4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-1376]

Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; 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 final guidance entitled "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; Guidance for Industry and Food and Drug Administration Staff." This guidance explains the circumstances in which it may be appropriate to extrapolate existing medical device data to support pediatric device indications in premarket approval applications (PMAs), humanitarian device exemptions (HDEs) and de novo requests. This guidance also describes FDA's approach for determining whether extrapolation may be appropriate and the factors that should be considered within a statistical model for extrapolation. Extrapolation may be appropriate when there are few differences in safety or effectiveness of the proposed device when used in adult as compared to the intended pediatric populations and the adult data are of high quality for borrowing.

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-2015-D-1376 for "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; Guidance for Industry and Food and Drug Administration 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.

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 "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; Guidance for Industry and Food and Drug Administration Staff" 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; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request.

FOR FURTHER INFORMATION CONTACT: Jacqueline Francis, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. G426, Silver Spring, MD 20993-0002, 301-796-6405; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7301, Silver Spring, MD 20993, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

The objectives of this final guidance are: (1) To increase the availability of safe and effective pediatric devices by providing a roadmap for leveraging relevant existing clinical data for use in demonstrating a reasonable assurance of safety and effectiveness in PMAs and de novo requests, as well as for use in supporting approvals of HDEs; (2) to explain the circumstances in which it may be appropriate to leverage existing clinical data to support pediatric device indications and labeling; (3) to outline the approach FDA uses to determine whether extrapolation is appropriate, and, to what extent the data can be leveraged; and (4) to describe statistical methodology that can be used to leverage the data in a way that increases precision for pediatric inferences. This approach will potentially streamline the process for establishing a pediatric intended use claim, and enhance and encourage pediatric device development programs.

This guidance does not change the regulatory threshold for valid scientific evidence. Instead, the document seeks to provide clarity and predictability for device sponsors and to ensure consistency within FDA regarding the specific criteria that should be considered when deciding whether leveraging existing clinical data to support pediatric claims is appropriate, and if so, to what extent. When considering extrapolation, sponsors are encouraged to engage FDA early in product development planning.

For the purposes of this document, "extrapolation" refers to the leveraging process whereby an indication for use of a device in a new pediatric patient population can be supported by existing clinical data from a studied patient population. That is, when existing data are relevant to a pediatric indication and determined to be valid scientific evidence, it may be scientifically appropriate to attempt to extrapolate such data to a pediatric use in support of

demonstrating a reasonable assurance of effectiveness or probable benefit and, occasionally, safety.

FDA published in the Federal Register of May 6, 2015 (80 FR 26061), the document entitled "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; Guidance for Industry and Food and Drug Administration Staff" and the comment period closed on August 4, 2015. FDA has considered all of the comments received in finalizing this guidance. The comments from the docket sought further clarification of the scope of the document, the extent of extrapolation that may be feasible across various pediatric subpopulations, and the concept of "borrowing strength" from existing adult data. Accordingly, this guidance document has been updated to include de novo requests within the scope and to provide additional explanation on the concepts of extrapolation of data across pediatric subpopulations and "borrowing strength."

This guidance should be used in conjunction with other device-specific guidances to help ensure that medical devices intended for use in pediatric population provide reasonable assurance of safety and effectiveness.

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 the extrapolation of data for pediatric uses of medical devices. 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.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm or http://www.regulations.gov. Persons unable to download an electronic copy of "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; Guidance for Industry and Food and Drug Administration Staff" may send an email request to CDRH-Guidance@fda.hhs.gov to receive an electronic copy of the document. Please use the document number 1827 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 parts 801 and 809 have been approved under OMB control number 0910-0485 (medical device labeling); the collections of information in 21 CFR part 812 have been approved under OMB control number 0910-0078 (investigational device exemptions); the collections of information in 21 CFR part 814 have been approved under OMB control number 0910-0231 (subparts A through E, premarket approval).

V. References

The following references are on display in the Division of Dockets Management (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m.,

Monday through Friday; they are also available electronically at http://www.regulations.gov. FDA has verified the Web site addresses, as of the date this document publishes in the Federal Register, but Web sites are subject to change over time.

1. FDA guidance entitled "Premarket Assessment of Pediatric Medical Devices," March 24, 2014, available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089740.htm.

Dated: June 16, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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