**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: October 16, 2007

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

THROUGH: Vince Tolino /S/ 10-31-07
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Michael F. Ortwerth, Ph.D. /S/ 11-8-07
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 Aman Buzdar, M.D.

I am writing to request a waiver for Aman Buzdar, M.D., a Temporary Voting 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. Buzdar 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. Buzdar 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. Buzdar has been asked to participate in all official matters concerning supplemental BLA 125085/91, Avastin (bevacizumab), sponsored by Genentech, Inc., proposed indication, in combination with paclitaxel, for the treatment of patients who have not received chemotherapy for their locally recurrent or metastatic, HER2 negative breast cancer.

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

**Dr. Buzdar 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. Aman Buzdar's employer, University of Texas M.D. Anderson Cancer Center, was awarded a research contract by ——— to conduct a study on the evaluation of ——— . The drugs being studied are ———, ——— and ———. The goal of the study is to compare ——— to ——— in the treatment of breast cancer to see which treatment is better for preventing recurrence. Another important goal is to determine which treatment is more effective at eradicating tumor in the breast and lymph nodes. The study started in —— and is ongoing. It is anticipated to end in Year 2009. The study is co-funded by ——— for $ ——— per year. Dr. Buzdar is the Principal Investigator (PI) for the study but he does not receive any personal remuneration.**

**——— is used in combination ——— and is not used as stand alone therapy for the proposed indication. ——— and ——— are not competing products to Avastin (bevacizumab). ———is the sponsor of ——— . ——— . —— is the sponsor of ——— and ——, competing products to Avastin.**

**In addition, Dr. Buzdar's employer, University of Texas M.D. Anderson Cancer Center, has a research contract with ——— that is unrelated to the issues to be discussed. Arguably, his employer's interest does not constitute a financial interest in the particular matter under section 208(a) since it is unrelated to the issue at hand. Nevertheless, in the utmost of caution, I recommend that this wavier be granted.**

As a Temporary Voting Member of the Oncologic Drugs Advisory Committee, Dr. Buzdar 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. Buzdar 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. Buzdar 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, the study Dr. Buzdar is involved in is for an indication unrelated to the indication being sought for Avastin. The study population is different from that of which approval/labeling claims for Avastin (bevacizumab) are being sought. Specifically, the study Dr. Buzdar is involved in is being conducted in patients with newly diagnosed, localized breast cancer and enrollment was permitted in patients with HER2 positive tumors without this being a requirement. However, Avastin was studied in patients with metastatic (inoperable) breast cancer and only enrolled patients with HER2 negative tumors. It is highly unlikely that Dr. Buzdar's participation in the matter coming before the committee will have an impact on the trial. It is difficult to predict that any action, short of "clinical hold", would lead to the discontinuation of the trial or a modification of the protocol that would directly affect the financial interest of Dr. Buzdar and his employer.

Second, although Dr. Buzdar's employer has current interest in ——— and ——— he himself has no financial interest in the firms. Generally, there is less likelihood that the judgment of the individual will be affected by the imputed interest of an employer than by a personal financial interest.

Third, according to the Review Division, the uniqueness of Dr. Buzdar's qualification justifies granting this waiver. Dr. Buzdar has been involved in the treatment and research of Breast Cancer for the past 32 years. His research involves defining and improving the short- and long-term benefits of systemic adjuvant therapies for breast cancer; endocrine therapies; and, biologic therapies. He is also involved in testing several new hormonal therapies in the treatment of breast cancer. Dr. Buzdar's extensive research and experience in Breast Cancer therapy will provide the agency with expert advice on specific topic issues and broader issues of drug development and clinical trial design related to Breast Cancer. I believe that participation by Dr. Buzdar in the committee's deliberations will contribute to the diversity of opinions and expertise represented on the committee.

Lastly, locating qualified individuals without disqualifying financial interest to serve on this advisory committee has been very difficult. According to the division, it was difficult to find any other breast cancer specialists who were not conflicted since many of these individuals hold positions within the National Cancer Institute with this group conducting the trial being reviewed at the meeting. The division is interested in gaining the perspective of more than one breast cancer expert in an effort to remain objective in discussing a resubmitted supplemental BLA for a breast cancer indication and in doing so requests that a waiver be granted for Dr. Buzdar to participate in this meeting. A total of 7 members or Special Government Employees (SGEs) with expertise in breast cancer were invited, of which Dr. Buzdar is one of two able to attend. However, both of these two individuals require waivers. Also, the FDA Modernization Act (FDAMA) requires that at least two individuals with expertise in the disease or condition for which the application under review is indicated be present. In order to have the proper expertise to review an application with a breast cancer indication and to meet the FDAMA requirement, the Division feels that it is imperative that Dr. Buzdar be present at this meeting. To that end, we are requesting that the

waiver be granted for Dr. Buzdar to participate as there has been a genuine effort to secure individual participation and representation with minimal conflict of interest.

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. Buzdar is Professor of Medicine and Deputy Department Chair for the Department of Breast Oncology at the University of Texas, M.D. Anderson Cancer Center. He has served as the Principal Investigator in numerous breast cancer clinical trials and has also published in such journals as the Archives of Internal Medicine, Cancer and the Journal of the American Medical Association. Dr. Buzdar was also previously named in Consumers' Research Council of America, America's Top Physicians in 2003.

Accordingly, I recommend that you grant Aman Buzdar, M.D., a waiver that would allow him to participate in all official matters concerning supplemental BLA 125085/91, Avastin (bevacizumab), Genentech, Inc., proposed indication, in combination with paclitaxel, for the treatment of patients who have not received chemotherapy for their locally recurrent or metastatic, HER2 negative breast cancer. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Buzdar outweighs the potential for a conflict of interest created by the financial interest attributed to him.

DECISION:

X 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.

/s/

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

11/15/07
Date