4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-1630]

Draft Guidance for Industry on Qualification for the Use of Galactomannan in Serum and Bronchoalveolar Lavage Fluid; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Draft Guidance on Qualification of Biomarker--Galactomannan in Studies of Treatments of Invasive Aspergillosis." This draft guidance provides recommendations on the use of Galactomannan detection in serum and/or bronchoalveolar lavage (BAL) fluid as the sole microbiological criterion to classify patients as having probable invasive Aspergillosis (IA) for enrollment in clinical trials. This draft guidance provides the context of use for which this biomarker drug development tool (DDT) is qualified through the Center for Drug Evaluation and Research (CDER) DDT Qualification Program. In the Federal Register of January 7, 2014, FDA announced the availability of a guidance for industry entitled "Qualification Process for Drug Development Tools," which described the process that would be used to qualify 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 The qualification recommendations in this draft guidance were developed using the process described in that guidance.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on any guidance at any time (see 21 CFR 10.115(g) (5)), to ensure that the Agency considers your comment on this draft guidance before it begins work

on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, 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 See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov.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 "Draft Guidance on Qualification of Biomarker--Galactomannan in studies of treatments of invasive Aspergillosis." This draft guidance provides recommendations on the use of Galactomannan detection in serum and/or BAL fluid as the sole microbiological criterion to classify patients as having probable IA for enrollment in clinical trials. The draft guidance provides the context of

use for which this biomarker DDT is qualified through the CDER DDT Qualification Program. Qualification of this biomarker for this specific context of use represents the conclusion that analytically valid measurements of the biomarker can be relied on to have a specific use and interpretable meaning. Further, the biomarker can be used by drug developers for the qualified context in submission of investigational new drug applications, new drug applications, and biologics licensing applications without the relevant CDER review group reconsidering and reconfirming the suitability of the DDT. Qualification means that the use of this biomarker in the specific context of use 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. The draft guidance is an attachment to the guidance for industry entitled "Qualification Process for Drug Development Tools."

In March 2006, FDA issued the "Critical Path Opportunities Report and List," in which FDA described six key areas along the critical path to improved therapies and listed specific opportunities for advancement within these topic areas. The report noted that a new product development toolkit containing new scientific and technical methods was needed to improve the efficiency of drug development.

In 2008, the Mycoses Study Group proposed using Galactomannan in serum and BAL fluid as an indicator of IA in lieu of culture in patients with hematologic malignancies and recipients of allogeneic hematopoietic stem cell transplants and who also have radiologic evidence suggestive of invasive fungal infection (Ref. 1). A qualification review team of experts evaluated the data supporting the proposed context of use and rendered a qualification recommendation. The qualification recommendation in the draft guidance includes the following information:

- A use statement;
- conditions for qualified use of the assay;
- patient populations;
- limitations for use of the Galactomannan assay;
- considerations for sample acquisition and documentation;
- analysis of study results; and
- performance characteristics of the assay.

Innovative and improved DDTs can help streamline the drug development process, improve the chances for clinical trial success, and yield more information about a treatment and/or disease. DDTs include, but are not limited to, biomarkers, clinical outcome assessments and animal models. Refer to DDTs Qualification Programs at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm for additional information.

As stated previously in the Federal Register of January 7, 2014 (79 FR 831), FDA announced the availability of the guidance for industry entitled "Qualification Process for Drug Development Tools," which 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. CDER has developed this formal process to work with developers of these biomarker DDTs to guide the developers as they refine the tools and rigorously evaluate them for use in the regulatory context. Once qualified, DDTs will be publicly available for use in any drug development program for the qualified context of use. As described in the January 2014 guidance, biomarker DDTs should be developed and reviewed using this process.

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 Galactomannan in serum and BAL fluid. 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 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 the 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.

V. Reference

The following reference has 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 is available electronically at http://www.regulations.gov.

1. De Pauw, B., T. J. Walsh, J. P. Donnelly, et al., "Revised Definitions of Invasive Fungal Disease from European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group," Clinical Infectious Diseases (2008) 46: 1813-1821.

Dated: October 21, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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