DEPARTMENT OF HEALTH & HUMAN SERVICES

MEMORANDUM

Food and Drug Administration
Rockville MD 20857

DATE: February 2, 2006

TO: Jason D. Brodsky
Acting Associate Commissioner
Office of 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 Ralph D'Agostino, Ph.D.

I am writing to request a waiver for Ralph D'Agostino, Ph.D. a consultant to the Center for Drug Evaluations and Research, 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. D'Agostino 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. D'Agostino 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

negotiating for, or as an arrangement concerning, prospective employment.

Dr. D'Agostino has been asked to participate in all official matters concerning NDA 20-509, S-039 Gemzar (Gemcitabine HCl), sponsored by Eli Lilly & Company, proposed for use in combination with Carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy. This matter is coming before the Oncology Drugs Advisory Committee for consideration.

In addition, Dr. D'Agostino has been invited to participate in the Pediatric Subcommitte of the Oncologic Drugs Advisory Committee meeting to discuss clinical trials of studies of methotrexate and daunomycin to be conducted under the Best Pharmaceuticals for Children Act. Methotrexate is sponsored by Mayne Pharma USA, a Mayne Group Ltd. Cerubidine (daunorubicin, daunomycin) is sponsored by Bedford Laboratories, a division of Ben Venue Laboratories, Inc., a wholly owned subsidiary of Boehringer Ingelheim Corporation, the U.S. affiliate of Boehringer Ingelheim GmbH.

The function of the Oncologic 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 cancer, and to make appropriate recommendations to the Commissioner of Food and Drugs. Temporary subcommittees consisting of two or more committee members may be established as needed to address specific issues within their respective areas of expertise. Subcommittees make preliminary recommendations regarding specific issues for subsequent action by the full Committee.

Dr. D'Agostino has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the matters previously described. Dr. D'Agostino is a consultant for [redacted] on an unrelated matter. [redacted] a competing product to Methotrexate.

Dr. D'Agostino serves as a member of two Advisory Committees for [redacted] on unrelated matters, one on [redacted] observational study of cardiac outcomes, and the other on cardiovascular [redacted]

Dr. D'Agostino consults for [redacted] on products used to treat [redacted] competing product to Cerubidine.

In addition, he serves as a member of [redacted] Advisory Committee regarding personal products. He receives nominal compensation for his service. [redacted], a competing product to Gemzar, and [redacted], a competing product to Cerubidine.

As a consultant advising the Pediatric Subcommittee and the Oncologic Drugs Advisory Committee, Dr. D'Agostino 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. D'Agostino 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. D'Agostino that would permit him to participate in the matters previously described.

First and foremost, arguably, Dr. D'Agostino's interests in [redacted] do not constitute financial interests in the particular matter within the meaning of 18 U.S.C. §208(b)(3), since his consulting is unrelated to Gemzar, Methotrexate, Cerubidine, or their competing products. Nevertheless, I recommend that this waiver be granted.

Moreover, Dr. D'Agostino's financial interest in [redacted] is not so substantial as to preclude his participation in the matters described previously. He receives minimal compensation for his consulting.

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. D'Agostino's 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. D'Agostino is the Executive Director of Biostatistics at the Harvard Clinical Research Institute (HCRI). He is an internationally recognized expert in the areas of longitudinal data analysis, multivariate data analysis, biostatistics and robust procedures. He is also a professor of mathematics, statistics, and public health at Boston University, and is an expert in statistical evaluations of data. Dr. D'Agostino is a member of the American Statistical Association and the Cardiovascular Epidemiology section of the American Heart Association. He is a co-author of four books on Factor Analysis, Goodness-of-Fit Techniques, Mathematical Models in Health Service Research, and Engineering Statistics, and has served on the editorial board of the journal of the American Statistical Association, Biostatistics, and Statistics in Medicine. I believe that Dr. D'Agostino's expertise in statistical analysis 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 Ralph D'Agostino, Ph.D., a waiver that will permit him to participate in all official matters concerning New Drug Application (NDA) 20-509, S-039 Gemzar (Gemcitabine HCl), sponsored by Eli Lilly & Company, proposed for use in combination with Carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy; and, discussions of clinical trials of methotrexate and daunomycin to be conducted under the Best Pharmaceuticals for Children Act. Methotrexate is sponsored by Mayne Pharma USA, a Mayne Group Ltd.

Cerubidine (daunorubicin, daunomycin) is sponsored by Bedford Laboratories, a division of Ben Venue Laboratories, Inc., a wholly owned subsidiary of Boehringer Ingelheim Corporation, the U.S. affiliate of Boehringer Ingelheim GmbH. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. D'Agostino outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: Mary Ann Kellogan for 2/6/04

Jenny Slaughter
Director, Ethics and
Integrity Staff
Office of Management Programs
Office of Management

Date

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.

2-9-06

Jason D. Brodsky
Acting Associate Commissioner
Office of External Relations
Food and Drug Administration

Date