



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

DATE: April 14, 2008

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 Maha Hussain, M.D.

I am writing to request a waiver for Maha Hussain, M.D., a Member of the Oncologic 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 section 712(c)(2)(B). Therefore, you have the authority to grant Dr. Hussain 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. Hussain is a special Government employee, she 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 her.

The function of the Oncologic Drugs Advisory Committee 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.

Dr. Hussain has been asked to chair the May 30, 2008, meeting to discuss New Drug Application (NDA) 022-291, Promacta (eltrombopag olamine), originally developed by Ligand Pharmaceuticals Inc., in collaboration agreement with GlaxoSmithKline, for the proposed indication for short-term treatment of previously-treated patients with chronic idiopathic thrombocytopenic purpura (ITP) to increase platelet counts and reduce or prevent bleeding.

This matter is coming before the Oncologic Drugs Advisory Committee. This issue is a particular matters involving specific parties.

Dr. Hussain has advised the Food and Drug Administration (FDA) that she \_\_\_\_\_ have current financial interests which could potentially be affected by her participation in the matter described above. Dr. Hussain \_\_\_\_\_ own stock in \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, and \_\_\_\_\_. Dr. Hussain \_\_\_\_\_ do not have management control of \_\_\_\_\_ stock holdings. A fiduciary third party has complete management discretion.

\_\_\_\_\_ is the sponsor of \_\_\_\_\_;  
\_\_\_\_\_ makes \_\_\_\_\_, \_\_\_\_\_ makes \_\_\_\_\_,  
\_\_\_\_\_ makes \_\_\_\_\_ (generic) and \_\_\_\_\_ (generic), \_\_\_\_\_,  
\_\_\_\_\_, a subsidiary of \_\_\_\_\_ makes \_\_\_\_\_),  
\_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_,  
\_\_\_\_\_, \_\_\_\_\_, and \_\_\_\_\_  
\_\_\_\_\_, \_\_\_\_\_ makes \_\_\_\_\_,  
\_\_\_\_\_, part of \_\_\_\_\_ makes \_\_\_\_\_,  
\_\_\_\_\_ makes \_\_\_\_\_ (generic), \_\_\_\_\_,  
\_\_\_\_\_, and \_\_\_\_\_ (generic), all are competing products to Promacta.

As a Member of the Oncologic Drugs Advisory Committee, Dr. Hussain could become involved in matters that could affect her financial interests. Under section 712(c)(2)(A), she 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. Hussain 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. Hussain that would allow her to participate fully in the matters described because her voting participation is necessary to afford the committee essential expertise.

First, Dr. Hussain's stock interests are not so substantial as to preclude her participation in the matters coming before the committee. Additionally, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, and \_\_\_\_\_ are large, well-established firms with multiple product lines and global presence. It is unlikely that the committee's recommendations will significantly impact the economic stability of these companies.

Second, the need for Dr. Hussain's participation outweighs the conflict created by her financial interests. The first topic involves the marketing consideration for the first drug in a new class of hematologic growth factors. This class of drugs has a hypothetical risk for inducing or worsening cancer and/or leukemia. This drug, Promacta (also known as eltrombopag) acts within megakaryocytes to increase the production of platelets and is proposed for use to treat a deficiency in blood platelet production. The specific deficiency of platelets occurs in a very uncommon condition called chronic idiopathic (immunogenic) thrombocytopenic purpura (ITP). The rarity of the condition is exemplified by the fact that less than 300 patients were included in the studies of Promacta. Dr. Hussain has unparalleled experience in critical analysis of clinical study data from small sample size clinical studies (especially for products that may alter cancer growth), and interpreting these data in the context of actual physician usage of a drug. All studies of Promacta were small sample size studies and Dr. Hussain's experience with these types of studies is essential to thoroughly assessing the risks and benefits of the drug.

The Food and Drug Administration has determined that it is important to try to maximize attendance among the standing members of the Oncologic Drugs Advisory Committee (due to the cancer-related nature of Promacta considerations) and also to try to supplement the committee with additional experts. Of the thirty-four non-member SGEs that were invited to this meeting, twenty-six are unable to attend. Fourteen of these SGEs not attending have a background in either Hematology or Hematology/Oncology as does Dr. Hussain. Dr. Hussain's expertise in the analysis of small sample size clinical studies and cancer considerations will be important to informing the discussion at this meeting.

Dr. Hussain is the current chair of the Oncologic Drugs Advisory Committee and has chaired the Oncologic Drugs Advisory Committee meetings since 2006. She has participated as a voting member of the committee since 2004. In considering the issues involved with this topic, it is paramount that the panel chair be someone who is both qualified and experienced to guide and advise the clinicians on Oncologic Drugs Advisory Committee as to the most scientifically valid interpretation of the topic at hand. Although other members or SGEs that are attending this meeting have a similar background as Dr. Hussain, the division strongly feels that Dr. Hussain is capable of delivering this guidance in the most qualified manner to provide balance in approach and ensure a sound scientific discussion. Furthermore, according to the Review Division, the uniqueness of Dr. Hussain's qualification justifies granting this waiver. I believe that participation by Dr. Hussain in the committee's deliberations will contribute to the diversity of opinions and expertise represented on the committee.

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. Hussain currently serves as Professor of Medicine and Urology in the Departments of Internal Medicine and Urology, Division of Hematology/Oncology at the University of Michigan. Dr. Hussain is a national expert and leader in the management of prostate and bladder cancer and chairs the Advanced Prostate Cancer Subcommittee of the Southwest Oncology Group. Dr. Hussain is the author of more than 60 articles and book chapters and actively participates in clinical trials in urologic malignancies and development of novel therapies.

Accordingly, I recommend that you grant Maha Hussain, M.D., a waiver that would allow her voting participation in all official matters concerning New Drug Application (NDA) 022-291, Promacta (eltrombopag olamine), originally developed by Ligand Pharmaceuticals Inc., in collaboration agreement with GlaxoSmithKline, for the proposed indication for short-term treatment of previously-treated patients with chronic idiopathic thrombocytopenic purpura (ITP) to increase platelet counts and reduce or prevent bleeding. I believe that such a waiver is appropriate because in this case, Dr. Hussain'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.

\_\_\_\_\_/S/\_\_\_\_\_  
Randall W. Lutter, Ph.D.  
Deputy Commissioner for Policy  
Food and Drug Administration

\_\_\_\_4/29/08\_\_\_\_  
Date