

56469, September 18, 2015, or access the information at: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

**Docket:** For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://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 Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building., 4th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, or 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 See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:** Amalia Himaya, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6439, Silver Spring, MD 20993-0002, 301-796-0700; or 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.

#### **SUPPLEMENTARY INFORMATION:**

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

FDA is announcing the availability of a draft guidance for industry entitled "Special Protocol Assessment." SPA is a process by which sponsors may request to meet with FDA to reach agreement on the design and size of certain trials, clinical studies, or animal trials to determine if they adequately address scientific and regulatory requirements. After completing the SPA review, FDA issues a letter including an assessment of the protocol, agreement or nonagreement with the proposed protocol, and answers to the sponsor's relevant questions. Section 119 of the Food and Drug Administration Modernization Act of 1997 amended section 505(b) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(b)) and directed FDA to

meet with sponsors who request to meet, provided certain conditions are met, to reach agreement on the design and size of the well-controlled clinical trials intended to form the primary basis for a demonstration of effectiveness in a marketing application submitted under section 505(b) of the FD&C Act or section 351 of the Public Health Service (PHS) Act (42 U.S.C. 262). These provisions subsequently were amended in section 7002(d)(1) of the Biologics Price Competition and Innovation Act of 2009 to include any necessary clinical study or studies for biosimilar biological product applications under section 351(k) of the PHS Act. In 2013, the Pandemic and All Hazards Preparedness Reauthorization Act of 2013 (Pub. L. 113-5) further amended the SPA provisions to provide for SPA agreements regarding animal and associated clinical trials conducted in support of applications for products developed under 21 CFR part 314 subpart I, and 21 CFR part 601 subpart H (the animal rule). Such marketing applications include new drug applications (NDAs), biologics license applications (BLAs), and efficacy supplements to approved NDAs and BLAs.

In conjunction with the Prescription Drug User Fee Amendments of 2012 (PDUFA V), enacted as part of the Food and Drug Administration Safety and Innovation Act (FDASIA), and with the Biosimilar User Fee Act of 2012 (BsUFA), enacted as part of FDASIA, FDA agreed to specific performance goals (PDUFA V goals and BsUFA goals, respectively) for SPA. Per section 505(b)(5)(B) of the FD&C Act, the PDUFA V goals, and the BsUFA goals, the following protocols are eligible for SPA: (1) Animal carcinogenicity protocols; (2) drug substance and drug product stability protocols; (3) animal efficacy protocols for studies intended to provide primary evidence of effectiveness required for approval or for licensure for products developed under the animal rule; (4) protocols for clinical trials or studies intended to form the primary basis of an efficacy claim; and (5) protocols for clinical studies necessary to prove biosimilarity and/or interchangeability.

This draft guidance revises the guidance of the same name issued in May 2002. After it has been finalized, this guidance will replace the May 2002 guidance. Significant changes from the 2002 version include the following: (1) Clarifying which protocols are eligible for SPA; (2) adding animal rule efficacy protocols intended to support approval under part 314 subpart I, and part 601 subpart H, for drugs and biological

products, respectively; (3) adding protocols intended to support approval of a biosimilar biological product; (4) providing greater detail about the content of an SPA submission; and (5) clarifying the process for rescinding an SPA agreement. FDA seeks comments to aid in finalizing this draft guidance.

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 the procedural aspects of SPA. 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. The Paperwork Reduction Act of 1995**

This draft 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 referred to in the guidance entitled "Special Protocol Assessment" have been approved under OMB control number 0910-0470. The collections of information for FDA Form 1571 have been approved under OMB control number 0910-0014.

##### **III. Electronic Access**

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

Dated: April 28, 2016.

**Leslie Kux,**

*Associate Commissioner for Policy.*

[FR Doc. 2016-10391 Filed 5-3-16; 8:45 am]

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#### **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

##### **Food and Drug Administration**

[Docket No. FDA-2013-P-1654]

##### **Determination That LEUCOVORIN CALCIUM (Leucovorin Calcium) Injectable and Other Drug Products 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 the drug products listed in this document 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:**

Stacy Kane, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6207, Silver Spring, MD 20993-0002, 301-796-8363, [Stacy.Kane@fda.hhs.gov](mailto:Stacy.Kane@fda.hhs.gov).

**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 approved 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 generally known as the "Orange Book." Under FDA regulations, a drug is 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).

Under § 314.161(a) (21 CFR 314.161(a)), the Agency must determine whether a listed drug was withdrawn from sale for reasons of safety or effectiveness: (1) Before an ANDA that refers to that listed drug may be approved, (2) whenever a listed drug is voluntarily withdrawn from sale and ANDAs that refer to the listed drug have been approved, and (3) when a person petitions for such a determination under 21 CFR 10.25(a) and 10.30. Section 314.161(d) provides that if FDA determines that a listed drug was withdrawn from sale for safety or effectiveness reasons, the Agency will initiate proceedings that could result in the withdrawal of approval of the ANDAs that refer to the listed drug.

FDA has become aware that the drug products listed in the table in this document are no longer being marketed.

