Canada and Swissmedic. Additionally, the Membership of ICH has expanded to include other regulatory authorities and industry associations from around the world (refer to *https://www.ich.org/*).

ICH works by involving technical experts from both regulators and industry parties in detailed technical harmonization work and the application of a science-based approach to harmonization through a consensus-driven process that results in the development of ICH guidelines. The regulators around the world are committed to consistently adopting these consensus-based guidelines, realizing the benefits for patients and for industry.

As a Founding Regulatory Member of ICH, FDA plays a major role in the development of each of the ICH guidelines, which FDA then adopts and issues as guidance for industry. FDA's guidance documents do not establish legally enforceable responsibilities. Instead, they describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

In the **Federal Register** of November 13, 2017 (82 FR 52306), FDA published a notice announcing the availability of a draft guidance entitled ''S5(R3) Detection of Toxicity to Reproduction for Human Pharmaceuticals.'' The notice gave interested persons an opportunity to submit comments by February 12, 2018.

After consideration of the comments received and revisions to the guideline, a final draft of the guideline was submitted to the ICH Assembly and endorsed by the regulatory agency members in January 2020.

The guidance finalizes the guidance issued on November 13, 2017. The guidance has undergone revisions to align with other ICH guidances, elaborate on concepts to consider when designing studies, and identify potential circumstances in which a risk assessment can be made based on preliminary studies. It also clarifies the qualification and potential use of alternative assays.

The purpose of this guidance is to provide key considerations for developing a testing strategy to identify hazard and characterize reproductive risk for human pharmaceuticals. The guidance informs on the use of existing data and identifies potential study designs to supplement available data to identify, assess, and convey risk. General concepts and recommendations are provided that should be considered when interpreting study data and assessing reproductive risk in support of clinical development and marketing approval.

This guidance applies to pharmaceuticals, including biotechnology-derived pharmaceuticals; vaccines (and their novel constitutive ingredients) for infectious diseases; and novel excipients that are part of the final pharmaceutical product. It does not apply to cellular therapies, gene therapies, and tissue-engineered products. The methodological principles (*e.g.,* study design, dose selection, and species selection) outlined in this guidance can also apply to all compounds for which the conduct of reproductive and/or developmental toxicity studies is appropriate, including vaccines for other indications (*e.g.,* cancer). (see ICH guidance for industry ''S9 Nonclinical Evaluation for Anticancer Pharmaceuticals'' (March 2010), available at *https://www.fda.gov/media/73161/download*).

The guidance reflects revisions made in response to comments received on the draft guidance. These include reorganization of the guidance to improve readability and clarity, to introduce discussion of conventional assessment strategies earlier in the document, and to clarify which elements of the guidance are more appropriate for biotechnology-derived therapies. To accommodate the rapidly evolving nature of alternative assay development, the discussion of alternative assays was placed in an Annex, subject to a maintenance procedure, to allow for more frequent updating of this material.

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 ''S5(R3) Detection of Reproductive and Developmental Toxicity for Human 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.

II. Paperwork Reduction Act of 1995

This guidance contains no collection of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521) is not required.

However, this guidance refers to previously approved FDA collections of information. These collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 58 have been approved under OMB control number 0910–0119; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001; the collections of information in 21 CFR part 312 have been approved under OMB control number 0910–0014; and the content and format requirements for pregnancy and lactation labeling of human prescription drug and biological products have been approved under OMB control number 0910–0624.

III. Electronic Access

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

Dated: May 6, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–10017 Filed 5–11–21; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–D–1370]

COVID–19: Developing Drugs and Biological Products for Treatment or Prevention; 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 ''COVID–19: Developing Drugs and Biological Products for Treatment or Prevention.'' This guidance describes FDA's current recommendations regarding phase 2 or phase 3 trials for drugs or biological products under development for the treatment or prevention of COVID–19. Given the public health emergency presented by COVID–19, this guidance document is being implemented without prior public comment because FDA has determined that prior public participation is not feasible or appropriate, but it remains subject to comment in accordance with the Agency's good guidance practices. This final guidance revises and replaces the final guidance of the same name issued

on May 11, 2020. Revisions were made to address the evolving landscape of COVID–19 drug development, including the emergence of SARS-CoV–2 variants and the availability of COVID–19 vaccines. The revision to this guidance was posted to the FDA website on February 22, 2021.

DATES: The announcement of the guidance is published in the **Federal Register** on May 12, 2021. The guidance document is immediately in effect, but it remains subject to comment in accordance with the Agency's good guidance practices.

ADDRESSES: You may submit 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–2020–D–1370 for ''COVID–19: Developing Drugs and Biological Products for Treatment or Prevention.'' 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, 240–402–7500.

- 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.govinfo.gov/content/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, 240–402–7500.

