Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Peripheral and Central Nervous System Drugs Advisory Committee Meeting
October 23, 2008

Topics: The committee discussed the clinical development of radionuclide imaging products for the detection of amyloid to assist in the diagnosis of Alzheimer's Disease.

These summary minutes for the October 23, 2008 Peripheral and Central Nervous System Drugs Advisory Committee meeting were approved on October 29, 2008.

I certify that I attended the October 23, 2008 Peripheral and Central Nervous System Drugs Advisory Committee meeting and that these minutes accurately reflect what transpired.

_____*-Signed-*_____
Diem-Kieu H. Ngo, Pharm.D., BCPS
(Designated Federal Official)

_____*-Signed-*_____
Larry B. Goldstein, M.D.
(Acting Chair)

Summary Minutes of the Peripheral and Central Nervous System Drugs Advisory Committee Meeting
October 23, 2008

The following is the final report of the Peripheral and Central Nervous System Drugs Advisory Committee meeting held on October 23, 2008. A verbatim transcript will be available in approximately six weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cder08.html#PeripheralCentralNervousSystem

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

The Peripheral and Central Nervous System Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on October 23, 2008 at the Hilton Washington DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the background materials from the FDA. The meeting was called to order by Larry B. Goldstein, M.D. (Acting Chair); the conflict of interest statement was read into the record by Diem-Kieu H. Ngo, Pharm.D., BCPS (Designated Federal Official). There were approximately 200 people in attendance. There were three Open Public Hearing (OPH) speakers.

Issue: On October 23, 2008, the committee discussed the clinical development of radionuclide imaging products for the detection of amyloid to assist in the diagnosis of Alzheimer's Disease.

Attendance:
Peripheral and Central Nervous System Drugs Advisory Committee members present (voting): Larry B. Goldstein, M.D. (Acting Chair); Britt Anderson, M.D., Ph.D.; Mark W. Green, M.D., Ph.D.; Gregory L. Holmes, M.D., Ph.D.; Lily K.F. Jung, M.D., M.M.M.; Ying Lu, Ph.D.; Matthew Rizzo, M.D.; Stacy A. Rudnicki, M.D.

Peripheral and Central Nervous System Drugs Advisory Committee members absent (voting): Sandra F. Olson, M.D.

Temporary Voting Members: Twyla Bridgwater (Patient Representative); William E. Bridgwater (Patient Representative); Peter Herscovitch, M.D.; Elizabeth C. Jones, M.D., M.P.H.; Robert F. Mattrey, M.D.; Henry D. Royal, M.D.; Harvey A. Zeissman, M.D.

Industry Representative present (non-voting): Roy E. Twyman, M.D.

Guest Speakers (non-voting): Madhav Thambisetty, M.D., Ph.D.; G. William Rebeck, Ph.D.

FDA Participants (non-voting): Robert Temple, M.D.; Russell G. Katz, M.D.; CAPT Rafel Dwaine Rieves, M.D.; Alexander Gorovets, M.D.; Qi Feng, M.D., Ph.D.

Open Public Hearing Speakers: William Thies, Ph.D..; Samantha Budd, Ph.D.; Michael Weiner, M.D.

The agenda was as follows:

8:00 a.m.	Call to Order and Opening Remarks	**Larry B. Goldstein, M.D.** Acting Chair Peripheral and Central Nervous System Drugs Advisory Committee
	Introduction of Committee	
	Conflict of Interest Statement	**Diem-Kieu H. Ngo, Pharm.D., BCPS** Designated Federal Official
8:15 a.m.	FDA Introductory Remarks	**CAPT Rafel Dwaine Rieves, M.D.** Director, Division of Medical Imaging and Hematology Products (DMIHP), Office of Oncology Drug Products (OODP), OND, CDER, FDA

FDA PRESENTATION

8:30 a.m.	Overview of Potential Imaging Claims	**Alexander Gorovets, M.D.** Medical Officer Team Leader DMIHP, OODP, OND, CDER, FDA
8:45 a.m.	Clinical Presentation, Diagnosis and Management of Alzheimer's Disease	**Madhav Thambisetty, M.D., Ph.D.** Staff Clinician Section of Brain Physiology and Metabolism National Institute on Aging
9:25 a.m.	Amyloid and Amyloid Deposition in the Brain	**G. William Rebeck, Ph.D.** Associate Professor Department of Neuroscience Georgetown University Medical Center
9:45 a.m.	**BREAK**	

