



**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 [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

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.

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

Submit written requests for single copies of this 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. 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.

FOR FURTHER INFORMATION CONTACT: John Leighton, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2204, Silver Spring, MD 20993-0002, 301-796-7550; or Haleh Saber, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2117, Silver Spring, MD 20993-0002, 301-796-7550.

SUPPLEMENTARY INFORMATION:

#### I. Background

FDA is announcing the availability of a guidance for industry entitled “Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals.” The purpose of this guidance is to assist sponsors in the design of nonclinical studies for the development of pharmaceuticals used to treat patients with SDLTHDs. 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 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.

SDLTHDs include conditions in which life expectancy is short or quality of life is greatly diminished despite available therapies. FDA has defined life-threatening and severely debilitating diseases in regulations (21 CFR 312.81). A streamlined approach to drug development is necessary to allow patients with SDLTHDs earlier and continued access to new and potentially effective therapies. The draft guidance for industry entitled "Rare Diseases: Common Issues in Drug Development" (available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm458485.pdf>) does not specifically facilitate the nonclinical development of pharmaceuticals for treatment of SDLTHDs. Because SDLTHDs are not all rare diseases, they can fall outside the scope of the draft guidance for rare diseases. The present document provides consistent guidance for all nononcology SDLTHDs, independent of disease incidence or prevalence.

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 "Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals." 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.

## II. Paperwork Reduction Act of 1995

This 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 collection of information submitted under 21 CFR part 312 has been approved under OMB control number 0910-0014. The collection of information submitted under 21 CFR part 314 has been approved under OMB control number 0910-0001.

### III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <https://www.regulations.gov>.

Dated: March 11, 2019.

Lowell J. Schiller,

Acting Associate Commissioner for Policy.

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