over the 3-year approved information collection request (ICR) period for a more comprehensive burden table.

Based on updated data, we have revised our estimate for sections 905(b), 905(c), 905(d), 905(h), or 905(i) of the FD&C Act. Based on FDA's experience with current establishment registration and product listing information submitted to the agency, FDA has lowered the estimated annual respondents for (1) initial tobacco product establishment registration and listing (via Form FDA 3741) from 200 to 37 respondents, and (2) renewal of tobacco product establishment and listing (via Form FDA 3741) from 2,572 to 900 respondents.

The agency estimates that up to 37 new establishments will each submit one initial establishment registration and product listing via the current Form FDA 3741. The agency retains the hours per response estimate of 1.60 hours (or 96 minutes) for the initial tobacco product establishment registration and listing via the current Form FDA 3741, which FDA estimates manufacturers will need to use through the first year of the 3-year ICR approval period. Once the updated Form FDA 3741 is released, FDA estimates its completion to take 1.67 hours (100 minutes) for an initial registration of a tobacco product establishment and material file submission. As shown in Table 1, averaged across the 3-year ICR period, FDA estimates an average annual burden of 1.65 hours (99 minutes) for a total of 61 burden hours (across the 37 annual respondents). FDA estimates up to 37 establishments will each submit 1 initial product listing spreadsheet each year using the new Form FDA 3741b, which is expected to take 0.33 hours (20 minutes), for a total of 12 burden hours. Averaged across the 3-year ICR approval period, FDA estimates an average annual hours per response of 0.22 hours (8 average total hours) because, as noted above, the agency estimates that tobacco product manufacturers will not start using this new form until Year 2 of the 3-year ICR approval period.

Based on updated data, FDA estimates that the annual number of respondents for establishment registration and product listing renewals required under FD&C Act section 905 (Form FDA 3741) will decrease from 2,572 to 900. FDA retains the hours per response estimate of 10 minutes (0.17 hours) for the registration renewal via the current Form FDA 3741, which FDA estimates manufacturers will need to use through the first year of the 3-year ICR approval period. For Years 2 and 3, FDA estimates that the updated Form FDA 3741 will take 20 minutes (0.33 hours) for registration renewal. The renewal time increases with the updated Form FDA 3741 because the consolidated registration renewal process now encompasses establishment registration, product listing updates, and material file updates. Averaged across the 3-year ICR period, FDA estimates an average annual burden of 0.28 hours (17 minutes) for a total of 252 burden hours (across the 900 annual respondents).

FDA estimates that the submission of ingredient listings required by section 904(a)(1) of the FD&C Act for each establishment will take 2 hours initially. Ingredients may be submitted electronically through the CTP Portal Next Generation or if unable to submit ingredients electronically then by mail using Form FDA 3742. FDA estimates that 16 establishments will initially submit one report annually at 2 hours per report, for a total of 32 hours.

Based on FDA's experience and the number of new products authorized to be introduced or delivered for introduction into interstate commerce submitted over the past 3 years, FDA estimates that 37 establishments will each submit 10 reports (one every 6 months). FDA also estimates that the confirmation or updating of product (ingredient) listing information required by section 904(c) of the FD&C Act is expected to take 0.40 hour (24 minutes) for a total 148 burden hours. FDA estimates that obtaining a D–U–N–S number will take 30 minutes. FDA assumes that all new establishment facilities that will be required to initially register under section 905 of the FD&C Act would obtain a D–U–N–S number. FDA estimates that up to 37 establishments that would need to obtain this number each year. The total industry burden to obtain a D–U–N–S number is 19 hours.

