



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: 208(b)(3) Conflict of Interest Waiver for Andrew Winokur, M.D., Ph. D.

I am writing to request a waiver for Andrew Winokur, M.D., Ph. D.. a Temporary Voting Member of the Psychopharmacologic Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a). Waivers under section 208(b)(3) may be granted by the appointing official where "the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved" and where the individual has made a disclosure of the financial interests at issue. We have determined that you are the appointing official for purposes of section 208. Therefore, you have the authority to grant Dr. Winokur a waiver under section 208(b)(3).

Section 208(a) prohibits Federal executive branch employees, including special Government employees, from participating personally and substantially in matters in which the employee or his employer has a financial interest. Because Dr. Winokur 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 or his employer.

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. Winokur 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. Winokur has advised the Food and Drug Administration (FDA) that he has a current financial interest which could potentially be affected by his participation in the matter described above. **Dr. Andrew Winokur's employer, University of Connecticut Health Center, was awarded a research contract by ----- to conduct a multi-center, long-term, open-label study to assess the safety and tolerability of ----- in the treatment of outpatients with Major Depressive Disorder. The study period was February 2006 to December 2007. The study is funded by ----- for \$-----.** The study has ended but Dr. Winokur's employer, University of Connecticut Health Center, has not received the final funds yet. Dr. Winokur is the Co-investigator for the study but he does not receive any personal remuneration.

In addition, Dr. Winokur's employer, the University of Connecticut Health Center, has past and current contracts with -----, -----, -----, ----- and is currently in negotiation with ----- for a study. In addition Dr. Winokur's ----- is currently employed at -----. Arguably, his employer's and ----- interests do not constitute a financial interest in the particular matter under section 208(a) since these interests are unrelated to the issue at hand. Nevertheless, in the utmost of caution, I recommend that this waiver be granted.

As a Temporary Voting Member of the Psychopharmacologic Drugs Advisory Committee, Dr. Winokur potentially could become involved in matters that could affect his financial interest. Under section 208, he is prohibited from participating in such matters. However, as noted above, you have the authority under section 208(b)(3) to grant a waiver permitting Dr. Winokur to participate in such matters as you deem appropriate.

For the following reasons, I believe that it would be appropriate for you to grant a waiver to Dr. Winokur that would allow him to participate fully in the matter described because the need for his services greatly outweighs the conflict of interest created by these financial interests.

First, although Dr. Winokur's employer has current interest in -----, he himself has no financial interest in the firm. Generally, there is less likelihood that the judgment of the individual will be affected by the imputed interest of an employer than by a personal financial interest.

Second, the ----- sponsored study of ----- is for an indication unrelated to the indication being sought for Zyprexa Adhera. It is highly unlikely that Dr. Winokur's participation in the matter coming before the committee will have an impact on the trial. It is difficult to predict that any action, short of "clinical hold", would lead to the discontinuation of the trial or a modification of the protocol that would directly affect the financial interest of Dr. Winokur and his employer.

Third, according to the Review Division, the uniqueness of Dr. Winokur's qualification justifies granting this waiver. Dr. Andrew Winokur is the only Adult psychopharmacology expert conducting schizophrenia research on the Psychopharmacologic Drugs Advisory Committee (PDAC). Dr. Winokur is a Professor of Psychiatry at the University of Connecticut Health Center who has authored upwards of 121 publications in the field of psychopharmacology with a particular focus on the effects of sedative hypnotics. The upcoming meeting will examine the psychopharmacologic safety and efficacy of the parenteral treatment of schizophrenia with olanzapine long-acting injection. Severe sedation as a drug related effect of parenteral olanzapine is the issue of greatest importance in the risk benefit evaluation in terms of the unique properties of this parenteral treatment. Consequently, Dr. Winokur's contribution to the pharmacokinetic and pharmacodynamic issues will greatly enhance our knowledge of the subject. I believe that participation by Dr. Winokur in the committee's deliberations will contribute to the diversity of opinions and expertise represented on the committee.

Lastly, locating qualified individuals without disqualifying financial interest to serve on this advisory committee has been very difficult. The Division of Psychiatry Products (DPP) feels that it would be pertinent to have a panel of experts that includes more than one expert in the area of psychiatry to consider a wider perspective and account for all aspects of the product under review. In an attempt to gain the appropriate representation, DPP and Advisors and Consultants Staff (ACS) contacted 20 individuals listed as current Special Government Employees (SGEs) and/or Federal Employees of the National Institutes of Health with specialties in the field of psychiatry. Of the 20 psychiatrists contacted, 18 accepted the offer to represent the Agency's interest, 2 others declined due to a scheduling conflict or prior commitment. Of the 18, 8 of the interested parties disclosed conflicts of a significant nature, resulting in the need for waivers. Out of the 8 people that needed waivers, DPP is only supporting waivers for SGEs with much needed expertise. As mentioned above, the Division is interested in gaining the perspective of more than one expert in an effort to remain objective, and in doing so requests that a waiver be granted for Dr. Andrew Winokur to participate as there has been a genuine effort to secure individual participation and representation with minimal conflict of interest.

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. Dr. Winokur is Director of the Neuropsychopharmacology Treatment, Research and Training Center (NTRTC) in the Department of Psychiatry at the University of Connecticut Health Center. He participates in clinical trials with established and investigational drugs for the treatment of mood and anxiety disorders. He also coordinates the teaching of psychopharmacology in the

Psychiatry Residency Program and he serves as the section leader for the Diseases of the Nervous System section of the second year medical school course Mechanisms of Disease. Accordingly, I recommend that you grant Andrew Winokur, M.D., Ph.D., a waiver that would allow him 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 for treatment, sponsored by Eli Lilly & Company, of schizophrenia. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Winokur outweighs the potential for a conflict of interest created by the financial interest attributed to him.

DECISION:

Waiver granted based on my determination, made in accordance with section 208(b)(3), that the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest attributable to the individual.

Waiver denied.

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

Date 1/14/08