



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 15/  
Director, Ethics and Integrity Staff  
Office of Management Programs  
Office of Management

Michael F. Ortwerth, Ph.D. 15/  
Deputy Director, Advisory Committee Oversight and Management Staff  
Office of Policy, Planning, and Preparedness

FROM: Igor Cerny, Pharm.D. 15/  
Director, Advisors and Consultants Staff  
Center for Drug Evaluation and Research

SUBJECT: 208(b)(1) Conflict of Interest Waiver for Joseph Cullen, M.D.

I am writing to request a waiver for Joseph Cullen, M.D., a temporary 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)(1) may be granted by the appointing official where "the [financial] interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from such employee" 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. Joseph Cullen a waiver under section 208(b)(1).

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. Cullen 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. Joseph Cullen 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. Joseph Cullen 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. Cullen is a co-investigator for a study of \_\_\_\_\_ at the University of Iowa. \_\_\_\_\_ is providing a total of \$\_\_\_\_\_ to the University for direct and indirect costs. The University anticipates enrolling a total of 6 patients. Dr. Cullen's only involvement is that he performs gastrointestinal surgery and some of his patients may receive \_\_\_\_\_ as part of this trial. The study is run by the Department of Anesthesia and the Principle Investigator is Dr. \_\_\_\_\_, an anesthesiologist. Dr. Cullen doesn't receive any personal remuneration or salary support from the funds received. \_\_\_\_\_ is an investigational competing product to Entereg.**

As a temporary member to the Gastrointestinal Drugs Advisory Committee, Dr. Cullen 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)(1) to grant a waiver permitting Dr. Cullen 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. Cullen that would allow him to participate in the matter described because the financial interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from him.

First, it is important to consider that Dr. Cullen's only role in this study is as a surgeon, performing the gastrointestinal surgery. He is not involved with entering patients into the study or follow-up on the patients for the study.

Second, this interest is not so substantial as to preclude Dr. Cullen's participation. Dr. Cullen himself receives no additional compensation from the funding his employer receives for this study. In addition, the total funding to his employer for this study is nominal.

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 couldnot 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. Joseph Cullen, M.D., FACS, is currently the Chief of General Surgery and Chief of Surgical Service, Veterans Affairs Medical Center, Iowa City, Iowa. He also is an Associate Professor of Surgery and Associate Professor of Radiation Oncology, the University of Iowa, College of Medicine, Iowa City, Iowa. He has extensive experience in the area of gastrointestinal operations and gastrointestinal motility. He is uniquely qualified because of his work in the area of gastrointestinal operations and gastrointestinal motility over many years. The Division of Gastrointestinal Products (DGP) feels that it would be pertinent to have a panel of experts that include more than one expert in the area of GI surgery, to consider a wider perspective and account for all aspects of the product under review. It is especially important as this committee engages in the discussion of the indication at hand, accelerating the time of upper and lower gastrointestinal recovery following partial small or large bowel resection with primary anastomosis. It is of vital importance to have Dr. Cullen as someone with extensive experience and knowledge of treating and managing patients for upper and lower gastrointestinal recovery following partial small or large bowel resection with primary anastomosis. He would be able to evaluate the risks and benefits of the proposed new therapy. We have had extreme difficulty in locating a similarly qualified individual without a disqualifying financial interest to serve on the committee. As mentioned above, the division is interested in gaining the perspective of more than one expert in an effort to remain objective and in doing so requests that a waiver be granted for Dr. Joseph Cullen, M.D. to participate. Dr. Cullen is one of the few surgeon SGEs with CDER and is uniquely qualified because he is the only GI surgeon. Two surgeons were invited, but Dr. Cullen's specific expertise is in gastrointestinal surgery, whereas the other surgeon is specialized in abdominal surgery. I believe that participation by Dr. Cullen in the committee's deliberations will contribute to the diversity of opinions and expertise represented on the committee.

Accordingly, I recommend that you grant Joseph Cullen, 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

**APPEARS THIS WAY  
ON ORIGINAL**

case, Dr. Cullen's imputed financial interest is not so substantial as to be deemed likely to affect the integrity of the services that the agency may expect from him.

DECISION:

Waiver granted based on my determination, made in accordance with section 208(b)(1), that the [financial] interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from this individual.

Waiver denied.

15/  
Randall W. Lutter, Ph.D.  
Deputy Commissioner for Policy  
Food and Drug Administration

12/21/07  
Date