

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, or to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, 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:** Sarah Venti, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-3130, [drugtrackandtrace@fda.hhs.gov](mailto:drugtrackandtrace@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:**

### I. Background

FDA is announcing the availability of a guidance for industry entitled "Wholesale Distributor Verification Requirement for Saleable Returned Drug Product—Compliance Policy." FDA is issuing this guidance consistent with the good guidance practices regulation (21 CFR 10.115). FDA is implementing this guidance without prior public comment because the Agency has determined that prior public participation is not feasible or appropriate (21 CFR 10.115(g)(2)). FDA made this determination because this guidance document provides information pertaining to the statutory requirement that takes effect November 27, 2019, for wholesale distributors to verify saleable returned drug products prior to redistribution under section 582(c)(4)(D) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360eee-1(c)(4)(D)). It is important that FDA provide this information before that date. Although this guidance document is immediately in effect, it remains subject to comment in accordance with the Agency's good guidance practices (21 CFR 10.115(g)(3)).

The DSCSA (Title II of Pub. L. 113-54) was signed into law on November 27, 2013. Section 202 of the DSCSA added section 582 to the FD&C Act. This section established product tracing, product identifier, authorized trading partner, and verification requirements for manufacturers, wholesale distributors, repackagers, and

dispensers to facilitate the tracing of a product through the pharmaceutical distribution supply chain. Failure to comply with the requirements of section 582 is prohibited under section 301(t) of the FD&C Act (21 U.S.C. 331(t)) and subject to enforcement action under the FD&C Act.

Beginning November 27, 2019, wholesale distributors are required, under section 582(c)(4)(D) of the FD&C Act, to verify the product identifier, including the standardized numerical identifier, on each sealed homogeneous case of saleable returned product, or, if such product is not in a sealed homogeneous case, on each package of saleable returned product, prior to further distributing such returned product.

As described in the guidance, FDA has received comments and feedback from wholesale distributors as well as other trading partners and stakeholders expressing concern with industry-wide readiness for implementation of the verification of saleable returned product requirement for wholesale distributors and the challenges stakeholders face with developing interoperable, electronic systems to enable such verification and achieve interoperability between networks. Given the concerns expressed, FDA recognizes that some wholesale distributors may need additional time beyond November 27, 2019, before they can begin verifying the product identifier on returned products prior to further distribution in an efficient, secure, and timely manner.

To minimize possible disruptions in the distribution of prescription drugs in the United States, FDA has adopted the compliance policy described in this guidance. Under this compliance policy, FDA does not intend to take action before November 27, 2020, against wholesale distributors who do not verify a product identifier prior to further distribution of a package or sealed homogeneous case of product as required by section 582(c)(4)(D) of the FD&C Act.

Additionally, section 582 of the FD&C Act requires certain trading partners (manufacturers, repackagers, wholesale distributors, and dispensers) to exchange transaction information, transaction history, and a transaction statement when engaging in transactions involving certain prescription drugs. Section 581(27)(E) of the FD&C Act (21 U.S.C. 360eee(27)(E)) requires that the transaction statement include a statement that the entity transferring ownership in a transaction had systems and processes in place to comply with verification requirements under section 582. This guidance also explains that, prior to November 27, 2020, FDA does

not intend to take action against a wholesale distributor for providing a transaction statement to a subsequent purchaser of product on the basis that such wholesale distributor does not yet have systems and processes in place to comply with the saleable return verification requirements under section 582(c)(4)(D). The guidance document explains the scope of the compliance policy in further detail.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). This guidance represents the current thinking of FDA on "Wholesale Distributor Verification Requirement for Saleable Returned Drug Product—Compliance Policy." 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. This guidance is not subject to Executive Order 12866.

### II. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics>, or <https://www.regulations.gov>.

Dated: September 18, 2019.