Our estimated burden for the information collection reflects an overall decrease of 442 hours and a decrease of 1,861 annual responses. We attribute this adjustment to the proposed revisions to this information collection to add the updated and comprehensive Form FDA 3741, ''Registration and Product Listing of Tobacco Product Manufacturing Establishments'' and add Form FDA 3741b, ''Tobacco Product List Spreadsheet''.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–17222 Filed 9–8–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–D–2102]

Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations; 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 ''Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations.'' This guidance describes the Agency's recommendations on the design and evaluation of comparative analytical studies intended to support a demonstration that a proposed therapeutic protein product is biosimilar to a reference product licensed under the Public Health Service Act (PHS Act). Additionally, this guidance is intended to provide recommendations to sponsors on the scientific and technical information for the chemistry, manufacturing, and controls (CMC) portion of a marketing application for a proposed product submitted under the PHS Act. This guidance finalizes and replaces the draft guidance of the same title issued on May 22, 2019, and replaces the final guidance ''Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product'' issued on April 30, 2015.

DATES: The announcement of the guidance is published in the **Federal Register** on September 9, 2025.

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–2019–D–2102 for ''Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations.'' 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 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: Mustafa Unlu, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 1139, Silver Spring, MD 20993, 301–796–3396, *mustafa.unlu@fda.hhs.gov.* Philip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a final guidance for industry entitled ''Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations.'' This final guidance describes the Agency's recommendations on the design and evaluation of comparative analytical studies intended to support a demonstration that a proposed therapeutic protein product is biosimilar to a reference product licensed under section 351(a) of the PHS Act (42 U.S.C. 262(a)). Additionally, this final guidance is intended to provide recommendations to sponsors on the scientific and technical information for the CMC portion of a marketing application for a proposed product submitted under section 351(k) of the PHS Act. Although the 351(k) pathway applies generally to biological products, this final guidance focuses on therapeutic protein products.

Section 351(k) of the PHS Act (42 U.S.C. 262(k)) provides an abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed reference product and sets forth the requirements for an application for a proposed biosimilar product and an application for a proposed interchangeable biosimilar product. Under this abbreviated licensure pathway, FDA will license a proposed biological product submitted under section 351(k) of the PHS Act if, among other things, FDA determines that the information submitted in the application is sufficient to show that the biological product is biosimilar to the reference product.

This guidance finalizes the draft guidance entitled ''Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations'' issued on May 22, 2019 (84 FR 23569). FDA considered comments received on the draft guidance as the guidance was finalized. Comments submitted to the docket of the draft guidance addressed a range of issues, including clarifying questions on reference product lots and on the analyses of the comparative analytical data. FDA provided additional information and clarifying edits in response to comments as appropriate. In addition, 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 ''Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations.'' 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. The previously approved collections of information are subject to

review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The collections of information related to the submission of: (1) An investigational new drug application under 21 CFR part 312 have been approved under OMB control number 0910–0014; (2) a new drug application, under 21 CFR part 314 have been approved under OMB control number 0910–0001; (3) a biologics license application (BLA) under 21 CFR part 601 have been approved under OMB control number 0910–0338; and (4) a BLA under section 351(k), under 21 CFR part 601 have been approved under OMB control number 0910–0718. The collections of information regarding current good manufacturing processes for drug products and biological products under 21 CFR part 211 and 21 CFR parts 600, 601, and 610 have been approved under OMB control numbers 0910–0139 and 0910–0338.

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/biologics-guidances, https://www.fda.gov/regulatory-information/search-fda-guidance-documents,* or *https://www.regulations.gov.*

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–17226 Filed 9–8–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2023–D–1955]

E6(R3) Good Clinical Practice; International Council for Harmonisation; 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 ''E6(R3) Good Clinical Practice.'' The guidance was prepared under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The guidance includes a principles document and annex 1 and is the precursory guidance to the draft guidance entitled ''E6(R3) Good Clinical Practice: Annex 2.'' Once complete, the guidance will be composed of a principles document, annex 1, and annex 2. The guidance is intended to outline flexible and modern good clinical practices for conducting clinical trials. Notably, the guidance highlights the importance of quality-by-design, proportionality, and risk-based approaches in conducting clinical trials to ensure safety and reliability of results. The guidance also encourages use of innovative design elements and technology in clinical trials, while avoiding unnecessary complexities. The guidance finalizes the draft guidance of the same title issued on June 7, 2023.

DATES: The announcement of the guidance is published in the **Federal Register** on September 9, 2025.

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–2023–D–1955 for ''E6(R3) Good Clinical Practice.'' 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)).