OMB control number 0910–0139; 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 601 have been approved under OMB control number 0910–0338; the collections of information in 21 CFR part 610 have been approved under OMB control numbers 0910–0116, 0910–0139, and 0910–0338; the collections of information in 21 CFR part 630 have been approved under OMB control number 0910–0116; the collections of information in 21 CFR part 640 have been approved under OMB control number 0910–0116; the collections of information in 21 CFR part 812 have been approved under OMB control number 0910–0078; and the collections of information in 21 CFR part 814 have been approved under OMB control number 0910–0231.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either *https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics* or *https://www.regulations.gov.*

Dated: December 16, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–27520 Filed 12–19–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–D–4964]

Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products.'' This guidance complements and expands on the 1998 guidance entitled ''Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products'' (the 1998 guidance). Although FDA's evidentiary standard for effectiveness has not changed since 1998, the evolution of drug development and science has led to changes in the types of drug development programs submitted to the Agency. Specifically, there are more programs studying serious diseases lacking effective treatment, more programs in rare diseases, and more programs for therapies targeted at disease subsets. There is a need for more Agency guidance on the flexibility in the amount and type of evidence needed to meet the substantial evidence standard in these circumstances.

DATES: Submit either electronic or written comments on the draft guidance by February 18, 2020 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–4964 for ''Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products.'' 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 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 or

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: Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911 or Ei Thu Lwin, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6236, Silver Spring, MD 20993–0002, 301–796–0728.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products.'' This guidance complements and expands on the 1998 guidance. The 1998 guidance was issued in response to the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105–115), which stated that the substantial evidence requirement for effectiveness, which had generally been interpreted as calling for two adequate and well-controlled trials, could also be met by a single trial plus confirmatory evidence. The 1998 guidance, therefore, provided many examples of the types of evidence that could be considered confirmatory evidence, with a specific focus on adequate and well-controlled trials of the test agent in related populations or indications, as well as a number of illustrations of a single adequate and well-controlled trial supported by convincing evidence of the drug's mechanism of action in treating a disease or condition.

FDAMA, thus, introduced a specific new area of flexibility in the evidence needed to support effectiveness, but there are many other characteristics of the evidence supporting effectiveness that can vary (notably, trial designs, trial endpoints, statistical methodology), and evidence that varies in such ways potentially can provide substantial evidence of effectiveness but because of these characteristics may provide greater or lesser certainty. These characteristics also deserve consideration and were not discussed in the 1998 guidance. FDA's use of these various designs, endpoints, and analyses which can differ in the strength of evidence they provide, reflects the Agency's longstanding flexibility when considering the types of data and evidence that can meet the substantial evidence requirement.

Although FDA's evidentiary standard for effectiveness has not changed since 1998, the evolution of drug development and science has led to changes in the types of drug development programs submitted to the Agency. Specifically, there are more programs studying serious diseases lacking effective treatment, more programs in rare diseases, and more programs for therapies targeted at disease subsets. There is a need for more Agency guidance on the flexibility in the amount and type of evidence needed to meet the substantial evidence standard in these circumstances. The approaches discussed in this guidance can yield evidence that meets the statutory standard for substantial evidence and reflect the evolving landscape of drug development.

This guidance discusses the quality of evidence to establish effectiveness, including trial designs and trial endpoints. It also discusses the quantity of evidence needed in a given development program, *i.e.,* two adequate and well-controlled trials, one adequate and well-controlled trial plus confirmatory evidence, or reliance on a previous finding of effectiveness of an approved drug when scientifically justified and legally permissible (*i.e.,* no new effectiveness or pharmacodynamic data would be needed). The guidance also expands upon the discussions included in the 1998 guidance on the types of mechanistic and pharmacologic evidence and non-clinical evidence that can constitute confirmatory evidence.

Although randomized superiority trials with a placebo- or active-control design generally provide the strongest evidence of effectiveness, this guidance discusses the circumstances under which trials not using a placebo control, superiority design, or randomization may be acceptable. In addition, this guidance also discusses situations in which human efficacy trials are not ethical or feasible, and the animal rule may be applied. In all cases, FDA must reach the conclusion that there is substantial evidence of effectiveness to approve a drug; however, the degree of certainty supporting such a conclusion may differ, depending on clinical circumstances (*e.g.,* severity and rarity of the disease and unmet medical need).

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 ''Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products.'' 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.

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 312 for submission of an investigational new drug application have been approved under OMB control number 0910–0014. The collections of information in 21 CFR 314.50 for submission of an NDA have been approved under OMB control number 0910–0001. The collections of information in 21 CFR part 601 for submission of a BLA have been approved under OMB control number 0910–0338.

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, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics,* or *https://www.regulations.gov.*

Dated: December 16, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–27524 Filed 12–19–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Indian Health Service

Request for Public Comment: 60 Day Information Collection: Indian Health Service Medical Staff Credentials

AGENCY: Indian Health Service, HHS.

ACTION: Notice and request for comments. Request for revision to a collection.

SUMMARY: In compliance with the Paperwork Reduction Act of 1995, the Indian Health Service (IHS) invites the general public to comment on the information collection titled, ''Indian