



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

DATE: October 9, 2008

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

THROUGH: Vince Tolino \_\_\_\_\_/S/  
Director, Ethics and Integrity Staff  
Office of Management Programs  
Office of Management

Michael F. Ortwerth, Ph.D. \_\_\_\_\_/S/  
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 John Bradley, M.D.

I am writing to request a waiver for John Bradley, M.D., a temporary member of the Antiviral 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. Bradley 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. Bradley 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 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. John Bradley has been asked to participate in the meeting to provide advice on types of studies and trial designs needed for an influenza antiviral MedKit for the treatment or prophylaxis of pandemic influenza and discuss publicly the proposed development program that would support an application for such a MedKit. Issues such as the role of personal MedKits, home stockpiling, nonprescription availability of influenza medications and interfaces of home readiness with public health systems will be raised in the course of the discussions.

This matter is coming before a joint meeting of the Antiviral Drugs Advisory Committee and the Nonprescription Drugs Advisory Committees. This issue is a particular matter involving specific parties.

Dr. Bradley has advised the Food and Drug Administration (FDA) that he has a financial interest that could potentially be affected by his participation in the matter described above. The University of Alabama was recently awarded a contract by the National Institutes of Health, through its Collaborative Antiviral Study Group, for an open-label study of Tamiflu in the treatment of influenza in infants less than one year old. Tamiflu is one of the products that could potentially be affected by the committee meeting. Dr. Bradley's employer, Rady Children's Hospital of San Diego, is a subcontractor for this trial. Dr. Bradley will be a site principal investigator and the hospital's goal is to enroll 2-3 patients. Rady Children's Hospital will receive a nominal fee per patient enrolled from the University of Alabama.

As a temporary member to the Antiviral Drugs Advisory Committee, Dr. Bradley potentially could become involved in matters that could affect his imputed financial interest. 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. Bradley 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. Bradley that would allow him to participate in the matter described because the need for his services greatly outweighs the conflict of interest created by this financial interest.

First, it is important to consider that the study involved is a federally funded, open-label study for a patient population that is not approved for Tamiflu. Dr. Bradley's site is one of many sites collecting data on the efficacy of Tamiflu in infants less than one year of age to determine dosage and what adverse events there might be. This specific patient population will not be discussed at the advisory committee meeting.

Second, it is unlikely that Dr. Bradley's participation in the committee's discussions of the types of studies and trials designs needed for a pandemic influenza MedKit will have an effect on this efficacy and pharmacokinetic trial for an unrelated patient population. It is difficult to predict that

any action, short of a "clinical hold," would lead to the discontinuation of the federally funded trial or a modification of the protocol that would directly affect Dr. Bradley's employer's financial interest.

Additionally, this financial interest is not so substantial as to preclude Dr. Bradley's participation in the committee meeting. The fee per patient is nominal and the number of patients to be enrolled is small.

Moreover, although the special Government employee has an imputed interest under the law because his employer is a subcontractor to a University which has a grant from NIH to study a drug that could be used in a MedKit, Dr. Bradley himself has no personal financial interest in the matter. The fact that this financial interest is imputed to him from his employer should lessen any potential conflict the interest may present.

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.

The Division is in need of Dr. Bradley's unique expertise, training and research in pediatric infectious diseases and respiratory viral and bacterial infections in the evaluation of an antiviral MedKit for influenza for home use during a pandemic. An antiviral MedKit for use during a pandemic is an idea being put forth by the Department of Health and Human Services to encourage personal and shared responsibility in the setting of an influenza pandemic. The product, an antiviral MedKit containing either oral oseltamivir (Tamiflu) or inhaled zanamivir (Relenza) for treatment and/or prophylaxis of influenza is a complex, precedent-setting product. It is being brought to the Committee prior to submission of a supplemental New Drug Application so that the Committee can provide expert advice on the design and conduct of trials necessary for the public to understand how and when to use this product.

A crucial part of the advisory committee's risk-benefit discussion of an antiviral MedKit for use during a pandemic will involve discussions of viral resistance in general and in the setting of misuse of the product and misdiagnosis of bacterial infections in the setting of circulating influenza. Dr. Bradley has extensive expertise in the area of resistance and has published in this area as well as in the topic of defining pneumonia in critically ill children. He is a participant of the American Academy of Pediatrics Committee on Infectious Diseases and was recently involved in developing recommendations for influenza immunization of children. He also was involved with the Infectious Diseases Society of America (IDSA) national committee that developed guidelines for diagnosis and therapy of influenza. Whereas most of our committee members have expertise in HIV, including the other pediatric infectious disease expert serving on the committee, Dr. Bradley provides expertise in the area of pediatric respiratory illnesses and resistance which will be a major component of the advisory committee discussion. Dr. Bradley's work on Tamiflu in children less than 1 year of age is unrelated to any of the discussions that will be held during the October 29<sup>th</sup> meeting since the MedKit discussion on use of antiviral treatments during a pandemic will not encompass children less than 1 year of age. The antiviral treatments for influenza are not

