DEPARTMENT OF HEALTH & HUMAN SERVICES

HFA-305

Public Health Service

Food and Drug Administration
Rockville MD 20857

3955 7 AUG 13 P2:16

August 10, 2007

Tania Hoffman
Project Specialist, Regulatory Affairs
SICOR Pharmaceuticals, Inc.
19 Hughes
Irvine, CA 92618-1902

Re: Docket No. 2006P-0520/CP1

Dear Ms. Hoffman:

This letter responds to your citizen petition, dated December 15, 2006, requesting that the Food and Drug Administration (FDA) determine whether methotrexate injection, USP, preservative free, equivalent to (Eq.) 500 milligrams (mg) base/20 milliliters (mL) (25 mg/mL)(new drug application No. 11-719 held by Mayne Pharma USA) was withdrawn from sale for reasons of safety or effectiveness.

The FDA has reviewed its records and determined that methotrexate injection, USP, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), was not withdrawn from sale for reasons of safety or effectiveness. Thus, the FDA will maintain methotrexate injection, USP, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), in the "Discontinued Drug Product List" of the *Approved Drugs With Therapeutic Equivalence Evaluations* (the Orange Book).

Enclosed is a copy of the *Federal Register* notice that announces the FDA determination. If you require further information, please feel free to call me at (301) 594-2041.

Sincerely,

Elena Cohen
Division of Regulatory Policy II
Office of Regulatory Policy
Center for Drug Evaluation and Research

Enclosure

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of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

Under § 314.161(a)(1) (21 CFR 314.161(a)(1)), the agency must determine whether a listed drug was withdrawn from sale for reasons of safety or effectiveness before an ANDA that refers to that listed drug may be approved. FDA may not approve an ANDA that does not refer to a listed drug.

MIVACRON (mivacurium chloride) injection EQ 2 mg base/mL is the subject of approved NDA 20–098 held by Abbott Laboratories, Inc. (Abbott). MIVACRON is a short-acting neuromuscular blocking agent indicated for inpatients and outpatients, as an adjunct to general anesthesia, to facilitate tracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation. FDA approved the NDA for MIVACRON on January 22, 1992. Abbott ceased marketing MIVACRON in July 2006.

Regulus Pharmaceutical Consulting, Inc., submitted a citizen petition dated October 25, 2006 (Docket No. 2006P–0445/CP1), under 21 CFR 10.30, requesting that the agency determine, as described in § 314.161, whether MIVACRON (mivacurium chloride) injection EQ 2 mg base/mL was withdrawn from sale for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that MIVACRON was withdrawn from sale as a result of safety or effectiveness concerns.

We have reviewed our records and determined that Abbott's MIVACRON (mivacurium chloride) injection EQ 2 mg base/mL was not withdrawn from sale for reasons of safety or effectiveness. We have also independently evaluated relevant literature and data for adverse event reports and have determined that this product was not withdrawn for reasons of safety or effectiveness.

After considering the citizen petition and reviewing its records, FDA has determined that, for the reasons outlined in this notice, Abbott's MIVACRON (mivacurium chloride) injection EQ 2 mg base/mL was not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will list MIVACRON (mivacurium chloride) injection EQ 2 mg base/mL 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. ANDAs that refer to MIVACRON (mivacurium chloride) injection EQ 2 mg base/mL may be approved by the agency as long as they meet all relevant legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the agency will advise ANDA applicants to submit such labeling.

Dated: July 30, 2007.

Randall W. Lutter,

Deputy Commissioner for Policy.

[FR Doc. E7–15488 Filed 8–7–07; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2006P–0520]

Determination That Methotrexate Injection, USP, Preservative Free, Equivalent to 500 Milligrams Base/20 Milliliters (25 Milligrams/Milliliter), Was 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) has determined that methotrexate injection, USP, preservative free, equivalent to (Eq.) 500 milligrams (mg) base/20 milliliters (mL) (25 mg/mL), was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for methotrexate injection, preservative free, Eq. 500 mg base/20 mL (25 mg/mL).

FOR FURTHER INFORMATION CONTACT: Elena Cohen, Center for Drug Evaluation and Research (HFD–7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–2041.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 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 typically 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 only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

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, 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).

Under 21 CFR 314.161(a)(1), the agency must determine whether a listed drug was withdrawn from sale for reasons of safety or effectiveness before an ANDA that refers to that listed drug may be approved. FDA may not approve an ANDA that does not refer to a listed drug.

