DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: March 26, 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 Stephen George, Ph.D.

I am writing to request a waiver for Stephen George, Ph.D., a temporary voting member of the Oncologic 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 Stephen George, Ph.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. George 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. George has been asked to participate in all official matters concerning New Drug Application (NDA) 022-092, proposed trade name Junovan (mifamurtide), formerly known as L-MTP-PE, liposomal muramyl tripeptide phosphatidyl ethanolamine, sponsored by IDM Pharma, Inc., for treatment of high-grade resectable non-metastatic osteosarcoma in combination with adjuvant chemotherapy for osteosarcoma. Genzyme Corporation, NOF Corporation, Ben Venue Laboratories, owned by Boehringer Ingelheim Corporation, the U.S. affiliate of Boehringer Ingelheim GmbH, and Solvias AG are the contract manufacturers of the liposomal formulation of muramyl tripeptide phosphatidyl- ethanolamine. This matter is coming before the Oncologic Drugs Advisory Committee for consideration and is a particular matter involving specific parties.

The functions of the Oncologic Drugs Advisory Committee, as stated in its Charter, are to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cancer, and to make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. George 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. George is a member of ——————— 's Independent Data Monitoring Committee for two unrelated studies. He also serves on a Steering Committee for ——————— on a matter unrelated to that coming before the committee for consideration. ——————— makes several competing products to Junovan, the product at issue, and ——— ——— is a contract manufacturer for ———.

As a temporary voting member of the Oncologic Drugs Advisory Committee, Dr. George 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. George 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. George that would permit him to participate in the matter previously described.

First, given the nature of the unrelated consulting Dr. George provides to both [redacted] and [redacted], it is unlikely that Committee's recommendations will impact the economic stability of the companies or his continued relationship with them. The possibility that Dr. George's impartiality will be called into question should be minimal.

Second, the Committee's role is advisory in nature and the Agency officials making the decisions are not bound by the recommendations of the Committee. Therefore, the Agency will take into consideration Dr. George's involvements when determining the action to be taken.

Further, the uniqueness of Dr. George's expertise makes him an invaluable resource to FDA for this important meeting. Dr. George is one of two invited participants with a primary background in biostatistics, with specific emphasis on clinical trial data analysis, including analyses of studies utilizing a multi-factorial design and evaluation for potential interactions. He also has extensive background and experience in oncology trial design and analysis. According to the Division of Oncologic Drug Products, Dr. George's participation is essential to assess whether the subset analyses proposed by the sponsor in support of this application is robust and reproducible, and that the data submitted demonstrates the efficacy of Junovan for its proposed indication. It is critical that a statistician who is an expert on the analytic methodology be present to guide and advise the clinicians in Oncologic Drugs Advisory Committee as to the most scientifically valid interpretation of these results and any limitations with respect to the study design in the analytic approach. The division strongly feels that at least two statisticians be present on the Committee to provide such advice and guidance to provide balance in approach and ensure these technical issues be thoroughly communicated and evaluated.

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. Dr. George is Director and Professor of Biostatistics, Department of Biostatistics and Bioinformatics at the Duke University Medical Center. Dr. George also serves as the Director of the Statistical Center and Group Statistician for the Cancer and Leukemia Group B (CALGB), a National Cancer Institute-funded cooperative clinical trials group, at Duke University. He is an expert in biostatistical and clinical trials methodology and has spent his career in the design and analysis of clinical oncology trials in oncology at tertiary care cancer centers, including pediatric oncology trials conducted by St. Jude Children's Research Hospital. Dr. George has written over 150 articles on such topics as sequential clinical trials in cancer, practical problems in the design, conduct, and analysis of cooperative clinical trials, and monitoring practices in cancer trials. In addition, Dr. George has served as a member or guest on the Oncologic Drugs Advisory Committee over a period of 5 years. Dr. George's extensive background in oncology trials, and especially in pediatric oncology trials, provide a unique expertise among statisticians available to provide advice to this Committee, thus no additional SGEs have been given consideration with respect to participation at this meeting.

Accordingly, I recommend that you grant Stephen George, Ph.D., a waiver that would allow him to participate in all official matters concerning New Drug Application (NDA) 022-092, proposed trade name Junovan (mifamurtide), sponsored by IDM Pharma, Inc., for treatment of high-grade resectable non-metastatic osteosarcoma in combination with adjuvant chemotherapy for osteosarcoma. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. George

outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: /s/ 4/10/07

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/ 4/20/07

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

Date