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 Terry Davis, Ph.D.

I am writing to request a waiver for Terry Davis, Ph.D., a member of the Drug Safety and Risk Management 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. Davis 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. Davis is a special Government employee, she 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 her, her spouse, minor child, or general partner; an organization or entity for which she serves as an officer, director, trustee, general partner, or employee; and, a person with whom she is

negotiating for, or has an arrangement concerning, prospective employment.

Dr. Davis 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 of the Drug Safety and Risk Management Advisory Committee, as stated in its Charter, is to advise the Commissioner of Food and Drugs on risk management, risk communication, and quantitative evaluation of spontaneous reports for drugs for human use and for any other product for which the Food and Drug Administration has regulatory responsibility. The committee also advises the Commissioner of Food and Drugs regarding the scientific and medical evaluation of all information gathered by the Department of Health and Human Services and the Department of Justice with regard to safety, efficacy, and abuse potential of drugs or other substances, and recommends actions to be taken by the Department of Health and Human Services with regard to the marketing, investigation, and control of such drugs or other substances.

Dr. Davis has advised the Food and Drug Administration (FDA) that she has financial interests that could potentially be affected by her participation in the matters described above. **Dr. Davis owns modest amounts of stock in ——————— and ———————. These firms manufacture competing products to Tysabri.**

As a member of the Drugs Safety and Risk Management Advisory Committee, Dr. Davis potentially could become involved in matters that could affect her financial interests. Under 18

U.S.C. §208(a), she 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. Davis 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. Davis that would permit her to participate in the matters previously described.

First, the stocks represent only a small percentage of Dr. Davis' total net worth and are not so substantial as to preclude her participation in these matters. Moreover, this waiver for Dr. Davis is further justified because the affected products made by the companies in which Dr. Davis holds stock represent a quite small percentage of the total revenue of each company.

Second, the uniqueness of Dr. Davis' qualification justifies granting this waiver. According to the review Division, Dr. Davis is the only risk communication expert on the advisory committee. Her expertise is especially critical to this meeting because the risk management program for Tysabri will be discussed. Risk management programs are designed to minimize significant risks of a product by using one or more risk management tools such as education and outreach to inform patient and healthcare practitioners about a product's risks and how to prevent or mitigate the risk, reminder systems to prompt or guide prescribing, dispensing, or using a product in ways that minimize risks, and performance linked systems that link product access to required laboratory testing or other documentation. For the committees to have an informed discussion about how to best communicate risks to healthcare practitioners and patients, Dr. Davis' expertise in risk communication is essential.

Third, the difficulty of locating a similarly qualified individual without a disqualifying financial interest to serve on the committees' also justifies granting this waiver. It has been exceedingly difficult to find qualified risk communication experts. The Division searched and polled a number of current special Government employees for their availability. Of the three risk communication experts contacted, only Dr. Davis accepted the offer to represent the agency's interests, the rest declining due to a scheduling conflicts and prior commitments. Therefore, we request to use the services of Dr. Davis who will serve as the only representative with expertise in risk communication. Dr. Davis' participation in this meeting will ensure the level of expertise and objectivity required to provide advice and recommendations required to discuss the

optimum method of communicating the potential risks associated with Tysabri to healthcare practitioners and patients.

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. Dr. Davis is Professor of Medicine and Pediatrics, Louisiana State University Health Sciences Center and, Director of Behavioral Science Section, Feist-Weiller Cancer Center. Dr. Davis' research interest is in work centered education materials and methods, e.g. pamphlets, posters, video tapes, peer educators. She works with providers, federal health agencies, and professional organizations to develop best practices for continuing education for practicing physicians (e.g. office based in-services, computer based Continuing Medical Education (CME), train-the-trainer models). She works with key stakeholders to design primary care clinics that are user-friendly for patients with limited literacy and test the efficacy in regard to health care quality and outcomes. I believe her participation will contribute to the diversity of opinions and expertise represented on the committee and will provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant Terry Davis, Ph.D., a waiver that will permit her 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. Terry Davis outweighs the potential for a conflict of interest created by the financial interests attributable to her.

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/ 7/6/07

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

Date