DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-928/S-008

Pfizer Inc
235 East 42nd Street
New York City, NY 10017

Attention: Samantha McNamara
Director, US Regulatory Affairs

Dear Ms. McNamara:

Please refer to your supplemental new drug application dated and received on January 18, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Chantix (varenicline).

We acknowledge receipt of your submission dated April 10, 2008.

This supplemental new drug application provides for the addition of a Medication Guide to the Chantix product labeling, which replaces the previously-approved Patient Package Insert.

We have completed our review of this supplemental new drug application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the Medication Guide).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA.* Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 21-928/S-008.**" Approval of this submission by FDA is not required before the labeling is used.

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENT

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a REMS for an approved drug if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since Chantix was approved on May 10, 2006, as an aid to smoking cessation treatment, we have become aware of postmarketing reports of neuropsychiatric symptoms, including changes in behavior, agitation, depressed mood, and suicidal thoughts or actions associated with Chantix. This information was not available when Chantix was granted marketing authorization as an aid to smoking cessation treatment. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

Your proposed REMS must contain the following:

Medication Guide: As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Under 21 CFR Part 208 and in accordance with 505-1, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Chantix. Pursuant to 21 CFR Part 208, FDA has determined that Chantix poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Chantix. FDA has determined that Chantix is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use Chantix.

Communication Plan: We have determined that a communication plan to healthcare providers who are likely to prescribe Chantix will support implementation of the elements of your REMS. The communication plan must provide for the dissemination of information about Chantix, including the Medication Guide and other prescriber materials, to encourage implementation by health care providers.

Timetable for Assessment: The proposed REMS must include a timetable for assessment of the REMS that shall be no less frequent than at 18 months, 3 years, and 7 years after the REMS is approved. The REMS, once approved, will create enforceable obligations.

Information needed for assessment of the REMS should include but may not be limited to:

a. A survey of patients' and prescribers' understanding of the serious risks of Chantix
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

In accordance with section 505-1, within 120 days of the date of this letter, you must submit a prior-approval supplement containing your proposed REMS.

A suggested template for the REMS is included in Attachment A.

You should also provide a REMS Supporting Document that explains the rationale for each of the elements of the REMS. It should include the following sections:

1. Background
2. Goals
3. Rationale for proposed REMS
    a. Description of and rationale for each of the REMS elements (see section 505-1(e) of the FDCA, as amended by FDAAA)

b. Description of and rationale for the proposal for assessing the REMS (see section 505-1(d) of the FDCA)

Use the following designator to prominently label all submissions, including supplements, relating to the REMS:

Risk Evaluation and Mitigation Strategy (REMS)

You should not wait for approval of your proposed REMS to begin to use the Medication Guide approved with this letter.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Title IX, Subtitle A, Section 901 of FDAAA amends the FDCA to authorize FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)). This provision took effect on March 25, 2008.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the known serious risk of neuropsychiatric symptoms, including changes in behavior, agitation, depressed mood, and suicidal thoughts or actions related to the use of Chantix.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to assess this known serious risk.

Therefore, based on the new safety information described above, FDA has determined that you are required, pursuant to section 505(o)(3) of the FDCA, to conduct postmarketing clinical study(ies) or trial(s) of Chantix to assess the known serious risk of neuropsychiatric symptoms, including changes in behavior, agitation, depressed mood, and suicidal thoughts or actions. The specific details of the required postmarketing clinical study(ies) or trial(s) will be described more fully in a future letter.

REPORTING REQUIREMENTS

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

PROMOTIONAL MATERIALS

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the revised product labeling and has determined that it contains significant new risk information relating to your drug product. All promotional materials for your drug product that include representations about your drug product must be revised to include the new risk information promptly as provided for under 21 CFR 314.70(a)(4). These revisions should include prominent disclosure of the important new information presented in the Medication Guide and further described in the WARNINGS and PRECAUTIONS sections in the revised package insert labeling.

If you have any questions, call Dominic Chiapperino, Regulatory Project Manager, at (301) 796-1183.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, M.D.
Director
Division of Anesthesia, Analgesia, and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Attachment A (recommended format for REMS proposal) and package insert and Medication Guide labeling

Attachment A

NDA 21-928 Chantix (varenicline)

PROPOSED RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL:

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each Chantix prescription. [Describe in detail how you will comply with 21 CFR 208.24.]

B. Communication Plan

Pfizer will implement a communication plan to healthcare providers to support implementation of this REMS:

1. The audience is healthcare professionals (HCPs)
2. Pfizer will provide physicians and pharmacists with the educational materials listed below that describe the key risks and benefits of Chantix:
    a. Prescriber materials:
        i. List materials
    b. Pharmacist materials (if applicable)
        i. List any pharmacist materials
    c. All final communication and educational materials listed above are to be appended to the REMS.
3. List other communication plans if applicable
4. Distribution of materials:
    a. Describe how materials will be distributed.

C. Elements To Assure Safe Use

Chantix has been shown to be effective but is associated with a risk of neuropsychiatric adverse events. This REMS for Chantix can be approved without any elements to assure safe use.

D. Implementation System

Because this REMS for Chantix can be approved without any elements to assure safe use, an implementation system is not required.

III. ASSESSMENT OF REMS:

A. Timetable for Assessments

REMS Assessments will be submitted to FDA no less frequently than at 18 months, 3 years, and 7 years after approval.

B. Information Needed for Assessments

a. A survey of patients' and prescribers' understanding of the serious risks of Chantix
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

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/s/

Bob Rappaport

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