DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: March 13, 2007

TO: Randall W. 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 David A. Schoenfeld, Ph.D.

I am writing to request a waiver for David Schoenfeld Ph.D., a member of the Pulmonary and Allergy 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. Schoenfeld, 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. Schoenfeld 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. Shoenfeld has been asked to participate in all official matters concerning the efficacy supplement to New Drug Application (NDA) 21-077 for the approved product Advair Diskus 500/50 (fluticasone propionate/ salmeterol inhalation powder) for the proposed indication of increased survival and reduced exacerbations in patients with chronic obstructive pulmonary disease (COPD). Advair Diskus 500/50 is sponsored by GlaxoSmithKline. This matter is coming before the Pulmonary and Allergy Drugs Advisory Committee and is a particular matter involving specific parties.

The function of Pulmonary-Allergy 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 pulmonary disease and diseases with allergic and/or immunologic mechanisms and make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Schoenfeld has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the deliberations concerning GlaxoSmithKline's Advair Diskus 500/50. Dr. Schoenfeld is a consultant for ———, a Contract Research Organization. He does work part-time for an hourly fee. ——— has an agreement with a law firm representing ——— in a patent litigation suit against———. ——— has filed an intention to produce a generic formulation of a combination——— produced by ———. It involves whether the patent claims for the combination product are supported by the available data from an animal experiment conducted at the time the original patent was filed. The product involved in the suit is unrelated to products that could be affected by the committees' discussion. ——— is the parent company of ———, who makes ———, a competing product of Advair Diskus.

[redacted] also has a contract with [redacted] for a Health Canada application concerning a generic nasal decongestant spray. [redacted] received $[redacted] in funding and Dr. Schoenfeld expects to receive $[redacted] for analyzing the pharmacokinetic study. [redacted], an affiliate of [redacted], makes [redacted], a competing product of Advair Diskus.

Dr. Schoenfeld is the Director of the Biostatistics Unit at the Massachusetts General Hospital. [redacted] and the [redacted] are negotiating a contract for a study of an [redacted] treatment. If both parties accept the contract, the [redacted] will likely subcontract with the Biostatistics Unit at Massachusetts General Hospital (MGH). Dr. Schoenfeld would be compensated for his work as part of his MGH salary. Should [redacted] decide to do the study through [redacted], it is likely that [redacted] would hire Dr. Schoenfeld as a statistical consultant. In this instance, he would receive minimal compensation from [redacted].

As a member participating in the Pulmonary and Allergy Drugs Advisory Committee meeting, Dr. Schoenfeld 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)(3) to grant a waiver permitting Dr. Schoenfeld 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. Schoenfeld, which would permit him to participate in the matter previously described.

First, Dr. Schoenfeld's interests are not so substantial as to preclude his participation in this meeting. Dr. Schoenfeld receives minimal compensation for his work.

Second, the uniqueness of Dr. Schoenfeld's qualification justifies granting this waiver. Dr. Schoenfeld developed the first omnibus goodness of fit test for the proportional hazards regression model, a model that is used extensively in clinical trials which have survival or time to progression as

an endpoint. He also developed widely used graphical techniques for this model. In addition to his experience developing statistical analytic techniques, he has extensive experience designing and analyzing clinical trials. He authored a popular web site for sample size considerations for clinical trials. He has been director of the ARDS Clinical Network since its founding and was instrumental in initiating the procedures that have made that a successful ongoing group studying new therapies for the Adult Respiratory Distress Syndrome. In addition to his work with ARDS Net which is a national group supported by the NIH he collaborates with diverse clinical groups at the Massachusetts General Hospital. He has participated in collaborative work with the Endocrine Division, the Transplant Program and with the Cancer Genetics Network and Burn Unit. Dr. Schoenfeld's expertise is essential for an appropriate discussion of biostatistics and epidemiology which will take up significant portion of the discussion of this meeting.

Third, Dr. Schoenfeld has participated in past PADAC meetings and is cognizant of the needs of the Agency. In past meetings he has been quick to grasp the important issues and to make useful suggestions during the deliberations. The study that will be discussed at the May 1, 2007 meeting is large and complex. There were many analyses conducted each with a specific type of statistical analysis and each will require careful consideration. It is absolutely essential that we have an experienced biostatistician on the panel.

Lastly, Division of Pulmonary and Allergy Products feels that because of the nature of the issues to be discussed it is essential to have a number of experts in clinical trials and epidemiology participate in the advisory committee meeting. Further, the Division feels that biostatistics will be a key component of the discussions. In an attempt to gain the necessary expertise, the Division along with the Advisors and Consultants Staff contacted two Special Government Employee consultants in addition to the one standing biostatistician member. Of the three biostatisticians contacted, two accepted indicating that they were interested and available to attend the AC meeting. The one who declined, did so as a result of scheduling conflicts. The two who accepted will both require a waiver to participate in the

meeting due to their current financial interests. After consultation with the Division, it was determined that they would seek waivers for both statisticians because the expertise required for the analysis of controlled clinical trials is different from that used in the analysis of epidemiologic data. Therefore, both biostatisticians are needed for an adequate evaluation of the issues that will be discussed. The Division is seeking broad and diverse perspectives on the issues at hand in an effort to approach the topic in an objective and scientific manner. If any of the biostatisticians are recused, it will leave insufficient biostatistical expertise on the panel to adequately address the meeting issues. To that end, we are requesting that the waiver be granted for Dr. Shoenfeld to participate as there has been a genuine effort to secure individual participation and representation with minimal conflict of interest.

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 committee. 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. He is currently a professor in the Department of Biostatistics in the Harvard School of Public Health and a professor of medicine, HMS. Because the focus of the discussion will center upon a large, multi-national, long-term clinical trial in patients with COPD, his experience will provide valuable insight regarding issues in conducting and analyzing the results unique to such studies. I believe that Dr. Schoenfeld's participation will help provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant David A. Schoenfeld, Ph.D., a waiver that will permit him to participate fully in all official matters concerning the efficacy supplement to New Drug Application (NDA) 21-077 for the approved product Advair Diskus 500/50 (fluticasone propionate/ salmeterol inhalation powder) for the proposed indication of increased survival and reduced exacerbations in patients with chronic obstructive pulmonary disease (COPD). I

believe that such a waiver is appropriate because in this case, the need for the services of Dr. Schoenfeld outweighs the potential for a conflict of interest created by the financial interests involved.

CONCURRENCE: _____/s/_____ __3/30/07__
Vince Tolino Date
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

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/_____ __4/2/07___
Randall W. Lutter, Ph.D. Date
Associate Commissioner for
Policy and Planning
Food and Drug Administration