DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: August 28, 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: 208(b)(3) Conflict of Interest Waiver for Ralph D'Agostino, Ph.D.

I am writing to request a waiver for Ralph D'Agostino, Ph.D., a member of the Nonprescription Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a). Waivers under section 208(b)(3) may be granted by the appointing official 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 section 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 his employer has a financial interest. Since Dr. D'Agostino is a special Government employee, he is under a statutory obligation to refrain from participating in any deliberations that involve a particular matter having a direct and predictable effect on a financial interest attributable to him or his employer.

The function of the Nonprescription Drugs Advisory Committee is to review and evaluate available data concerning the safety and effectiveness of over-the-counter (nonprescription) human drug products, or any other FDA-regulated product, for use in the treatment of a broad spectrum of human symptoms and diseases and advise the Commissioner either on the promulgation of monographs establishing conditions under which these drugs are generally recognized as safe and effective and not misbranded or on the approval of new drug application for such drugs. The Committee also serves as a forum for the exchange of views regarding the prescription and nonprescription status, including switches from one status to another, of these various drug products and combinations thereof.

The function of the Pediatric Advisory Committee is to advise and makes recommendations to the Commissioner of Food and Drugs on matters relating to pediatric therapeutics, pediatric research, and any other matter involving pediatrics for which the Food and Drug Administration has regulatory responsibility. The Committee also advises and makes recommendations to the Secretary pursuant to 45 CFR 46.407 on research involving children as subjects that is conducted or supported by the Department of Health and Human Services.

Dr. D'Agostino has been asked to participate in all official matters at the joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee to discuss the safety and efficacy of over-the-counter (OTC) cough and cold products marketed for pediatric use. A citizen petition was submitted to FDA on March 1, 2007, that raised concerns about the safety and efficacy of cough and cold products in children under six years of age. The petition requested among other things that FDA amend the OTC drug monograph for Cold, Cough, Allergy, Bronchodilator, and Ant asthmatic Drug Products (CCABADP) in 21 CFR Part 341 to require that labeling for over-the-counter antitussive, expectorant, nasal decongestant, antihistamine, and combination cough and cold products state that these products have not been found to be safe or effective in children under 6 years of age for the treatment of cough and cold, and that these products should not be used for the treatment of cough and cold in children under 6 years of age. In addition, the petitioner requested the Agency to notify manufacturers of these products whose labeling either uses such terms as “infant” or “baby” or displays images of children under the age of 6, that such marketing is not supported by scientific evidence and that manufacturers will be subject to enforcement action at any time.

This matter is coming before a joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee. This issue is a particular matter involving specific parties.

Dr. D'Agostino has advised the Food and Drug Administration (FDA) that he has a financial interest that could potentially be affected by his participation in the matter described above. Dr. D'Agostino is on a Data Safety Monitoring Board (DSMB) for ------ on an unrelated issue. ------ is a firm that could potentially be affected by the committees’ discussions and recommendations. ------ makes over-the-counter (OTC) cough and cold products marketed for pediatric use, such as ------.

In addition, Dr. D'Agostino's employer, Harvard Clinical Research Institute, has contracts with ------ that are unrelated to the issues to be discussed. Arguably, his employer's interests do not constitute a financial interest in the particular matter under section 208(a) since they are unrelated to the issue at hand. Nevertheless, in the utmost of caution, I recommend that this waiver be granted.

As a member of the Nonprescription Drugs Advisory Committee, Dr. D'Agostino potentially could become involved in matters that could affect his financial interests. Under section 208, 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 allowing 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 allow him to participate fully in the matter described because the need for his services greatly outweighs the conflict of interest created by this financial interest.

First, it is important to consider that Dr. D'Agostino's interest in ------ is unrelated to over-the-counter (OTC) cough and cold products marketed for pediatric use.

Second, Dr. D'Agostino's financial interest in ------ is not so substantial as to preclude his participation in this meeting. He receives minimal compensation for serving on the Data Safety Monitoring Board.

Third, according to the Division of Nonprescription Clinical Evaluation, the uniqueness of Dr. D'Agostino's qualifications justifies granting this waiver. Dr. D'Agostino received his doctorate in Mathematical Statistics from Harvard University. He has an outstanding record of research and publications in biostatistics. He has received numerous honors for his work including the Commissioner's Special Citation from the FDA, twice. Dr. D'Agostino has received numerous federal grants supporting his work. He presently serves as a consultant to the Divisions of Biometrics, Oncology, and to the Office of Nonprescription Products at the FDA, and he has previously served as a member of advisory committees including the Nonprescription Drugs Advisory Committee (1995-1998), and the Gastrointestinal Advisory Committee (1990-1994). He also participated on the committee that recently (2006) discussed issues regarding consumer studies such as label comprehension and actual use studies that are instrumental to approval of nonprescription drug products.

The Division's experience with Dr. D'Agostino has been unmatchable. His ability to analyze statistical problems and present concise interpretation to non-statistical advisory committee members has been and continues to be invaluable. Due to his previous experience on the Nonprescription Drugs Advisory Committee, Dr. D'Agostino understands the complex regulatory scheme by which nonprescription drug products are marketed and the data that is required to amend any existing monographs. With his extensive experience in reviewing clinical trial data, Dr. D'Agostino is able to discuss clinical issues as they relate to statistical certainty. For this meeting, one of the important issues for discussion is whether clinical studies reported in the medical literature establish that cough and cold products are not effective in children. Dr. D'Agostino will be able to opine on the quality and validity of these studies in determining whether cough and cold

products are not effective. Dr. D'Agostino's unique combination of experience in matters where epidemiologic surveillance and complex statistical analysis are required, his in-depth knowledge of nonprescription drug products, and his experience with the advisory committee process makes him uniquely qualified. For these reasons, the Division believes that Dr. D'Agostino is uniquely qualified and, therefore, a search was not done for an alternate statistician. The Center believes the benefits of Dr. D'Agostion's participation in this meeting will greatly outweigh any potential financial conflicts of interest.

Moreover, 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. 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 broad clinical and research experience will contribute to the diversity of opinions and expertise represented on the committee.

Accordingly, I recommend that you grant Ralph D'Agostino, Ph.D., a waiver that would allow him to participate in all official matters concerning the safety and efficacy of over-the-counter (OTC) cough and cold products marketed for pediatric use. 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 interest attributed to him.

CONCURRENCE: /S/ 10/2/07

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 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/ 10/2/07

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

Date