4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-D-0112]

Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development." This guidance is intended to provide a framework for considering whether and what type of long-term neurologic, sensory, and/or developmental evaluations could be useful in supporting a determination of safety of a regulated product for use in neonates, and which domains of assessment may be most pertinent. Although short-term safety evaluations may be acceptable for adults or other populations, such short-term evaluations may not identify important adverse events in the neonatal population, as latent effects may follow early-life exposures and drug treatment during the neonatal period coincides with a time of critical growth and physiologic development. Consideration of these potential long-term neurologic, sensory, and development effects in the neonatal population early in a drug development program will help ensure a safer product.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2022-D-0112 for "Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development; Draft Guidance for Industry." 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 draft guidance to An Massaro, Office of Pediatric Therapeutics, Office of Clinical Policy and Programs, Office of the Commissioner,

Food and Drug Administration, 10903 New Hampshire Avenue, Bldg. 32, 5th Floor, Silver Spring, MD 20993-0002, 301-467-8507; Gerri Baer, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Silver Spring, MD 20993-0002, 240-402-2865; Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Room 3128, Silver Spring, MD 20993-0002, 240-402-7911; Vasum Peiris, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Silver Spring, MD 20993-0002, 301-796-6089. 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: An Massaro, Office of Pediatric Therapeutics, Office of Clinical Policy and Programs, Office of the Commissioner, Food and Drug Administration, 10903 New Hampshire Avenue, Bldg. 32, 5th Floor, Silver Spring, MD 20993-0002, 301-467-8507; Gerri Baer, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Silver Spring, MD 20993-0002, 240-402-2865; Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, 240-402-7911; and Vasum Peiris, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Silver Spring, MD 20993-0002, 301-796-6089.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development; Draft Guidance for Industry."

Treatment with drugs, biological products, or devices, medical products (referred to as "medical products") during the neonatal period coincides with a time of critical growth and physiologic development. Although short-term safety evaluations may be acceptable for adults or other populations, such short-term evaluations may not identify important adverse events in the neonatal population, as latent effects may follow early-life exposures. Historically, most medical products used to treat neonates and young infants were not approved for use in these populations for the relevant indications, and thus long-term impacts were infrequently systematically evaluated.

Clinical investigators and sponsors of neonatal studies should consider and assess both the potential short- and long-term effects of an investigational therapy, whether novel or developed for a different indication. Prospectively designed long-term follow-up is helpful to understand medical product safety in growing and developing neonates.

Neonates should have the same access as other populations to drugs and biologics that have been adequately evaluated for optimal dosing, efficacy, and safety. There are unique conditions that occur in term or preterm neonates that will not have analogous development programs in older populations. As products are developed for unique neonatal conditions, it may be useful for novel development programs and first-in-human studies to occur in neonates, and these development programs should demonstrate long-term neurologic, sensory, and developmental safety. This guidance will discuss general, patient-specific and product-specific considerations ranging from neurodevelopmental screening through a comprehensive neurodevelopmental evaluation. It will also address what to measure in a risk assessment, when, and for how long. 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 "Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development; Draft Guidance for Industry." 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 submission of investigational new drug applications, 21 CFR part 312, have been approved under 0910-0014. The collections of information for submission of new drug applications, 21 CFR part 314, have been approved under 0910-0001. The collections of information for submission of biologic license applications, 21 CFR part 601, have been approved under 0910-0338. The collections of information for submission of premarket approval applications, 21 CFR part 807, subpart E; investigational device exemptions, 21 CFR part 812; premarket notifications, 21 CFR part 814, subparts A through E; humanitarian device exemptions, 21 CFR part 814, subpart H; and De Novo classification requests, 21 CFR part 860, subpart D, have been approved under OMB control numbers 0910-0120, 0910-0078, 0910-0231, 0910-0332, and 0910-0844, respectively.

III. Electronic Access

Persons with access to the internet may obtain the draft 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.

Dated: February 7, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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