

will have a significant impact on small entities.

In addition, section 1102(b) of the Act requires us to prepare a regulatory impact analysis if a rule may have a significant impact on the operations of a substantial number of small rural hospitals. This analysis must conform to the provisions of section 604 of the RFA. For purposes of section 1102(b) of the Act, we define a small rural hospital as a hospital that is located outside of a Metropolitan Statistical Area for Medicare payment regulations and has fewer than 100 beds. We are not preparing an analysis for section 1102(b) of the Act because we have determined, and the Secretary certifies, that this notice would not have a significant impact on the operations of a substantial number of small rural hospitals.

Section 202 of the Unfunded Mandates Reform Act of 1995 (UMRA) also requires that agencies assess anticipated costs and benefits before issuing any rule whose mandates require spending in any 1 year of \$100 million in 1995 dollars, updated annually for inflation. In 2014, that threshold is approximately \$141 million. The Agency has determined that there will be minimal impact from the costs of this notice, as the threshold is not met under the UMRA.

Executive Order 13132 establishes certain requirements that an agency must meet when it promulgates a proposed rule (and subsequent final rule) that imposes substantial direct requirement costs on state and local governments, preempts state law, or otherwise has federalism implications. Since this notice does not impose substantial direct costs on state or local governments, the requirements of Executive Order 13132 are not applicable.

In accordance with the provisions of Executive Order 12866, this notice was reviewed by the Office of Management and Budget.

Dated: October 22, 2014.

**Marilyn Tavenner,**

*Administrator, Centers for Medicare & Medicaid Services.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2014-D-1891]

#### How To Obtain a Letter From the Food and Drug Administration Stating That Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable Risk Evaluation and Mitigation Strategies for Reference Listed Drugs; Draft Guidance for Industry; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD.” This draft guidance describes how a prospective abbreviated new drug application (ANDA) applicant may request a letter stating that FDA has determined the following: The potential applicant’s bioequivalence (BE) study protocol contains safety protections comparable to those in the risk evaluation and mitigation strategy (REMS) with elements to assure safe use (ETASU) applicable to the reference listed drug (RLD) and FDA will not consider it a violation of the REMS for the RLD sponsor to provide a sufficient quantity of the RLD to the interested generic firm or its agent to allow the firm to perform the testing necessary to support its ANDA.

**DATES:** Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by February 3, 2015.

**ADDRESSES:** 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, 10903 New Hampshire Ave., Bldg. 51, Rm. 2201, 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.

Submit electronic comments on the guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

#### FOR FURTHER INFORMATION CONTACT:

Elizabeth Giaquinto, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 1670, Silver Spring, MD 20993, 240-402-7930, [Elizabeth.Giaquinto@fda.hhs.gov](mailto:Elizabeth.Giaquinto@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

FDA is announcing the availability of a draft guidance for industry entitled “How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD.” Section 505-1(a)(1) of the FD&C Act authorizes FDA to require applicants to submit a proposed REMS as a part of the relevant application<sup>1</sup> if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh its risks (21 U.S.C. 355-1(a)(1)). A REMS is a required risk management plan that uses tools beyond routine professional labeling (such as a medication guide, a patient package insert, and/or a communication plan) to ensure that the benefits of a drug outweigh its risks (section 505-1(f) of the FD&C Act). In addition, FDA may require ETASU in some circumstances when such elements are necessary to mitigate the risks associated with the drug. ETASU may include, for example, requirements that health care providers who prescribe or administer the drug have particular training or certification; that patients using the drug be monitored and/or enrolled in a registry; or that pharmacies, practitioners, or health care settings that dispense the drug be specially certified.

FDA is aware of instances in which an RLD sponsor has refused to sell drug products to a prospective ANDA applicant seeking to conduct the testing needed to obtain approval, and the RLD sponsor has cited the REMS ETASU as justification. In the interest of facilitating prospective generic applicants’ access to RLD products to conduct the testing necessary to support ANDA approval, FDA has, on request, reviewed the BE study protocols proposed by a prospective ANDA

<sup>1</sup> Section 505-1 of the FD&C Act applies to any application for approval of a prescription drug submitted under section 505(b) or (j) of the FD&C Act (including both NDAs submitted under section 505(b)(2) and ANDAs submitted under section 505(j)), as well as applications submitted under section 351 of the Public Health Service Act (42 U.S.C. 262).

applicant to assess whether they provide safety protections comparable to those in the applicable REMS ETASU. When the Agency has determined that comparable protections existed, FDA has issued letters to the RLD sponsor stating so, and indicating that FDA would not consider it to be a violation of the REMS for the RLD sponsor to provide drug product to the prospective ANDA applicant or its agent.

