



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: December 13, 2007

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

THROUGH: Vince Tolino 151 12/21/07
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Michael F. Ortwerth, Ph.D. 151
Deputy Director, Advisory Committee Oversight and Management Staff
Office of Policy, Planning, and Preparedness

FROM: Igor Cerny, Pharm.D. 151
Director, Advisors and Consultants Staff
Center for Drug Evaluation and Research

SUBJECT: 712(c)(2)(B) Conflict of Interest Waiver for Robert Harrington, M.D.

I am writing to request a waiver for Robert Harrington, M.D., a member of the Drug Safety and Risk Management Committee of the Center for Drug Evaluation and Research, 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 section 712(c)(2)(B). Therefore, you have the authority to grant Dr. Harrington 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. Harrington 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 Drug Safety and Risk Management Advisory Committee, as stated in its Charter, is to advise the Commissioner of Food and Drugs on risk management, risk communication, and quantitative evaluation of spontaneous reports for drugs for human use and for any other product for which the Food and Drug Administration has regulatory responsibility. The committee also advises the Commissioner of Food and Drugs regarding the scientific and medical evaluation of all information gathered by the Department of Health and Human Services and the Department of Justice with regard to safety, efficacy, and abuse potential of drugs or other substances, and recommends actions to be taken by the Department of Health and Human Services with regard to the marketing, investigation, and control of such drugs or other substance.

Dr. Harrington has been asked to participate in the discussions of the safety and efficacy of new drug application (NDA) 22-054, INJECTAFER (ferric carboxymaltose injection), used for the treatment of iron deficiency anemia in patients with postpartum hemorrhage or heavy uterine bleeding. INJECTAFER is sponsored by Luitpold Pharmaceuticals, Inc., a wholly owned subsidiary of Daiichi Sankyo Co., Ltd. Of Japan. If approved, INJECTAFER will be marketed in the U.S. by American Regent, Inc., a subsidiary of Luitpold Pharmaceuticals, Inc.

This matter is coming before a meeting of Drug Safety and Risk Management Advisory Committee. This issue is a particular matter involving specific parties.

Dr. Harrington 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. Harrington is a member of _____ Data Safety Monitoring Committee for _____ for the treatment of _____, an issue unrelated to the Committee's agenda. _____ is the manufacturer of _____, a competing product to INJECTAFER.

As a temporary voting member of the Drug Safety and Risk Management Advisory Committee, Dr. Harrington could become involved in matters that could affect his financial interest. Under section 712(c)(2)(A), 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. Harrington to participate in such matters if necessary to afford this committee essential expertise.

For the following reasons, I believe that it would be appropriate for you to grant a waiver to Dr. Harrington that would allow him to participate in the matter described because the need for his services greatly outweighs the conflict of interest created by this financial interest.

According to the review division, this Drug Safety and Risk Management (DSaRM) advisory committee will discuss the risks and benefits of a new drug to treatment iron deficiency anemia (iron carboxymaltose, Luitpold, Inc). FDA anticipates that the committee will make recommendations regarding market approval of the drug. FDA has identified three major safety concerns for the drug: excessive numbers of deaths, excessive risks for severe decreases in blood phosphate (mineral) levels and excessive risks for serious adverse reactions. FDA's concerns are based upon epidemiological assessment of the new products' safety database and considerations of the potential cardiac causes for the safety risks.

As a prelude to questions of overall marketing consideration, FDA plans to ask the DSaRM committee about the importance of epidemiological data assessments and cardiac considerations for people with iron deficiency anemia. FDA has chosen the DSaRM committee as the venue because the new drug is a variant of other FDA-approved drugs that are currently marketed and because epidemiological, statistical, hematological and cardiovascular expertise is essential to fully interpreting the new drug's safety database and because drug safety is the major FDA concern for the drug (not efficacy). FDA is working to supplement the drug safety experts on DSaRM committee with experts in cardiovascular and hematologic diseases as well as other subspecialists familiar with the management of iron deficiency anemia.

Dr. Robert Harrington is currently a Director of Cardiovascular Clinical Trials at the Duke Clinical Research Institute in North Carolina. He has an extensive experience in cardiovascular research and the clinical care of patients with cardiac problems. His particular research background focuses upon coronary artery disease and specifically acute myocardial ischemia and death, one of the major safety concerns applicable to review of safety issues for the new drug to be discussed at the DSaRM. Dr. Harrington has extensive experience in the review of clinical trial data, including service as a chairman of an FDA advisory Committee. The DSaRM lacks cardiovascular expertise and the participation of at least two cardiovascular experts is essential to a thorough discussion of the drug's risk. Dr. Harrington is uniquely qualified and essential to the review of this new drug due to his overall clinical trial experience as well as his expertise in the review of mortality data from clinical trials, especially mortality related to cardiovascular disease (which is the main safety consideration for this new drug). Dr. Harrington's participation will help to ensure adequate and varied scientific analysis and discourse. Therefore, Dr. Harrington's participation is critical to include a variety of viewpoints from the pharmacoepidemiology and cardiovascular/renal community.

At this time, of the three individuals considered as possible alternatives to Dr. Harrington, all were more seriously conflicted, requiring 208 and 712 waivers or unavailable to participate in this advisory committee meeting, leaving Dr. Harrington, the least conflicted. The Division believes that Dr. Harrington's participation will bring an enormous amount of experience, knowledge and expertise in the field of cardiovascular medicine and clinical trials that is essential to the committee's discussions and will help provide a foundation for developing advice and recommendations that are fair and comprehensive. Due to the safety issues involved with this product, it is essential to have more than one cardiovascular expert on the panel. If Dr. Harrington is recused, it will leave the committee with insufficient cardiovascular expertise on this panel.

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 Robert Harrington, M.D., a waiver that would allow his voting participation in all official matters concerning the discussions of the safety and efficacy of new drug application (NDA) 22-054, INJECTAFER (ferric carboxymaltose injection), used for the treatment of iron deficiency anemia in patients with postpartum hemorrhage or heavy uterine bleeding. I believe that such a waiver is appropriate because in this case, Dr. Harrington's voting participation is necessary to afford the committee essential expertise.

DECISION:

- 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.

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

1/3/08
Date