4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-0350]

Use of International Standard ISO 10993-1, "Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process"; Guidance for Industry and Food and Drug Administration 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 the guidance entitled "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process.' " FDA has developed this guidance document to assist industry in preparing Premarket Applications (PMAs), Humanitarian Device Exceptions (HDEs), Investigational Device Applications (IDEs), Premarket Notifications (510(k)s), and de novo requests for medical devices that come into direct contact or indirect contact with the human body in order to determine the potential for an unacceptable adverse biological response resulting from contact of the component materials of the device with the body.

The purpose of this guidance is to provide further clarification and updated information on the use of International Standard ISO 10993-1, "Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process" to support applications to FDA. This guidance supersedes Office of Device Evaluation (ODE) Blue Book Memorandum

#G95-1 (1995), entitled "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices--Part 1: Evaluation and Testing.' "

DATES: Submit either electronic or written comments on this guidance at any time. General comments on Agency guidance documents are welcome 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-2013-D-0350 for "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process.' " 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.

An electronic copy of the guidance document is available for download from the Internet. See the SUPPLEMENTARY INFORMATION section for information on electronic access to the guidance. Submit written requests for a single hard copy of the guidance document entitled "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process' " to the Office of the Center Director, Guidance and Policy Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5431, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request.

FOR FURTHER INFORMATION CONTACT: Jennifer Goode, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 1212, Silver Spring, MD 20993-0002, 301-796-6374.

SUPPLEMENTARY INFORMATION:

I. Background

FDA has developed this guidance document to assist industry in PMAs, HDEs, IDEs, 510(k)s, and de novo requests for medical devices that come into direct contact or indirect contact with the human body in order to determine the potential for an unacceptable adverse biological response resulting from contact of the component materials of the device with the body.

The purpose of this guidance is to provide further clarification and updated information on the use of International Standard ISO 10993-1, "Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process" to support applications to FDA. This guidance supersedes ODE Blue Book Memorandum #G95-1 (1995), entitled "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices--Part 1: Evaluation and Testing.' "

The scope of this document is limited to the biological evaluation of sterile and non-sterile medical devices that come into direct or indirect contact with the human body and covers the following topics: Use of risk assessments for biocompatibility evaluations for a proposed medical device; use of ISO 10993-1 and the FDA-modified matrix to determine the relevant biocompatibility endpoints for an evaluation; general biocompatibility testing considerations, including test article preparation; specific considerations for the following testing: Cytotoxicity, sensitization, hemocompatibility, pyrogenicity, implantation, genotoxicity, carcinogenicity, reproductive and developmental toxicity, and degradation assessments; chemical assessment recommendations; and considerations for labeling devices as "-free."

A draft of this guidance was made available in the Federal Register on April 23, 2013, and the comment period closed on July 22, 2013. The final guidance was revised in response to the comments to emphasize use of risk assessment and leveraging of prior information within a submission to potentially reduce the need for new biocompatibility testing.

Commenters also requested additional details regarding biocompatibility testing of devices in contact with gas pathways and color additives used in medical devices. FDA has determined that these concepts would be appropriately addressed in separate guidance documents and have therefore been removed from this final guidance.

II. Significance of Guidance

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 Use of International Standard ISO 10993-1, "Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process." 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.

III. Electronic Access

Persons interested in obtaining a copy of the guidance may do so by downloading an electronic copy from the Internet. A search capability for all Center for Devices and Radiological Health guidance documents is available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm. Guidance documents are also available at http://www.regulations.gov. Persons unable to download an electronic copy of "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process'

" may send an email request to CDRH-Guidance@fda.hhs.gov to receive an electronic copy of the document. Please use the document number 1811 to identify the guidance you are requesting.

IV. 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). The collections of information in 21 CFR part 58 have been approved under OMB control number 0910-0119; the collections of information in 21 CFR parts 801 and 809 have been approved under OMB control number 0910-0485; the collections of information in 21 CFR part 807, subpart E, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 812 have been approved under OMB control number 0910-0078; the collections of information in 21 CFR part 814, subparts A through E, have been approved under OMB control number 0910-0231; the collections of information in 21 CFR part 814, subpart H, have been approved under OMB control number 0910-0332; the collections of information in 21 CFR part 820 have been approved under OMB control number 0910-0073; and the collections of information in the guidance document "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff" have been approved under OMB control number 0910-0756.

Dated: June 8, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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