



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 1271

[Docket No. FDA-2015-D-3719]

Draft Guidances Relating to the Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products; Rescheduling of Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of rescheduling of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing a 2-day public hearing to obtain input on four draft guidance documents relating to the regulation of human cells, tissues, and cellular and tissue-based products (HCT/Ps). FDA had announced a 1-day public hearing for April 13, 2016, to obtain input on the guidances, but on February 29, 2016, announced that due to considerable interest in the public hearing and to give stakeholders additional time to provide comments to the Agency, the hearing was postponed. FDA also stated its intent to extend the comment period for the four draft guidance documents and to schedule a scientific workshop to identify and discuss the scientific considerations and challenges to help inform the development of HCT/Ps subject to premarket approval, including stem cell-based products. FDA will consider information it obtains from the public hearing in the finalization of the four draft guidance documents.

DATES: The public hearing will be held on September 12 and 13, 2016, from 9 a.m. to 5 p.m.

The hearing on September 13 may be extended or end early depending on the number of speakers scheduled. Persons (including FDA employees) seeking to view the hearing via a live

Webcast are not required to register. Persons (including FDA employees) seeking to attend in person or to attend and speak at the public hearing must register by June 1, 2016. FDA will notify registered speakers of their scheduled times, and make available an agenda at <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm462125.htm> on or before July 1, 2016. Once FDA notifies registered speakers of their scheduled times, speakers should submit an electronic copy of their presentation to [CBERPublicEvents@fda.hhs.gov](mailto:CBERPublicEvents@fda.hhs.gov) by August 1, 2016. Section IV of this document provides attendance and registration information. Electronic or written comments will be accepted after the public hearing until September 27, 2016.

ADDRESSES: The public hearing will be held at the National Institutes of Health (NIH), 9000 Rockville Pike, Bldg. 10, Masur Auditorium, Bethesda, MD 20892. Entrance for the public hearing attendees and speakers (non-FDA employees) is through Bldg. 66 (Gateway Center), where routine security check procedures will be performed. For parking and security information, please refer to <http://www.nih.gov/about-nih/visitor-information>.

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-3719 for “Draft Guidances Relating to the Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products; Rescheduling of Public Hearing; Request for Comments.” 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.

A link to the live Webcast of this public hearing will be available at <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm462125.htm> on the day of the public hearing. Persons seeking to view the hearing via the live

Webcast are not required to register. A video record of the public hearing will be available at <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm462125.htm>. A video record of the public hearing will be available at the same Web address for 1 year.

FOR FURTHER INFORMATION CONTACT: Lori Jo Churchyard, 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, [lori.olsenchurchyard@fda.hhs.gov](mailto:lori.olsenchurchyard@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

HCT/Ps are defined in § 1271.3(d) (21 CFR 1271.3(d)) as articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. FDA has implemented a risk-based approach to the regulation of HCT/Ps. Under the authority of section 361 of the Public Health Service (PHS) Act (42 U.S.C. 264), FDA established regulations for all HCT/Ps to prevent the introduction, transmission, and spread of communicable diseases. These regulations can be found in part 1271. HCT/Ps are regulated solely under section 361 of the PHS Act and part 1271, if they meet all of the following criteria (§ 1271.10(a)):

- The HCT/P is minimally manipulated;
- The HCT/P is intended for homologous use, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
- The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving or storage

agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and

- Either
  - The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function, or
  - The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and is for the following uses:
    - Autologous,
    - Allogeneic, in a first-degree or second-degree blood relative, or
    - Reproductive.

If an HCT/P does not meet all of the criteria set forth under § 1271.10(a), the HCT/P will be regulated as a drug, device, and/or biological product under the Federal Food, Drug, and Cosmetic Act, and/or section 351 of the PHS Act (42 U.S.C. 262).

In certain circumstances as provided in § 1271.15, an establishment may not be required to comply with some or all of the requirements in part 1271. For example, an establishment is exempted from the requirements in part 1271 if it “removes HCT/P’s from an individual and implants such HCT/P’s into the same individual during the same surgical procedure” (§ 1271.15(b)).

## II. Draft Guidances

As part of its commitment to public outreach and to explain the Agency’s current thinking on the regulatory framework for HCT/Ps, FDA has issued the following four draft guidances<sup>1</sup>:

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<sup>1</sup><http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/default.htm>.

- Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception; Draft Guidance for Industry (Same Surgical Procedure Exception Draft Guidance);
- Minimal Manipulation of Human Cells, Tissues, and Cellular and Tissue-Based Products; Draft Guidance for Industry and Food and Drug Administration Staff (Minimal Manipulation Draft Guidance);
- Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) from Adipose Tissue: Regulatory Considerations; Draft Guidance for Industry (Adipose Tissue Draft Guidance); and
- Homologous Use of Human Cells, Tissues, and Cellular and Tissue-Based Products; Draft Guidance for Industry and FDA Staff (Homologous Use Draft Guidance).

The Same Surgical Procedure Exception Draft Guidance was announced in the Federal Register of October 23, 2014 (79 FR 63348), and provides answers to common questions regarding the scope of the exception. Comments were requested by December 22, 2014.

The Minimal Manipulation Draft Guidance was announced in the Federal Register of December 23, 2014 (79 FR 77012), and provides recommendations for meeting the § 1271.10(a)(1) criterion of minimal manipulation. Comments were requested by February 23, 2015.

The Adipose Tissue Draft Guidance was announced in the Federal Register of December 24, 2014 (79 FR 77414), and provides those who manufacture and use adipose tissue with recommendations for complying with the regulatory framework for HCT/Ps. Comments were requested by February 23, 2015.

