DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–D–0332]

Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices; 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 guidance entitled ''Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices.'' National outbreaks of Toxic Anterior Segment Syndrome (TASS) have been associated with single-use intraocular ophthalmic devices (IODs) and single-use intraocular ophthalmic surgical instruments/accessories that are contaminated with endotoxins. These devices can become contaminated as part of the manufacturing, sterilization, or packaging processes. This guidance document provides recommendations for endotoxin limits as well as endotoxin testing to manufacturers and other entities involved in submitting premarket applications (PMAs) or premarket notification submissions (510(k)s) for different categories of IODs to mitigate future outbreaks of TASS.

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: 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 ''Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices'' 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.

Submit electronic comments on the 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: Michelle Tarver, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 2504, Silver Spring, MD 20993–0002, 301–796–5620.

SUPPLEMENTARY INFORMATION:

I. Background

TASS has been increasing in frequency over the past decade from approximately 1 in 1,000 to about 2 in 100. Some cases of TASS are severe enough to require secondary surgical interventions including glaucoma surgery and corneal transplantation. The use of inadequately or improperly processed ophthalmic surgical instruments is one of many factors suggested as a potential cause of TASS. In many TASS cases, bacterial endotoxin from medical devices is believed to cause the inflammation.

This guidance document was developed to notify manufacturers and other entities involved in submitting PMAs or 510(k)s for different categories of IODs of the recommended endotoxin limit for the release of IODs and single-use intraocular ophthalmic surgical instruments/accessories in an effort to mitigate future TASS outbreaks.

The draft of this guidance was made available in the **Federal Register** on April 17, 2014 (79 FR 21777), and the comment period closed July 16, 2014. Only two sets of comments were received. The comments were minor, and FDA made revisions to the document in response to the comments where appropriate. FDA also removed posterior segment devices from the scope of the guidance document. FDA may address endotoxin testing recommendations for this device type in future guidance documents.

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 endotoxin testing and limits for single-use IODs. 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 ''Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic 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 1836 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 814 have been approved under OMB control number 0910–0231.

V. 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: August 12, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–20229 Filed 8–14–15; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2015–D–2843]

Qualification of Biomarker—Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Qualification of Biomarker—Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease.'' This draft guidance provides a qualified context of use (COU) for total kidney volume (TKV), measured at baseline, to be used as a prognostic enrichment biomarker to select patients with autosomal dominant polycystic kidney disease (ADPKD) at high risk for a ''progressive decline'' in renal function, defined as a confirmed 30 percent decline in the patient's estimated glomerular filtration rate (eGFR), for inclusion in interventional clinical trials. This draft guidance also describes the experimental conditions and constraints for which this biomarker is qualified through the Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program. This biomarker can be used by drug developers for the qualified COU in submissions of investigational new drug applications, new drug applications, and biologics license applications without the relevant CDER review group reconsidering and reconfirming the suitability of the biomarker.

In the **Federal Register** of January 7, 2014, FDA announced the availability of a final guidance for industry entitled ''Qualification Process for Drug Development Tools'' that described the process that would be used to qualify Drug Development Tools (DDTs) and to make new DDT qualification recommendations available on FDA's Web site. The qualification recommendations in this draft guidance were developed using the process described in that guidance.

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 on 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 October 16, 2015.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, 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 draft guidance document.

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.

FOR FURTHER INFORMATION CONTACT: Marianne Noone, Center for Drug Evaluation and Research (Office of Translational Sciences, Immediate Office), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 21, Rm. 4528, Silver Spring, MD 20993–0002, 301–796–2600.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Qualification of Biomarker—Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease.'' This draft guidance provides qualification recommendations for the use of TKV, measured at baseline, as a prognostic enrichment biomarker to select patients with ADPKD at high risk for a ''progressive decline'' in renal function, defined as a confirmed 30 percent decline in the patient's eGFR, for inclusion in interventional clinical trials. This biomarker may be used in combination with the patient's age and baseline eGFR as an enrichment factor in these interventional clinical trials. Specifically, this draft guidance provides the COU for which this biomarker is qualified through the CDER Biomarker Qualification Program. Qualification of this biomarker for this specific COU represents the conclusion that analytically valid measurements of the biomarker can be relied on to have a specific use and interpretable meaning. This biomarker can be used by drug developers for the qualified COU in submission of investigational new drug applications, new drug applications, and biologics license applications without the relevant CDER review group reconsidering and reconfirming the suitability of the biomarker. ''Qualification'' means that the use of this biomarker in the specific COU is not limited to a single, specific drug development program. Making the qualification recommendations widely known and available for use by drug developers will contribute to drug innovation, thus supporting public health.

