DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-875

Cephalon, Inc.
Attention: Paul M. Kirsch
Senior Director, Regulatory Affairs
41 Moores Road
P.O. Box 4011
Frazer, PA 19355

Dear Mr. Kirsch:

Please refer to your New Drug Application (NDA) dated March 31, 2005, received March 31, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nuvigil™ (armodafinil) Tablets 50 mg, 100 mg, 150 mg, and 250 mg.

We acknowledge receipt of your additional submissions dated:

April 16, 2007	May 15, 2007	June 1, 2007	June 14, 2007
May 8, 2007	May 17, 2007	June 11, 2007	June 15, 2007
May 11, 2007	May 23, 2007	June 13, 2007	

The April 16, 2007 submission constituted a complete response to our March 28, 2007 action letter.

This new drug application provides for the use of Nuvigil™ (armodafinil) Tablets to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome, narcolepsy and shift work sleep disorder.

We have completed our review of this application, as amended. It 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 patient package insert) and submitted labeling (immediate container and carton labels submitted June 11, 2007). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 NDA 21-875**." Approval of this submission by FDA is not required before the labeling is used.

PEDIATRIC STUDY REQUIREMENTS

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages less than 6 years for all approved indications and for pediatric patients ages 6 to 17 years with obstructive sleep apnea/hypopnea syndrome and shift work sleep disorder, and deferring pediatric studies for patients ages 6 to 17 years with narcolepsy for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitment(s) are listed below.

1. Deferred pediatric study under PREA to improve wakefulness in patients with excessive sleepiness associated with narcolepsy in pediatric patients ages 6 to 17.

   Final Report Submission: June 15, 2012

   Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

POSTMARKETING COMMITMENTS

We remind you of your postmarketing study commitments described in your submissions dated April 16, 2007, May 8, 2007, June 11, 2007, June 13, 2007 and June 15, 2007. These commitments are listed below.

1. Description of Commitment – Conduct a 2-year oral (gavage) carcinogenicity study of armodafinil in mouse.

Protocol Submission:	by 04/08
Study Start:	by 08/08
Final Report Submission:	by 08/11

2. Description of Commitment – Provide a Risk Minimization Action Plan (RiskMAP) for Nuvigil to address the risk of serious rash and other hypersensitivity reactions (See **Risk Minimization Action Plan (RiskMAP)** below for additional comments).

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

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

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

4. Description of Commitment – Provide a thorough literature search to determine whether there is any information on the P-glycoprotein induction potential of modafinil in vivo.

   Final Report Submission: by 06/15/08

5. Description of Commitment – Conduct a comprehensive literature search for any in-vivo P-glycoprotein drug-drug interaction information.

   Final Report Submission: by 06/15/08

Submit non-clinical and 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 Nuvigil.
- Implementation of a plan to promote Nuvigil 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 Nuvigil 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.

CLINICAL PHARMACOLOGY

We note your agreement, included in your January 25, 2006 submission, to accept the dissolution specification proposed by the Agency in our December 27, 2005 communication. Accordingly, the agreed upon dissolution method and specifications for NUVIGIL tablets are as follows:

Apparatus: USP apparatus 2 (Paddle)
Stirring Speed: 50 rpm
Dissolution Medium: 0.1N HCl
Volume of Medium: 900 mL
Temperature: 37.0 °C
Specification: Q =------ in 30 minutes

PROMOTIONAL MATERIALS

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert(s) directly 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

"DEAR HEALTHCARE PROFESSIONAL" LETTERS

Although a Dear Healthcare Professional letter is a planned part of the RiskMAP, we note your agreement to mail the Dear Healthcare Professional letter within 4 weeks of the Nuvigil product launch. 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 post-marketing 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, regardless of seriousness or severity, 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

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