Register of April 28, 2017, FDA announced its determination that Wellcovorin (leucovorin calcium) tablets, EQ 5 mg base and EQ 25 mg base, were not withdrawn from sale for reasons of safety or effectiveness under 21 CFR 314.161.

Under 21 CFR 314.160, FDA, on its own initiative or upon request of an applicant, may, on the basis of new data, approve an application or abbreviated application which it had previously refused, suspended, or withdrawn approval. With respect to leucovorin calcium tablets, FDA has conducted a systematic analysis of literature published between 2009–2024 and has determined that the information supports a finding that orally administered leucovorin calcium tablets improve certain symptoms in adults and pediatric patients with cerebral folate deficiency (CFD). Published case reports provided patient-level data on over 40 patients, including both adults and pediatric patients, with genetically confirmed CFD due to variants in the FOLR1 gene who were treated with oral leucovorin. Patients had heterogenous clinical symptoms that included global developmental delays with autistic features and psychomotor regression, intractable epilepsy, and cerebellar ataxia. In some patients, leucovorin dosing was titrated based on levels of 5-methyltetrahydrofolate (5-MTHF) in the cerebrospinal fluid (CSF) or symptoms. Clinical outcomes were compared to the known natural history of CFD due to variants in the FOLR1 gene as historic control. The majority of patients demonstrated substantial improvement of symptoms of CFD that would not be expected when compared to the natural history of CFD due to FOLR1 gene variants. In addition, we reviewed mechanistic data that demonstrated a normalization in CSF 5-MTHF levels in 80% of patients who had CSF samples available for analysis following administration of leucovorin. We note that CFD has been reported in patients with neuropsychiatric symptoms, including autistic features, and detectable serum autoantibodies to the folate receptor alpha; however, data on the use of leucovorin is limited in this population and additional studies are needed.

Subsequent to the approval of NDA 018342 for Wellcovorin (leucovorin calcium) tablets, EQ 5 mg base and EQ 25 mg base, that is being announced in this Notice, FDA intends to request that GSK submit a prior approval supplemental NDA to revise the prescribing information for Wellcovorin (leucovorin calcium) tablets, EQ 5 mg base and EQ 25 mg base, to include the essential scientific information needed for the safe and effective use of these drug products for the treatment of CFD in adults and pediatric patients.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–18510 Filed 9–22–25; 4:15 pm]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2022–D–0795]

Computer Software Assurance for Production and Quality System Software; 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 a final guidance entitled ''Computer Software Assurance for Production and Quality System Software.'' FDA is issuing this guidance to provide recommendations on computer software assurance for computers and automated data processing systems used as part of medical device production or the quality system. FDA believes that these recommendations will help foster the adoption and use of innovative technologies that promote patient access to high-quality medical devices and help manufacturers to keep pace with the dynamic, rapidly changing technology landscape, while promoting compliance with laws and regulations implemented by FDA.

DATES: The announcement of the guidance is published in the **Federal Register** on September 24, 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–2022–D–0795 for ''Computer Software Assurance for Production and Quality System Software.'' 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 guidance document entitled ''Computer Software Assurance for Production and Quality System Software'' to the Office of Policy, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5431, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your request.

FOR FURTHER INFORMATION CONTACT: Daniel Walter, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 1526, Silver Spring, MD 20993–0002, 301–796–5587 or Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA envisions a future state where the medical device ecosystem is inherently focused on device features and manufacturing practices that promote product quality and patient safety. FDA has sought to identify and promote successful manufacturing practices and help device manufacturers raise their manufacturing quality level. In doing so, one goal is to help manufacturers produce high-quality medical devices that align with the laws and regulations implemented by FDA. Compliance with quality system obligations including those in 21 CFR part 820 is required for manufacturers of finished medical devices to the extent they engage in operations to which those obligations apply. This guidance addresses practices relating to computers and automated data processing systems used as part of production or the quality system.

