DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: November 2, 2005

TO: Sheila 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 David DeMets, Ph.D.

I am writing to request a waiver for David DeMets, Ph.D., a member of the Cardiovascular and Renal Drugs Advisory Committee, 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. DeMets 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. DeMets 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 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. DeMets has been asked to participate in all official matters concerning New Drug Application (NDA) 21-628, proposed trade name Certican (everolimus) Tablets (0.25mg, 0.5mg, 0.75mg and 1.0mg) sponsored by Novartis Pharmaceuticals Corporation, the U.S. affiliate of Novartis AG., for the proposed indication of prophylaxis of rejection in heart transplantation.

Dr. DeMets has advised the Food and Drug Administration (FDA) that he has financial interests that could potentially be affected by his participation in this matter. Dr. DeMets is a member of an advisory board for Novartis Pharmaceuticals. The board advises on Health Outcomes and Related Incidence with Zoledronic Acid Once Yearly (HORIZON 2301) in osteoporosis. Novartis Pharmaceuticals is the sponsor of Certican, the product at issue and the distributor of Myfortic (mycophenolic acid), one of the competing products.

In addition, Dr. DeMets is a consultant and Data Safety Monitoring Board member for [redacted] and [redacted] co-partner on a study [redacted]: to measure the safety and efficacy of [redacted] with atrial arrhythmia. [redacted] is the sponsor of [redacted], one of the competing products to Certican.

As a member of the Cardiovascular and Renal Drugs Advisory Committee, Dr. DeMets could potentially 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 18 U.S.C. §208(b)(3) to grant a waiver permitting Dr. DeMets 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. DeMets that would allow him to participate fully in the matter described above.

First, arguably, Dr. DeMets' interests in Novartis Pharmaceuticals and [redacted] do not constitute financial interest in the particular matter within the meaning of 18 U.S.C. §208(b)(3), since his interests are unrelated to the product at issue or the competing products. Nevertheless, I recommend that this waiver be granted.

In addition, Dr. DeMets' interests are not so substantial as to preclude his participation in this matter. Dr. DeMets receives minimal compensation for his service.

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. DeMets 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. DeMets is Chairman and Professor, Department of Biostatistics, University of Wisconsin. He is a highly regarded biostatistician who specializes in the statistical analysis of clinical trials and research studies. Dr. DeMets has published numerous articles, book chapters and policy papers on such topics as "Discrete Sequential Boundaries for Clinical Trials," "An Aid to Data Monitoring in Long-term Clinical Trials," and "Practical Aspects in Data Monitoring." He is a member of numerous professional societies, such as the American Mathematical Society, the American Statistical Association, and the Society for Controlled Clinical Trials. We believe that Dr. DeMets participation will contribute to the diversity of expertise and viewpoints represented and will provide a foundation for developing advice and recommendations that will be fair and comprehensive.

Accordingly, I recommend that you grant Dr. DeMets a waiver that would allow him to participate in all official matters concerning New Drug Application (NDA) 21-628, proposed trade name Certican (everolimus) Tablets (0.25mg, 0.5mg, 0.75mg and 1.0mg) sponsored by Novartis Pharmaceuticals Corporation, the U.S. affiliate of Novartis AG., for the proposed indication of prophylaxis of rejection in heart transplantation. I believe that such a waiver is appropriate because in this case, the need for the services of David DeMets, Ph.D., outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: _____ 11/04/05
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 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.

_____ 11-8-05
Sheila Dearybury Walcoff, Esq. — Date
Associate Commissioner for External Relations
Food and Drug Administration

Disclosure Document for a 18 U.S.C. §208(b)(3) Waiver

David DeMets, Ph.D.

Committee: Cardiology and Renal Drugs Advisory Committee

Meeting Date: November 16, 2005

I acknowledge that contingent upon public disclosure of the financial interests listed below, related to the agenda item, New Drug Application (NDA) 21-628, proposed trade name Certican (everolimus) Tablets (0.25mg, 0.5mg, 0.75mg and 1.0mg) sponsored by Novartis Pharmaceuticals Corporation, the U.S. affiliate of Novartis AG., for the proposed indication of prophylaxis of rejection in heart transplantation, I am eligible to receive a waiver under 18 U.S.C. §208(b)(3).

Type of Interest	Nature	Magnitude
Advisory Board	Sponsor	Less than $10,001
Consultant and Member of Data Safety Monitoring Board	Competitor	Less than $10,001

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 interests the waiver is not valid.

D L DeMets

Signature of SGE

11/03/05

Date