Food and Drug Administration
Center for Drug Evaluation and Research
Holiday Inn, The Ballroom, 2 Montgomery Village Avenue, Gaithersburg, MD.

Summary Minutes of the Peripheral and Central Nervous System Drugs Advisory Committee November 18, 2002

Members Present

Claudia H., Kawas, M.D.	Richard D. Penn, M.D.	Gerald Van Belle, Ph.D
Jerry S. Wolinsky, M.D.	Michael Grundman, M.D., M.P.H	

Consultants

Lee C. Chiu, M.D.	Ruth Ramsey, M.D.	Craig Beam, M.D.
Walter Wolf, Ph.D.	Gregory Sorensen, M.D.	Hyun Kwon Kim, Ph.D
Mark Fogel, M.D.	James M. Provenzale, M.D.	

Guests

Charles DeCarli, M.D.	Clifford Jack, M.D.	Nick Fox, M.D.
H. Cecil Charles, Ph.D.	Michael W. Weiner, M.D.	P. Murali Doraiswamy, M.D.
William Jagust, M.D.	Michael Hughes,Ph.D.	Gary W. Small, M.D.

FDA Participants

Russell G. Katz, M.D.	Robert Temple, M.D.	Ranjit B. Mani, M.D.	Patricia Love, M.D.

These summary minutes for the November 18, 2002 meeting of the Peripheral and Central Nervous System Drugs Advisory Committee were approved on November 29, 2002.

I certify that I attended the November 18, 2002 meeting of Peripheral and Central Nervous System Drugs Advisory Committee, and that these minutes accurately reflect what transpired.

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Thomas H. Perez, M.P.H., R.Ph.
Executive Secretary

Claudia H., Kawas, M.D., Chair

The Peripheral and Central Nervous System Drugs Advisory Committee, of the Food and Drug Administration, Center for Drug Evaluation and Research met November 18, 2002 at the Holiday Inn, The Ballroom, 2 Montgomery Village Avenue, Gaithersburg, MD.

The Committee discussed the role of brain imaging as an outcome measure in Phase 3 trials of putative therapeutic drugs for Alzheimer's Disease and whether brain imaging modalities can be utilized as surrogate markers; that is, as primary outcomes in definitive clinical trials to measure drug effect in lieu of clinical outcomes. The committees specifically discussed the following issues in reference to each imaging modality:

1. How is the surrogate imaging modality best validated?
2. If one uses an imaging modality to support a disease-modifying effect claim, how does one establish that such an effect occurs?
3. Has any surrogate imaging modality been validated at the present time?
4. Even if no surrogate imaging modality has currently been validated, is it appropriate to use one or more such modalities as primary or ancillary outcome measures of efficacy in Phase 3 clinical trials?

The Committee had received a briefing document from the FDA.

There were approximately 140 persons in the audience. The meeting was called to order at 8:10 a.m. by the Chair, Claudia H., Kawas, M.D. The Committee members and discussants introduced themselves. Thomas H. Perez, Executive Secretary of the Peripheral and Central Nervous System Drugs Advisory Committee read the Meeting Statement. A welcome and opening remarks were provided by Patricia Love, M.D., Director, Division of Medical Imaging and Radiopharmaceutical Drug Producst, and Russell G. Katz, M.D., Director, Division of Neuropharmacological Drug Products, provided an FDA overview of Issues for the meeting.

The scheduled presentations began at 8:30 a.m. and proceeded as follows.

Overview of Imaging - Charles De Carli, M.D.
Surrogate Endpoints as Measures of Efficacy: Complexities and Limitations - Michael Hughes, Ph.D.

Volumetric MRI and Related Subjects
- Clifford Jack, M.D.
- Nick Fox, M.D.
- H. Cecil Charles, Ph.D.
- Michael Grundman, M.D.

The meeting was reconvened at 11:05 a.m. after a 15 minute break, and proceeded with the following presentations.

MR Spectroscopy and PET
- Michael Weiner, M.D.
- Murali Doraiswamy, M.D.
- William Jaqust, M.D.
- Gary Small, M.D.

Validating Surrogate Endpoints - Michael Hughes, Ph.D.

At 12:40 p.m. the Committee had a break for Lunch, and reconvened at 1:45 with the Open Public Hearing, which had two presenters.

- Eric Reiman, M.D., University of Arizona & Good Samaritan Positron Emission Tomography Ctr
- Mary Pendergast, Elan Pharmaceutical Management Corp.

The Committee began its discussion of the issues presented by the FDA at 2 p.m., and meeting was adjourned at 4:45 p.m.

The Committee expressed a wide variety of opinions on the issues presented for discussion by the FDA. No official votes were taken at this meeting. Transcripts of the meeting will be placed on the web when they become available, in approximately 2 to 3 weeks at www.fda.gov/ohrms/dockets/ac/acmenu.htm

The Committee discussed the following issues in reference to each imaging modality:

1. How is the surrogate imaging modality best validated?

2. If one uses an imaging modality to support a disease-modifying effect claim, how does one establish that such an effect occurs?

3. Has any surrogate imaging modality been validated at the present time?

4. Even if no surrogate imaging modality has currently been validated, is it appropriate to use one or more such modalities as primary or ancillary outcome measures of efficacy in Phase 3 clinical trials?