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4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-N-5776]

Equivalence of Complex Products; Public Workshop; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the following public workshop entitled “Demonstrating Equivalence of Generic Complex Drug Substances and Formulations: Advances in Characterization and In Vitro Testing.” The purpose of the workshop is to share FDA’s current experiences on the evaluation and characterization of critical quality attributes for complex drug substances (e.g. polymeric and naturally derived substances and peptides) and formulations (e.g. liposomes, emulsions, suspensions, and polymeric inserts); discuss current and future innovative approaches for the development and regulatory review of equivalent complex drug products; obtain input from various stakeholders on how to conduct and assess critical quality attribute measurements to demonstrate equivalence of complex drug products; and request comments on these topics.

DATES: The public workshop will be held on October 6, 2017, from 8:30 a.m. to 4:30 p.m.

Submit either electronic or written comments on this public workshop by November 10, 2017.

See the SUPPLEMENTARY INFORMATION section for registration date and information.

ADDRESSES: The public workshop will be held at FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (Rm. 1503 B+C), Silver Spring,

MD 20993-0002. Entrance for the public workshop participants (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information, please refer to

<https://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before November 10, 2017. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of November 10, 2017. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://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 <https://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): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, 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-2017-N-5776 for “Demonstrating Equivalence of Generic Complex Drug Substances and Formulations: Advances in Characterization and In Vitro Testing.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff 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 <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. 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: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://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 Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Xiaohui Jiang, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 4716, Silver Spring, MD 20993, 240-402-4468, Xiaohui.Jiang@fda.hhs.gov; or Darby Kozak, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 4710, Silver Spring, MD 20993, 240-402-2647, Darby.Kozak@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

In July 2012, Congress passed the Generic Drug User Fee Amendments (GDUFA) (Title III of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144)). GDUFA is designed to enhance public access to safe, high-quality generic drugs and reduce costs to industry. To support this goal, FDA agreed in the GDUFA commitment letter to work with industry and interested stakeholders on identifying regulatory science research priorities specific to generic drugs for each fiscal year covered by GDUFA. The commitment letter outlines FDA's performance goals and procedures under the GDUFA program for the years 2012 to 2017. The commitment letter can be found at

<https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf>.

In the Regulatory Science section of the GDUFA Commitment Letter, FDA outlined its plans to advance regulatory science, including research to support the development of guidance and policy that clarifies the ANDA pathway for complex drug products. This regulatory science research includes but is not limited to: (1) Assessing innovative analytical methods and procedures for characterizing the active ingredient sameness and pharmaceutical equivalence of complex drug substances, such as peptides and naturally derived substances, and (2) developing and evaluating new techniques to measure the critical quality attributes of complex formulations, such as liposomes, emulsions, suspensions, and polymeric inserts, with the goal of providing robust in vitro alternatives to in vivo bioequivalence studies, and (3) developing and evaluating critical quality attributes for complex drug-device combination products. To facilitate communication of recent advances in this regulatory science, including those supported by GDUFA funds, FDA plans to hold a public workshop on new analytical methods and assessment criteria for demonstrating the equivalence of complex drug substances and formulations.

II. Topics for Discussion at the Public Workshop

The purposes of the workshop are to:

1. Share FDA's current experiences on the evaluation and characterization of critical quality attributes for complex drug substances (e.g. polymeric and naturally derived substances and peptides) and formulations (e.g. liposomes, emulsions, suspensions, and polymeric inserts);
2. Discuss current and future innovative approaches for the development and regulatory review of equivalent complex drug products;
3. Obtain input from various stakeholders on how to conduct and assess critical quality attribute measurements to demonstrate equivalence of complex drug products; and
4. Request comments on these topics.

The scope of the workshop covers the current status, from an academic, industry, and regulatory perspective, of methods for assessing the pharmaceutical equivalence of complex drug substances and the bioequivalence of complex generic drug product formulations.

Complex drug substances and formulations present unique development and regulatory challenges for generic drugs as establishing equivalence may not be straightforward by conventional practices. New and innovative analytical and statistical approaches may overcome these hurdles and thereby reduce product development time and cost, and inform regulatory decisions. For example, new high resolution analytical methods and advanced statistical models can provide better understanding of the complex structure, and greater confidence of structural sameness, needed for demonstrating the pharmaceutical equivalence of a generic peptide, carbohydrate, or other naturally-sourced complex drug substance. In the same fashion, new and innovative *in vitro* characterization methods can provide an accurate measure of the critical

quality attributes of generic liposomal, emulsion, suspension, or polymeric matrix drug products. These in vitro tests can often be used to support a demonstration of bioequivalence, in lieu of in vivo studies, depending, among other factors, on the sensitivity, robustness and/or correlation of these in vitro tests to the product performance. The focus of this public workshop is on the evaluation of new analytical and statistical methods for demonstrating equivalence of complex products, including discussing the areas in which these methods can contribute significantly, how and when the methods should be conducted and evaluated, and inherent scientific challenges.

Public input will improve FDA's current understanding of present and future methods available for evaluating complex product equivalence. The knowledge gained from, and consensus reached, through this workshop will be summarized and disseminated to the scientific community by publication(s).

FDA seeks input from the public on when, where, and how to utilize new methods for development of equivalent complex drug products and in the regulatory review of pharmaceutical equivalence and bioequivalence. Specific topics to be addressed include:

1. Identifying the areas in which new in vitro analytical and statistical methods can contribute to the development of equivalent complex products and regulatory evaluation of pharmaceutical equivalence and bioequivalence;
2. Discussing how in vitro testing for demonstrating complex product equivalence should be conducted and evaluated; and
3. Addressing the scientific challenges in assessing critical quality attributes of complex products and in developing new analytical methods for demonstrating complex product equivalence.

III. Participating in the Public Workshop

Registration: Persons interested in attending this public workshop must register online at https://survey.co1.qualtrics.com/jfe/form/SV_6X23XS8WXHtfWAJ. Please provide complete contact information for each attendee, including name, title, affiliation, address, email, and telephone.

Registration is free and based on space availability, with priority given to early registrants. Persons interested in attending this public workshop must register by October 2, 2017, midnight, Eastern Time. Early registration is recommended because seating is limited; therefore, FDA may limit the number of participants from each organization.

If you need special accommodations due to a disability, please contact Xiaohui Jiang (see FOR FURTHER INFORMATION CONTACT) no later than October 2, 2017.

Streaming Webcast of the public workshop: This public workshop will also be webcast. A live webcast of this workshop will be viewable at <https://collaboration.fda.gov/complexgenericdrugs/> on the day of the workshop.

If you have never attended a Connect Pro event before, test your connection at https://collaboration.fda.gov/common/help/en/support/meeting_test.htm. To get a quick overview of the Connect Pro program, visit https://www.adobe.com/go/connectpro_overview. FDA has verified the website addresses in this document, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

Transcripts: Please be advised that as soon as a transcript of the public workshop is available, it will be accessible at <https://www.regulations.gov>. It may be viewed at the Dockets Management Staff (see ADDRESSES). A link to the transcript will also be available on the Internet at <https://www.fda.gov/drugs/newsevents/ucm552461.htm>.

Dated: September 26, 2017.

Anna K. Abram,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.

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