



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

DATE: June 10, 2011

TO: Jill Hartzler Warner, J.D.
Associate Commissioner for Special Medical Programs (Acting),
FDA

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 Special Medical Programs

FROM: Jayne E. Peterson, J.D. _____ /S/
Director, Division of Advisory Committee and Consultant
Management
Center for Drug Evaluation and Research

Name of Advisory Committee Member: Steven Czinn, M.D.

Committee: Gastrointestinal Drugs Advisory Committee

Meeting date: July 21, 2011

Description of the Facts on Which the Waiver is Based:

Type, Nature, and Magnitude of the Financial Interest:

Dr. Czinn owns (b) (6) shares of stock in a competing firm, (b) (6). The current market value of the stock is between (b) (6).

Description of the Particular Matter to Which the Waiver Applies:

On July 21, 2011, the committee will discuss the results from a clinical trial of supplement biologics license application 103772/5301, REMICADE (infliximab), by Janssen Biotech, Inc. (formerly known as Centocor Ortho Biotech Inc.), in the treatment

of pediatric patients with moderately to severely active ulcerative colitis, a type of Inflammatory Bowel Disease (IBD).

Additional Facts: None

Basis for Granting the Waiver:

Steven J. Czinn, MD is a nationally-recognized pediatric gastroenterologist who currently serves as Professor and Chair of Department of Pediatrics at University of Maryland Medical Center (UMMC).

Prior to joining UMMC in 2006, Dr. Czinn served as Professor of Pediatrics and Chief of the Division of Pediatric Gastroenterology and Nutrition at Rainbow Babies & Children's Hospital in Cleveland, Ohio. Dr. Czinn has 29 years of clinical experience in pediatric gastroenterology, and his research interests include mucosal immunology, inflammatory bowel diseases (IBD), gastrointestinal infections, and the *Helicobacter pylori* micro-organism. He is the lead author or co-author on more than 80 peer-reviewed publications and has served as an associate editor of the American Journal of Gastroenterology since 2003. He has authored multiple book chapters on pediatric gastroenterology topics and served as a reviewer for more than 15 academic journals. Dr. Czinn has also co-organized the first International Symposium on Pediatric Inflammatory Bowel Disease in 2003.

The July 21, 2011 Gastrointestinal Drugs Advisory Committee (GIDAC) meeting has been convened to discuss a number of key issues that require expertise in the treatment of pediatric IBD. The committee currently has a paucity of physicians who have the substantial background and depth of knowledge that Dr. Czinn possesses. It should be noted that the pediatric IBD community is relatively small. About 150,000 of the approximately 1.4 million patients with IBD in the United States are children under age 17. Many pediatric IBD experts are leaders at medical centers and institutions that actively engage in clinical research, most of which are commercially funded; therefore, it is difficult to find experts without conflicts.

Increasingly, the care of IBD children is being directed to IBD centers within these academic institutions, as they use a multidisciplinary approach to treat patients in the hope for a better clinical outcome. During the pre-screening process for the upcoming GIDAC meeting, we have learned that the majority of pediatric IBD experts in the academic centers have served as site PIs for the pediatric REMICADE (infliximab) trial and/or for pediatric trials involving competing products. For the REMICADE trial alone, 17 U.S. pediatric IBD experts served as site PIs and, therefore, were not eligible to participate in the upcoming GIDAC meeting. Since IBD is less common in pediatric population and it is more difficult to enroll children into clinical trials, 27 sites (17 U.S. sites) were required to participate to enroll 60 pediatric ulcerative colitis (UC) patients into the REMICADE trial (4 sites failed to enroll any patients). Similar clinical trials each involving 20-30 centers are currently ongoing for competing products.

We currently have one pediatric IBD expert attending the committee meeting, and one other pediatric IBD specialist requiring a waiver for participation. It is also important

that the advisory committee have experts with a broader perspective in pediatric gastroenterology. Dr. Czinn is an expert in pediatric gastroenterology with a research background in IBD. In an attempt to gain the appropriate representation, at least 31 other pediatric gastroenterology and adult and pediatric IBD experts were contacted, but could not attend the meeting due to conflict of interests, self-recused at the beginning of the conflict of interest screening process, unable to attend due to schedule conflicts, or incomplete paperwork. Additional pediatric IBD experts were considered but were found to be involved in one of the abovementioned clinical trials or advisory panels to pharmaceutical companies.

It should be noted that REMICADE (infliximab) is already approved in children for other indications, including a subtype of inflammatory bowel disease called Crohn's disease. This advisory committee will discuss the results from a clinical trial in the treatment of pediatric patients with moderately to severely active ulcerative colitis. The use of Tumor Necrosis Factor (TNF) blockers, such as REMICADE, in a pediatric population presents a number of clinical challenges that require input from pediatric gastroenterologists who have experience with this drug class. The clinical study to be discussed will require a risk/benefit assessment unique to the IBD pediatric population, with which Dr. Czinn has considerable clinical experience. The application under review has given the division an opportunity to review their approach to guiding drug development for TNF blockers in children with IBD. Dr. Czinn's contributions to the advisory committee discussion could potentially result in the division changing their approach to the design and conduct of pediatric studies in ulcerative colitis.

In summary, the division believes that it is critical to have at least a minimum of two experienced pediatric IBD experts and there has been a genuine effort to secure individual participation and representation without conflicts of interest. We currently have one pediatric IBD expert attending the committee meeting, and one other pediatric IBD expert requiring a waiver for participation. Dr. Czinn is a highly skilled and knowledgeable pediatric gastroenterology expert, with a research background in pediatric IBD. Due to the strong need for experienced pediatric gastroenterologists, his expertise will contribute to the diversity of opinions and expertise represented on the committee and will provide a foundation for developing advice that is fair and comprehensive.

Accordingly, we recommend that you grant a waiver for Dr. Steven J. Czinn, a temporary member of Gastrointestinal Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a) as well as the conflict of interest prohibitions of section 712(c)(2)(B) of the Federal Food, Drug, and Cosmetic Act.

Certification:

- 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.
- The individual may participate, pursuant to 21 U.S.C. 379d-1 – The individual's service is necessary to afford the advisory committee essential expertise.

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 (Acting)

06/30/2011
Date