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4164-01-P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-1835]

### Smallpox (Variola Virus) Infection: Developing Drugs for Treatment or Prevention; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Smallpox (Variola Virus) Infection: Developing Drugs for Treatment or Prevention.” The purpose of this draft guidance is to assist sponsors in all phases of development of antiviral drugs for the treatment or prevention of smallpox (variola virus) infection. This draft guidance revises the draft guidance for industry entitled “Smallpox (Variola) Infection: Developing Drugs for Treatment or Prevention” issued on November 23, 2007.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2018-D-1835 for “Smallpox (Variola Virus) Infection: Developing Drugs for Treatment or Prevention; Draft Guidance for Industry; Availability.” 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. 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: Jeffrey Murray, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6370, Silver Spring, MD 20993-0002, 301-796-1500.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Smallpox (Variola Virus) Infection: Developing Drugs for Treatment or Prevention.” The purpose of this draft guidance is to assist sponsors in all phases of development of antiviral drugs for the treatment or prevention of smallpox (variola virus) infection. This draft guidance addresses nonclinical development, key study design considerations for animal efficacy studies to support potential new drug application (NDA)/biologics license application (BLA) submissions under the animal rule (21 CFR part 314, subpart I, for drugs and 21 CFR part 601, subpart H, for biologics), and considerations for obtaining a human safety database.

This draft guidance revises the draft guidance for industry entitled “Smallpox (Variola) Infection: Developing Drugs for Treatment or Prevention” issued on November 23, 2007 (72 FR 65750). The revisions intend to streamline the guidance and incorporate input from a public workshop in 2009 and an advisory committee meeting in 2011. This revision contains the following changes:

- Modification and integration of several sections to focus on multidisciplinary considerations for studies in animal models of orthopoxvirus disease, including:

- Considerations for preliminary assessments of antiviral activity in animal models
- Key study design considerations for animal efficacy studies to support potential NDA/BLA submissions under the animal rule
- Selection of an effective dose in humans
- Additional clarification on the following:
  - Key nonclinical virology issues related to drug development under the animal rule
  - Key pharmacology/toxicology issues
  - Considerations regarding healthy volunteer safety trials, safety data from non-smallpox clinical experience, clinical trials in the event of a public health emergency, individual patient expanded access investigational new drug applications for emergency use, and emergency use authorization
  - Key clinical pharmacology issues that may be affected by limitations in collecting clinical data
  - Key chemistry, manufacturing, and controls issues, such as the importance of developing formulations for patients who are unable to swallow solid oral dosage formulations, as well as the importance of generating stability data needed to support a long expiration dating period

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 developing drugs for the treatment and prevention of smallpox (variola virus) infection. 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. The Paperwork Reduction Act of 1995

This 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 collection of information in 21 CFR part 312 (investigational new drug applications) has been approved under OMB control number 0910-0014. The collection of information in 21 CFR part 314 (NDAs) has been approved under OMB control number 0910-0001. The collection of information resulting from special protocol assessments has been approved under OMB control number 0910-0470. The collection of information resulting from emergency use authorization of medical products has been approved under OMB control number 0910-0595. The collection of information resulting from individual patient expanded access applications has been approved under OMB control number 0910-0814. The collection of information resulting from good laboratory practices has been approved under OMB control number 0910-0119.

## III. Electronic Access

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

Dated: July 2, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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