Food and Drug Administration
Center for Drug Evaluation and Research

SUMMARY MINUTES OF THE
PSYCHOPHARMACOLOGIC DRUGS ADVISORY COMMITTEE

March 23, 2006

Members Present (Voting)
Wayne Goodman, M.D. *(Chair)*
Jorge Armenteros, M.D.
Jean Bronstein, R.N., M.S.
Andrew Leon, Ph.D.
Daniel S. Pine M.D.
Delbert Robinson, M.D.
Philip Wang, M.D., Dr. P.H.
Barbara Wells, Pharm.D.

Consultants to the Psychopharmacologic Drugs Advisory Committee (Voting)
Michael Bigby, M.D.
Richard Malone, M.D.
Cynthia Pfeffer, M.D.
Marsha Rappley, M.D.
Deborah Dokken, MPA *(Patient Representative)*

Psychopharmacologic Drugs Advisory Committee Industry Representative (Non-voting)
Dilip Mehta, M.D., Ph.D.

FDA Participants
Robert Temple, M.D.
Thomas Laughren, M.D.
Paul Andreason, M.D.
Glenn Mannheim, M.D.

Designated Federal Officer
Cicely Reese, Pharm.D.

Members Not Present
James J. McGough, M.D.
Bruce G. Pollock, M.D., Ph.D.

These summary minutes for the March 23, 2006 meeting of the Psychopharmacologic Drugs Advisory Committee were approved on March 27, 2006

I certify that I attended the March 23, 2006 meeting of the Psychopharmacologic Drugs Advisory Committee and that these minutes accurately reflect what transpired.

_____/s/_____ ____/s/_____
Cicely Reese, Pharm.D. Wayne Goodman, M.D.
Designated Federal Official Chair

Summary Minutes
Food and Drug Administration (FDA)
Center for Drug Evaluation and Research (CDER)
Psychopharmacologic Drugs Advisory Committee

March 23, 2006

The following is an internal report which has not been reviewed. A *verbatim* transcript will be available in approximately two weeks, sent to the Division and posted on the FDA website at:

http://www.fda.gov/ohrms/dockets/ac/cder06.html#PsychopharmacologicDrugs

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA and written statements submitted by the public. The meeting was called to order by Wayne Goodman, M.D. (Committee Chair); the conflict of interest statement was read into the record by Cicely Reese, Pharm.D. (Executive Secretary). There were approximately 180 in attendance.

Attendance:
Psychopharmacologic Drugs Advisory Committee Members Present (voting):
Wayne Goodman, M.D.(Chair), Jorge Armenteros, M.D., Jean Bronstein, R.N., M.S., Andrew Leon, Ph.D., Daniel Pine, M.D., Delbert Robinson, M.D., Philip Wang, M.D., Dr. P.H., Barbara Wells, Pharm.D.

Psychopharmacologic Drugs Advisory Committee Member (Industry Representative- non-voting):
Dilip Mehta, M.D., Ph.D.

Psychopharmacologic Drugs Advisory Committee Consultants (voting):
Michael Bigby, M.D., Richard Malone, M.D., Cynthia Pfeffer, M.D., Marsha Rappley, M.D.

Psychopharmacologic Drugs Advisory Committee Patient Representative (voting):
Deborah Dokken, MPA

FDA Participants at the Table:
Robert Temple, M.D., Thomas Laughren, M.D., Paul Andreason, M.D., Glenn Mannheim, M.D.

Topic: issues and questions regarding efficacy and safety of new drug application (NDA) 20-717/S-019, trade name PROVIGIL Tablets, Cephalon, Inc., proposed indication is for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents.

FDA Introductory Remarks	Thomas Laughren, M.D. Director, Division of Psychiatry
Products	CDER, FDA
FDA Clinical Review	Glenn Mannheim, M.D. Medical Officer, Division of Psychiatry
Products	CDER, FDA
Modafinil for the Treatment of ADHD	Paul Andreason, M.D. Deputy Director, Division of Psychiatry
Products	CDER, FDA
Serious Adverse Cutaneous Reactions	Michael Bigby, M.D. Associate Professor Harvard University and Beth Israel Deaconess Medical Center
Sponsor Presentation	
Introduction	Victor Raczkowski, M.D. Vice President Worldwide Regulatory Affairs Cephalon, Inc.
Overview of ADHD	Joseph Biederman, M.D. Professor of Psychiatry Massachusetts General Hospital and Harvard Medical School
Clinical Pharmacology and Efficacy	Lesley Russell, M.R.C.P. Senior Vice President Worldwide Clinical Research Cephalon, Inc.
General Safety	Srdjan Stankovic, M.D Vice President Neuroscience Clinical Research Cephalon, Inc.
Benefit-Risk/Conclusions	Lesley Russell, M.R.C.P. Senior Vice President Worldwide Clinical Research Cephalon, Inc.

Open Public Hearing:

S. DuBose Ravenel

Grace Jackson

Fred Baughman

Ben Hanson

Committee Discussion

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Questions to the Committee

1. **Has modafinil been shown to be effective for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents?**

Yes – 13 No – 0 Abstain – 0

The Committee consensus was that the data presented on efficacy was sufficient however there is no clear advantage for its use over currently available treatments for ADHD. A trial using an active comparator is recommended, as well as one to better clarify the optimal dosing regimen.
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2. Has modafinil been shown to be acceptably safe in the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents?

Yes – 1 *No – 12* *Abstain – 0*

In the discussion of safety, the Committee consensus was that additional safety testing should be considered and the post marketing is not the best arena to detect serious adverse cutaneous effects such as Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), or Erythema Multiforme (EM). The Committee believes that the one main case presented raises a significant level of doubt about serious adverse events. In general, the Committee decided that the available data is not adequate to assure the safety of the drug in the pediatric population, and recommends conduction of trials designed to get a better estimation of the risk. Overall, it was determined that the efficacy and safety data were not compelling enough to endorse marketing of modafinil for the treatment of ADHD.

Since modafinil was not considered for approval by the Committee, comments on the following additional questions to the Committee were <u>not</u> addressed directly:

In addition to your deliberations on the above two questions, we ask for comment on additional questions, assuming modafinil were to be considered for approval:

- What kind of a risk management plan should be implemented with regard to the
- signal for serious skin rashes with this drug in the ADHD program?
- How should the concern about serious skin rashes be addressed in product labeling (you have been provided our labeling proposal in the approvable letter and also the sponsor's currently proposed labeling)?
- Should there be a requirement for a post-marketing study(ies) to better understand the serious skin rashes, and what type of study(ies) might be considered?

The Meeting adjourned for the day at approximately 4:20 p.m.