DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: April 23, 2007

TO: Randall W. Lutter, Ph.D.
Associate Commissioner for Policy and Planning
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 Maha Hussain, M.D.

I am writing to request a waiver for Maha Hussain, M.D., a Member and Chair of the Oncologic 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 Maha Hussain, M.D., 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. Hussain 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. Hussain has been asked to participate in all official matters concerning New Drug Application (NDA) 022-092, proposed trade name Junovan (mifamurtide), formerly known as (L-MTP-PE, liposomal muramyl tripeptide phosphatidyl ethanolamine), sponsored by IDM Pharma, Inc., for treatment of resectable high-grade resectable non-metastatic osteosarcoma in combination with adjuvant chemotherapy for osteosarcoma. Genzyme Corporation, NOF Corporation, Ben Venue Laboratories, owned by Boehringer Ingelheim Corporation, the U.S. affiliate of Boehringer Ingelheim GmbH, and Solvias AG are the key manufacturers of the liposomal formulation of muramyl tripeptide phosphatidyl ethanolamine. This matter is coming before the Oncologic Drugs Advisory Committee for consideration and is a particular matter involving specific parties.

The functions of the Oncologic Drugs Advisory Committee, as stated in its Charter, are 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. Hussain has advised the Food and Drug Administration that she ———— have financial interests that could potentially be affected by her participation in the matters previously described. Dr. Hussain's ——— owns stock in ————, ————, ————, ————, and ————. ——— is one of the manufacturers of ———— ————. ————, a subsidiary of ————, ——— and ————, subsidiaries of ———— ————, and ——— an affiliate of ————, make competing products to Junovan. ————'s ———— is an investigational product under development.

As a Member of the Oncologic Drugs Advisory Committee, Dr. Hussain 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. Hussain 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. Hussain that would permit her to participate in the matters described previously.

First, the value of each stock is not so substantial as to preclude her participation.

Second, with respect to her ——— stock interests in firms that make competing products to Junovan, it is important to consider that there are over 20 firms that market or are pursuing development of a directly competing product. The availability of multiple firms and products should mitigate the potential perception of bias on the part of Dr. Hussain.

Third, her ——— stock holdings are in large, diverse pharmaceutical firms that manufacture and distribute a variety of products. They do not depend on one or two products for their economic survival. Given the above considerations, I believe that the potential for a conflict of interest is minimal.

Moreover, Dr. Hussain's expertise makes her an invaluable resource to FDA for this meeting and her expertise will greatly enhance the deliberations of the Committee. Dr. Hussain is the current chair of the Oncologic Drugs Advisory Committee and has chaired Oncologic Drugs Advisory Committee meetings since 2006. She has participated as a voting member of the Committee since 2004. Her background, breadth of knowledge, and experience with the issues involved with the product coming before the Committee, make her uniquely qualified to participate on this advisory committee meeting. It is critical to the discussions of Junovan that the Committee chair be both qualified and experienced to guide and advise the clinicians in the Oncologic Drugs Advisory Committee as to the interpretation of study results and limitations of study design in the analytic approach. The division strongly feels that Dr. Hussain is

capable of delivering this guidance in the most qualified manner to provide balance in approach and ensure the issues are clearly communicated and assessed. The difficulty of locating a similarly qualified individual without a disqualifying financial interest to serve on the Committee also justifies granting this waiver.

In addition to schedule conflicts that prevented both members and additional consultants from attending this meeting, three of the Oncologic Drugs Advisory Committee members were disqualified from participating in the Junovan discussion because of their financial interests. The Division added consultants with the needed expertise. However, identifying an individual with the expertise in a subject area is important, but even more essential is having a chair with advisory committee experience. Dr. Hussain's experience in conducting clinical trials, her familiarity with the Advisory Committee issues and processes, and understanding of FDA's regulatory framework are critical for this discussion and justify granting her a waiver to participate in this meeting.

Further, 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. Hussain is a recognized national and international expert in the clinical management and clinical research of genitourinary malignancies with a special focus on prostate and bladder cancer. As the co-chair of the prostate cancer subcommittee of the Southwest Oncology Group, she has led the group in directing the clinical research activities in advanced prostate cancer at a national level. Dr. Hussain is the Principal Investigator of several national and institutional clinical trials that are investigating novel treatments in bladder and prostate cancers. She directs the Research Developmental Program of the University of Michigan SPORE in prostate cancer, she chairs the University of Michigan Comprehensive Cancer Center Protocol Review Committee, which reviews all new patient related clinical and translational research protocols, and she is a member of the University of

Michigan Medical School Dean's Advisory Council on Clinical Research. Dr. Hussain's expertise in clinical design and her vast experience as a cancer researcher is essential for an appropriate discussion of Junovan. I believe that Dr. Hussain's expertise 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 Maha Hussain, M.D., a waiver that would allow her to participate in all official matters concerning New Drug Application (NDA) 022-092, proposed trade name Junovan (mifamurtide), sponsored by IDM Pharma, Inc., for treatment of high-grade resectable non-metastatic osteosarcoma in combination with adjuvant chemotherapy for osteosarcoma. I believe that such a waiver is appropriate because in this case, the need for the services of Maha Hussain, M.D., outweighs the potential for a conflict of interest created by the financial interests attributable to her.

CONCURRENCE: /s/ 4/24/07

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/ 4/24/07

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