4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration.

[Docket No. FDA-2019-D-0297]

Smoking Cessation and Related Indications: Developing Nicotine Replacement Therapy Drug Products; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Smoking Cessation and Related Indications: Developing Nicotine Replacement Therapy Drug Products." The document provides guidance to assist sponsors in the clinical development of nicotine replacement therapy (NRT) drug products, including but not limited to those intended for smoking cessation and related chronic indications.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2019-D-0297 for "Smoking Cessation and Related Indications: Developing Nicotine Replacement Therapy Drug Products." 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)).

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: Alina Salvatore, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave, Bldg. 22, Rm. 5418, Silver Spring, MD 20993-0002, 240-402-0379.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Smoking Cessation and Related Indications: Developing Nicotine Replacement Therapy Drug Products." This draft guidance reflects the FDA's current recommendations regarding overall development programs to support the approval of NRT drug products for smoking cessation and related chronic indications. There are several FDA-approved prescription and nonprescription NRT drug products for cessation of smoking cigarettes, but the Agency encourages the development of additional NRT drug products, which could help more smokers quit. In November 2017, FDA published a notice in the *Federal Register* requesting comments on the Agency's approach to evaluating the safety and efficacy of NRT drug products, including how they should be used and

labeled (82 FR 56759; Docket No. FDA-2017-N-6529). The Agency hosted a public hearing in January 2018 to obtain input from stakeholders on these issues. This draft guidance takes into consideration the feedback received and is intended to serve as a focus for continued discussions among the Agency, pharmaceutical sponsors, the academic community, and the public on this topic.

The draft guidance focuses on drug development and trial design issues that are specific to the study of NRT drug products. NRT drug products are typically studied and labeled for use as adjuncts to behavioral self-help materials and to date have involved single treatment regimens that begin on the patient's quit day. Alternate treatment regimens (e.g., pretreatment before quit day, quitting by gradual reduction (reduce to quit), using multiple NRT drug products together) are discussed in the guidance.

As outlined in the guidance, NRT drug products can be developed for smoking cessation and/or reduction in risk of relapse. NRT drug products that first have demonstrated efficacy for at least one of these indications can also include additional information in labeling by demonstrating efficacy in certain secondary endpoints. Sponsors can evaluate reduction in the urge to smoke or relief of cue-induced craving in former smokers, as secondary endpoints. Additionally, sponsors that can demonstrate, via a secondary endpoint, that the drug product provides relief of withdrawal symptoms in smokers *who are not trying to quit smoking*, may be able to include labeling instructions to address situations when such individuals are required to abstain and therefore experience withdrawal symptoms (e.g., while traveling on an airplane).

FDA is aware of the serious risks associated with smoking and is committed to facilitating the development of therapies to support smoking cessation efforts. Both the regulatory pathway for an NRT drug product and the amount of nonclinical or clinical data

needed to support approval will depend on the characteristics of the proposed NRT drug product relative to an approved NRT drug product. This guidance outlines general considerations for NRT drug development and trial design, and FDA encourages sponsors to contact FDA for feedback on their proposed development plans. Sponsors developing an over-the-counter drug product should bear in mind that it is often not possible to answer all regulatory questions in a single trial, and additional sequential steps may be needed.

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 "Smoking Cessation and Related Indications: Developing Nicotine Replacement Therapy Drug Products." 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 draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information 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 collection of information in 21 CFR part 314 for the submission of new drug applications (NDAs), including the submission of labeling under §§ 314.50(e)(2)(ii) and 314.50(l)(1)(i), as well as the submission of 505(b)(2) applications and abbreviated new drug applications, has been approved under OMB control number 0910-0001. The submission of biologics license applications (BLAs) has been approved under OMB control number 0910-

0338. The collection of information in 21 CFR part 312 has been approved under OMB control number 0910-0014.

The submission of prescription drug labeling under 21 CFR 201.56 and 201.57 has been approved under OMB control number 0910-0572. The collections of information in 21 CFR parts 50 and 56 (*Protection of Human Subjects: Informed Consent; Institutional Review Boards*) have been approved under OMB control number 0910-0755.

The collection of information in the draft guidance for industry entitled "Formal Meetings Between FDA and Sponsors and Applicants for PDUFA Products," (available at https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm590547.pdf) including requests for pre-NDA and pre-BLA meetings, has been approved under OMB control number 0910-0429.

The submission of special protocol assessments has been approved under OMB control number 0910-0470.

In accordance with the PRA, prior to publication of any final guidance document, FDA intends to solicit public comment and obtain OMB approval for any information collections recommended in this guidance that are new or that would represent material modifications to those previously approved collections of information found in FDA regulations or guidances.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or https://www.regulations.gov.

Dated: February 15, 2019.

Lowell J. Schiller,

Acting Associate Commissioner for Policy.

[FR Doc. 2019-03064 Filed: 2/21/2019 8:45 am; Publication Date: 2/22/2019]