In the **Federal Register** of January 7, 2014 (79 FR 831), FDA announced the availability of a final guidance for industry entitled ''Qualification Process for Drug Development Tools'' that described the process that would be used to qualify DDTs and to make new DDT qualification recommendations available on FDA's Web site at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*. The current draft guidance is an attachment to that final guidance.

CDER has initiated this formal qualification process to work with developers of these biomarker DDTs to guide them as they refine and evaluate DDTs for use in the regulatory context. Once qualified, biomarker DDTs will be publicly available for use in any drug development program for the qualified COU. As described in the January 2014 guidance, biomarker DDTs should be developed and reviewed using this process. For more information on FDA's DDTs Qualification Programs, refer to the following Web page: *http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm*.

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 the use of TKV, measured at baseline, as a prognostic enrichment biomarker to select patients with ADPKD at high risk for a progressive decline in renal function, defined as a confirmed 30 percent decline in eGFR, for inclusion in interventional clinical trials. This biomarker may be used in combination with patient age and baseline eGFR, as an enrichment factor in these interventional clinical trials. It does not establish any rights for any person and not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

This guidance contains an information collection that is 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 information collection has been approved under the OMB control numbers 0910–0001 and 0910–0014. The information requested in this guidance is currently submitted to FDA to support medical product effectiveness (see 21 CFR 312.30, 21 CFR 314.50(d)(5), and 21 CFR 314.126(b)(6)).

III. 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*.

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: August 12, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2015–D–2818]

Rare Diseases: Common Issues in Drug Development; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Rare Diseases: Common Issues in Drug Development.'' The purpose of this draft guidance is to advance and facilitate the development of drugs and biologics to treat rare diseases. Drug development for rare diseases has many challenges related to the nature of these diseases. This draft guidance is intended to assist sponsors of drug and biological products for treating rare diseases in conducting more efficient and successful development programs.

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 on 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 October 16, 2015.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002; or 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 requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

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.

FOR FURTHER INFORMATION CONTACT: Jonathan Goldsmith, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6480, Silver Spring, MD 20903–0002, 240–402–9959; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Rare Diseases: Common Issues in Drug Development.'' This guidance is intended to assist sponsors of drug and biological products for treating rare diseases in conducting more efficient and successful development programs through a discussion of selected issues commonly encountered in rare disease drug development. Although these issues are encountered in other drug development programs, they are frequently more difficult to address in the context of a rare disease than a common disease for which there is greater and more widespread medical experience. These issues are also more acute with increasing rarity of the disorder. A rare disease is defined by the Orphan Drug Act as a disorder or condition that affects less than 200,000 persons in the United States; however, most rare diseases affect far fewer persons.

Most rare disorders are serious conditions with no approved treatments, and rare disease patients have considerable unmet medical needs. Collectively, rare diseases are highly diverse. FDA is committed to helping sponsors of drugs for rare diseases create successful programs that address the particular challenges posed by each disease.

This guidance addresses the following important components of drug development:

- Adequate description and understanding of the disease's natural history
- Adequate understanding of the pathophysiology of the disease and the drug's proposed mechanism of action
- Nonclinical pharmacotoxicology considerations to support the proposed clinical investigation(s)
- Standard of evidence to establish safety and effectiveness
- Drug manufacturing considerations during drug development

Early consideration of these issues allows sponsors to efficiently and adequately address them during the course of drug development, from drug discovery to confirmatory efficacy and safety studies, and to have productive meetings with FDA.

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 current thinking of FDA on common issues in drug development for rare diseases. 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.

II. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that 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 312 have been approved under OMB control number 0910–0014, and the collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001.

III. 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