

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.

**FOR FURTHER INFORMATION CONTACT:** Beverly Friedman, Office of Regulatory Policy, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6250, Silver Spring, MD 20993, 301-796-3600.

#### **SUPPLEMENTARY INFORMATION:**

##### **I. Background**

The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) and the Generic Animal Drug and Patent Term Restoration Act (Pub. L. 100-670) generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product’s regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical

investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Director of USPTO may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA’s determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA has approved for marketing the human drug product XOFIGO (radium 223 dichloride). XOFIGO is indicated for treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease. Subsequent to this approval, the USPTO received a patent term restoration application for XOFIGO (U.S. Patent No. 6,635,234) from Algeta ASA, and the USPTO requested FDA’s assistance in determining this patent’s eligibility for patent term restoration. In a letter dated March 19, 2015, FDA advised the USPTO that this human drug product had undergone a regulatory review period and that the approval of XOFIGO represented the first permitted commercial marketing or use of the product. Thereafter, the USPTO requested that FDA determine the product’s regulatory review period.

##### **II. Determination of Regulatory Review Period**

FDA has determined that the applicable regulatory review period for XOFIGO is 1,945 days. Of this time, 1,792 days occurred during the testing phase of the regulatory review period, while 153 days occurred during the approval phase. These periods of time were derived from the following dates:

1. *The date an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(i)) became effective:* January 19, 2008. Algeta ASA claims that February 21, 2008, is the date the investigational new drug application (IND) became effective. However, FDA records indicate that the IND effective date was January 19, 2008, which was 30 days after FDA receipt of the IND.

2. *The date the application was initially submitted with respect to the human drug product under section 505(b) of the FD&C Act:* December 14, 2012. FDA has verified the applicant’s claim that the new drug application

(NDA) for XOFIGO (NDA 203971) was initially submitted on December 14, 2012.

3. *The date the application was approved:* May 15, 2013. FDA has verified the applicant’s claim that NDA 203971 was approved on May 15, 2013.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the USPTO applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 1,032 days of patent term extension.

##### **III. Petitions**

Anyone with knowledge that any of the dates as published are incorrect may submit either electronic or written comments and ask for a redetermination (see **DATES**). Furthermore, any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period. To meet its burden, the petition must be timely (see **DATES**) and contain sufficient facts to merit an FDA investigation. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41–42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Submit petitions electronically to <http://www.regulations.gov> at Docket No. FDA-2013-S-0610. Submit written petitions (two copies are required) to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Dated: June 15, 2016.

**Leslie Kux,**

*Associate Commissioner for Policy.*

[FR Doc. 2016-14551 Filed 6-20-16; 8:45 am]

**BILLING CODE 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](mailto: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.*

[FR Doc. 2016–14640 Filed 6–20–16; 8:45 am]

**BILLING CODE 4164–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA–2012–N–0977]

### Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco To Protect Children and Adolescents

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of availability.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Fax written comments on the collection of information by July 21, 2016.

**ADDRESSES:** To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202–395–7285, or emailed to [oir\\_submission@omb.eop.gov](mailto:oir_submission@omb.eop.gov). All comments should be identified with the OMB control number 0910–0312. Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE–14526, Silver Spring, MD 20993–0002, [PRAStaff@fda.hhs.gov](mailto:PRAStaff@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:** In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.