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 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; or 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. 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: Eithu 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; or 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.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''COVID–19: Developing Drugs and Biological Products for Treatment or Prevention.'' There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named SARS-CoV–2, and the disease it causes has been named Coronavirus Disease 2019 (COVID–19). On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health emergency related to COVID–19 and mobilized the Operating Divisions of HHS. The public health emergency declaration has been subsequently renewed. In addition, on March 13, 2020, the President declared a national emergency in response to COVID–19. The revision to this guidance was posted to the FDA website on February 22, 2021.

This guidance describes FDA's current recommendations regarding phase 2 or phase 3 trials for drugs under development to treat or prevent COVID–19. This guidance focuses on the patient population, trial design, efficacy endpoints, safety considerations, and statistical considerations for such trials. Drugs should have undergone sufficient development before their evaluation in phase 2 or phase 3.

This guidance focuses on the development of drugs with direct antiviral activity or immunomodulatory activity. However, the recommendations in this guidance may be applicable to development plans for drugs for COVID–19 with other mechanisms of action. The mechanism of action of the drug may impact key study design

elements (*e.g.,* population, endpoints, safety assessments, duration of followup, etc.).

Preventative vaccines are not within the scope of this guidance. Nor does this guidance provide general recommendations on early drug development in COVID–19, such as use of animal models.

In light of the public health emergency related to COVID–19 declared by the Secretary of HHS, FDA has determined that prior public participation for this guidance is not feasible or appropriate and is issuing this guidance without prior public comment (see section 701(h)(1)(C)(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 371(h)(1)(C)(i)) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

This guidance is intended to remain in effect for the duration of the public health emergency related to COVID–19 declared by HHS, including any renewals made by the Secretary in accordance with section 319(a)(2) of the Public Health Service Act (42 U.S.C. 247d(a)(2)). However, the recommendations and processes described in the guidance are expected to assist the Agency more broadly in its continued efforts to assist sponsors in the clinical development of drugs for the treatment of COVID–19 beyond the termination of the COVID–19 public health emergency and reflect the Agency's current thinking on this issue. Therefore, within 60 days following the termination of the public health emergency, FDA intends to revise and replace this guidance with any appropriate changes based on comments received on this guidance and the Agency's experience with implementation.

This final guidance revises and replaces the final guidance with the same title issued on May 19, 2020 (85 FR 29949). The revision addresses the potential impact of the emergence of SARS-CoV–2 variants and the availability of COVID–19 vaccines. Additional updates reflecting the evolving landscape of COVID–19 drug development were made to the recommendations on patient population, trial design, efficacy endpoints, safety considerations, and statistical considerations. In addition, FDA considered comments received on the previous guidance, and editorial changes were made to improve clarity.

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 ''COVID–19: Developing Drugs and Biological Products for Treatment or Prevention.'' 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

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001; the collections of information in 21 CFR parts 312 and 320 have been approved under OMB control number 0910–0014; the collections of information in 21 CFR part 58 regarding good laboratory practice for nonclinical laboratory studies have been approved under OMB control number 0910–0119; the collections of information in 21 CFR parts 50 and 56 have been approved under OMB control number 0910–0130; the collections of information in 21 CFR part 320 have been approved under OMB control number 0910–0291; the collections of information in 21 CFR part 601 have been approved under OMB control number 0910–0338; the collections of information in FDA's draft guidance for industry entitled ''Formal Meetings Between the FDA and Sponsors or Applicants of Prescription Drug User Fee Act Products'' have been approved under OMB control number 0910–0429; the collections of information in FDA's final guidance for clinical trial sponsors entitled ''Establishment and Operation of Clinical Trial Data Monitoring Committees'' have been approved under OMB control number 0910–0581; and the collections of information in FDA's final 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 guidance at *https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics, https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders,* or *https://www.regulations.gov*.

Dated: May 7, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–D–1156]

Q3D(R2)—Guideline for Elemental Impurities; International Council for Harmonisation; 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 ''Q3D(R2)—Guideline for Elemental Impurities.'' The draft guidance was prepared under the auspices of the International Council for Harmonisation (ICH), formerly the International Conference on Harmonisation. The draft guidance provides Permissible Daily Exposures (PDEs) for the cutaneous and transcutaneous routes of administration and relevant risk assessment considerations to supplement previous guidance for the oral, parenteral, and inhalation routes of administration. In addition, error corrections to previously identified PDEs for gold (oral, parenteral, and inhalation routes), silver (parenteral route), and nickel (inhalation route) are provided. The draft guidance is intended to recommend acceptable amounts for the listed elemental impurities in pharmaceuticals for the safety of the patient and provide recommendations for conducting a risk assessment for pharmaceutical products.

DATES: Submit either electronic or written comments on the draft guidance by June 11, 2021 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: