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

DATE: February 9, 2017

TO: Janice M. Soreth, M.D.
Associate Commissioner for Special Medical Programs
Office of Medical Products and Tobacco
Office of the Commissioner, FDA

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

FROM: Pediatric Advisory Committee
Marieann Brill, MBA, RAC, MT(ASCP)
Designated Federal Officer
Office of Pediatric Therapeutics

Name of Advisory Committee Meeting Speaker: James S. Leeder, Ph.D.

Committee: Pediatric Advisory Committee

Meeting date: March 6 – 7, 2017

Description of the Particular Matter to Which the Waiver Applies:

The Pediatric Advisory Committee (PAC) is chartered to provide advice and make recommendations regarding FDA-regulated pediatric research, including the identification of research priorities related to pediatric therapeutics. In addition, the PAC reviews adverse event reports for drugs and biologics that have had pediatric labeling based on studies conducted under the Best Pharmaceuticals for Children Act (21 USC §355b) (BPCA) and/or the Pediatric Research Equity Act (21 USC §355a) (PREA).

The Pediatric Advisory Committee (PAC) will meet on the afternoon of March 6, 2017 to discuss the role of pharmacogenomics in pediatric product development and labeling. During that session, Strattera® (atomoxetine) will be used as an example in the FDA public presentations to frame the discussion of the non-voting questions before the committee. Strattera®, a selective

norepinephrine reuptake inhibitor, is indicated for the treatment of attention-deficit/hyperactivity disorder (ADHD) and is marketed by Eli Lilly and Co. The PAC will not be asked to make any specific recommendations about Strattera®, or for that matter about any of the other products that will be used as examples during this session. Dr. Leeder is a Special Government Employee (SGE) who has been invited for the sole purpose of giving a presentation at the pharmacogenomics session of the PAC meeting, and will not participate in the discussion. Dr. Leeder, who has specialized expertise in pharmacogenomics in children, will provide critical information to assist the committee in their discussion of the role of pharmacogenomics studies in pediatric product development. Although the particular matter before the PAC involves the broader discussion of pharmacogenomics in pediatric product development, because the committee will be discussing Strattera as an example, the particular matter potentially could impact agency decisions regarding Strattera, individually or as part of a class of products, and Dr. Leeder's financial interests, as described below, could be affected.

During the remainder of the meeting on March 6 and 7, 2017, the PAC will be discussing the pediatric-focused safety reviews of selected products following pediatric-labeling as a result of studies conducted under either BPCA and/or PREA, and to make recommendations about continued pediatric safety monitoring and/or labeling changes as a result of those safety reviews. Dr. Leeder will not be participating in that portion of the PAC meeting.

Type, Nature, and Magnitude of the Financial Interest(s):

Dr. Leeder is a principal investigator for a five year grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), awarded to Children's Mercy Hospital (his employer), to investigate the role of genetic variation on the observed variability in the response to Strattera® of patients with attention deficit hyperactivity disorder (ADHD).

The total grant awarded to Children's Mercy Hospital over a period of five years is (b)(4); the amount awarded per year is (b)(4) with direct costs of (b)(4) for year one (divided among an Administrative Core, a Clinical Project, a Translational Project and a Pilot Project). The Clinical Project has a first-year budget of (b)(4) in direct costs, from which Dr. Leeder receives a salary of (b)(4) plus (b)(4) fringe for a total of (b)(4). Overall, Dr. Leeder's total salary and fringe is (b)(4) for the entire grant. The overall project period is from September 2016 through June 2021. Dr. Leeder has a personal financial interest in the NICHD grant to Children's Mercy Hospital based on the salary support he receives from the grant, and he has an imputed financial interest based on his employment with Children's Mercy Hospital, the grant recipient.

Basis for Granting the Waiver:

The role of pharmacogenomics in pediatric product development is an emerging field, and there are few scientists with the necessary clinical expertise in this area. In addition, the PAC will not be discussing the safety and/or efficacy of Strattera®. Although Dr. Leeder's interest involves Strattera®, the grant is sponsored by NICHD which is not a party to a matter before the committee. In addition, as a speaker, Dr. Leeder will not be participating in the committee deliberations.

Dr. Leeder has unique qualifications and specialized expertise needed for this particular matter.

Dr. Leeder earned his Doctor of Pharmacy at the University of Minnesota and his Doctor of Philosophy in the Department of Pharmacology at the University of Toronto. He is currently the Deputy Director of the Children's Research Institute at Children's Mercy Hospital. Dr. Leeder is an Associate Chair-Research of the Department of Pediatrics at Children's Mercy and University of Missouri-Kansas City School of Medicine. He serves as the Marion Merrell Dow/Missouri Endowed Chair in Pediatric Clinical Pharmacology and is the Director of the Division of Clinical Pharmacology, Toxicology and Therapeutic Innovation at Children's Mercy Hospital. Dr. Leeder is also a Professor in Pediatric and Pharmacology at the University of Missouri and is an Adjunct Professor at the School of Medicine, University of Utah; School of Pharmacy, University of Kansas; and University of Kansas Medical Center. He has held various positions in Pharmacology at different hospitals. Dr. Leeder's research has produced over 160 peer-reviewed publications which include highly cited reviews on the application of pharmacogenetic and pharmacogenomics strategies to observe variability in drug disposition and response in children.

Dr. Leeder is essential for this PAC meeting because of his exceptional experience in pharmacogenomics, a critical aspect of the discussion. It would be very difficult to replicate his knowledge and experience as a speaker before the committee.

There is limited expertise available and it is difficult to locate similarly qualified individuals without a disqualifying financial interest.

Pharmacogenomics uses information about a person's genetic makeup, or genome, to choose the drugs and drug doses that are likely to work best for that particular person. This new field combines the science of how drugs work, called pharmacology, with the science of the human genome, called genomics. It has been difficult to identify individuals with pharmacogenomics expertise in pediatrics who are free of conflicts to attend this meeting. In the interest of public health, it is critical that Dr. Leeder participate to ensure a fully-informed discussion of this issue.

In our meeting preparation process, we reviewed current SGEs in the Center for Drug Evaluation and Research (CDER) with experience in this area. Out of the 1600 CDER SGEs, we identified 16 that have experience in clinical pharmacology. However, we were unsuccessful in finding the range of expertise to match that of Dr. Leeder for this particular meeting- i.e., pharmacogenomics expertise in pediatrics.

The particular matter is not sensitive.

The particular matter to be addressed by the PAC is not considered sensitive. There will be no questions involving the efficacy, safety and/or labeling of Strattera® for the treatment of patients with ADHD. The goal of this part of the meeting is to have a better understanding of the role of pharmacogenomics in products used in children and its implications for product labeling.

Dr. Leeder's expertise in this particular matter is necessary in the interest of public health.

In the interest of public health, it is critical for the agency to be able to solicit advice and recommendations from the PAC regarding the role of pharmacogenomics in FDA-regulated pediatric research, including the identification of research priorities related to pediatric therapeutics.

The dollar value of the potential gain or loss that may result from Dr. Leeder's participation in the particular matter is small relative to the amount of the total grant.

The total cost of the grant over five years is (b)(4) the total costs per year are (b)(4) with direct costs for year one at (b)(4). In year one, Dr. Leeder receives a salary of (b)(4) plus (b)(4) fringe for a total of (b)(4) ((b)(4) of the direct costs). Overall, Dr. Leeder's total salary and fringe is (b)(4) or (b)(4) for the entire grant.

Any potential for a conflict of interest is greatly outweighed by the strong need for Dr. Leeder's expertise in this matter.

Dr. Leeder is an employee of Children's Mercy Hospital, the awardee of a NICHD grant to study Strattera for treatment of ADHD in children. Dr. Leeder is a principal investigator on the grant. The PAC discussion involves pharmacogenomics in pediatric product development, not ADHD, and the discussion of Strattera will not relate to its safety, efficacy, or labelling. Any potential conflict of interest created by this grant is greatly outweighed by the need for Dr. Leeder's special expertise in providing expert information to enable the PAC to provide advice and make recommendations regarding the role of pharmacogenomics in FDA-regulated pediatric research. As such, Dr. Leeder's involvement as a speaker at the March 6, 2017 PAC meeting is essential to the success of this particular matter.

Accordingly, I recommend that you grant a waiver for Dr. Leeder, a speaker at the Pediatric Advisory Committee meeting being held March 6, 2017, from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

__X__ The individual may participate as a speaker at the meeting, 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 Special Government Employee's Ability to Act: Dr. Leeder will only be providing a presentation to the committee. He will not be participating in the committee discussion. The Committee will not vote on the particular matter.

_____ Denied – The individual may not participate.

/S/ February 16, 2017

Janice M. Soreth, M.D. Date
Associate Commissioner for Special Medical Programs
Office of Medical Products and Tobacco
Office of the Commissioner, FDA