DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: October 11, 2007

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

THROUGH: Vince Tolino_____/s/_____
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Michael F. Ortwerth, Ph.D._____/s/_____
Deputy Director, Advisory Committee Oversight and Management Staff
Office of Policy, Planning, and Preparedness

FROM: Igor Cerny, Pharm.D._____/s/_____
Director, Advisors and Consultants Staff
Center for Drug Evaluation and Research

SUBJECT: 712(c)(2)(B) 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 section 712(c)(2)(A) of the Federal Food, Drug, and Cosmetic Act. Waivers under section 712(c)(2)(B) may be granted by the appointing official where it is "necessary to afford the advisory committee essential expertise" and where the individual has made a disclosure to FDA of the financial interests at issue. We have determined that you are the appointing official for purposes of section712(c)(2)(B). Therefore, you have the authority to grant Dr. D'Agostino a waiver under section 712(c)(2)(B).

Section 712(c)(2)(A) prohibits Federal executive branch employees, including special Government employees, from participating in any particular matter in which the employee or an immediate family member has a financial interest that could be affected by the advice given to the FDA with respect to the matter. Because 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.

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 make 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 ------.

As a member of the Nonprescription Drugs Advisory Committee, Dr. D'Agostino could become involved in matters that could affect his financial interest. Under section 712(c)(2)(B), he is prohibited from participating in such matters. However, as noted above, you have the authority under section 712(c)(2)(B) to grant a waiver permitting Dr. D'Agostino to participate in such matters if necessary to afford these committees essential expertise.

For the following reasons, I believe that it would be appropriate for you to grant a waiver to Dr. Ralph D'Agostino that would allow him to participate fully in the matter described because his voting participation is necessary to afford the committee essential expertise.

First, 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. I believe that participation by Dr. D'Agostino in the committees' deliberations will contribute to the diversity of opinions and expertise represented on the committees.

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.

Accordingly, I recommend that you grant Ralph D'Agostino, Ph.D., a waiver that would allow his voting participation 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, Dr. D'Agostino's voting participation is necessary to afford the committee essential expertise.

DECISION:

__x__ Waiver granted based on my determination, made in accordance with section 712(c)(2)(B) of the Federal Food, Drug, and Cosmetic Act, that voting participation is necessary to afford the committee essential expertise.

____ Waiver granted based on my determination, made in accordance with section 712(c)(2)(B) of the Federal Food, Drug, and Cosmetic Act, that nonvoting participation is necessary to afford the committee essential expertise.

_____ Waiver denied.

_____/s/_____ 10/16/07

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