

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-1020]

Draft Guidance for Industry on Bioanalytical Method Validation; Availability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SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Bioanalytical Method Validation." The draft guidance is intended to provide recommendations regarding analytical method development and validation for the measurement of drugs and/or metabolites, therapeutic biologics, and biomarkers for sponsors of investigational new drug applications (INDs), new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biologics license applications (BLAs) for therapeutic biologics regulated by the Center for Drug Evaluation and Research. This draft guidance may apply to some studies related to the veterinary drug approval process (Investigational New Animal Drugs (INADs), New Animal Drug Applications (NADAs), and Abbreviated New Animal Drug Applications (ANADAs)) regulated by the Center for Veterinary Medicine. This guidance was originally issued in 2001. FDA is revising the guidance to reflect advancements in the science and technology of bioanalytical method validation.

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comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by December 12, 2013.

ADDRESSES: Submit written requests for single copies of the revised draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2201,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, or Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. See

the **SUPPLEMENTARY INFORMATION** section for electronic access to the 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Submit electronic comments on the draft guidance to 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:

Brian Booth, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2186, Silver Spring, MD 20993-0002, 301-796-1508; or John Kadavil, Center for Veterinary Medicine (HFV-151), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240-276-9589.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Bioanalytical Method Validation." The measurement of drug and/or metabolite, therapeutic biological product, or biomarker concentrations in in vivo studies provides critical support for many types of drug and therapeutic biologic development studies. The accuracy and the reliability of these data are of critical importance to the interpretation of the study outcomes. The draft guidance reflects the Agency's view that the reliability of these data is, in part, assured by adequate method development and validation prior to study conduct. The method validation should provide assurance that the samples are unaffected by handling conditions, and that the measurements are accurate and can be repeated without significant change.

The draft guidance provides recommendations for sponsors of INDs, NDAs, ANDAs, and BLAs regarding measurement of drug, therapeutic biological product, and biomarker concentrations in nonclinical and clinical study samples. The guidance provides recommendations for sponsors of INADs, NADAs, and ANADAs regarding measurement of drug concentrations in some bioavailability, bioequivalence, and pharmacokinetic studies. The guidance lists the recommendations for sample handling and stability; method acceptance criteria for accuracy and precision; and reproducibility. The guidance also addresses the fit-for-purpose concept, biomarkers, and novel technologies.

On May 23, 2001 (66 FR 28526), FDA issued the first version of this guidance. Since then, substantial scientific and technical advancements have taken

place related to the validation of bioanalytical methods. FDA revised the guidance to reflect these advancements and is issuing the revised guidance in draft to solicit public input. The revised draft guidance contains a number of new sections, including sections on endogenous compounds, incurred sample reanalysis, biomarker assays, use of diagnostic kits and new technologies, system suitability, and examples of report formats for tabular data listings. In addition, FDA has updated sections where needed, such as the sections on chromatography and ligand-binding assays. The changes and additions are intended to reflect the many advances in the field during the last decade.

This revised draft guidance is 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 Bioanalytical Method Validation. 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 requirement of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This revised draft 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 58 have been approved under OMB control number 0910-0119; the collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001; the collections of information in 21 CFR part 514 have been approved under OMB control number 0910-0032; the collections of information in 21 CFR part 511 have been approved under OMB control number 0910-0117; and the collections of information in section 360b(n)(1) (21 U.S.C 512(n)(1)) of the Federal Food, Drug and Cosmetic Act have been approved in OMB control number 0910-0669.

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> or <http://www.regulations.gov>.

Dated: September 7, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0322]

Draft Guidance for Industry on Arsenic in Apple Juice: Action Level; Supporting Document for Action Level for Arsenic in Apple Juice; A Quantitative Assessment of Inorganic Arsenic in Apple Juice; Extension of Comment Period

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; extension of comment period.

SUMMARY: The Food and Drug Administration (FDA or we) is extending the comment period for the draft guidance for industry entitled “Arsenic in Apple Juice: Action Level” that appeared in the **Federal Register** of July 15, 2013 (78 FR 42086). The draft guidance identifies for the industry an action level for inorganic arsenic in apple juice that FDA considers protective of human health and achievable with the use of good manufacturing practices. It also describes FDA’s intended sampling and enforcement approach. In the notice, we requested comments on the draft guidance. We are taking this action in response to a request for an extension to allow interested persons additional time to submit comments.

DATES: FDA is extending the comment period on the draft guidance. Submit either electronic or written comments by November 12, 2013.

ADDRESSES: Submit electronic comments on the draft guidance to <http://www.regulations.gov>. Submit written comments on the draft guidance

to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit written requests for single copies of the draft guidance to the Office of Food Safety, Center for Food Safety and Applied Nutrition (HFS-317), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740. Send two self-addressed adhesive labels to assist that office in processing your request. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance.

FOR FURTHER INFORMATION CONTACT:

Lauren Posnick Robin, Center for Food Safety and Applied Nutrition (HFS-317), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, 240-402-1639.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of July 15, 2013 (78 FR 42086), we published a notice announcing the availability of three documents, a draft guidance for industry entitled “Arsenic in Apple Juice: Action Level,” a draft supporting document entitled “Supporting Document for Action Level for Arsenic in Apple Juice,” and a risk assessment document entitled “A Quantitative Assessment of Inorganic Arsenic in Apple Juice.” The draft guidance identifies an action level for inorganic arsenic in apple juice of 10 micrograms/kilogram (µg/kg) or 10 parts per billion (ppb), and identifies FDA’s intended sampling and enforcement approach. The draft supporting document reviews data on arsenic levels, health effects, and achievability, and explains FDA’s rationale for identifying an action level for inorganic arsenic in apple juice of 10 µg/kg. The risk assessment document provides estimates of arsenic exposure and risk to humans at different hypothetical limits for inorganic arsenic in apple juice. The notice invited comments on the draft guidance by September 13, 2013.

As of August 28, 2013, we have received two requests for an extension of the comment period. The requests, from the Arsenic Science Task Force and the Juice Products Association, explained that they needed more time to complete their analyses of the supporting documents.

We have considered the request and are extending the comment period for the notice for 60 days, until November 12, 2013. We believe that a 60-day extension allows adequate time for interested persons to submit comments

without significantly delaying further FDA action on this guidance.

II. Request for 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: September 10, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-0001]

Challenging Regulatory and Reimbursement Paradigms for Medical Devices in the Treatment of Metabolic Diseases: How to Estimate and Reward True Patient-Centric Value in Innovation; Public Workshop

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop.

The Food and Drug Administration (FDA) is announcing a public workshop entitled “Changing Regulatory and Reimbursement Paradigms for Medical Devices in the Treatment of Metabolic Diseases: How to Estimate and Reward True Patient-Centric Value in Innovation.” FDA is cosponsoring the workshop with the American Gastroenterological Association (AGA). The purpose of the workshop is to facilitate discussion between FDA, AGA, and other interested parties of the development of medical devices for the treatment of morbid obesity and other metabolic diseases and evolving approaches for the regulation and reimbursement of minimally invasive procedures.

Dates and Times: The public workshop will be held on October 17, 2013, from 8:30 a.m. to 5 p.m. and October 18, 2013, from 8:30 a.m. to 12:15 p.m.

Location: The public workshop will be held at the Grand Hyatt Washington,