DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: March 1, 2007

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

THROUGH: Vince Tolino
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 John R. Teerlink, M.D.

I am writing to request a waiver for John R. Teerlink, M.D., a member of Cardiovascular and Renal Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a). Waivers under section 208(b)(1) may be granted by the appointing official where "the [financial] interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from such employee" 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 John R. Teerlink, M.D., a waiver under section 208(b)(1).

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. Teerlink is a full-time 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.

The function of the Cardiovascular and Renal Drugs Advisory Committee, as stated in its Charter, is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cardiovascular and renal disorders and to make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Teerlink has been asked to participate in all official matters concerning Supplemental New Drug Application (NDA) 20-758/S-037, Avalide (irbesartan/HCTZ), sponsored by Bristol Myers Squibb and Sanofi-Synthelabo, a subsidiary of Sanofi-Aventis, for use in the treatment of hypertension in patients unlikely to achieve blood pressure goals on one drug. This matter is coming before the Cardiovascular and Renal Drugs Advisory Committee and is a particular matter involving specific parties.

Dr. Teerlink has advised the Food and Drug Administration that he has financial interests which could potentially be affected by his participation in the matter described above. **Dr. Teerlink serves on the steering committee for one of the pivotal trials in ——— 's ——————— development program ——————— and has been assisting in the continued development of the program. He receives moderate compensation for his role. ——————— is a ——————————— for the treatment of heart failure. ——— is the manufacturer of ———, a competing product to Avalide (irbesartan/HCTZ).**

In addition, Dr. Teerlink serves as a blinded endpoint reviewer for the ——————in heart failure———————— ——————————————— clinical trial, sponsored by ——————————————————————. The purpose of this study is to determine whether ——————————— is superior to placebo in reducing mortality and cardiovascular morbidity, defined as the occurrence of death from any cause or hospitalization due to cardiovascular disease, in subjects with heart failure ——————————————————. ————— is one of the components of ——————————— in combination with ——————————————————————.

Finally, Dr. Teerlink owns a moderate number of shares in a health sector mutual fund. This fund is a ——————— ——— and represents less than -% of his total net worth.

As a member of the Cardiovascular and Renal Drugs Advisory Committee, Dr. Teerlink 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)(1) to grant a waiver permitting Dr. Teerlink 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. Teerlink that would permit him to participate in the matter described above.

First, Dr. Teerlink's interest in ——— is unrelated to the matter coming before the committee for consideration.

Second, with respect to Dr. Teerlink's financial interest in a health sector mutual fund, it is important to consider that he has no influence over the specific investments in fund or the strategies that are employed by the fund manager. It is also important to consider that this fund represents a small portion of his total net worth.

Third, with respect to Dr. Teerlink's interest in ———. It is important to consider that he serves as a blinded reviewer on a study to determine whether ——— is superior to placebo in reducing mortality and cardiovascular morbidity, defined as the occurrence of death from any cause or hospitalization due to cardiovascular disease, in subjects with heart failure ———, an indication unrelated to irbesartan in combination with hydrochlorothiazide (HCTZ), trade name Avalide, the product at issue.

Further, considering that Dr. Teerlink is one of the few experts in the area of endothelin receptor antagonists, his advice is sought by regulated industry and government alike, it seems unlikely that ——— and ——— ——— would terminate their contracts or be less likely, in the future, to retain the services of an expert such as Dr. Teerlink.

Moreover, the uniqueness of Dr. Teerlink's qualification justifies granting this waiver. The upcoming meeting is intended to explore the novel basis for the approval for first-line use of a combination antihypertensive drug

product. Dr. Teerlink is board-certified in internal medicine and cardiology, but his specific research experience in mostly in regard to heart failure, much of which is the long-term consequence of cardiovascular disease that began with hypertension. Thus, Dr. Teerlink brings highly relevant clinical expertise and a strong sense for the public health implications of better treatment for hypertension. Many of Dr. Teerlink's publications and speaking engagements are about the translation of clinical trial findings to clinical practice. Dr. Teerlink's contributions to past meetings have been very thoughtful and insightful. The Center for Drug Evaluation and Research's Division of Cardiovascular and Renal Drugs believes Dr. Teerlink's contributions to the upcoming meeting to be essential.

In addition, the standing core CRDAC committee was instrumental in providing significant guidance and recommendations to the Agency during a 2006 Advisory Committee discussing important considerations for labeling changes for hypertensive drugs. The discussions surrounding this topic of discussion are germane to regulatory decisions that will affect the broader class of combination hypertensive products. Thus what is key is that those previously involved in these discussions are able to weigh in and provide the continuity needed for this meeting. Thus no additional non-member SGEs have been given consideration with respect to participation in this meeting.

Finally, 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. Teerlink is Director of the Heart Failure Clinic and Director of Clinical echocardiography at the San Francisco Veterans Administration Medical Center. He is also Associate Professor of Medicine at the University of California, San Francisco. Dr. Teerlink's clinical research interests include the study of the pathogenesis and therapy of heart failure on both an experimental and clinical level. Dr. Teerlink has served as a principal investigator for a multi-center international acute heart failure trial and is active in multiple chronic

heart failure therapeutics development programs. He is a member of several prestigious medical societies including the American College of Physicians, the American Heart Association and the American College of Cardiology. He has given numerous national and international presentations, and has published extensively on various cardiology issues, such as acute heart failure and acute coronary syndrome. I believe that Dr. Teerlink will bring an enormous amount of experience and knowledge that is critical to the committee's discussions and his participation will help provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant John R. Teerlink, M.D., a waiver that will permit him to participate in all official matters concerning Supplemental New Drug Application (NDA) 20-758/S-037, Avalide (irbesartan/HCTZ), sponsored by Bristol Myers Squibb and Sanofi-Synthelabo, a subsidiary of Sanofi-Aventis, for use in the treatment of hypertension in patients unlikely to achieve blood pressure goals on one drug. This matter is coming before the Cardiovascular and Renal Drugs Advisory Committee and is a particular matter involving specific parties. I believe that

in this case, Dr. Teerlink's financial interests are not so substantial as to be deemed likely to affect the integrity of the services that the Government may expect from him.

CONCURRENCE: /S/ 3/20/07

Vince Tolino
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)(1), that the interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from such employee.

_____ Waiver denied.

/S/ 3/22/07

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

Date