DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

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 David S. Schade, M.D

I am writing to request a waiver for David S. Schade 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 David S. Schade M.D., 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. Schade 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. Schade has been asked to participate in the discussions of 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 functions 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. Schade has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the matter previously described. Dr. Schade is currently a member of ———— Speaker's Bureau for ————. ———— is the sponsor of ———— and ————, competing products to the products at issue.

In addition, Dr. Schade serves as a consultant to ——— regarding an unrelated product, ————. ——— manufactures several competing products to the thiazolinediones.

Lastly, Dr. Schade attended a ———— sponsored forum in the past, which was a one time meeting. Arguably, his interest do not constitue a financial interest in the matter under 18 U.S.C. § 208(a). Nevertheless, in the utmost of caution, I recommend that this wavier be granted.

As a Temporary Voting Member of the Endocrinologic and Metabolic Drugs Advisory Committee, Dr. Schade 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. Schade 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. David Schade that would permit him to participate in the matter described previously.
First, it is significant to note that Dr. Schade's consulting and Speaker's Bureau activities are unrelated to the issue coming before the committees.

Second, Dr. Schade's interests are not so substantial as to preclude his participation in this meeting. He receives minimal compensation for his speaking and consulting activities.

Third, Dr. Schade's expertise makes him an invaluable resource to FDA for this important meeting. Dr. David Schade is one of two diabetologists identified whose background training is critical to this meeting as it will be discussing oral anti-diabetic drug rosiglitazone. At issue is the finding of a 40% increase in cardiac ischemic events in a population of patients with type 2 diabetes mellitus who are treated with Avandia (rosiglitazone) based on a pooling of 42 short-term clinical trials. As a diabetologist, Dr. Schade will provide expertise on the management of diabetic patients, the need for multiple/combination drug therapies, and the risk of disease balanced against the risk of drug therapy.

Lastly, the difficulty in locating a similarly qualified individual without a disqualifying financial interest to serve on the committee also justifies this waiver. The Division of Metabolism of Endocrinology Products contacted all current members of its advisory committee and also contacted Special Government Employees/past members with experience in the field of diabetology. Only two members with the level of expertise were available; one member was recused because he was on the speaker's bureau for GlaxoSmithKline, the manufacturer of rosiglitazone. The Division was able to invite a diabetologist from the National Institutes of Health; however, the importance of this meeting to the diabetes field requires more than one diabetologist to consider the data and inform other members as well as the agency on appropriate actions to take for rosiglitazone.

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 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.
Although cardiac safety of a drug is the main point of discussion, this is specific to the diabetes population. Dr. Schade's clinical experience will provide perspective on the day-to-day management of patients treated with a thiazolidinedione and other anti-diabetics. He has also been involved in numerous clinical trials of patients with type 2 diabetes mellitus which assess short-term and long-term benefits of blood sugar control. An understanding of short-term benefits of glucose control on complications such as infections, kidney failure, peripheral vascular disease, and visual disturbance is critical in this meeting, as it will place into perspective the importance of diabetes control even in the setting when benefits to cardiovascular risk reduction have not been established.

Accordingly, I recommend that you grant David S. Schade M.D., a waiver that would allow him to participate in the discussions of 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 David S. Schade, M.D., outweighs the potential for a conflict of interest created by the financial interest attributable to him.

CONCURRENCE: /S/ 7/3/07

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/ 7/5/07

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

Date