

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2020-D-1794]

**Evaluation of Gastric pH-Dependent Drug Interactions With Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications; Draft Guidance for Industry; Availability**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**SUMMARY:** The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Evaluation of Gastric pH-Dependent Drug Interactions With Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications.” This draft guidance focuses on specific recommendations pertinent to gastric pH-dependent drug-drug interaction (DDI) assessment and describes the FDA’s recommendations regarding when clinical DDI studies with acid-reducing agents (ARAs) are needed; design of the clinical studies; interpretation of study results; and communicating findings and options for managing pH-dependent DDIs in product labeling.

**DATES:** Submit either electronic or written comments on the draft guidance by March 1, 2021 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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:

*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-1794 for “Evaluation of Gastric pH-Dependent Drug Interactions With Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications.” 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.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.

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:** Anuradha Ramamoorthy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3118, Silver Spring, MD 20993, 240-402-6426.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a draft guidance for industry entitled “Evaluation of Gastric pH-Dependent Drug Interactions With Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications.” ARAs such as antacids, histamine H2-receptor antagonists, and proton pump inhibitors are widely used, and many of these drugs are available over-the-counter. Because ARAs can elevate the gastric pH, concomitant administration of a drug with an ARA could alter the solubility, dissolution, and bioavailability of the drug, potentially resulting in a loss of efficacy for weak-base drugs or increased toxicity for weak-acid drugs. Therefore, it is important to assess the susceptibility of an investigational drug to gastric pH change-mediated DDIs early in drug development, characterize the DDI effect with clinical studies when needed, and communicate the findings in the drug product labeling. This draft guidance addresses when clinical DDI studies with ARAs should be conducted, the design and conduct of clinical pH-

dependent DDI studies, alternative approaches for evaluating pH-dependent DDIs, and extrapolating clinical DDI study results with drug classes of ARAs.

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 "Evaluation of Gastric pH-Dependent Drug Interactions With Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications." 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 for submissions of investigational new drug applications, new drug applications, and biologic license applications in 21 CFR parts 312, 314, and 601 have been approved under OMB control numbers 0910–0014; 0910–0001; and 0910–0338, respectively. In addition, the submission of prescription drug labeling under 21 CFR 201.56 and 201.57 has been approved under OMB control number 0910–0572.

## III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs> or <https://www.regulations.gov>.

Dated: November 25, 2020.

**Lauren K. Roth,**

*Acting Principal Associate Commissioner for Policy.*

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**BILLING CODE 4164–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA–2011–N–0076]

#### Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Electronic Records; Electronic Signatures

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Submit written comments (including recommendations) on the collection of information by December 31, 2020.

**ADDRESSES:** To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to <https://www.reginfo.gov/public/do/PRAMain>. Find this particular information collection by selecting "Currently under Review—Open for Public Comments" or by using the search function. The OMB control number for this information collection is 0910–0303. Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–5733, [PRAStaff@fda.hhs.gov](mailto:PRAStaff@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:** In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

#### Electronic Records; Electronic Signatures—21 CFR Part 11

*OMB Control Number 0910–0303—Extension*

This information collection supports FDA regulations in part 11 (21 CFR part 11), which govern criteria for acceptance of electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records. Under these regulations, records and reports may be submitted to us

electronically provided that we have stated our ability to accept the records electronically in an Agency-established public docket and that the other requirements of part 11 are met.

The recordkeeping provisions in §§ 11.10, 11.30, 11.50, and 11.300 (21 CFR 11.10, 11.30, 11.50, and 11.300) require the following standard operating procedures to ensure appropriate use of and precautions for systems using electronic records and signatures: (1) § 11.10 specifies procedures and controls for persons who use closed systems to create, modify, maintain, or transmit electronic records; (2) § 11.30 specifies procedures and controls for persons who use open systems to create, modify, maintain, or transmit electronic records; (3) § 11.50 specifies procedures and controls for persons who use electronic signatures; and (4) § 11.300 specifies controls to ensure the security and integrity of electronic signatures based upon use of identification codes in combination with passwords. The reporting provision (§ 11.100) requires persons to certify to us in writing that they will regard electronic signatures used in their systems as the legally binding equivalent of traditional handwritten signatures.

The burden created by the information collection provision of this regulation is a one-time burden associated with the creation of standard operating procedures, validation, and certification. We anticipate that the use of electronic media will substantially reduce the paperwork burden associated with maintaining FDA-required records. The respondents are businesses and other for-profit organizations, State or local governments, Federal Agencies, and nonprofit institutions.

To assist respondents with the information collection we have developed the guidance document entitled "Guidance for Industry: Part 11, Electronic Records; Electronic Signatures—Scope and Application," available on our website at <https://www.fda.gov/media/75414/download>. While we do not believe the guidance creates any attendant burden, it describes the Agency's thinking regarding persons who, in fulfillment of a requirement in a statute or another part of FDA's regulations to maintain records or submit information to FDA, have chosen to maintain the records or submit designated information electronically and, as a result, have become subject to part 11. Part 11 applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted under any records requirements set forth in Agency regulations. Part 11 also