INDUSTRY PRESENTATION

AVID RADIOPHARMACEUTICALS

10:00 a.m.	Introduction and Development Overview of ^{18}F-AV-45	**Daniel Skovronsky, M.D., Ph.D.** CEO, Avid Radiopharmaceuticals
	Clinical Utility and Reference Standard for Amyloid Imaging	**Christopher Clark, M.D.** University of Pennsylvania, Department of Neurology Medical Director, Avid Radiopharmaceuticals
	Development Plan Proposal	**Daniel Skovronsky, M.D., Ph.D.** CEO, Avid Radiopharmaceuticals
10:30 a.m.	Clarifying Questions to Presenters	

BAYER HEALTH CARE PHARMACEUTICALS

10:40 a.m.	Introduction and Bayer Position	**Madhu Anant, M.Sc., RAC** Deputy Director, Global Regulatory Affairs Bayer Health Care Pharmaceuticals
	Clinical Utility	**Kenneth Marek, M.D.** Director, Institute of Neurodegenerative Disorders Yale University Medical School
	Phase 3 Study Design – Standard Of Truth	**Cornelia Reininger, M.D., Ph.D.** Director, Global Clinical Development Bayer Health Care Pharmaceuticals
	Conclusion	**Madhu Anant, M.Sc., RAC** Deputy Director, Global Regulatory Affairs Bayer Health Care Pharmaceuticals
11:10 a.m.	Clarifying Questions to Presenters	

GE HEALTHCARE

11:20 a.m.	Product Introduction, Proposed Indication and Clinical Development Plan for GE-067	**David Brooks, M.D., D.Sc.** Head of Neurology in Clinical Development, GE Healthcare Hartnett Professor of Neurology, Imperial College London
	Data to Support [11C]PIB as a Standard of Truth (SoT)	**William Klunk, M.D., Ph.D.** Professor of Psychiatry and Neurology University of Pittsburgh, Pittsburgh, PA
	Clinical Utility for Amyloid Imaging	**Keith A. Johnson, M.D.** Assistant Professor of Neurology, Harvard University Director of Molecular Imaging, Massachusetts General Hospital, Boston, MA
11:50 a.m.	Clarifying Questions to Presenters	
12:00 p.m.	FDA Summary and Considerations	**Qi Feng, M.D., Ph.D.** Medical Officer DMIHP, OODP, OND, CDER, FDA
12:30 p.m.	**LUNCH**	
1:30 p.m.	Open Public Hearing	
2:30 p.m.	Clarifying Questions to Presenters	
2:45 p.m.	Panel Discussion/Committee Questions	
3:30 p.m.	**BREAK**	

3:45 p.m. Panel Discussion/Committee Questions, Continued

5:00 p.m. **ADJOURNMENT**

Questions to the Committee:

1. To what extent, if any, would an indication for the use of an *in vivo* diagnostic radiopharmaceutical agent for the "detection of cerebral amyloid" provide useful clinical information?

   Committee Discussion:
   The committee discussed question #2 first before it discussed question #1. The committee agreed that a" negative" amyloid test could have clinical utility in ruling out a diagnosis of Alzheimer's Disease (AD). Additionally, the committee noted that a" positive" test would have very limited utility since cerebral amyloid is known to be present in multiple conditions, including normal aging. Hence, the clinical usefulness of a "positive" amyloid test was regarded as tenuous. Some committee members noted that a "positive" test might ultimately be useful to help characterize AD, but not to diagnose it. The committee agreed that such a test would probably be a powerful tool for future research. (See Transcript for Complete Discussion)

2. If an *in vivo* diagnostic radiopharmaceutical is clinically useful in the "detection of cerebral amyloid," what should be a "standard of truth" in phase 3 clinical studies?

   Committee Discussion:
   The committee discussed this question first, before question #1. In regards to the indication of detecting amyloid in the brain, the committee overwhelmingly agreed that histopathological correlation should be the "standard of truth" in phase 3 clinical studies. There was discussion about the feasibility of obtaining "enough" pathological studies or the ability to follow study patients to autopsy. A few committee members noted that [11C]PIB may also be a standard of truth; however, other committee members expressed concern that [11C]PIB is not an FDA-approved product and data are insufficient to establish its reliability as a marker for cerebral amyloid. (See Transcript for Complete Discussion)

3. Please comment on the strengths and weaknesses of the phase 3 study outlines supplied by the companies.

   Committee Discussion:
   The committee did not discuss this question specifically since it was agreed upon by the Review Division and the committee that the strengths and weaknesses of the phase 3 study outlines were addressed during the earlier discussions for questions #1 and #2. (See Transcript for Complete Discussion)

The meeting was adjourned at approximately 4:30 p.m.