assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Jason Bunting, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6366, Silver Spring, MD 20993, 301–796–1292, *Jason.Bunting@fda.hhs.gov;* 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, *Stephen.Ripley@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''REMS: FDA's Application of Statutory Factors in Determining When a REMS Is Necessary.'' The Food and Drug Administration Amendments Act of 2007 (FDAAA) (Pub. L. 110–85) created section 505–1 of the FD&C Act (21 U.S.C. 355–1),[1] which authorizes FDA to require a REMS for certain drugs if FDA determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks (see section 505–1(a) of the FD&C Act). FDA can require a REMS before initial approval of a new drug application or, should FDA become aware of ''new safety information'' (as defined in section 505–1(b)(3) of the FD&C Act) about a drug and determine that a REMS is necessary to ensure that the benefits of the drug outweigh its risks, after the drug has been approved (see section 505–1(a)(2) of the FD&C Act).

FDA's determination as to whether a REMS is necessary for a particular drug is a complex, drug specific inquiry, reflecting an analysis of multiple, interrelated factors. Section 505–1(a) of the FD&C Act, as added by FDAAA, requires FDA to consider the following six factors [2] in making a decision about whether to require a REMS:

- The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug;
- The expected benefit of the drug with respect to the disease or condition;
- The seriousness of the disease or condition that is to be treated with the drug;
- Whether the drug is a new molecular entity;
- The expected or actual duration of treatment with the drug; and
- The estimated size of the population likely to use the drug.

These six factors influence FDA's decisions with respect to whether a REMS is required for a particular drug and what type of REMS might be necessary (*i.e.,* what specific elements or tools should be included as part of the REMS). FDA makes decisions about requiring a REMS as part of a benefit-risk determination for a drug after an evaluation that includes integrated consideration of each of the statutory factors. All six factors are considered together to inform FDA's REMS decision making process and no single factor is determinative as to whether a REMS is necessary. The relative importance or weight of each factor is a case specific inquiry. This guidance describes how FDA considers each of these factors in conducting its REMS analysis.

This guidance finalizes the draft guidance entitled ''FDA's Application of Statutory Factors in Determining When a REMS Is Necessary,'' issued September 21, 2016 (81 FR 64911). Interested persons were invited to comment by November 21, 2016. FDA received comments related to how we weigh the six factors when determining if a REMS is necessary, minor clarifying comments on how we apply the six factors, and comments suggesting that FDA expand on which REMS elements or tools should be used when it is determined that a REMS is necessary. FDA has considered all of the public comments received in finalizing this guidance. Clarifying edits were made to address the comments as appropriate. Additionally, edits were made to streamline the guidance, extraneous background information was removed, and the title was modified for clarity.

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 ''REMS: FDA's Application of Statutory Factors in Determining When a REMS Is Necessary.'' 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/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm,* or *https://www.regulations.gov.*

Dated: April 1, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–06663 Filed 4–4–19; 8:45 am]

BILLING CODE 4164–01–P

[1] Section 505–1 of the FD&C Act applies to applications for prescription drugs submitted or approved under subsections 505(b) (*i.e.,* new drug applications) or (j) (*i.e.,* abbreviated new drug applications) (21 U.S.C. 355(b) or (j)) of the FD&C Act and to applications submitted or licensed under section 351 (*i.e.,* biologics license applications) of the Public Health Service Act (42 U.S.C. 262). In this document, unless otherwise specified, the term ''drug'' refers to drug and biological products (or biologics).

[2] Section 505–1(a)(1) of the FD&C Act requires the Agency to consider these factors in determining whether a REMS is necessary for a new drug. FDA also generally considers these factors in determining whether (based on new safety information), a REMS is necessary for a drug that is the subject of an approved application.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA–2011–P–0047, FDA–2012–P–0468, FDA–2015–P–3400, and FDA–2016–P–1667]

Determination That ANTIVERT Chewable Tablets, 25 Milligrams, and Tablets, 12.5 Milligrams, 25 Milligrams, and 50 Milligrams, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that ANTIVERT (meclizine hydrochloride) chewable tablets, 25 milligrams (mg), and tablets, 12.5 mg, 25 mg, and 50 mg, were not withdrawn from sale for reasons of safety or effectiveness. This determination means that FDA will not begin procedures to withdraw approval of abbreviated new drug applications (ANDAs) that refer to these drug products, and it will allow FDA to continue to approve ANDAs that refer to the products as long as they meet relevant legal and regulatory requirements.

