

MEMORANDUM

DATE: October 16, 2002

TO: Members, Peripheral and Central Nervous Systems Drugs and Nuclear Medicine Drugs Advisory Committees, and Invited Guests

FROM: Staff
Division of Neuropharmacological Drug Products

SUBJECT: Addendum to Background Document for Joint Advisory Committee Meeting of November 18, 2002: Issues Related to the Role of Brain Imaging as an Outcome Measure in Phase III Trials of Putative Drugs for Alzheimer's Disease

LIST OF PERTINENT PUBLICATIONS

The following publications are being supplied to the members of the Committees and invited guests in full text.

Fleming TR, DeMets DL. Surrogate end points in clinical trials: are we being misled? *Annals of Internal Medicine* 1996;125(7):605-13

Fox NC, Cousens S, Scahill R, Harvey RJ, Rossor MN. Using serial registered brain magnetic resonance imaging to measure disease progression in Alzheimer disease: power calculations and estimates of sample size to detect treatment effects. *Arch Neurol* 2000;57(3):339-44

Reiman EM, Caselli RJ, Chen K, Alexander GE, Bandy D, Frost J. Declining brain activity in cognitively normal apolipoprotein E epsilon 4 heterozygotes: A foundation for using positron emission tomography to efficiently test treatments to prevent Alzheimer's disease. *Proc Natl Acad Sci U S A* 2001;98(6):3334-9

Jack CR Jr, Petersen RC, Xu YC, O'Brien PC, Smith GE, Ivnik RJ, Boeve BF, Waring SC, Tangalos EG, Kokmen E. Prediction of AD with MRI-based hippocampal volume in mild cognitive impairment. *Neurology* 1999;52(7):1397-403.

Jack CR Jr, Petersen RC, Xu Y, O'Brien PC, Smith GE, Ivnik RJ, Boeve BF, Tangalos EG, Kokmen E. Rates of hippocampal atrophy correlate with change in clinical status in aging and AD. *Neurology* 2000;55(4):484-89.

Doraiswamy PM, Chen JG, Charles HC. Brain magnetic resonance spectroscopy. Role in assessing outcomes in Alzheimer's Disease. *CNS Drugs* 2000;14(6):457-472

Grundman M, Sencakova D, Jack CR Jr, Petersen RC, Kim HT, Schultz A, Weiner MF, DeCarli C, DeKosky ST, van Dyck C, Thomas RG, Thal LJ; Alzheimer's Disease Cooperative Study. Brain MRI hippocampal volume and prediction of clinical status in a mild cognitive impairment trial. *J Mol Neurosci* 2002;19(1-2):23-7

Styner MA, Charles HC, Park J, Gerig G. Multi-site validation of image analysis methods – assessing intra- and inter-site variability. SPIE MI-2002, San Diego.

Schuff N, Capizzano AA, Du AT, Amend DL, O'Neill J, Norman D, Kramer J, Jagust W, Miller B, Wolkowitz OM, Yaffe K, Weiner MW. Selective reduction of N-acetylaspartate in medial temporal and parietal lobes in AD. *Neurology* 2002;58(6):928-35