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 Marie Davidian, Ph.D.

I am writing to request a waiver for Marie Davidian, 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. Davidian, 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. Davidian is a special Government employee, she 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 her, her spouse, minor child, or general partner; an organization or entity for which she serves as an officer, director, trustee, general partner, or employee; and, a person with whom she is negotiating for, or has an arrangement concerning, prospective employment.

Dr. Davidian 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. Prior knowledge of disease change over time and covariates, placebo variation and drug effects can be used to make better decisions and design more informative clinical trials. Examples will be used to demonstrate these principles. The above issues to be discussed are particular matters of general applicability. Particular matters of general applicability focus on a discrete and identifiable class of persons, but do not involve 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. Davidian has advised the Food and Drug Administration that she has financial interests that could potentially be affected by her participation in the matters under discussion by the Clinical Pharmacology Subcommittee of the Advisory Committee for Pharmaceutical Science.

Dr. Davidian is a consultant to _____ _____ Research & Development. She assists members of the Preclinical Biostatistics Department with statistical

analysis of assay data and stability data using mixed effects and nonlinear statistical models. In addition, she is also negotiating a consulting position as a member of the Advisory Board for [redacted].

As a consultant advising the Clinical Pharmacology Subcommittee of the Advisory Committee for Pharmaceutical Science, Dr. Davidian potentially could become involved in matters that could affect her current and future financial interests. Under 18 U.S.C. §208(a), she 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. Davidian 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. Davidian, which would permit her to participate in the matters previously described.

First, 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 Dr. Davidian's current or future financial interests, other than as part of a class.

Second, arguably, Dr. Davidian's consulting does not constitute a financial interest in the particular matter within the meaning of 18 U.S.C. §208(a) since her consulting is unrelated to the issues at hand. Nevertheless, in the utmost of caution, I recommend that this waiver be granted.

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. Davidian's 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. Davidian is the William Neal Reynolds Professor, Department of Statistics, North Carolina University. Her research interests focus on mixed effects models, longitudinal data analysis, covariate measurement error, missing data, and analysis of assay data and calibration. She is also Adjunct Professor of Biostatistics and Bioinformation at Duke University where she works in the Duke Clinical Research Institute collaborating on problems in cardiovascular disease research. She is currently Executive Editor of Biometrics, the flagship journal of the International Biometric Society. Dr. Davidian has published extensively in books, monographs, peer-reviewed publications, manuscripts, articles, technical reports and abstracts. She is a member of several professional societies including the American Statistical Association (ASA), the International Statistical Institute (ISI), and the Institute of Mathematical Statistics (IMS). I believe that Dr. Davidian's expertise in biostatistics will help provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant Marie Davidian, Ph.D., a waiver that will permit her 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. Prior knowledge of disease change over time and covariates, placebo variation and drug effects can be used to make better decisions and design more informative clinical trials. Examples will be used to demonstrate these principles. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Davidian

outweighs the potential for a conflict of interest created by the financial interests attributable to her.

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