DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-717/S-020

Cephalon, Inc.
Attention: James M. Ciciriello, RPh
Director, Regulatory Affairs
41 Moores Road
P.O. Box 4011
Frazer, PA 19355

Dear Mr. Ciciriello:

Please refer to your supplemental new drug application dated May 4, 2005, received May 6, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Provigil® (modafinil) Tablets, 100 mg and 200 mg.

We acknowledge receipt of your additional submissions dated May 25, 2005, August 6, 2007 and August 15, 2007.

This supplemental new drug application originally provided for revisions to the CLINICAL PHARMACOLOGY and PRECAUTIONS sections.

We also refer to our action letter dated September 21, 2006 for ---------- This letter requested that revisions to the Provigil product labeling be made to include information regarding serious skin rash, psychiatric symptoms, multi-organ hypersensitivity, and pediatric use.

Furthermore, our March 28, 2007 action letter for NDA 21-875, Nuvigil™ (armodafinil) Tablets, requested that you adopt a bolded statement in the Warnings section of the labeling describing the risk of developing serious skin and other hypersensitivity reactions associated with the use of modafinil. Subsequent to this letter, it was agreed that the Warnings sections of both the Nuvigil and Provigil labeling would contain a bolded statement describing these risks. Your August 6, 2007 submission in conjunction with a telephone conversation on August 16, 2007, reflected these agreements. Specifically, in the August 16, 2007 telephone conversation, it was agreed that the following statement would be included as a bolded statement in the Warnings section of the Provigil labeling:

"**Modafinil is not approved for use in pediatric patients for any indication.**"

This supplemental new drug application, S-020, fulfills the label change requested in our September 21, 2006 letter and reflects the agreement that the aforementioned bolded statement would be adopted into the Provigil product labeling.

We have completed our review of this supplemental application, S-020, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon enclosed labeling text.

CONTENT OF LABELING

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 and text for the patient package insert) and/or submitted labeling (package insert and patient package insert submitted on August 6, 2007). 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 20-717."

SUPERCEDE

We have reviewed the content of the following labeling supplements, and we note that these changes have been incorporated into the enclosed labeling text. Therefore, the supplemental applications listed below have been superceded and will be retained in our files with no further action.

Supplement Number:	Date Submitted:
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POSTMARKETING COMMITMENTS

We remind you of your postmarketing study commitments in your submissions dated August 6, 2007 and August 15, 2007 to NDA 20-717 and June 11, 2007 to NDA 21-875. Your June 11, 2007 submission noted your agreement to provide a Risk Minimization Action Plan (RiskMAP) and Pregnancy Registry protocol for both Provigil and Nuvigil. These commitments are described in greater detail and are listed below.

1. Description of Commitment – Provide a RiskMAP for Provigil to address the risk of serious rash and other hypersensitivity reactions (See **RiskMAP** below for additional comments).

   Submission of Draft RiskMAP: Eight weeks after approval of S-020
   Implementation: Eight weeks after concurrence with the Agency

2. Description of Commitment – Provide a Pregnancy Registry protocol for Provigil to obtain systematically collected data on the effects of exposures during pregnancy, labor, and delivery in women of child-bearing age.

   Submission of Protocol: by 07/16/07
   Implementation: Upon concurrence with the Agency

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each

commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

RISK MINIMIZATION ACTION PLAN (RiskMAP)

You have agreed to submit a comprehensive RiskMAP to address the risk of serious skin and other hypersensitivity reactions. Your RiskMAP should include the following components:

- Implementation of a program and distribution of materials to educate prescribers, other healthcare providers and patients about the risks and benefits of Provigil.
- Implementation of a plan to promote Provigil only to prescribers for the approved indications in adult patients, and to limit prescribing in pediatric patients.
- Implementation of a reporting and data collection system for safety surveillance.
- Implementation of a plan to monitor and evaluate the effectiveness of the RiskMAP in communicating and minimizing the risk of serious skin and other hypersensitivity reactions and limiting the use of Provigil in pediatric patients.

The following documents should be submitted:

- A draft version of the RiskMAP document that includes the components listed above. We refer you to the RiskMAP guidance available at http://www.fda.gov/cder/guidance/6358fnl.htm.
- A copy of all healthcare provider and patient educational materials to be provided as part of the RiskMAP program.
- A plan for ongoing assessment (including monitoring for prescribing in pediatric patients) and periodic reporting to FDA of the operation of the RiskMAP and any needed revisions.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

"DEAR HEALTHCARE PROFESSIONAL" LETTERS

Although a Dear Healthcare Professional letter is a planned part of the Provigil RiskMAP, we note your agreement to mail the Dear Healthcare Professional letter within 4 weeks of the approval of this supplement. When that letter is mailed, we request that you submit a final copy of the Dear Healthcare Professional letter to the NDA and to the following address:

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

OTHER

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81). In addition to the postmarketing reporting requirements under CFR 314.80, you have agreed to submit the following reports received from any source (ie, clinical studies or spontaneous reports), and subsequent follow-up information, within 15 days of receipt as 15 day expedited reports using a MedWatch form (FDA Form 3500A):

- Any reports of serious skin and other hypersensitivity adverse events

If you have any questions, please call Tamy Kim, PharmD, Regulatory Project Manager, at (301) 796-2250.

Sincerely,

{See appended electronic signature page}

Russell Katz, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Package Insert, Patient 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/

Russell Katz
8/17/2007 11:37:54 AM