DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: September 12, 2006

TO: Randall Lutter, Ph.D.
Associate Commissioner for
Policy and Planning
Food and Drug Administration

THROUGH: Jenny Slaughter
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

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

SUBJECT: Conflict of Interest Waiver for Paul Watkins, Ph.D.

I am writing to request a waiver for Paul Watkins, Ph.D., a consultant to the Center for Drug Evaluation and Research, from the conflict of interest prohibitions of 18 U.S.C. §208(a). The appointing official may grant waivers under section 208(b) (3) 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. Watkins, a waiver under 18 U.S.C. §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 any other person whose interests are imputed to the employee under 18 U.S.C. §208, has a financial interest. Since Dr. Watkins is a special Government employee, he is under a statutory obligation to refrain from participating in an official capacity in any particular matter having a direct

and predictable effect on a financial interest attributable to him, his spouse, minor child, or general partner; an organization or entity for which he serves as an officer, director, trustee, general partner, or employee; and, a person with whom he is negotiating for, or has an arrangement concerning, prospective employment.

Dr. Watkins has been asked to participate in the Clinical Pharmacology Subcommittee, of the Advisory Committee for Pharmaceutical Science, meeting where the subcommittee will: (1) hear an update on previous CPSC meeting recommendations and receive an introduction to the three new topics of this meeting; (2) discuss and provide comments on the evaluation of transporter-based drug interactions; and, (3) consider the impact of using prior knowledge on drug development and regulatory decisions. These issues are particular matters of general applicability.

In addition, Dr. Watkins has been asked to participate in the subcommittee's discussions of the scope and strength of evidence to support the inclusion of pharmacogenetic information on CYP2D6 polymorphism in a revision of the label for tamoxifen to improve the benefit/risk of the drug. This is a particular matter involving specific parties.

The function of the Advisory Committee for Pharmaceutical Science, as stated in its charter, is to provide advice on scientific and technical issues concerning the safety, and effectiveness of human generic drug products for use in the treatment of a broad spectrum of human diseases, and as required, any other product for which the Food and Drug Administration has regulatory responsibility, and make appropriate recommendations to the Commissioner of Food and Drugs. The Committee may also review Agency sponsored intramural and extramural biomedical research programs in support of FDA's generic drug regulatory responsibilities.

Dr. Watkins has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the matters to be discussed.

Dr. Watkins consults on the hepatotoxicity of compounds in development for the following firms: ———, ———, ———, ———, ———, ———, ———, ———, ———

[redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted], and [redacted]. In addition, he is on the [redacted]'s Research and Development Advisory Board and he owns stock in [redacted]. These firms could be affected by the subcommittee's discussions of (1) previous Clinical Pharmacology Subcommittee meeting recommendations and introduction to the three new topics of this meeting; (2) the evaluation of transporter-based drug interactions; and,(3) the impact of using prior knowledge on drug development and regulatory decisions.

In addition, Dr. Watkins has an active consulting agreement with [redacted]; however, he has not consulted for the firm in the past 12 months. [redacted] could be affected by the particular matters of general applicability and the subcommittee's discussion of tamoxifen. [redacted] makes [redacted], a competing product to tamoxifen.

As a consultant advising the Clinical Pharmacology Subcommittee of the Advisory Committee for Pharmaceutical Science, Dr. Watkins potentially could become involved in matters that could affect his financial interests. Under 18 U.S.C. §208(a), he is prohibited from participating in such matters. However, as noted above, you have the authority under 18 U.S.C. §208(b)(3) to grant a waiver permitting Dr. Watkins 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. Watkins, which would permit him to participate in the matters previously described.

First, with respect to the subcommittee's discussion of (1) previous Clinical Pharmacology Subcommittee meeting recommendations and introduction to the three new topics of this meeting; (2) discussion of the evaluation of transporter-based drug interactions; and, (3) the impact of using prior knowledge on drug development and regulatory decisions, this waiver is justified, in part, because of the general nature of particular matters of general applicability. It is well recognized that particular matters of general applicability pose far less risk of a conflict of interest. Particular matters of general applicability include regulations, points-

to-consider, guidelines, and policies governing classes of individuals, products, and organizations. Particular matters of general applicability do not include particular matters involving specific parties, such as recommendations regarding a specific product, or enforcement matters involving known parties. Particular matters of general applicability will not have a special or distinct impact on any of Dr. Watkins' financial interests, other than as part of a class.

Second, arguably, Dr. Watkins' consulting interests do not constitute financial interests in the matters to be discussed within the meaning of 18 U.S.C. §208(a), since his consulting is unrelated to the issues to be discussed. Nevertheless, in the utmost of caution, I recommend that this waiver be granted.

In addition, Dr. Watkins' stock interest in _____ is not so substantial as to preclude his participation. It represents a small percentage of his total net worth.

Further, 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 various advisory committee members and Dr. Watkins' participation will contribute to the balance of views represented and the diversity of opinions and expertise. 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. Watkins is Director of the General Clinical Research Center, and Professor of Pharmacotherapy at the University of North Carolina. He is a hepatologist with a special interest in liver toxicity. He has consulted widely in both industry and government on issues involving drug-and toxin-induced liver disease. His research has focused on the molecular basis for inter-individual differences in drug disposition, particularly as it involves cytochromes P450 and drug transporters present in human liver and intestine. Dr. Watkins is a member of various professional societies, such as the American Association for the Study of Liver Diseases, the American Gastroenterological Association, the International Association for the Study of Liver, and the American Federation for Clinical Research. Liver toxicity is one of the leading

reasons that drugs fail in clinical trials or are withdrawn from the market. Dr. Watkins' expertise in gastroenterology and hepatic events will help provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant Paul Watkins, Ph.D., a waiver that will permit him to participate in the Clinical Pharmacology Subcommittee, of the Advisory Committee for Pharmaceutical Science, meeting where the committee will: (1) hear an update on previous CPSC meeting recommendations and receive an introduction to the three new topics of this meeting; (2) discuss and provide comments on the evaluation of transporter-based drug interactions; and, (3) consider the impact of using prior knowledge on drug development and regulatory decisions; and, (4) discuss and provide comments on the scope and strength of evidence to support the inclusion of pharmacogenetic information on CYP2D6 polymorphism in a revision of the label for tamoxifen to improve the benefit/risk of the drug. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Watkins outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: /S/ 9/22/06

Jenny Slaughter
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Date

DECISION:

_X_ Waiver granted based on my determination, made in accordance with section 18 U.S.C. §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/ 9/25/06

Randall Lutter, Ph.D.
Associate Commissioner for
Policy and Planning
Food and Drug Administration

Date