



Waiver to Allow Participation in a Food and Drug Administration Advisory Committee

DATE: April 15, 2016

TO: Jill Hartzler Warner, J.D.
Associate Commissioner for Special Medical Programs

THROUGH: Division of Ethics and Integrity
Office of Operations

Michael F. Ortwerth, Ph.D.
Director, Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

FROM: Kathleen L. Walker, RN, M.Ed.
Chief, Integrity, Committee and Conference Management Branch
Division of Ethics and Management Operations, OMO
Center for Devices and Radiological Health

Name of Advisory Committee Member: Richard L. Page, M.D.

Committee: Circulatory System Devices Panel of the Medical Devices Advisory Committee

Meeting date: May 24, 2016

Type of Meeting: Particular Matter Involving Specific Parties.

Description of the Facts on Which the Waiver is Based:

Type, Nature, and Magnitude of the Financial Interest:

Richard L. Page, M.D. serves as Chairman of the Circulatory System Devices Panel, which reviews and evaluates data concerning the safety and effectiveness of marketed and investigational devices for use in the circulatory system and makes appropriate recommendations to the Commissioner of Food and Drugs. Dr. Page's employer, University of Wisconsin School of Medicine and Public Health (UWSMPH), has been identified as a clinical site for St. Jude Medical's AMPLATZER Patent Foramen Ovale (PFO) Occluder study, the Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment (RESPECT) trial. The premarket approval

application (PMA) for the AMPLATZER PFO Occluder device is the particular matter under review by the Panel at this meeting. Data from the RESPECT trial supports the PMA.

Dr. Page is not personally involved with the RESPECT trial at UWSMPH. The study's investigator is on the faculty of the Division of Cardiovascular Medicine and reports to the Chief of the Division, which is one of 23 divisions within the Department of Medicine. Dr. Page is chair of the Department of Medicine, which has over 1,200 staff and 350 faculty members. Dr. Page has no direct input on this investigator's activities, including any clinical trial involvement. As Chair of the Department of Medicine, Dr. Page does not directly oversee or have knowledge of industry grants, contracts or other relationships. Chair/Department approval of all extramural awards within the Department of Medicine has been delegated to the Senior Administrative Program Specialist.

Dr. Page's employer was awarded between \$10,001 and \$25,000 in 2015 and between \$5001 and \$10,000 to date in 2016 in funding for RESPECT trial-related activities. Payments are allocated between \$10,001 and \$25,000 for annual visits of patients who are in the follow-up phase.

Description of the Particular Matter to Which the Waiver Applies:

The Panel will discuss, make recommendations and vote on information regarding the PMA for the AMPLATZER[®] PFO Occluder. The AMPLATZER device is a permanently implanted cardiac device that is delivered percutaneously to close patent foramen ovale for the prevention of recurrent stroke in patients who have had a cryptogenic stroke due to presumed paradoxical embolism.

Additional Facts: None

Basis for Granting the Waiver:

Dr. Page is a highly regarded clinical cardiologist, electrophysiologist and clinical trialist. He received his M.D. and B.S. degrees from Duke University. He was a Resident at the Massachusetts General Hospital and performed cardiology and clinical cardiology fellowships at Duke University Medical Center. He has had academic appointments at medical schools since 1989 and since 2009 has been the Chair of the Department of Medicine at University of Wisconsin School of Medicine and Public Health in Madison, Wisconsin. Dr. Page has served on the Circulatory System Devices Panel as a member and chair on multiple occasions, and his contributions to the panel's discussions have been significant, demonstrating a commitment to the interests of public health.

The topic for discussion is a PFO Occluder device specifically indicated for percutaneous, transcatheter closure of a PFO to prevent recurrent ischemic stroke in patients who have had a cryptogenic stroke due to presumed paradoxical embolism. We expect that the Panel deliberations will be complex and potentially contentious, such that an experienced Chair like Dr. Page is essential. Dr. Page has a full understanding of the benefit-risk issues associated with PFO closure. Furthermore, he did an excellent job chairing a very

challenging and controversial advisory panel meeting, and the major focus of the PFO Occluder Panel meeting (prevention of embolic stroke) shares many of the same considerations as the previous panel meeting.

Dr. Page is being sought for participation in this panel meeting because of his experience as a panelist, his expertise in clinical trial design, his in-depth understanding of the treatment strategies for this specific disease, as well as for his understanding and experience in chairing Circulatory System Devices Advisory Panels. It is also critical to have an advisory panel that has a good balance between surgical and non-surgical perspective because while PFO closure has traditionally been in the surgical field of practice, this device is intended for use by a cardiologist.

The AMPLATZER PFO trial included 925 subjects at 62 US sites. Due to the large number of study sites, it was very difficult to identify panelists with relevant expertise who had no affiliation with a clinical study site for the PFO Occluder Advisory Panel. In our panel preparation process, we approached multiple individuals who have experience in these areas, but were unsuccessful in finding the range of experience equivalent to that of Dr. Page. The panelists we contacted who had expertise in this area were either ineligible due to financial conflicts or unavailable due to scheduling conflicts, including physicians from the other CDRH panels, the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research and the National Institutes of Health. Although Dr. Page is employed by a participating study site, he does not have any involvement or oversight with the AMPLATZER PFO trial. Additionally, the study site enrolled a total of 23 (2.5%) subjects, a small percentage of the U.S. sample size. No additional subjects have been enrolled since August 2011, and no additional subjects are being recruited to participate in the study at the site. Follow-up visits for patients previously enrolled are currently being conducted.

Further, in the interest of public health, it is critical for the agency to review new products that can potentially provide treatment for PFO closure. A patent foramen ovale serves as an open conduit for passage of thrombus from a venous source and can potentially expose patients with a PFO to risk of recurrent stroke. Dr. Page's knowledge of cardiovascular diseases and clinical trial design will provide the necessary expertise for this important discussion.

Accordingly, I recommend that you grant a waiver for Dr. Richard L. Page, Chairperson of the Circulatory System Devices Panel, from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

 X The individual may participate, pursuant to 18 U.S.C. 208(b)(3). The need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved.

Limitations on the Regular Government Employee's or Special Government Employee's Ability to Act:

_____ Non-voting

_____ Other (specify):

_____ Denied – The individual may not participate.

/S/
Jill Hartzler Warner, J.D.
Associate Commissioner for Special
Medical Programs

4/28/2016
Date