



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

DATE: December 6, 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: 208(b)(3) Conflict of Interest Waiver for Michael Epstein, M.D.

I am writing to request a waiver for Michael Epstein, M.D., a member of the Gastrointestinal 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. Michael Epstein 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. Epstein 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 Gastrointestinal Drugs Advisory Committee, as stated in its charter 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 gastrointestinal diseases and to make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Michael Epstein has been asked to participate in the discussions of the safety and efficacy of Entereg (alvimopan), new drug application (NDA) 21-775, Adolor Corporation, for the proposed indication of acceleration of time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis. Originally developed by Eli Lilly, licensed to Shire Pharmaceuticals Group, currently GlaxoSmithKline and Adolor Corporation are in collaborative agreement for development and commercialization

This matter is coming before a meeting of the Gastrointestinal Drugs Advisory Committee. This issue is a particular matter involving specific parties.

**Dr. Epstein 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. Epstein is on \_\_\_\_\_ Speakers Bureau and lectures regarding their product \_\_\_\_\_, for use in \_\_\_\_\_ constipation, an indication unrelated to the indication coming before the committee. \_\_\_\_\_ is a competing product to Entereg.**

As a member of the Gastrointestinal Drugs Advisory Committee, Dr. Epstein 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 18 U.S.C. §208(b)(3) to grant a waiver permitting Dr. Epstein 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. Epstein that would allow him to participate in the matter described above because the need for his services greatly outweighs the conflict of interest created by this financial interest.

First, although Dr. Epstein lectures with regards to \_\_\_\_\_ a competing product, it is for a different indication.

Second, this interest is not so substantial as to preclude Dr. Epstein's participation. Dr. Epstein receives nominal compensation for his lecturing.

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. Michael Epstein is Assistant Professor of Medicine at the Uniformed Services of Health Sciences, Bethesda, Maryland, and Staff Gastroenterologist, Anne Arundel Medical Center, Annapolis, MD. He has had broad experience treating a variety of gastrointestinal disorders over his lengthy career. He is very knowledgeable regarding clinical trial conduct and practice, having participated in several studies on a wide variety of gastroenterological diseases. His broad experience gives him a unique ability to understand the complications of extended hospital recovery and the potential benefits of earlier discharge from the hospital. This is highly

important, as one of the major factors balancing the potential cardiovascular risk is a practical evaluation of the shortened hospital time weighed against such risk. In addition, Dr. Epstein will have the unique perspective of being able to comment on the proposed risk management plan and its potential to mitigate the potential risks. We have had extreme difficulty in locating similarly qualified gastroenterologists without a disqualifying financial interest to serve on the committee. The division feels that it is very important to gain the perspective of several gastroenterologists to consider a wider perspective and account for all aspects of the product under review. After inviting 16 gastroenterologists, 2 are cleared to participate, 3 were recused, 6 declined to participate, and 4 had minimal financial interests. We are requesting a waiver only for Dr. Epstein. I believe that participation by Dr. Epstein in the committee's deliberations will contribute to the diversity of opinions and expertise represented on the committee.

Accordingly, I recommend that you grant Michael Epstein, M.D., a waiver that would allow him to participate in all official matters concerning the discussions of the safety and efficacy of Entereg (alvimopan), new drug application (NDA) 21-775, Adolor Corporation, for the proposed indication of acceleration of time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Epstein outweighs the potential for a conflict of interest created by the financial interest attributed to him.

DECISION:

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.

151  
Randall W. Lutter, Ph.D.  
Deputy Commissioner for Policy  
Food and Drug Administration

12/21/07  
Date