Requesting or obtaining such a letter from FDA is not a legal requirement. If a prospective ANDA applicant chooses to request such a letter, this guidance is intended to clarify the process for doing so.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on how a prospective generic applicant can obtain a letter stating that its BE study protocols contain safety protections comparable to those in the applicable REMS for the RLD. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public.

**II. Comments**

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and

will be posted to the docket at <http://www.regulations.gov>.

**III. The 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 under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR parts 312 and 314 have been approved under OMB control numbers 0910–0014 and 0910–0001.

**IV. Electronic Access**

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: December 1, 2014.

**Leslie Kux,**

*Associate Commissioner for Policy.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA–2014–N–1795]

**Mallinckrodt Inc. et al.; Withdrawal of Approval of 23 New Drug Applications and 68 Abbreviated New Drug Applications**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is withdrawing approval of 23 new drug applications (NDAs) and 68 abbreviated new drug applications (ANDAs) from multiple applicants. The holders of the applications notified the Agency in writing that the drug products were no longer marketed and requested that the approval of the applications be withdrawn.

**DATES:** *Effective Date:* January 5, 2015.

**FOR FURTHER INFORMATION CONTACT:**

Florine P. Purdie, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6248, Silver Spring, MD 20993–0002, 301–796–3601.

**SUPPLEMENTARY INFORMATION:** The holders of the applications listed in table 1 in this document have informed FDA that these drug products are no longer marketed and have requested that FDA withdraw approval of the applications pursuant to the process in § 314.150(c) (21 CFR 314.150(c)). The applicants have also, by their requests, waived their opportunity for a hearing. Withdrawal of approval of an application or abbreviated application under § 314.150(c) is without prejudice to refiling.

TABLE 1

Application No.	Drug	Applicant
NDA 002852 .....	Plexofer (multivitamins) Syrup .....	Mallinckrodt Inc., 675 McDonnell Blvd., Hazelwood, MO 63042.
NDA 008719 .....	Levo-Dromoran (levorphanol tartrate) Injection, 2 milligrams (mg)/milliliter (mL).	Valeant Pharmaceuticals North America LLC, 400 Somerset Corporate Blvd., Bridgewater, NJ 08807.
NDA 008720 .....	Levo-Dromoran (levorphanol tartrate) Tablets, 2 mg .....	Do.
NDA 011777 .....	Sodium Phosphate P 32 Solution .....	Mallinckrodt Inc.
NDA 012366 .....	Soma Compound with Codeine (carisoprodol, aspirin, and codeine phosphate).	Meda Pharmaceuticals Inc., 265 Davidson Ave., Suite 300, Somerset, NJ 08873–4120.
NDA 012708 .....	Diutensen-R (methyclothiazide and reserpine) Tablets, 2.5 mg/0.1 mg.	Do.
NDA 016245 .....	Vercyte (pipobroman) Tablets .....	AbbVie, Inc., 1 North Waukegan Rd., Dept. PA 77/Bldg. AP30, North Chicago, IL 60064.
NDA 017463 .....	Motrin (ibuprofen) Tablets, 300 mg, 400 mg, 600 mg, and 800 mg.	McNeil Consumer Healthcare Division of McNeil-PPC, Inc., 7050 Camp Hill Rd., Fort Washington, PA 19034–2299.
NDA 018310 .....	Lymphazurin (isosulfan blue), 1% .....	Covidien, 60 Middletown Ave., North Haven, CT 06473.
NDA 018340 .....	Aerobid (flunisolide) Inhalation Aerosol <sup>1</sup> .....	Roche Palo Alto LLC, c/o Genentech Inc., 1 DNA Way, South San Francisco, CA 94080–4990.
NDA 018731 .....	Buspar (buspirone hydrochloride (HCl)) Tablets, 5 mg, 10 mg, 15 mg, and 30 mg.	Bristol-Myers Squibb Co., P.O. Box 4000, Princeton, NJ 08543–4000.
NDA 019453 .....	Drixoral (dextbrompheniramine maleate, pseudoephedrine sulfate, and acetaminophen) Extended-Release Tablets, 3 mg, 60 mg, and 500 mg.	Merck Consumer Care, 556 Morris Ave., Summit, NJ 07901.