DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM

DATE: September 15, 2006

TO: Randall Lutter, Ph.D.
Associate Commissioner for
Policy and Planning
Food and Drug Administration

THROUGH: Jenny Slaughter
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 Kenneth Sherman, M.D., Ph.D.

I am writing to request a waiver for Kenneth Sherman, M.D., Ph.D., a member of the Antiviral Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a). The appointing official may grant waivers under 18 U.S.C. §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. Sherman 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. Since Dr. Sherman 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.

Dr. Sherman has been asked to participate in all official matters concerning clinical trial design issues in the development of products for the treatment of chronic hepatitis C virus infections, particularly those related to the identification of appropriate control arms, populations for study, endpoints, and long-term follow-up. These matters are coming before the Antiviral Drugs Advisory Committee for consideration and are particular matters of general applicability.

The function of the Antiviral 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 acquired immune deficiency syndrome, human immunodeficiency virus related illnesses, and other viral, fungal and mycobacterial infections, and to make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Sherman has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the matters described above. **Dr. Sherman's employer, the University of Cincinnati, was awarded research contracts by ——————— and ——————— ——— to conduct clinical studies of affected products for the treatment of Hepatitis C Virus (HCV) infections. Dr. Sherman is the principal site investigator for the studies. However, he does not receive any personal remuneration or salary support for his work on the studies.**

Dr. Sherman is also a member of ——'s and ——————— ———'s Speaker's Bureaus. He lectures on HCV and HIV infections for ——— and on HCV infections for ———. Although he received no direct payments from ——— or ——————— in the last calendar year, he does report speaking in Continued Medical Education (CME) programs sponsored by these firms. He does not have any future speaking engagements scheduled at this time.

As a member of the Antiviral and Renal Drugs Advisory Committee, Dr. Sherman could potentially become involved in matters that could affect his or his employer's financial interests. 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)(3) to grant a waiver permitting Dr. Sherman 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. Sherman that would allow him to participate fully in the matters described previously.

First, Dr. Sherman's interests in ——————— and ——————— are not so substantial as to preclude his participation in this matter. He receives no personal remuneration or salary support for his work on the studies and receives minimal compensation for his membership in the firms' Speaker's Bureaus. The funding for these studies is also not a significant financial interest to the University of Cincinnati. For the 2005 fiscal year, the University received more than ——— in research funding from a variety of public, private, and governmental agencies in support of its research activities.

Second, with respect to the current studies sponsored by ——————— and ———————, it is important to note that all but one of the affected products that are being studied are already approved and marketed for the treatment of HCV infections.

Third, the uniqueness of Dr. Sherman's qualification justifies granting this waiver. Dr. Sherman is one of few hepatologists on the committee with the requisite expertise to discuss both the treatment of hepatitis C virus (HCV) infections and clinical trial design issues. Dr. Sherman has participated in clinical trials of antiviral therapies for chronic viral hepatitis as well as human immunodeficiency virus (HIV) infections, and understands the elements that are needed to execute a successful clinical trial. He also has special expertise in the area of HCV viral kinetics, and is scheduled to give a presentation on this topic at the meeting. His presentation will provide critical background information on various virologic endpoints for the committee to consider and discuss. In addition, Dr. Sherman is the planned Chair for this meeting. The division feels that he is the only regular member of the committee with the requisite hepatology experience to lead the discussions at the meeting and function as the Chair.

Fourth, the difficulty of locating a similarly qualified individual without a disqualifying financial interest to serve on the committee also justifies granting this waiver. Because the universe of hepatologists is small, and that of those involved in the care and clinical evaluation of therapy for hepatitis C virus infections is even smaller, it has been exceedingly difficult to find consultants and committee members, who are knowledgeable about it has been exceedingly difficult to find consultants and committee members, who are knowledgeable about clinical trial design issues, such as HCV viral kinetics, in the development of products for the treatment of the chronic HCV infected population, yet have not had any involvement with sponsors in the development of new treatments for this disease. The division feels that only hepatologists have the requisite expertise to discuss both treatment of HCV infections and clinical trial design. A reduction in the number of hepatologists in the committee, therefore, will render much of the discussion useless, and may call into question the validity of any committee recommendations to the Agency.

Moreover, this waiver is also justified, in part, because of the general nature of particular matters of general applicability. It is well recognized that particular matters of general applicability pose far less risk of a conflict of interest. Particular matters of general applicability include regulations, legislation, guidelines, points-to-consider, and policies governing classes of organizations, individuals, and products. Particular matters of general applicability do not include particular matters involving specific parties, such as specific grants, contracts, recommendations regarding a specific product, or enforcement matters involving known parties. The committee's discussions of clinical trial design issues such as the identification of appropriate control arms, populations for study, endpoints, and long-term follow-up in the development of products for the treatment of chronic hepatitis C infections will not have a unique and distinct impact on Dr. Sherman's financial interest, but rather may affect classes of similarly situated products and manufacturers to the same extent. While this participation may be covered by section 208, it poses far less risk of bias than participation in matters that relate specifically to a particular firm or organization in which Dr. Sherman has an interest.

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. Kenneth Sherman, M.D., Ph.D., is Director, Hepatology & Liver Transplant Medicine, Associate Professor of Medicine, Director of Clinical Trials, Department of Medicine, and Associate Professor of Pathology and Laboratory Medicine. He specializes in hepatology and liver transplant medicine. Dr. Sherman is a member of numerous professional societies, such as the American College of Physicians, the American Society of Microbiology, the American Society for Gastrointestinal Endoscopy, and the American Gastroenterological Association. His research interests include liver disease in immunosuppressed populations, viral hepatitis, autoimmune hepatitis and steatohepatitis. He has written numerous articles on topics such as Hepatitis and HIV. I believe that Dr. Sherman's 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 Dr. Sherman a waiver that would allow him to participate in all official matters concerning clinical trial design issues in the development of products for the treatment of chronic hepatitis C virus infection, particularly those related to the identification of appropriate control arms, populations for study, endpoints, and long-term follow-up. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Kenneth Sherman outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: /s/ 9/26/06

Jenny Slaughter
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 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/ 9/28/06

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

Date