



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: 208(b)(3) Conflict of Interest Waiver for Gary Lyman, M.D.

I am writing to request a waiver for Gary Lyman, M.D., a Member of the Oncologic 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. Lyman 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. Because Dr. Lyman 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 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. Lyman has been asked to participate in 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 a meeting of the Oncologic Drugs Advisory Committee. This issue is a particular matter involving specific parties.

Dr. Lyman has advised the Food and Drug Administration (FDA) that he has a current financial interest which could potentially be affected by his participation in the matter described above. Dr. Lyman is a member of _____ Speaker's Bureau regarding _____ and _____ issues, topics unrelated to the meetings discussions of Promacta. _____ makes _____, a competing product to Promacta.

As a Member of the Oncologic Drugs Advisory Committee, Dr. Lyman potentially could become involved in matters that could affect his financial interest. Under section 208, he is prohibited from participating in such matters. However, as noted above, you have the authority under section 208(b)(3) to grant a waiver permitting Dr. Lyman 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. Lyman 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 significant to note that Dr. Lyman's _____ interest is unrelated to the issue coming before the committee. Dr. Lyman's lectures concern _____ and _____ _____ is a condition marked by _____ and _____ effects of cancer chemotherapy. Having _____

Second, Dr. Lyman's interest is not so substantial as to preclude his participation in this meeting. He receives minimal compensation for his services to _____

Third, Dr. Lyman's expertise makes him an invaluable resource to FDA for this important meeting. Dr. Lyman's expertise includes Medical Oncology, Hematology, Biostatistics and Epidemiology. This multidisciplinary expertise is important for this advisory committee because the Promacta (eltrombopag olamine) clinical studies were predominantly short term (six week) clinical studies even though the product will likely be used long term (potentially life-long) in

some patients. The evaluation of short term clinical data in the context of a chronic treatment need is an area that Dr. Lyman's expertise would be especially useful since he has both the clinical as well as statistical background to thoroughly weigh the issues.

The division feels strongly that Dr. Lyman has the background and expertise to engage in an appropriate and stimulating discussion during the meeting. His areas of expertise will bring a wide range of knowledge to this meeting. Promacta (eltrombopag olamine), the drug to be discussed at the meeting, is proposed for use among patients with chronic immune (idiopathic) thrombocytopenic purpura, a bleeding condition in which the blood doesn't clot as it should due to a low number of platelets. The number of individuals in the United States with ITP has been estimated to be approximately 200,000. Promacta (eltrombopag olamine) is a member of a class of products that have been thought to serve a role in the initiation or promotion of cancer (especially leukemia). Hence, Dr. Lyman's extraordinary combination of expertise in statistical aspects of data (especially from small sample clinical studies) combined with his knowledge of cancer will provide a unique perspective that should importantly bolster the regulatory review of Promacta (eltrombopag olamine). As a new molecular entity, a close review of Promacta's (eltrombopag olamine) safety and efficacy is essential, since the available data are much more limited than FDA usually receives.

Dr. Lyman's expertise includes Medical Oncology, Hematology, Biostatistics and Epidemiology. Three other statisticians/biostatisticians were invited to the meeting, all with a background in Medical Oncology. One requires an appearance determination for the meeting, one is cleared to attend the meeting and the other is unable to attend due to a schedule conflict. 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. Lyman. However, Dr. Lyman's expertise differs in that he has experience in Biostatistics and Epidemiology as well as Medical Oncology and Hematology.

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. Gary Lyman currently holds the position of Director of the Health Services and Outcomes Research Program in Oncology at Duke University. In addition, Dr. Lyman serves as Senior Fellow for the Duke Center for Clinical Health Policy Research and is a member of the Duke University Comprehensive Cancer Center. He is also a reviewer for the Breast Cancer Review Group and is a member of the Health Services Research Committee for the American Society of Clinical Oncology.

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