Application No.	Drug name	Active ingredient(s)	Strength(s)	Dosage form/route	Applicant
NDA 008107 .....	LEUCOVORIN CALCIUM.	Leucovorin Cal- cium.	Equivalent to (EQ) 3 milligrams (mg) base/milliliter (mL); EQ 50 mg base/ vial; EQ 100 mg base/vial; EQ 350 mg base/vial.	Injectable; Injection	Hospira, Inc.
NDA 009986 .....	DELTASONE .....	Prednisone .....	2.5 mg; 5 mg; 10 mg; 20 mg; 50 mg ..	Tablet; Oral .....	Pharmacia & Upjohn Co.
NDA 010392 .....	ATARAX .....	Hydroxyzine Hy- drochloride.	10 mg; 25 mg; 50 mg; 100 mg .....	Tablet; Oral .....	Pfizer Inc.
NDA 016727 .....	PROLIXIN DECANOATE.	Fluphenazine Decanoate.	25 mg/mL .....	Injectable; Injection	Bristol-Myers Squibb
NDA 018031 .....	INDERIDE-40/25 and IINDERIDE 80/20.	Hydrochlorothiazid- e; Propranolol.	Hydrochloride 25 mg; 40 mg and 25 mg; 80 mg.	Tablet; Oral .....	Wyeth Pharma- ceuticals Inc.
NDA 019279 .....	DIMETANE-DX ....	Brompheniramine Maleate; Dextromethorphan Hydrobromide; Pseudoephedrine Hydrochloride.	2 mg/5 mL; 10 mg/5 mL; 30 mg/5 mL	Syrup; Oral .....	A.H. Robins Com- pany
NDA 050007 .....	VIBRAMYCIN .....	Doxycycline Hyclate.	EQ 50 mg base .....	Capsule; Oral .....	Pfizer Inc.
ANDA 061639 ..	E.E.S. 200 and E.E.S. 400.	Erythromycin Ethylsuccinate.	EQ 200 mg base/5 mL; EQ 400 mg base/5 mL.	Suspension; Oral ..	Arbor Pharma- ceuticals, LLC
ANDA 062736 ..	BACTOCILL .....	Oxacillin Sodium ...	EQ 1 gram (g) base/vial; EQ 2 g base/ vial.	Injectable; Injection	GlaxoSmithKline
ANDA 065012 ..	CEFOXITIN .....	Cefoxitin Sodium ..	EQ 1 g base/vial; EQ 2 g base/vial .....	Injectable; Injection	Fresenius Kabi USA

FDA has reviewed its records and, under § 314.161, and has determined that the drug products listed in this document were not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the Agency will continue to list the drug products listed in this document in the "Discontinued Drug Product List" section of the Orange Book. The

"Discontinued Drug Product List" identifies, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness.

Approved ANDAs that refer to the NDAs and ANDAs listed in this document are unaffected by the discontinued marketing of the products subject to those NDAs and ANDAs. Additional ANDAs that refer to these

products may also be approved by the Agency if they comply with relevant legal and regulatory requirements. 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 27, 2016.

**Leslie Kux,**

*Associate Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2016-P-0159]

#### Medical Devices; Exemption From Premarket Notification: Method, Metallic Reduction, Glucose (Urinary, Non-Quantitative) Test System in a Reagent Tablet Format

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

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that it has received a petition requesting exemption from the premarket notification requirements for a method, metallic reduction, glucose (urinary, non-quantitative) test system in a reagent tablet format that is intended to measure glucosuria (glucose in urine). Method, metallic reduction, glucose (urinary, non-quantitative) test systems in a reagent tablet format are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, hypoglycemia, and hyperglycemia. FDA is publishing this notice to obtain comments in accordance with procedures established by the Food and Drug Administration Modernization Act of 1997 (FDAMA).

**DATES:** Submit either electronic or written comments by June 3, 2016.

**ADDRESSES:** You may submit comments as follows:

#### Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal:* <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://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 <http://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):* Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, 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-2016-P-0159 for "Medical Devices; Exemption From Premarket Notification: Method, Metallic Reduction, Glucose (Urinary, Non-Quantitative) Test System in a Reagent Tablet Format." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management 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 <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. 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: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://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 Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Ana Loloei Marsal, Center for Devices and Radiological Health (CDRH), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4552, Silver Spring, MD 20993-0002, 301-796-8774, [anahita.loloeimarsal@fda.hhs.gov](mailto:anahita.loloeimarsal@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Statutory Background

Under section 513 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360c), FDA must classify devices into one of three regulatory classes: class I, class II, or class III. FDA classification of a device is determined by the amount of regulation necessary to provide a reasonable assurance of safety and effectiveness. Under the Medical Device Amendments of 1976 (1976 amendments) (Pub. L. 94-295), as amended by the Safe Medical Devices Act of 1990 (Pub. L. 101-629), devices are to be classified into class I (general controls) if there is information showing that the general controls of the FD&C Act are sufficient to assure safety and effectiveness; into class II (special controls) if general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide such assurance; and into class III (premarket approval) if there is insufficient information to support classifying a device into class I or class II and the device is a life sustaining or life supporting device, or is for a use which is of substantial importance in preventing impairment of human health or presents a potential unreasonable risk of illness or injury.

Most generic types of devices that were on the market before the date of