FDA recognizes the potential for advances in manufacturing technologies, including the adoption of automation, robotics, simulation, and other digital capabilities, to provide significant benefits for enhancing the quality, availability, and safety of medical devices. Medical device manufacturers have expressed a desire for greater clarity regarding the Agency's expectations for software validation for computers and automated data processing systems used as part of production or the quality system. Given the rapidly changing nature of software, manufacturers have also expressed a desire for a more iterative, agile approach for validation of computer software used as part of production or the quality system.

Traditionally, software validation has often been accomplished via software testing and other verification activities conducted at each stage of the software development life cycle. However, software testing alone is often insufficient to establish confidence that the software is fit for its intended use. FDA believes that applying a risk-based approach to computer software used as part of production or the quality system would better focus manufacturers' assurance activities to help ensure product quality while helping to fulfill validation requirements. This guidance provides recommendations on computer software assurance for computers and automated data processing systems used as part of medical device production or the quality system. FDA believes that these recommendations will help foster the adoption and use of innovative technologies that promote patient access to high-quality medical devices and help manufacturers to keep pace with the dynamic, rapidly changing technology landscape, while promoting compliance with laws and regulations implemented by FDA.

This guidance supplements FDA's guidance entitled ''General Principles of Software Validation,'' [1] except this guidance supersedes Section 6 (''Validation of Automated Process Equipment and Quality System Software'') of the ''General Principles of Software Validation'' guidance.

A notice of availability of the draft guidance appeared in the **Federal Register** of September 13, 2022 (87 FR 56059). FDA considered comments received and revised the guidance as appropriate in response to the comments, including adding a definitions section to provide clarity on commonly used terms in the guidance, updating examples of manual and automated testing, and adding examples throughout the guidance that apply the concepts in the guidance to different types of software.

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 Computer Software Assurance for Production and Quality System Software. 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. Electronic Access

Persons interested in obtaining a copy of the 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 ''Computer Software Assurance for Production and Quality System Software'' may send an email request to *CDRH-Guidance@fda.hhs.gov* to receive an electronic copy of the document. Please use the document number GUI00017045 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 OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–

[1] Available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-principles-software-validation.*

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.
11	Electronic records; Electronic signatures	0910–0303
814, subparts A through E	Premarket approval	0910–0231
814, subpart H	Humanitarian Device Exemption	0910–0332
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. 2025–18468 Filed 9–23–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2025–N–3708]

ADUFA V Third-Party Assessment Report: Notice of Availability; Virtual Public Meeting; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability; announcement of virtual public meeting; and request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the availability of a report entitled ''ADUFA V Third-Party Assessment Report'' and a related virtual public meeting. The purpose of the virtual public meeting is to provide an overview of a third-party assessment that examines the implementation of the Animal Drug User Fee Act (ADUFA). FDA is soliciting comments on the assessment.

DATES: The virtual public meeting will be held on Thursday, October 30, 2025, at 10:00 a.m. (EST). Either electronic or written/paper comments on this public workshop must be submitted by December 30, 2025. See the **SUPPLEMENTARY INFORMATION** section for registration date and information.

ADDRESSES: This public meeting is virtual only. Persons interested in attending this virtual public meeting must register at: *https://events.gcc.teams.microsoft.com/event/0c499308-1f4e-49ef-8c23-a3d3b0712963@7d2fdb41-339c-4257-87f2-a665730b31fc.* Additional details about the virtual public meeting are available on the ADUFA V Third-Party Assessment meeting web page listed on the Center for Veterinary Medicine's ''Workshops, Conferences and Meetings'' page: *https://www.fda.gov/animal-veterinary/news-events/workshops-conferences-meetings.*

You may submit comments identified by Docket No. FDA–2025–N–3708 as follows. Please note that late, untimely filed comments will not be considered. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of December 30, 2025. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

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'').

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- 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–N–3708 for ''ADUFA V Third-Party Assessment Report.'' Received comments, those filed in a timely manner (see **ADDRESSES**), 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