DEPARTMENT OF HEALTH & HUMAN SERVICES

MEMORANDUM

Food and Drug Administration
Rockville MD 20857

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 Karen Murray, M.D.

I am writing to request a waiver for Karen Murray, M.D., a consultant to the Center for Drug Evaluation and Research, 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. Karen Murray 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 her employer has a financial interest. Since Dr. Murray is a special Government employee, she 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 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. Murray has been asked to participate in all official matters concerning the discussion of the 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. This matter is 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. Murray has advised the Food and Drug Administration (FDA) that her employer has financial interests that could potentially be affected by her participation in the matter at issue. **Dr. Murray is an employee of University of Washington's Department of Pediatrics. As part of her official duties to the University, Dr. Murray conducts pediatric research at the Children's Hospital and Regional Medical Center. She is the co-investigator for a study of Pegylated Interferon +/- Ribavirin for children with Hepatitis C Virus (HCV) infections. The study is sponsored by a Cooperative Research and Development Agreement (CRADA) between the National Institutes of Health (NIH), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the FDA, and Roche. Roche also supplies the medications to the government who then supplies Johns Hopkins University for dispersal to the various study sites. Johns Hopkins University awarded the Children's Hospital and Regional Medical Center (CHRMC) a subcontract to be one of the eleven trial sites for the study. The CHRMC reimburses the University of Washington for Dr. Murray's time on the study. [redacted] and [redacted] are affected products.**

The CHRMC is also involved in a long-term follow-up study of pediatric patients who participated in ————————'s trial to assess the safety, efficacy, tolerability, and pharmacokinetics of ———— plus ———————— in pediatric patients with chronic Hepatitis C. The CHRMC also reimburses the University for the time Dr. Murray spends on the trial from the subcontract with Johns Hopkins University.

As a consultant to the Center for Drug Evaluation and Research, Dr. Murray could potentially become involved in matters that could affect her employer's financial interest. Under section 208, 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. Murray 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. Karen Murray that would allow her to participate fully in the matter described above.

First, although Dr. Murray's employer currently has financial interests in Roche and ————————., she herself does not have any financial interest in either the firms or their products. Although the financial interests of an employer impute to the individual under 18 U.S.C. §208, 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.

Second, Dr. Murray's personal and imputed financial interests are not so substantial as to preclude her from participating in this matter. Dr. Murray does not receive any personal remuneration for her work on the studies. The funding from the subcontract with Johns Hopkins University is not a significant financial interest to the Children's Hospital and Regional Medical Center or to the University of Washington. For the 2005 fiscal year, the Children's Hospital and Regional Medical Center received approximately ———— from Federal, State and Private sources for its research activities. For 2005, the University of Washington received ———— in contracts and grants from Federal, State and Private for its research activities.

Third, the uniqueness of Dr. Murray's qualification justifies granting this waiver. Dr. Murray is the only pediatric hepatologist invited to the meeting and therefore is the only person with the requisite expertise to discuss the clinical trial design issues pertaining to the pediatric HCV infected population.

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 a pediatric hepatologist who is knowledgeable about clinical trial design issues for in the development of products for the treatment of the pediatric HCV infected population, yet have not had any involvement with sponsors in the development of new treatments for this disease. Locating a qualified pediatric hepatologist has been further hampered by the scheduling of a pediatric gastroenterology meeting scheduled for the same day. Therefore, it is highly unlikely that the division will be able to find another pediatric hepatologist with similar qualifications should Dr. Murray be recused.

Fifth, **the products that are being studied, ——— and ——— , are already approved and marketed for the treatment of HCV infections.**

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 HCV infections will not have a unique and distinct impact on Dr. Murray'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. Murray 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. Karen Murray, M.D., is President-elect Medical Staff, Program Director for Gastroenterology Education, Co-Chair for Program Sub-Committee at the Children's Hospital and Regional Medical Center, Associate Professor of Pediatrics, and Director of the Hepatobiliary Program, Department of Pediatrics. She received her medical degree from Johns Hopkins University School of Medicine. She is board certified in Pediatric Gastroenterology & Nutrition. Her clinical research experiences are in Pathogenesis, epidemiology, viral hepatitis and other pediatric liver disease. She is a member of many organizations such as American Board of Pediatrics, American Association for the Study of Liver Disease, North American Society of Pediatric Gastroenterology, Hepatology and Nutrition. She has published many articles regarding children with chronic hepatits C, Acute liver failure and Prevalence of hepatitis C and risk factors in an incarcerated juvenile population. I believe that Dr. Murray'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 Karen Murray, M.D., a waiver that would allow her to participate in all official matters concerning the discussion of the 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. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Murray outweighs the potential for a conflict of interest created by the financial interest attributable to her.

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