Methotrexate injection, USP, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), is the subject of approved NDA 11–719 currently held by Mayne Pharma USA (Mayne). Although NDA 11–719 was originally approved in 1959, this formulation and dosage was approved in April 2005 (S–108). Methotrexate is an antifolate cytotoxic drug used in the treatment of a variety of malignancies, including acute lymphoblastic leukemia, osteosarcoma, advanced metastatic breast cancer, and others. It is also used to treat some inflammatory conditions such as rheumatoid arthritis. To date, Mayne has not marketed methotrexate injection, USP, preservative free, Eq. 500 mg base/20 mL (25 mg/mL). At the request of the sponsor, the product was moved to the discontinued section of the Orange Book in June 2005. In previous instances (see, e.g., the **Federal Register** document of December 30, 2002 (67 FR 79640), addressing a relisting request for Diazepam Autoinjector), the agency has determined that, for purposes of §§ 314.161 and 314.162, never marketing an approved drug product is equivalent to withdrawing the drug from sale.

SICOR Pharmaceuticals, Inc., submitted a citizen petition dated

December 15, 2006 (Docket No. 2006P-0520/CP1), under 21 CFR 10.30, requesting that the agency determine whether methotrexate injection, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), was withdrawn from sale for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that methotrexate injection, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), was withdrawn from sale for reasons of safety or effectiveness. FDA has independently evaluated relevant literature and data for possible postmarketing adverse events and has found no information that would indicate this product was withdrawn for reasons of safety or effectiveness.

After considering the citizen petition and reviewing agency records, FDA has determined that, for the reasons outlined in this document, methotrexate injection, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), was not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will continue to list methotrexate injection, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), 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. ANDAs that refer to methotrexate injection, preservative free, Eq. 500 mg base/20 mL (25 mg/mL), may be approved by the agency as long as they meet all relevant 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: July 30, 2007.

Randall W. Lutter,

Deputy Commissioner for Policy.

[FR Doc. E7-15490 Filed 8-7-07; 8:45 am]

BILLING CODE 4160-01-S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2002D-0081]

Guidance for Industry: Adequate and Appropriate Donor Screening Tests for Hepatitis B; Hepatitis B Surface Antigen Assays Used to Test Donors of Whole Blood and Blood Components, Including Source Plasma and Source Leukocytes; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a document entitled "Guidance for Industry: Adequate and Appropriate Donor Screening Tests for Hepatitis B; Hepatitis B Surface Antigen (HBsAg) Assays Used to Test Donors of Whole Blood and Blood Components, Including Source Plasma and Source Leukocytes" dated July 2007. The guidance document provides recommendations to manufacturers of HBsAg assays that are intended to test donors of Whole Blood and blood components, including Source Plasma and Source Leukocytes, and to establishments using an HBsAg assay. Topics include recommendations on minimum sensitivity standards for HBsAg assays. This guidance finalizes the draft guidance entitled "Guidance for Industry: A Modified Lot-Release Specification for Hepatitis B Surface Antigen (HBsAg) Assays Used to Test Blood, Blood Components, and Source Plasma Donations" dated April 2002.

DATES: Submit written or electronic comments on agency guidances at any time.

ADDRESSES: Submit written requests for single copies of the guidance to the Office of Communication, Training, and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist the office in processing your requests. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 301-827-1800. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

Submit written comments on the guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments.*

FOR FURTHER INFORMATION CONTACT: Joseph L. Okrasinski, Jr., Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448, 301-827-6210.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a document entitled "Guidance for Industry: Adequate and Appropriate Donor Screening Tests for Hepatitis B; Hepatitis B Surface Antigen (HBsAg) Assays Used to Test Donors of Whole Blood and Blood Components, Including Source Plasma and Source Leukocytes" dated July 2007. The guidance document provides recommendations to manufacturers of HBsAg assays that are approved donor screening tests intended to screen donors of Whole Blood and blood components, including Source Plasma and Source Leukocytes for Hepatitis B, and to establishments using an HBsAg assay (See § 610.40(b) (21 CFR 610.40(b)). The document represents FDA's current thinking on minimum sensitivity for such HBsAg assays as they relate to donor testing "to reduce adequately and appropriately the risk of transmission of communicable disease" under § 610.40(b). Under 21 CFR 610.44, the manufacturers of HBsAg assays used to test donations must verify acceptable sensitivity and specificity of such kits by testing the kit-lots using an FDA reference panel. This guidance document recommends that all HBsAg detection assays used to test donors of Whole Blood and blood components, including Source Plasma and Source Leukocytes, have a lower limit of detection standard of 0.5ng HBsAg/mL or less.

In the **Federal Register** of April 11, 2002 (67 FR 17704), FDA announced the availability of the draft guidance entitled "Guidance for Industry: A Modified Lot-Release Specification for Hepatitis B Surface Antigen (HBsAg) Assays Used to Test Blood, Blood Components, and Source Plasma Donations." FDA received a few comments on the draft guidance, and those comments were considered as the guidance was finalized. In addition, editorial changes were made to improve clarity. The recommended implementation date for the recommendations in this guidance is January 31, 2008. This guidance document finalizes the draft guidance document entitled "Guidance for