



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: December 6, 2007

TO: Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy
Food and Drug Administration

THROUGH: Vince Tolino / S /
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Michael F. Ortwerth, Ph.D. / S /
Deputy Director, Advisory Committee Oversight and Management Staff
Office of Policy, Planning, and Preparedness

FROM: Igor Cerny, Pharm.D. / S /
Director, Advisors and Consultants Staff
Center for Drug Evaluation and Research

SUBJECT: 712(c)(2)(B) Conflict of Interest Waiver for Andrew Leon, Ph.D.

I am writing to request a waiver for Andrew Leon, Ph.D., a Temporary Voting Member of the Psychopharmacologic Drugs Advisory Committee, from the conflict of interest prohibitions of section 712(c)(2)(A) of the Federal Food, Drug, and Cosmetic Act. Waivers under section 712(c)(2)(B) may be granted by the appointing official where it is "necessary to afford the advisory committee essential expertise" and where the individual has made a disclosure to FDA of the financial interests at issue. We have determined that you are the appointing official for purposes of section 712(c)(2)(B). Therefore, you have the authority to grant Dr. Leon a waiver under section 712(c)(2)(B).

Section 712(c)(2)(A) prohibits Federal executive branch employees, including special Government employees, from participating in any particular matter in which the employee or an immediate family member has a financial interest that could be affected by the advice given to the FDA with respect to the matter. Because Dr. Leon is a special Government employee, he is under a statutory obligation to refrain from participating in any deliberations that involve a particular matter having a direct and predictable effect on a financial interest attributable to him.

The functions of the Psychopharmacologic Drugs Advisory Committee, as stated in its Charter, are to review and evaluate data concerning the safety and effectiveness of marketed and investigational human drug products for use in the practice of psychiatry and related fields and make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Leon has been asked to participate in all official matters concerning new drug application (NDA) 22-173 Zyprexa Adhera (olanzapine pamoate depot) long acting intramuscular (IM) injection 210mg, 300mg, and 405 mg per/vial, sponsored by Eli Lilly & Company, for treatment of schizophrenia. A particular safety concern for discussion is the occurrence of severe somnolence in some patients who are administered this depot formulation of olanzapine.

This matter is coming before a meeting of the Psychopharmacologic Drugs Advisory Committee. This issue is a particular matter involving specific parties.

Dr. Leon has advised the Food and Drug Administration (FDA) that he has a financial interest that could potentially be affected by his participation in the matter described above. **Dr. Leon serves on _____'s Data Safety Monitoring Board (DSMB) for _____, and was recently recruited by _____ to serve on their DSMB for _____, _____ and _____ are competing products to Zyprexa Adhera, the product coming before the committee. Dr. Leon also serves on _____'s DSMB for _____, an obesity drug. This drug is unrelated to Zyprexa Adhera.**

As a Temporary Voting Member of the Psychopharmacologic Drugs Advisory Committee, Dr. Leon could become involved in matters that could affect his financial interest. Under section 712(c)(2)(A), he is prohibited from participating in such matters. However, as noted above, you have the authority under section 712(c)(2)(B) to grant a waiver permitting Dr. Leon to participate in such matters if necessary to afford this committee essential expertise.

For the following reasons, I believe that it would be appropriate for you to grant a waiver to Dr. Leon that would allow him to participate fully in the matter described because his voting participation is necessary to afford the committee essential expertise.

Although Dr. Leon serves on Data Safety Monitoring Boards (DSMBs) for _____ and _____, it is important to consider the main purpose of a DSMB. A Data Safety Monitoring Board is an independent group of experts who monitor patient safety and treatment efficacy data while a clinical trial is ongoing. It is a separate entity that conducts an independent, objective review of all accumulated data from both blinded and un-blinded clinical trials in such a manner as to maximize benefit to the trial participants and to the research effort. The primary mandate of the DSMB is to protect patient safety. Participants in the review of masked or confidential data and discussions regarding continuance or stoppage of the study should have no conflict of interest with or financial stake in the research outcome. And in this case, Dr. Leon does not have any financial stake in the competing product or firm. In addition, Dr. Leon's involvement with _____'s DSMB is unrelated to the matter coming before the committee.

According to the Division of Psychiatry Drug Products, the uniqueness of Dr. Leon's qualifications justifies granting this waiver. Not only is Dr. Leon the only biostatistician participating in the Psychopharmacologic Drugs Advisory Committee meeting, but he is a

biostatistician with expertise in psychiatric drugs which makes him even more vital for the required analysis of clinical trial data in this meeting. The meeting will examine the safety and efficacy of the parenteral treatment of schizophrenia with olanzapine long-acting injection. In order to have a balanced discussion of clinical trial design, a biostatistician is critical to provide input regarding time to onset of adverse drug reactions, clinical endpoints and related deltas, powering of studies, as well as comparator arms and treatment durations. Dr. Leon's vast research experience and knowledge of clinical trial design, adverse drug reactions in clinical trials, and protocol development as a statistician makes him uniquely qualified to participate and will allow a quantitative perspective in the determination of the overall risk and benefit assessment. I believe that participation by Dr. Leon in the committee's deliberations will contribute to the diversity of opinions and expertise represented on the committee.

Moreover, the Federal Advisory Committee Act requires that committee memberships be fairly balanced in terms of the points of view represented and the functions to be performed by the advisory committee. Also, the committee's intended purpose would be significantly impaired if the agency could not call upon experts who have become eminent in their fields, notwithstanding the financial interests and affiliations they may have acquired as a result of their demonstrated abilities. The Division's experience with Dr. Leon has been unmatched. Dr. Leon's participation in previous Psychopharmacologic Drugs Advisory Committee (PDAC) makes him an invaluable resource to FDA for this meeting. Dr. Leon is both qualified and experienced to guide and advise the clinicians on PDAC as to the most scientifically valid interpretation of the studies at matter. Due to his previous experience on the PDAC, Dr. Leon understands the complex regulatory scheme by which clinical trial data is reviewed and interpreted and how this is utilized to support the NDA at hand. Dr. Leon's unique combination of delivering this guidance in the most qualified manner to provide balance in approach and ensure a sound scientific discussion and his experience with the advisory committee process makes him uniquely qualified.

**APPEARS THIS WAY
ON ORIGINAL**