**Lowell J. Schiller,**

*Principal Associate Commissioner for Policy.*

[FR Doc. 2019-20651 Filed 9-23-19; 8:45 am]

**BILLING CODE 4164-01-P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2013-N-0035]

#### **Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment; 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 "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment." The guidance provides FDA's current thinking on the clinical development program and clinical trial designs for drugs to support an indication for the treatment of amyotrophic lateral

sclerosis (ALS). The guidance addresses the clinical development of drugs intended to treat the main motor aspects of ALS, *i.e.*, muscle weakness and its direct consequences, including shortened life expectancy. It does not address in detail the development of drugs to treat other symptoms that may arise in ALS, such as muscle cramps, spasticity, sialorrhea, pseudobulbar affect, and others. This guidance finalizes the draft guidance of the same name issued on February 16, 2018.

**DATES:** The announcement of the guidance is published in the **Federal Register** on September 24, 2019.

**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-2013-N-0035 for "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment." 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.gpo.gov/fdsys/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)).

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0002; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, 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:** Billy Dunn, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 4332, Silver Spring, MD 20993-0002, 301-796-2250; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

#### **SUPPLEMENTARY INFORMATION:**

##### **I. Background**

FDA is announcing the availability of a final guidance for industry entitled "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment." ALS is a progressive neurodegenerative disease that primarily affects motor neurons in the cerebral motor cortex, brainstem, and spinal cord, leading to loss of voluntary movement and the development of difficulty in swallowing, speaking, and breathing. The purpose of this guidance is to assist sponsors in the clinical development of drugs for the treatment of ALS.

The guidance addresses the clinical development of drugs intended to treat the main motor aspects of ALS (*i.e.*, muscle weakness and its direct consequences, including shortened survival). It does not address in detail the development of drugs to treat other symptoms that may arise in ALS, such as muscle cramps, spasticity, sialorrhea, and pseudobulbar affect.

The guidance covers considerations for early phase clinical development, drug development population, clinical efficacy study design and endpoints, and risk-benefit, as well as other factors, such as relevant nonclinical safety and pharmacokinetic/pharmacodynamic considerations. This guidance finalizes the draft guidance of the same name issued on February 16, 2018 (83 FR 7047). Changes made to the guidance took into consideration written and verbal comments received. Information was added about strategies to expedite clinical trials in ALS and minimize exposure to placebo, about the importance of broad inclusion criteria in ALS clinical trials, encouraging the use

of patient input and experience in the development of new outcome measures that are capable of measuring clinically meaningful effects in patients, and encouraging the incorporation of exploratory biomarkers in ALS development programs. Language was also added to provide greater context on the use of historical control data in ALS clinical trials, to suggest approaches to minimize patient burden during clinical trials, and to clarify safety data expectations for new ALS treatments. Finally, additions emphasize FDA's willingness to exercise flexibility in applying the statutory standards for approval of drugs for the treatment of serious diseases with unmet medical needs, while preserving appropriate assurances for safety and effectiveness.

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 "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment." 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. This guidance is not subject to Executive Order 12866.

## II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR part 312 have been approved under OMB control number 0910–0014, the collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001, and the collections of information referred to in the guidance for industry entitled "Establishment and Operation of Clinical Trial Data Monitoring Committees" (available at <https://www.fda.gov/media/75398/download>) have been approved under OMB control number 0910–0581.

## III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics>, or <https://www.regulations.gov>.

Dated: September 18, 2019.

**Lowell J. Schiller,**

*Principal Associate Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA–2019–D–3846]

#### Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations; Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders; 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 "Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations." The Patient Engagement Advisory Committee (PEAC) recommended that FDA and industry develop some type of framework to clarify how patient advisors can engage in the clinical investigation process. This draft guidance focuses on the applications, perceived barriers, and common challenges of patient engagement in the design and conduct of medical device clinical investigations. This draft guidance is not final nor is it in effect at this time.

**DATES:** Submit either electronic or written comments on the draft guidance by November 25, 2019 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–2019–D–3846 for "Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations." 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