DEPARTMENT OF HEALTH & HUMAN SERVICES

MEMORANDUM

Food and Drug Administration
Rockville MD 20857

DATE: November 14, 2005

TO: Shelia Dearybury Walcoff, Esq.
Associate Commissioner for External Relations
Food and Drug Administration

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

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

SUBJECT: Conflict of Interest Waiver for Michael Caldwell, M.D., Ph.D.

I am writing to request a waiver for Michael Caldwell, M.D., 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 18 U.S.C. §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. Caldwell 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. Since Dr. Caldwell 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 Pharmaceutical Science Advisory Committee, as stated in its Charter, are 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. Caldwell has been asked to give a presentation on the current status and next steps with integrating PGx information into safe and effective prescribing of warfarin and answer questions related to his presentation at the Clinical Pharmacology Subcommittee of the Advisory Committee for Pharmaceutical Science. The Subcommittee will discuss current evidence related to the pharmacogenetics of warfarin as a potential basis for label updates.

Dr. Caldwell 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. Caldwell's employer is [redacted] government agency, Agency for Healthcare Research and Quality (AHRQ), for a study [redacted] has agreed to supply the drug, if the study is funded by AHRQ.

Potential label updates with regards to the pharmacogenetics of warfarin is the issue before the Clinical Pharmacology Subcommittee.

As a consultant presenting to the Clinical Pharmacology Subcommittee, Dr. Caldwell could potentially become involved in matters that could affect his employer's financial interests. Under section 208, 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 limited waiver permitting Dr. Caldwell 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 limited waiver to Dr. Caldwell that would allow him to make a presentation to the committee regarding the current status and next steps with integrating PGx information into safe and effective prescribing of warfarin, and answer questions related to his presentation. Under the terms of this limited waiver, Dr. Caldwell will not participate in the committee's discussions, deliberations, or voting.

First, it is important to consider that Dr. Caldwell's conflict is mitigated by the fact that FDA has decided to limit his participation. Given the need for his expertise, Dr. Caldwell will give a presentation to the subcommittee and answer questions directly related to his presentation. He will not be allowed to participate in any of the committee's discussions, deliberations, or voting with respect to the current evidence related to the pharmacogenetics of warfarin as a potential basis for label updates.

Although the study that Dr. Caldwell is involved in, is related to the issue before the committee, it is important to note that this study is being funded by a government agency with [redacted] only supplying the drug. The fact that the source of funding is not from the pharmaceutical industry minimizes the likelihood or appearance that Dr. Caldwell is subject to influence by the manufacturers of warfarin or their competitor's. Thus, the potential for an actual or apparent conflict of interest is minimal.

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. Caldwell'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. Caldwell is Director, Wound Healing

Program, Marshfield Clinic; General Surgeon, St. Joseph's Hospital, and Marshfield Clinic. Dr. Caldwell's focus is in the area of personalized medicine. He has given numerous presentations in the field of pharmacogenomics. In addition, he is extensively published in books, book chapters, articles, and abstracts. He is appointed as a member of the Wisconsin technology Counsel. He is also a member of various medical societies including, the American Surgical Association, American Medical Association, and the American Physiological Society. Through his research specific to the pharmacogenetics of warfarin and his publishing from that research, Dr. Caldwell's presentation to the committee is essential for an appropriate discussion of the current evidence related to the pharmacogenetics of warfarin as a potential basis for label updates.

Accordingly, I recommend that you grant Michael Caldwell, M.D., Ph.D., a limited waiver that would allow him to give a presentation on the current status and next steps with integrating PGx information into safe and effective prescribing of warfarin and answer questions related to his presentation. Under the terms of this limited waiver, Dr. Caldwell will not be permitted to participate in the committee's discussions, deliberations, or voting with respect to the subcommittees discussions of the current evidence related to the pharmacogenetics of warfarin as a potential basis for label updates. I believe that such a limited waiver is appropriate because in this

case, the need for the services of Dr. Caldwell outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: _____ 11-14-05

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

DECISION:

✓ 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.

_____ 11.14.05

Shelia Dearybury Walcoff, Esq. Date
Associate Commissioner for External Relations
Food and Drug Administration

Acknowledgement and Consent for Disclosure of A Limited Waiver Under 18 U.S.C. §208(b)(3)

Michael Caldwell, M.D., Ph.D.

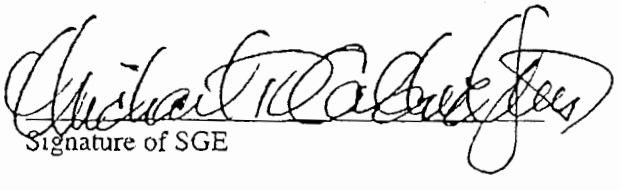
Committee: Clinical Pharmacology Subcommittee of the Advisory Committee for Pharmaceutical Science

Meeting Date: November 14, 2005

I acknowledge that contingent upon public disclosure of the financial interest listed below, I am eligible to receive a limited waiver under 18 U.S.C. §208(b)(3). Under the terms of the limited waiver, I will be permitted to give a presentation on the current status and next steps with integrating PGx information into safe and effective prescribing of warfarin, and answer questions directly related to my presentation. I will be excluded from participating in the committee's discussions, deliberations, or voting related to the current evidence related to the pharmacogenetics of warfarin as a potential basis for label updates.

Type of Interest	Nature	Magnitude
Negotiating for a related study.	**Federally funded with drug supplied by one of the sponsors of warfarin.**	**Between $100,001 and $300,000 per year.**

I hereby request that FDA make this information publicly available on my behalf at the start of the advisory committee meeting for which it is issued. The public disclosure will be accomplished by reading the statement into the record and by making a written copy publicly available at the time of the meeting. I understand that without public disclosure of the interest, the limited waiver is not valid.



Signature of SGE

11/8/05

Date