unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (2) the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included is unsafe under such conditions.[2]

The regulations at 21 CFR 314.94(a)(9)(iii) and (iv), with parallel provisions in the approval regulations at § 314.127(a)(8)(ii)(B) and (C), specify that FDA will consider an inactive ingredient in, or the composition of, a generic drug product intended for parenteral, ophthalmic, or otic use to be unsafe and will refuse to approve the ANDA unless the generic drug product contains the same inactive ingredients (with certain listed exceptions) in the same concentration as the RLD. Specifically, the inactive ingredient requirements in § 314.94(a)(9)(iii) and (iv) apply to pH adjusters, which are not expressly identified as one of the listed exceptions. Under § 314.99(b), however, an applicant may ask FDA to waive any requirement that applies to the applicant under §§ 314.92 through 314.99. Thus, an ANDA applicant for a drug product intended for parenteral, ophthalmic, or otic use who seeks to use a pH adjuster(s) that is Q1 or Q2 different from the RLD may ask the Agency to waive the inactive ingredient requirements at § 314.94(a)(9)(iii) or (iv) for the pH adjuster(s). This guidance document provides recommendations on (1) the type of information that applicants should consider submitting with a § 314.99(b) waiver request when an ANDA applicant asks the Agency to waive the inactive ingredient requirements for pH adjusters and (2) the format and process for submitting such waiver requests.

This guidance finalizes the draft guidance entitled ''Considerations for Waiver Requests for pH Adjusters in Generic Drug Products Intended for Parenteral, Ophthalmic, or Otic Use'' issued on April 14, 2022 (87 FR 22217). FDA considered comments received on the draft guidance as the guidance was finalized. Changes from the draft to the final guidance include recommendations for ANDA applicants to seek FDA feedback on a proposed approach for justifying a § 314.99(b) waiver request for a difference in pH adjuster, as well as in instances where the applicant also seeks to utilize a certain bioequivalence approach with a formulation that contains a Q1 or Q2 difference in pH adjuster.

In addition, this guidance includes information clarifying FDA's obligations to maintain the confidentiality of trade secret and confidential commercial information when responding to questions regarding drug product formulations, and to distinguish the regulatory provisions for requesting waiver of a Q1 or Q2 difference in a pH adjuster from the provisions that support a request to waive submission of evidence of in vivo bioequivalence.

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 ''Considerations for Waiver Requests for pH Adjusters in Generic Drug Products Intended for Parenteral, Ophthalmic, or Otic Use.'' 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 in 21 CFR part 314 relating to the submission of ANDAs, including requests for waiver for a pH adjuster difference under § 314.99(b) and waivers under § 314.90, have been approved under OMB control number 0910–0001. The collections of information in 21 CFR part 320 relating to the requirements for demonstrating bioavailability and bioequivalence, including waiver of evidence of in vivo bioavailability or bioequivalence under § 320.22(b), have been approved under OMB control numbers 0910–0014 and 0910–0291. The collections of information relating to the submission of controlled correspondence related to generic drug development and FDA approval have been approved under OMB control number 0910–0727.

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

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–19990 Filed 11–14–25; 8:45 am]

BILLING CODE 4164–01–P

[2] Section 505(j)(4)(H) of the FD&C Act.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2025–D–4051]

Quality Management System Information for Certain Premarket Submission Reviews; Draft Guidance for Industry and Food and Drug Administration Staff; 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 the draft guidance entitled ''Quality Management System Information for Certain Premarket Submission Reviews.'' The medical device current good manufacturing practice (CGMP) requirements, previously in the quality system regulation (QS regulation) and now the quality management system regulation (QMSR), have been amended effective February 2, 2026, to align more closely with the international consensus standard for devices by incorporating by reference an international standard specific for device quality management systems. This draft guidance document is intended to assist FDA staff and medical device manufacturers in understanding FDA expectations about preparing and maintaining a Quality Management System (QMS) and providing the information required to be included in certain marketing submissions regarding a QMS, in line with the QMSR. This draft guidance is not final nor is it for implementation at this time.