The Homologous Use Draft Guidance was announced in the Federal Register of October 30, 2015 (80 FR 66850), and provides recommendations for meeting the § 1271.10(a)(2) homologous use criterion. Comments were requested by April 29, 2016. Also in the Federal Register of October 30, 2015, FDA reopened the comment periods to FDA's public docket on the three draft guidance documents: Same Surgical Procedure Exception Draft Guidance (Docket No. FDA-2014-D-1584; 80 FR 66847); Minimal Manipulation Draft Guidance (Docket No. FDA-2014-D-1696; 80 FR 66844), and the Adipose Tissue Draft Guidance (Docket No. FDA-2014-D-1856; 80 FR 66849). Comments were requested by April 29, 2016.

In the Federal Register of October 30, 2015 (80 FR 66845), FDA announced a public hearing in a notice entitled "Draft Guidances Relating to the Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products; Public Hearing; Request for Comments," which was to be held on April 13, 2016. Comments were requested by April 29, 2016.

On February 29, 2016, FDA postponed the public hearing to give stakeholders additional time to provide comments to the Agency. FDA also stated its intent to extend the comment period for the four draft guidance documents and to schedule a scientific workshop to identify and discuss the scientific considerations and challenges to help inform the development of HCT/Ps subject to premarket approval, including stem cell-based products.

Elsewhere in this issue of the Federal Register, FDA is announcing the extension of the comment period for the four draft guidance documents. In a separate document, FDA is also announcing a public scientific workshop to identify and discuss scientific considerations and challenges to help inform the development of HCT/Ps subject to premarket approval, including stem cell-based products. FDA will provide a summary of the scientific workshop at the public hearing.

### III. Purpose and Scope of the Public Hearing

The purpose of this public hearing is to obtain comments on the four draft guidances. FDA is seeking feedback on the four draft guidances, both general and specific, from a broad group of stakeholders, including tissue establishments, biological and device product manufacturers, health care professionals, clinicians, biomedical researchers, and the public. For example, FDA would like comments on the scope of the four draft guidances, including the particular topics covered, the particular questions posed, whether there are additional issues for which guidance would be helpful, and whether FDA's recommendations for each topic are sufficiently clear and consistent within and across documents to provide meaningful guidance to stakeholders. In addition, FDA welcomes comments that will enhance the usefulness and clarity of these documents.

FDA recommends that comments exclude discussion of products that do not meet the definition of an HCT/P, such as platelet-rich plasma and other blood products. FDA also recommends that stakeholders coordinate comments when possible, in order to allow for presentation of a wide range of perspectives within the allotted time of the hearing.

### IV. Attendance and Registration

The NIH campus is a Federal facility with security procedures and limited seating. Attendance is free.

Persons (including FDA employees) seeking to view the hearing via a live Webcast are not required to register.

Persons (including FDA employees) who wish to attend in person, but not speak at the public hearing, must register at <https://www.eventbrite.com/e/part-15-hearing-on-draft-guidances-relating-to-the-regulation-of-hctps-registration-22921962206> on or before June 1,

2016, and provide complete contact information, including name, title, affiliation, email, and phone number. Those without email access may register by contacting Sherri Revell or Loni Warren Henderson at 240-402-8010. There will be no onsite registration for this hearing.

Persons (including FDA employees) who wish to attend and speak at the public hearing must register at <https://www.eventbrite.com/e/part-15-hearing-on-draft-guidances-relating-to-the-regulation-of-hctps-registration-22921962206> on or before June 1, 2016. Persons who wish to attend and speak at the public hearing will be required to provide complete contact information, including name, title, affiliation, email, and phone number. To help FDA organize the presentations, persons who wish to attend and speak must also indicate whether they are speaking on their own behalf or on behalf of an organization. If speaking on behalf of an organization, the name of the organization must be provided. Persons who wish to attend and speak must also indicate if they will be speaking on the draft guidance documents. Individuals and organizations with common interests should consolidate or coordinate their presentations and request time for a joint presentation. There will be no open public session at the public hearing.

FDA will do its best to accommodate requests to speak at the public hearing and will determine the amount of time allotted for each oral presentation, and the approximate time that each oral presentation will be scheduled to begin. Multiple speakers from the same organization will be given one presentation slot for that organization. If the number of persons or organizations requesting to speak is greater than can be reasonably accommodated, FDA will close registration for speakers. FDA will notify registered speakers of their scheduled times, and make available an agenda at <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm>

462125.htm on or before July 1, 2016. Once FDA notifies registered speakers of their scheduled times, presenters should submit an electronic copy of their presentation to [CBERPublicEvents@fda.hhs.gov](mailto:CBERPublicEvents@fda.hhs.gov) by August 1, 2016.

If you need special accommodations because of a disability, please contact Sherri Revell or Loni Warren Henderson at 240-402-8010 at least 7 days before the hearing.

A link to the live Webcast of this public hearing will be available at <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm462125.htm> on the day of the public hearing. A video record of the public hearing will be available at <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm462125.htm>. A video record of the public hearing will be available at the same Web address for 1 year.

#### V. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by FDA senior management from the Office of the Commissioner and the Center for Biologics Evaluation and Research.

Under § 15.30(f), the hearing is informal and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation. Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (21 CFR part 10, subpart C). Under § 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to

videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b) (see section VI of this document). To the extent that the conditions for the hearing, as described in this notice, conflict with any provisions set out in part 15, this notice acts as a waiver of those provisions as specified in § 15.30(h).

## VI. Transcripts

Please be advised that as soon as a transcript is available, it will be accessible at [www.regulations.gov](http://www.regulations.gov) and <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm462125.htm>. It may be viewed at the Division of Dockets Management (see ADDRESSES). A transcript will also be available in either hardcopy or on CD-ROM, after submission of a Freedom of Information request. The Freedom of Information office address is available on the Agency's Web site at <http://www.fda.gov>.

Dated: April 19, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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