FOR FURTHER INFORMATION CONTACT: Linda Jong, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6288, Silver Spring, MD 20993–0002, 301–796–3977.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98–417) (the 1984 amendments), which

authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the ''listed drug,'' which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the ''Approved Drug Products With Therapeutic Equivalence Evaluations,'' which is known generally as the ''Orange Book.'' Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

ANTIVERT (meclizine hydrochloride) chewable tablets, 25 mg, and tablets, 12.5 mg, 25 mg, and 50 mg, are the subject of NDA 010721, currently held by Casper Pharma LLC, and initially approved on February 14, 1957. ANTIVERT is indicated for the treatment of vertigo associated with diseases affecting the vestibular system.

ANTIVERT (meclizine hydrochloride) chewable tablets, 25 mg, and tablets, 12.5 mg, 25 mg, and 50 mg, are currently listed in the ''Discontinued Drug Product List'' section of the Orange Book.

Since 2011, the Agency has received four citizen petitions, submitted under 21 CFR 10.30, requesting that FDA determine whether one or more dosage forms and strengths of ANTIVERT were withdrawn from sale for reasons of safety or effectiveness.

- InvaGen Pharmaceuticals submitted a citizen petition dated January 14, 2011, and amendment dated February 24, 2011 (Docket No. FDA–2011–P–0047), requesting that the Agency determine whether ANTIVERT (meclizine hydrochloride) chewable tablets, 25 mg, was withdrawn from sale for reasons of safety or effectiveness.
- Modavar Pharmaceuticals LLC submitted a citizen petition dated May 4, 2012, (Docket No. FDA–2012–P–0468) requesting that the Agency determine whether ANTIVERT (meclizine hydrochloride) tablets, 12.5 mg and 25 mg, were withdrawn from sale for reasons of safety or effectiveness.
- Lupin Pharmaceuticals, Inc. submitted a citizen petition dated September 18, 2015 (Docket No. FDA–2015–P–3400), requesting that the Agency determine whether ANTIVERT (meclizine hydrochloride) tablets, 12.5 mg, 25 mg, and 50 mg, were withdrawn from sale for reasons of safety or effectiveness.
- Zydus Pharmaceuticals submitted a citizen petition dated June 14, 2016 (Docket No. FDA–2016–P–1667), requesting that the Agency determine whether ANTIVERT (meclizine hydrochloride) tablets, 12.5 mg and 25 mg, were withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petitions and reviewing Agency records, and based on the information we have at this time, FDA has determined under § 314.161 that ANTIVERT (meclizine hydrochloride) chewable tablets, 25 mg, and tablets, 12.5 mg, 25 mg, and 50 mg, were not withdrawn for reasons of safety or effectiveness. The petitioners have identified no data or other information suggesting that these drug products were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of ANTIVERT (meclizine hydrochloride) chewable tablets, 25 mg, and tablets, 12.5 mg, 25 mg, and 50 mg, from sale. We have also independently evaluated relevant literature and data for possible post marketing adverse events. We have found no information that would indicate that these drug products were withdrawn from sale for reasons of safety or effectiveness. Accordingly, the Agency will continue to list ANTIVERT (meclizine hydrochloride) chewable tablets, 25 mg, and tablets, 12.5 mg, 25 mg, and 50 mg, in the ''Discontinued Drug Product List'' section of the Orange Book. The ''Discontinued Drug Product List'' delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. FDA will not begin procedures to withdraw approval of approved ANDAs that refer to these drug products. Additional ANDAs for these drug products may also be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for these drug products should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: April 1, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–06656 Filed 4–4–19; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Office of the Director; Notice of Charter Renewal

In accordance with Title 41 of the U.S. Code of Federal Regulations, Section 102–3.65(a), notice is hereby given that the Charter for the Center for Scientific Review Advisory Council (CSRAC) was renewed for an additional two-year period on March 31, 2019.

It is determined that the CSRAC is in the public interest in connection with the performance of duties imposed on the National Institutes of Health by law, and that these duties can best be performed through the advice and counsel of this group.

Inquiries may be directed to Claire Harris, Acting Director, Office of Federal Advisory Committee Policy, Office of the Director, National Institutes of Health, 6701 Democracy Boulevard, Suite 1000, Bethesda, Maryland 20892 (Mail Code 4875), Telephone (301) 496–2123, or *harriscl@mail.nih.gov.*

Dated: April 1, 2019.

Ronald J. Livingston, Jr.,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2019–06615 Filed 4–4–19; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Proposed Collection; 60-day Comment Request: A Generic Submission for Formative Research, Pretesting and Customer Satisfaction of NCI's Communication and Education Resources (NCI)

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.