



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: January 10, 2008

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 David Shaffer, M.D.

I am writing to request a waiver for David Shaffer, M.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. Shaffer 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. Shaffer 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. Shaffer 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. Shaffer has advised the Food and Drug Administration (FDA) that his employer, Columbia University Medical Center, has current financial interests which could potentially be affected by his participation in the matter described above. **Dr. David Shaffer is the Chief of Division of Child and Adolescent Psychiatry at Columbia University Medical Research Center. One of the faculty members in his Division, Dr. -----, is the Principal Investigator (PI) for the following two ----- sponsored trials involving -----, ----- is a competing product to Zyprexa Adhera, the product coming before the committee. Dr. Shaffer has no direct involvement in these trials. His only involvement is managerial as Chief of the division. He does not receive any personal remuneration or salary support.**

1. **An open label trial of ----- with psychotic disorders -----**
2. **A double-blind placebo controlled phase III trial evaluating the efficacy, safety and pharmacokinetics of ----- in adolescents (13 to 17 years) with schizophrenia.**

Another faculty member, Dr. -----, is negotiating with ----- for a study of ----- for the treatment of -----, ----- is a competing product to Zyprexa Adhera. Dr. Shaffer will have no direct involvement in this trial. His only involvement will be managerial as Chief of the division. He will not receive any personal remuneration or salary support from the funds received.

As a Temporary Voting Member of the Psychopharmacologic Drugs Advisory Committee, Dr. Shaffer potentially could become involved in matters that could affect his financial interests. 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. Shaffer 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. Shaffer 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. Shaffer's employer has financial interests in ----- and potentially -----, he himself has no current personal financial interest in the companies. Generally, there is less likelihood that the judgment of the individual will be affected by an imputed interest of an employer than by a personal financial interest.

Second, it is highly unlikely that Dr. Shaffer's participation in the matter coming before the committee will have an impact on the trials currently underway at the Division of Child and Adolescent Psychiatry at Columbia University Medical Research Center. It is difficult to predict that any action, short of "clinical hold", would lead to the discontinuation of these trials or a modification of the protocols that would directly affect the financial interests of Dr. Shaffer's employer. -----'s ----- is already approved for the treatment of schizophrenia and any decision with respect to Eli Lilly's Zyprexa Adhera is unlikely to have an effect on ----- studying ----- for a totally different indication. In addition, the Columbia University Medical Research Center is a large, diverse, research institution which receives funding from a variety of public, private, and governmental agencies in support of its' research activities. It does not depend upon one or two sources for its funding. In 2006, the Columbia University Medical Research Center attracted more than \$----- in research grants.

Third, according to the Review Division, the uniqueness of Dr. Shaffer's qualification justifies granting this waiver. Dr. Shaffer is a professor of Child Psychiatry and Chief of the Division of Child and Adolescent Psychiatry at Columbia University Medical Center. His expertise is widely recognized in the field of general psychiatry, child psychiatry, and suicidality. This meeting will examine the safety and efficacy of the parenteral treatment of schizophrenia with olanzapine long-acting injection, and this formulation, if approved, will undoubtedly find some use in the community to treat adolescent patients with schizophrenia. A meaningful discussion of the efficacy and safety data will require contributions from multiple disciplines regarding the general patient population prescribed antipsychotic agents including experts in the subspecialties of schizophrenia, child and adolescent psychoses, neuropsychiatry, and biostatistics. Dr. Shaffer's input as an expert child and adolescent psychiatrist will allow a wider perspective in the determination of the overall risk assessment, particularly for younger patients with serious psychotic disorders. I believe that participation by Dr. Shaffer 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. David Shaffer 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. Shaffer is Chief of Division of Child and Adolescent Psychiatry at Columbia University Medical Center and Chief and Professor of Child Psychiatry and Pediatrics at College of Physicians and Surgeons at Columbia University. He is also the attending psychiatrist at New York Presbyterian Hospital. Dr. Shaffer has a long standing interest in developing new diagnostic instruments for children and adolescents. He was the lead investigator in developing the Children's Global Assessment Scale (C-GAS). Dr. Shaffer has led a team of colleagues and investigators in developing and modifying the Diagnostic Interview Schedule for Children (DISC) and more recently the Columbia Teen Screen.

Accordingly, I recommend that you grant David Shaffer, M.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, sponsored by Eli Lilly & Company, for treatment of schizophrenia. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Shaffer outweighs the potential for a conflict of interest created by the financial interests 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.

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

Date 1/18/08