transmissible disease and contains recommendations for documenting the source of animal tissue, conducting viral inactivation validation studies, as well as recommendations about the role of careful animal husbandry in ensuring safe tissue sources. The revised guidance also includes recommendations related to viral pathogens and all transmissible spongiform encephalopathies.

The information in this guidance is applicable to all medical devices that contain or are exposed to animal-derived materials (*e.g.,* bovine, ovine, porcine, avian materials) with the exception of in vitro diagnostic devices and materials generally recognized to be safe based on their method of manufacture. This guidance provides: (1) Information that FDA believes is important to document the safe and consistent manufacture of medical devices containing animal tissue; (2) information that should be included in a premarket submission for products within the scope of this guidance; (3) recommendations regarding how specific aspects of the Quality System (QS) Regulation should be applied to control and document the safe and consistent manufacture of medical devices containing animal tissue; and (4) additional information on specific approaches for determining the ability of manufacturing methods to eliminate viral contamination in the final product. Consideration of these items should aid in reducing the risk of infectious disease transmission by medical devices. FDA considered comments received on the draft guidance that appeared in the **Federal Register** of January 23, 2014 (79 FR 3826). FDA revised the guidance as appropriate in response to the comments.

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 medical devices containing materials derived from animal sources (except for in vitro diagnostic devices). 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. This guidance is not subject to Executive Order 12866.

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 *https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm.* This guidance document is also available at *https://www.regulations.gov.* Persons unable to download an electronic copy of ''Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic 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 2206 to identify the guidance you are requesting.

IV. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information. 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 the following FDA regulations and guidance have been approved by OMB as listed in the following table:

21 CFR part; guidance; or FDA form	Topic	OMB control No.
807, subpart E	Premarket notification	0910–0120
814, subparts A through E	Premarket approval	0910–0231
814, subpart H	Humanitarian Device Exemption	0910–0332
812	Investigational Device Exemption	0910–0078
''De Novo Classification Process (Evaluation of Automatic Class III Designation)''.	De Novo classification process	0910–0844
''Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff''.	Q-submissions	0910–0756
820	Current Good Manufacturing Practice (CGMP); Quality System (QS) Regulation.	0910–0073

Dated: March 11, 2019.

Lowell J. Schiller,

Acting Associate Commissioner for Policy.

[FR Doc. 2019–04883 Filed 3–14–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–D–0362]

A Risk-Based Approach To Monitoring of Clinical Investigations: Questions and Answers; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''A Risk-Based Approach to Monitoring of Clinical Investigations: Questions and Answers.'' The draft guidance provides information to sponsors on risk-based approaches to monitoring of investigational studies of human drug and biological products, medical devices, and combinations thereof. This guidance expands on the guidance for industry entitled ''Oversight of Clinical Investigations—A Risk-Based Approach to Monitoring'' (August 2013) (the RBM Guidance) by providing additional guidance to facilitate sponsors' implementation of risk-based monitoring.

DATES: Submit either electronic or written comments on the draft guidance by May 14, 2019 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

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–2019–D–0362 for ''A Risk-Based Approach to Monitoring of Clinical Investigations: Questions and Answers.'' Received comments 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.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

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; the 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; 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; or the Office of Good Clinical Practice, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5103, Silver Spring, MD 20993. 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.

FOR FURTHER INFORMATION CONTACT: Ansalan Stewart, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6312, Silver Spring, MD 20993–0002, 240–402–6631, *ansalan.stewart@fda.hhs.gov;* Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7268, Silver Spring, MD 20993–0002, 240–402–7911; Martin Hamilton, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5431, Silver Spring, MD 20993–0002, 301–796–5666, *CDRHClinicalEvidence@fda.hhs.gov;* Sheila Brown, Office of Good Clinical Practice, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5109, Silver Spring, MD 20993, 301–796–6563, *Sheila.Brown@fda.hhs.gov;* or Hector Colon, Office of Regulatory Affairs/Office of Bioresearch Monitoring Operations, 12420 Parklawn Dr., Rockville, MD 20857, 301–796–3899, *orabimoinspectionpoc@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''A Risk-Based Approach to Monitoring of Clinical Investigations: Questions and Answers.'' This document provides guidance to sponsors on risk-based approaches to monitoring investigational studies of human drug and biological products, medical devices, and combinations thereof. This guidance expands on the guidance for industry entitled ''Oversight of Clinical Investigations—A Risk-Based Approach to Monitoring'' (the RBM guidance) [1] by providing additional guidance to facilitate sponsors' implementation of risk-based monitoring.

FDA's experience since finalizing the RBM guidance in 2013 suggests that additional guidance would be beneficial regarding FDA's recommendations for planning a risk-based monitoring approach, developing the content of monitoring plans, and addressing and communicating monitoring results. The questions and answers in this draft guidance are intended to assist sponsors in planning and conducting risk-based monitoring.

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 a risk-based approach to monitoring of clinical investigations. 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. This

[1] Available at: *https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm269919.pdf.*

guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft 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 50 have been approved under OMB control number 0910–0755; 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 812 have been approved under OMB control number 0910–0078; and the collections of information in the guidance for industry entitled ''Oversight of Clinical Investigations: A Risk-Based Approach to Monitoring'' have been approved under OMB control number 0910–0733.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at *https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm, or https://www.regulations.gov.*

Dated: March 11, 2019.

Lowell J. Schiller,

Acting Associate Commissioner for Policy.

[FR Doc. 2019–04814 Filed 3–14–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–D–1328]

Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled ''Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals.'' This guidance outlines nonclinical studies recommended for the development of pharmaceuticals used to treat patients with severely debilitating or life-threatening hematologic disorders (SDLTHDs) and addresses comments received to the docket. This guidance is intended to streamline the development of pharmaceuticals used to treat patients with SDLTHDs, other than cancer, while protecting patients' safety and avoiding unnecessary use of animals, in accordance with the 3R (reduce, refine, replace) principles. This guidance applies to pharmaceuticals used both to treat the active disease and to prevent the recurrence of a life-threatening or debilitating event.

DATES: The announcement of the guidance is published in the **Federal Register** on March 15, 2019.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

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–2018–D–1328 for ''Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals.'' Received comments 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.