DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administrat
Rockville MD 20857

DATE: November 6, 2006

TO: Randall 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 John Edwards, Jr., M.D.

I am writing to request a waiver for John Edwards, Jr., M.D., a member of the Anti-Infective 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. Edwards 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. Edwards is a special Government employee, he 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 him, his spouse, minor child, or general partner; an organization or entity for which he serves as an officer, director, trustee, general partner, or employee; and, a person with whom he is

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

Dr. Edwards has been asked to participate in all official matters concerning the overall benefit to risk considerations for the approved product, Ketek (telithromycin), new drug application (NDA) 21-144, manufactured by Sanofi-Aventis with the current indications of acute bacterial exacerbations of chronic bronchitis, acute bacterial sinusitis, and community acquired pneumonia. This issue is coming before a joint meeting of the Anti-Infective Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee and is a particular matter involving specific parties.

The committees' functions, as stated in their Charters, are as follows: The Anti-Infective 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 infectious diseases and disorders. The Drug Safety and Risk Management Advisory Committee 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 committees make their appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Edwards has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the matter at issue. **Dr. Edwards is a member of ——— anti-infective advisory board. This advisory board meets to discuss general issues affecting ——— anti-infective program such as antibiotic resistance and on occasion, data on its antibacterial products. Dr. Edwards contacted ——— regarding this matter and they can't recall presenting data for competing products to Ketek to the board. According to ———, its only competing product to Ketek, ———, lost its patent in ——.**

As a member of the Anti-Infective Drugs Advisory Committee advising the committees, Dr. Edwards potentially could become involved in matters that could affect his financial interest. Under 18 U.S.C. §208(a), 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. Edwards 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. Edwards, which would permit him to participate in the matter described above.

First, Dr. Edwards's interest in ——— is not so substantial as to preclude his participation in this matter. He receives minimal compensation for his advisory board activity.

Second, the uniqueness of Dr. Edwards's qualification justifies granting this waiver. Dr. Edwards is the only physician on the committee with extensive experience in the use of non-inferiority trials used to define new antibiotic efficacy and the evolution of the Agency guidance on developing new antimicrobials. He has served as chairman or moderator for several Anti-Infective Drug Advisory Committee meetings and workshops in the past few years that have addressed antimicrobial drug development, antibiotic resistance, and non-inferiority trials specifically for several of the indications for which Ketek is approved (acute sinusitis and acute exacerbation of chronic bronchitis). Given his past experience, Dr. Edwards' participation in the upcoming Ketek meeting is essential, as the discussions of benefit/risk considerations will most certainly involve questions related to non-inferiority trials, and the development of Ketek for infections due to multi-drug resistant *Streptococcus pneumoniae*. Because this meeting involves joint participation of two committees and multiple consultants, the Division feels strongly that having an experienced chairman in that role will best serve the Agency. In addition, we were unable to find a similarly qualified individual, without a disqualifying financial interest, to serve on the committee despite considering all members of the Drug Safety and Risk Management Advisory Committee.

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. In addition, 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 because of their demonstrated abilities. Dr. Edwards is Professor of Medicine at the University of California at Los Angeles (UCLA) School of Medicine, and Chief, Division of Infectious Diseases, Department of Medicine, Harbor-UCLA Medical Center. He completed his internship, residency, and a research fellowship at UCLA School of Medicine. While on faculty at UCLA, he conducted research on the pathogenesis and

therapy of fungal infectious disease. Dr. Edwards is a member of the American Board of Internal Medicine, Subspecialty Board of Infectious Diseases, American Society for Microbiology, and the Infectious Disease Society of America. He has published over 40 scientific articles on the treatment of infectious diseases and is a member of the Editorial Board of the Journal of Infectious Diseases. I believe that Dr. Edwards' participation will bring an enormous amount of experience, knowledge, and expertise that is essential to the committee's discussions of the benefit/risk considerations for Ketek.

Accordingly, I recommend that you grant John Edwards, Jr., M.D., a waiver that will permit him to participate in all official matters concerning the overall benefit to risk considerations for the approved product, Ketek (telithromycin), new drug application (NDA) 21-144, manufactured by Sanofi-Aventis with the current indications of acute bacterial exacerbations of chronic bronchitis, acute bacterial sinusitis, and community acquired pneumonia. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Edwards outweighs the potential for a conflict of interest created by the financial interest attributable to him.

CONCURRENCE: /s/ 11/15/06

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/ 11/21/06

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

Date