



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Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices; Draft Guidance for Industry and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the draft guidance entitled "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices." This draft guidance is being issued to explain the circumstances in which it may be appropriate to leverage existing clinical data to support pediatric device indications in premarket approval applications (PMAs) and humanitarian device exemptions (HDEs). The draft guidance also describes the approach that FDA would use to determine whether extrapolation is appropriate in medical devices, and the factors that would be considered within a statistical model for extrapolation. Extrapolation may be appropriate when the course of the disease or condition and the effects of the device are sufficiently similar in adults and pediatric patients and the adult data are of high quality for borrowing. This draft guidance is not final nor is it in effect at this time.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment of this draft guidance before it begins work on

the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: 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 Submit written requests for a single hard copy of the draft guidance document entitled "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices" to the Office of the Center Director, Guidance and Policy Development, Center for Devices and Radiological Health (CDRH), 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.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify comments with the docket number found in brackets in the heading of this document.

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

SUPPLEMENTARY INFORMATION:

I. Background

Section 520(m)(6)(E)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360j) defines pediatric device patients as persons aged 21 or younger at the time of their diagnosis or treatment (i.e., from birth through the 21st year of life, up to but not including the 22d birthday). Pediatric subpopulations are defined in section 520(m)(6)(E)(ii) (and adopted by reference in section 515A(c) of the FD&C Act (21 U.S.C. 360e)) to be neonates, infants, children, and adolescents.

In an attempt to promote pediatric medical device development, CDRH published a final guidance document in 2004 entitled "Premarket Assessment of Pediatric Medical Devices" (Ref. 1). This 2004 document indicates that data can be extrapolated to support effectiveness and, on a limited basis, safety for premarket approval applications (PMAs) when consistent with scientific principles. Congress was aware of this 2004 document when it passed the Food and Drug Administration Amendments Act of 2007 (FDAAA). Title III of FDAAA is the Pediatric Medical Device Safety and Improvement Act (PMDSIA). The FDAAA specifically authorized the use of adult data to demonstrate pediatric effectiveness. While safety exploration is not discussed in PMDSIA, FDA believes that there are specific cases where it will be appropriate to consider extrapolation of existing clinical safety data to support or enhance evidence for pediatric indications. FDA seeks comment on the appropriateness of extrapolating from adult clinical data to support medical device safety in pediatric patients.

FDA aims to increase the availability of safe and effective pediatric devices while ensuring that the approval of these devices is based on valid scientific evidence. Extrapolation of adult data for pediatric use may benefit pediatric patients by making it possible for devices to be approved for pediatric-specific indications and labeling, even when there is little or no existing pediatric data. Extrapolation facilitates the use of available relevant data by making optimal use

of what is already known about device effects in other populations to support indications in the pediatric population. If extrapolation is found to be appropriate, FDA believes that statistical modeling and methods can be used to increase the precision of pediatric inferences.

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 draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on extrapolation of data for pediatric uses. 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 statute and regulations.

III. Electronic Access

Persons interested in obtaining a copy of the draft 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 "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices" 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 draft 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. Reference

The following reference have been placed on display in the Division of Dockets Management (see ADDRESSES), and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at <http://www.regulations.gov>. (FDA has verified the Web site address, but we are not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.)

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

VI. 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>.

Dated: April 30, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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