring, MD 20910.

Contact Person: Caryn Cohen, Center for Tobacco Products, Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 1–877–287–1373 (choose option 5), email: *TPSAC@fda.hhs.gov*, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area). A notice in the **Federal Register** about last minute modifications that impact a previously announced advisory committee meeting cannot always be published quickly enough to provide timely notice. Therefore, you should always check the Agency's Web site at *http://www.fda.gov/AdvisoryCommittees/default.htm* and scroll down to the appropriate advisory committee meeting link, or call the advisory committee information line, to learn about possible modifications before coming to the meeting.

Agenda: On August 16, 2013, the Committee will discuss possible approaches for evaluating information on the risks and potential benefits of a proposed modified risk tobacco product (MRTP) to the population as a whole. MRTPs are tobacco products that are sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products. Before an MRTP can be introduced or delivered for introduction into interstate commerce, an order from FDA under section 911(g) (21 U.S.C. 387k(g)) of the Federal Food, Drug, and Cosmetic Act must be in effect with respect to the tobacco product. 21 U.S.C. 387k(a).

In reviewing MRTP applications, among other things, FDA must evaluate the effects of a proposed product on the health of individual tobacco users and the population as a whole, taking into account: (1) The relative health risks to individuals of the MRTP; (2) the increased or decreased likelihood that existing users of tobacco products who would otherwise stop using such products will switch to the MRTP; (3) the increased or decreased likelihood that persons who do not use tobacco products will start using the MRTP; (4) the risks and benefits to persons from the use of the MRTP compared to the use of smoking cessation drug or device products approved by FDA to treat nicotine dependence; and (5) comments, data, and information submitted to FDA by interested persons. 21 U.S.C. 387k(g)(4).

FDA intends to make background material available to the public no later than 2 business days before the meeting. If FDA is unable to post the background material on its Web site prior to the meeting, the background material will be made publicly available at the location of the advisory committee meeting, and the background material will be posted on FDA's Web site after the meeting. Background material is available at *http://www.fda.gov/AdvisoryCommittees/Calendar/default.htm.* Scroll down to the appropriate advisory committee meeting link.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person on or before August 1, 2013. Oral presentations from the public will be scheduled between approximately 11 a.m. and 12 noon. Those individuals interested in making formal oral presentations should notify the contact person and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation on or before July 25, 2013. Time allotted for each presentation may be limited. If the number of registrants requesting to speak is greater than can be reasonably accommodated during the scheduled open public hearing session, FDA may conduct a lottery to determine the speakers for the scheduled open public hearing session. The contact person will notify interested persons regarding their request to speak by July 26, 2013.

Persons attending FDA's advisory committee meetings are advised that the Agency is not responsible for providing access to electrical outlets.

FDA welcomes the attendance of the public at its advisory committee meetings and will make every effort to accommodate persons with physical disabilities or special needs. If you require special accommodations due to a disability, please contact Caryn Cohen at least 7 days in advance of the meeting.

FDA is committed to the orderly conduct of its advisory committee meetings. Please visit our Web site at *http://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/ucm111462.htm* for procedures on public conduct during advisory committee meetings.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).