DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administrat
Rockville MD 20857

DATE: June 21, 2007

TO: Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy
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 Morris Schambelan, M.D.

I am writing to request a waiver for Morris Schambelan, M.D., a temporary voting member of the Endocrinologic and Metabolic Drugs Advisory Committee, 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. Schambelan 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. Schambelan 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. Schambelan has been asked to participate in all official matters concerning the cardiovascular ischemic/thrombotic risks of the thiazolidinediones, with focus on rosiglitazone, as presented by the FDA and GlaxoSmithKline. This matter is coming before a joint meeting of the Endocrinologic and Metabolic Drugs and the Drug Safety and Risk Management Advisory Committees. This meeting is a particular matter involving specific parties.

The function of the Endocrinologic and Metabolic Drugs Advisory Committee 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 endocrine and metabolic disorders and to make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Schambelan has advised the Food and Drug Administration that he has a financial interest that could potentially be affected by his participation in the matter at issue. Dr. Schambelan serves as a member of the ——————— entity called the ——————————. He serves on their "Complications Committee" which is focused on side effects (particularly HIV-associated lipodystrophy) of their antiviral medications. The Committee meets approximately 3 times per year. Dr. Schambelan receives modest compensation for his participation. ——————— is the manufacturer of ——————————— and ——— ——————————, two of the competing products to the products at issue.

As a temporary voting member of the Endocrinologic and Metabolic Drugs Advisory Committee, Dr. Schambelan potentially could become involved in matters that could affect his financial interest. 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. Schambelan 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. Schambelan that would permit him to participate in the matters previously described.

First, it is important to consider that Dr. Schambelan's interest is unrelated to the particular matter in which he is being asked to participate, or to the competing products.

Second, this interest is not so substantial as to preclude his participation in this matter. He receives modest compensation from ——————————.

Third, the uniqueness of Dr. Schambelan's qualification justifies granting this waiver. According to the review Division, Dr. Morris Schambelan is one of three endocrinologists available on the date of the meeting who has had experience serving as a member of the Endocrine and Metabolic Drugs Advisory Committee. His research and professional experience include leading the Division of Endocrinology at San Francisco General Hospital and the fellowship training program. He has shown a distinguished career in academic medicine. These attributes have served him well in previous controversial matters discussed before a public advisory committee meeting. Dr. Schambelan has always displayed critical analytical skills of data presented, asked relevant scientific and public health questions, and has formulated decisions based on consideration of all data available. This skill set will be particularly relevant to this meeting as the agency is considering very broad clinical data sources from completed studies and ongoing trials. The topic of discussion is cardiovascular risk associated with rosiglitazone use. This issue is relevant as the risk of cardiovascular disease is already increased in the diabetic patient. However, it is also important to note that treatment of diabetes targets normal glycemic control to reduce many risks, microvascular and macrovascular. Over the past several decades, evidence that good glycemic control reduces the risk of microvascular complications such as kidney failure, blindness, and neuropathy is extensive from several large clinical trials. The changing landscape of morbidities that diabetics face today is very similar to the changes observed in the treatment of HIV. Dr. Schambelan has conducted numerous research and clinical investigations into the endocrine complications of HIV and his experience in this field will add to the discussion of managing diabetic patients as they replace short-term complications of their disease with long-term complications as a result of better disease control contributing to longevity of disease.

Additionally, the Agency was unable to find a similarly qualified individual with out disqualifying financial interests to serve on the committee. There are only 3 other

endocrinologists available to attend this meeting. One is the current NIDDK director and has no notable conflicts. The remaining two require waivers which have been submitted for consideration.

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 committees' 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. Schambelan is Professor of Medicine at the University of California, San Francisco and Chief of the Division of Endocrinology and Metabolism at San Francisco General Hospital Medical Center. He is board certified in internal medicine with a subspecialty in endocrinology and metabolism. He is a member of numerous academic organizations, such as the American Association for the Advancement of Science, the American Diabetes Association, the American Federation for Clinical Research,and the American Society for Clinical Investigation. I believe his participation will contribute to the diversity of opinions and expertise represented on the committees' and will provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant Morris Schambelan, M.D., a waiver that will permit him to participate in all official matters concerning the cardiovascular ischemic/thrombotic risks of the thiazolidinediones, with focus on rosiglitazone, as presented by the FDA and GlaxoSmithKline. I believe that such a waiver is appropriate because in this case, the need for the

services of Dr. Morris Schambelan outweighs the potential for a conflict of interest created by the financial interest attributable to him.

CONCURRENCE: /s/ 6/22/07

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)(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/ 6/29/07

Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy
Food and Drug Administration

Date