DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: June 13, 2007

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

THROUGH: Vince Tolino
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

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

SUBJECT: Conflict of Interest Waiver for James Neaton, Ph.D.

I am writing to request a waiver for James Neaton, Ph.D., a temporary voting member to the Gastrointestinal Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a). The appointing official may grant waivers under section 208(b)(3) 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. Neaton a waiver under 18 U.S.C. §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 any other person whose interests are imputed to the employee under 18 U.S.C. §208, has a financial interest. Since Dr. Neaton is a special Government employee, he is under a statutory obligation to refrain from participating in an official capacity in any particular matter having a direct and predictable effect on a financial interest attributable to him, his spouse, minor child, or general partner; an organization or entity for which he serves as an officer, director, trustee, general partner, or employee; and, a person with whom he is negotiating for, or has an arrangement concerning, prospective employment.

Dr. Neaton has been asked to participate in all official matters concerning the safety and efficacy of Biologic License Application (BLA) 125104/33, Tysabri (Natalizumab) injection, for the proposed indication of inducing and maintaining sustained response and remission, and eliminating corticosteroid use in patients with moderately to severely active Crohn's disease with inflammation, as evidenced by elevated C-reactive protein (CRP) level or another objective marker. The committees will also discuss the risks (including progressive multifocal leukoencephalopathy) associated with TYSABRI (natalizumab) administration, its efficacy in the treatment of moderate to severe Crohn's disease, and proposed risk management plan(s). Tysabri is sponsored by Biogen Idec, Inc. and Elan Pharmaceuticals, a subsidiary of Elan Corporation, plc. These matters are coming before a joint meeting of the Gastrointestinal Drugs and the Drug Safety and Risk Management Advisory Committees. This meeting is a particular matter involving specific parties.

The function of the Gastrointestinal Drugs Advisory Committee, as stated in it's 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. Neaton has advised the Food and Drug Administration that he has a financial interest that could potentially be affected by his participation in the matters at issue. Dr. Neaton is a member of [redacted]'s Data Safety Monitoring Board for an on-going study of an unrelated drug, [redacted], for heart failure. [redacted] makes [redacted], a competing product to Tysabri (Natalizumab).

As a temporary voting member of the Gastrointestinal Drugs Advisory Committee, Dr. Neaton potentially could become involved in matters that could affect his financial interests. Under 18 U.S.C. §208(a), 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. Neaton 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. Neaton that would permit him to participate in the matters previously described.

First, it is important to consider that Dr. Neaton's interest in ———————— is unrelated to the product, competing products, and issues coming before the committees. Dr. Neaton is a member of ———————'s Data Safety Monitoring Board (DSMB) for a study of an unrelated drug, ————, for heart failure.

Second, Dr. Neaton's financial interest in ———— ——— is not so substantial as to preclude his participation in the meeting. Dr. Neaton receives minimal compensation for his membership in the DSMB.

Third, the uniqueness of Dr. Neaton's qualification justifies granting this waiver. According to the Review Division, Dr. Neaton's experience and background in biostatistics qualify him to adequately address statistical safety and efficacy issues for the Tysabri advisory committee meeting, especially issues pertinent to subpopulation effects and risk assessment evaluation.

Additionally, the Agency was unable to find a similarly qualified individual without disqualifying financial interests to serve on the committee. After inviting five biostatisticians, 3 declined to participate and one had such high interests that a waiver was not justified.

Finally, 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 committees' 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. James Neaton, Ph.D., is a Professor of biostatistics at the University of Minnesota's School of Public Health. Dr. Neaton has received many academic awards and honors for teaching and is a Fellow of the American Statistical Association. He is also principal investigator for clinical research programs on AIDS and other clinical programs and studies with National Institutes of Health (NIH) and the National Cancer Institute (NCI). Dr. Neaton has been involved in numerous clinical studies and programs in various roles as investigator, consultant, data analyst and member of data safety monitoring committees. Dr. Neaton has an extensive publication record in major statistical

and clinical journals which has emphasized drug safety, including cardiovascular risk and mortality assessment. I believe his participation will contribute to the diversity of opinions and expertise represented on the committees' and will provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant James Neaton, Ph.D., a waiver that will permit him to participate in all official matters concerning the safety and efficacy of Biologic License Application (BLA) 125104/33, Tysabri (Natalizumab) injection, for the proposed indication of inducing and maintaining sustained response and remission, and eliminating corticosteroid use in patients with moderately to severely active Crohn's disease with inflammation, as evidenced by elevated C-reactive protein (CRP) level or another objective marker, and the risks (including progressive multifocal leukoencephalopathy) associated with TYSABRI (natalizumab) administration, its efficacy in the treatment of moderate to severe Crohn's disease, and proposed risk management plan(s). I believe that such a waiver is appropriate because in this case, the need for the services of Dr. James Neaton outweighs the potential for a conflict of interest created by the financial interest attributable to him.

CONCURRENCE: /s/ 6/18/07

Vince Tolino
Director, Ethics and
Integrity Staff
Office of Management Programs
Office of Management
Date

DECISION:

__X__ Waiver granted based on my determination, made in accordance with section 18 U.S.C. §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.

/s/ 6/27/07

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