



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

DATE: October 18, 2007

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

THROUGH: Vincent Tolino /S/ 10/22/07  
Director, Ethics and Integrity Staff  
Office of Management Programs  
Office of Management

Michael F. Ortwerth, Ph.D. /S/ 10/30/07  
Deputy Director, Advisory Committee Oversight and Management Staff  
Office of Policy, Planning, and Preparedness

FROM: Kathleen L. Walker /S/ 10/18/07  
Chief, Integrity, Committee and Conference Management Branch  
Division of Ethics and Management Operations, OMO  
Center for Devices and Radiological Health

SUBJECT: 208(b)(3) Conflict of Interest Waiver for Jeffrey A. Brinker, M.D.

I am writing to request a waiver for Jeffrey A. Brinker, M.D., a temporary voting member of the Circulatory System Devices Panel of FDA's Medical Devices 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 Jeffrey A. Brinker, M.D., 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. Brinker 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 Medical Devices Advisory Committee, as stated in its Charter, is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational devices and advise the Commissioner of Food and Drugs regarding recommended classification of these devices into one of three regulatory categories; recommend the assignment of a priority for the application of regulatory requirements for devices classified in the standards or premarket approval category; advise on any possible risks to health associated with the use of devices; advise on formulation of product development protocols and review premarket approval applications for those devices classified in the premarket approval category; review classification as appropriate; recommend exemption to certain devices from the application of portions of the Act; advise on the necessity to ban a device; and respond to requests from the Agency to review and make recommendations on specific issues or problems concerning the safety and effectiveness of devices.

Dr. Brinker has been asked to participate in the Panel's discussion regarding a premarket approval application (PMA) submitted by Abbott Vascular (a subsidiary of Abbott Laboratories) for the *XIENCETM V Everolimus Eluting Coronary Stent System*. This system is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to de novo native coronary artery lesions (length  $\leq$  28 mm) with reference vessel diameter of 2.5mm to 4.0mm.

This matter is coming before a meeting of the Circulatory System Devices Panel of FDA's Medical Devices Advisory Committee. This issue is a particular matter involving specific parties.

Dr. Brinker has advised the FDA that his employer has a financial interest that could potentially be affected by his participation in the matter described above. His institute, Johns Hopkins Hospital (JHH), has been identified as a clinical site for the *XIENCETM V* study; [-----] is the principal investigator. Although the study occurred in the Division of Cardiology, where both Dr. Brinker and [-----] work, Dr. Brinker had no personal involvement in the trial and has no managerial responsibilities for [-----].

The Office of Device Evaluation within the Center for Devices and Radiological Health provided the following relevant study data:

- Total number of sites involved with the *XIENCETM V* study: [--]
- Total number of patients enrolled in the trial: [----]
- Total number of patients enrolled at JHH: [-]
- Percentage of patients treated at JHH: [----]
- Date of first study enrollment: [-----]
- Date of last study enrollment: [-----]
- Amount to institute: [-----]  
[-----]

As a temporary voting member to the Circulatory System Devices Panel, Dr. Brinker potentially could become involved in matters that could affect his 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. Brinker 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. Brinker that would allow him to participate fully in the matter described because the need for his services greatly outweighs the conflict of interest created by this financial interest.

First, although Dr. Brinker's institution was involved in the sponsor's trial, he had no direct, personal involvement and received no compensation. The fact that this financial interest is imputed to him from his employer should lessen any potential conflict the interest may present.

Second, Dr. Brinker's institution contributed a statistically insignificant portion of the trial data with only [----] of the total patient enrollment. This limitation should help to mitigate any concern that the SGE's impartiality might be called into question during Panel deliberations.

Third, there are over 20 firms that manufacture, market or plan to develop competing products or technologies for the same indication as the subject PMA device. The need for this individual's expertise outweighs the large market availability of similar products being considered.

Moreover, 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. Brinker is an interventional cardiologist at Johns Hopkins School of Medicine and a respected Fellow of the American College of Cardiology and the Society for Cardiac Angiography and Intervention. As an experienced panelist, he brings critical reasoning and an insightful dimension to Panel discussions. He was an active temporary member during the December, 2006 Panel meeting regarding general issues of drug-eluting stents (DES). He is currently practicing at Johns Hopkins as an adult clinical cardiovascular physician where he deals with the concerns of his patients on a daily basis. As a practicing cardiologist, he can speak from the perspective of patients who have received DES. One such issue that is expected to arise at this meeting is the topic of antithrombotic drug therapy and the need for patients to be on this therapy for an extended period of time, and to potentially delay or avoid certain invasive surgical procedures. Dr. Brinker's experience in working with patients will allow him to speak directly to this issue.

Dr. Brinker also brings to the Panel clinical trial design expertise and will add greatly to the discussion regarding appropriate trial designs for evaluation of drug-eluting stents. Because he is well informed in the history of bare metal stents (BMS), which this trial uses as a control group, he will be able to differentiate the risk/benefit profiles between the two different stents. He is considered to have the most expertise when dealing with BMS versus DES. The Center conducted a thorough evaluation of the 82 SGEs assigned to the Circulatory System Devices Panel and identified eight interventional cardiologists; five of whom were conflicted or unavailable. In order to have a comprehensive scientific discussion on the contents of this PMA, a minimum of three interventional cardiologists are considered essential.

