DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 20-632/S-032

Abbott Laboratories
Attention: Richard Leber
Manager, Global Pharmaceutical Regulatory Affairs (GPRA)
Dept. PA76, Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Mr. Leber:

Please refer to your supplemental new drug application dated and received April 15, 2009, submitted under section 505(b), of the Federal Food, Drug, and Cosmetic Act (FDCA) for Meridia (sibutramine hydrochloride monohydrate) Capsules, 5, 10, and 15 mg.

Reference is also made to our letter dated March 16, 2009, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Meridia. This information pertains to the risk of neuroleptic malignant syndrome (NMS) associated with use of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), both with and without co-administration of antipsychotic drugs.

This supplemental new drug application provides for revisions to the labeling for Meridia consistent with our March 16, 2009, letter. The following subsection has been added to the **WARNINGS** section of the package insert:

> **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-Like Reactions** —
>
> The development of a potentially life-threatening serotonin syndrome, or Neuroleptic Malignant Syndrome (NMS)-like reactions, has been reported with SNRIs and SSRIs alone, including Meridia treatment, but particularly with concomitant use of serotonergic drugs (including triptans), with drugs which impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms [e.g., nausea, vomiting, diarrhea] (see **PRECAUTIONS, Drug Interactions**). Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms.

In addition, the mention of serotonin syndrome in the **Postmarketing Reports** subsection (*Nervous System*) of the **ADVERSE REACTIONS** section of labeling has been deleted, since this reaction is discussed more prominently as a warning. The subsection now reads as follows:

> *Nervous System*
>
> abnormal dreams, abnormal gait, amnesia, anger, cerebrovascular accident, concentration impaired, confusion, depression aggravated, Gilles de la Tourette's syndrome, hypesthesia, libido decreased, libido increased, mood changes, nightmares, short term memory loss, speech disorder, transient ischemic attack, tremor, twitch, vertigo**.**

We have completed our review of this supplemental application and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revision listed below.

> To the first sentence of the new **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-Like Reactions** subsection of the **WARNINGS** section, change "of" to "or" (*To read "…with antipsychotics or other dopamine antagonists."*)

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). The revision noted above is a term of the supplemental NDA approval. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "**SPL for approved NDA 20-632/S-032**."

We also request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

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
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Pat Madara, Regulatory Project Manager in the Division of Metabolism and Endocrinology Products, at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Package Insert

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Eric Colman

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Eric Colman for Mary Parks