DATES: Submit either electronic or written comments on the draft guidance by January 16, 2026 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–2025–D–4051 for ''Quality Management System Information for Certain Premarket Submission Reviews.'' 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)).

An electronic copy of the guidance document is available for download from the internet. See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the guidance. Submit written requests for a single hard copy of the draft guidance document entitled ''Quality Management System Information for Certain Premarket Submission Reviews'' to the Office of Policy, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5441, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your request.

FOR FURTHER INFORMATION CONTACT: Erica Takai, Center for Devices and Radiological Health, Food and Drug Administration, 301–796–6353; or Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is issuing this draft document to provide guidance to industry and FDA staff about the expectations related to QMSR requirements and certain marketing submissions once the final rule amending 21 CFR part 820 goes into effect on February 2, 2026. The medical device CGMP requirements, formerly in the QS regulation and now in the QMSR, have been amended to align more closely with the international consensus standard for devices by incorporating by reference an international standard specific for device quality management systems (ISO 13485:2016). When final, this guidance is intended to assist medical device manufacturers in understanding FDA expectations about preparing and maintaining a QMS and providing the information required to be included in certain marketing submissions regarding a QMS, in line with the QMSR. In addition, this draft guidance is intended to make recommendations regarding information included in these marketing submissions that may help FDA determine compliance with QMSR.

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 Quality Management System Information for Certain Premarket Submission Reviews. 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.

As we develop final guidance on this topic, FDA will consider comments on costs or cost savings the guidance may generate, relevant for Executive Order 14192.

II. Electronic Access

Persons interested in obtaining a copy of the draft guidance may do so by downloading an electronic copy from the internet. A search capability for all Center for Devices and Radiological Health guidance documents is available at *https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products.* This guidance document is also available at *https://www.regulations.gov, https://www.fda.gov/regulatory-information/search-fda-guidance-documents* or *https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics.* Persons unable to download an electronic copy of ''Quality Management System Information for Certain Premarket Submission Reviews'' may send an email request to *CDRH-Guidance@fda.hhs.gov* to receive an electronic copy of the document. Please

use the document number GUI00001140 and complete title to identify the guidance you are requesting.

III. Paperwork Reduction Act of 1995

While this guidance contains no new 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 in the following table have been approved by OMB:

21 CFR part; guidance; or FDA form	Topic	OMB control No.
807, subpart E	Premarket notification	0910–0120
814, subparts A through E	Premarket approval	0910–0231
814, subpart H	Humanitarian Use Devices; Humanitarian Device Exemption	0910–0332
812	Investigational Device Exemptions	0910–0078
860, subpart D	De Novo classification process	0910–0844
''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program''.	Q-submissions and Early Payor Feedback Request Programs for Medical Devices.	0910–0756
810	Recalls	0910–0432
806	Medical Devices; Reports of Corrections and Removals	0910–0359
820	Current Good Manufacturing Practice (CGMP); Quality System (QS) Regulation.	0910–0073

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–19947 Filed 11–14–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HOMELAND SECURITY

Agreement Between the Government of the United States of America and the Government of the Republic of Ecuador Relating to the Transfer of Third-Country Nationals to Ecuador

AGENCY: Department of Homeland Security.

ACTION: Notice of Agreement.

SUMMARY: The Department of Homeland Security is publishing the Agreement between the Government of the United States of America and the Government of the Republic of Ecuador relating to the transfer of third-country nationals to Ecuador, effected by exchange of diplomatic notes on July 16, 2025 and July 23, 2025. The text of the diplomatic notes is set out below.

(Authority: 8 U.S.C. 1158(a)(2)(A).)

Joseph N. Mazzara,

Acting General Counsel, U.S. Department of Homeland Security.

BILLING CODE 9110–9M–P