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

DATE: September 27, 2019

TO: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

FROM: Jayne E. Peterson, B.S.Pharm., J.D.
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Meeting Temporary Member: David Eisenberg, M.D., MPH

Committee: Bone, Reproductive, and Urologic Drugs Advisory Committee

Meeting date: October 30, 2019

Description of the Particular Matter to Which the Waiver Applies:

Dr. David Eisenberg is a temporary voting member of the Bone, Reproductive, and Urologic Drugs Advisory Committee. The Committee's function is to review and evaluate data on the safety and effectiveness of marketed and investigational human drug products for use in the practice of osteoporosis and metabolic bone disease, obstetrics, gynecology, urology and related specialties, and make appropriate recommendations to the Commissioner of Food and Drugs.

On October 30, 2019, the committee will meet to discuss new drug application (NDA) 204017 (levonorgestrel and ethinyl estradiol) transdermal system, submitted by Agile Therapeutics, Inc., for the prevention of pregnancy in women of reproductive potential. The topic of this advisory committee meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Eisenberg is an Associate Professor in the Department of Obstetrics and Gynecology at Washington University School of Medicine in St. Louis (WUSTL). He has identified both a personal financial interest and a financial interest of his employer that is imputed to him under the federal conflict of interest statute, 18 U.S.C. § 208. Both financial interests can be affected by the particular matter that is the subject of the committee meeting.

Dr. Eisenberg serves as a scientific advisor to Medicines360, a competing firm. (b) (6) [redacted] Medicines 360 is a women's health entity so consulting in the next year could cover products for use in contraception. Dr. Eisenberg will receive between $0 and $2,000 per year for this consulting contract.

In addition, Dr. Eisenberg's employer, WUSTL, has a contract with Medicines360 for "A Phase 3, Multicenter, Open-Label Study of a Levonorgestrel 52 mg Intrauterine System for Long-Term, Reversible Contraception (NCT00995150)." The purpose of the study is to assess the efficacy of a levonorgestrel 52 mg intrauterine system in nulliparous and parous females of child-bearing potential who request long-term, reversible contraception for up to 10 years. Dr. Eisenberg is a Site Investigator for this study. The study began in March 2010 and will end in 2020. WUSTL receives between $100,000 and $150,000 per year for this study. Dr. Eisenberg does not receive salary support or personal remuneration for this study.

Basis for Granting the Waiver:

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

David Eisenberg, M.D., MPH, is an Associate Professor in the Department of Obstetrics and Gynecology at Washington University School of Medicine in St. Louis. Dr. Eisenberg specializes in all clinical aspects of family planning, including complex contraceptive care. Dr. Eisenberg attended the University of Alabama School of Medicine, after graduating *magna cum laude* from the University of Pittsburgh with a B.S. in Neuroscience. At Northwestern University, he completed his residency in Obstetrics & Gynecology and a 2-year fellowship in Family Planning and Contraception and obtained a Master of Public Health degree.

Dr. Eisenberg has lectured on various women's health topics including contraception, maternal mortality and the impact of family planning in the developing world. He is both a principal investigator and collaborator on various clinical research studies involving access to and education about contraception and new contraceptive methods and has published in this area.

In addition to his domestic work, Dr. Eisenberg has traveled to many countries, including sub-Saharan Africa, to provide clinical services and teaching focused on the same areas of family planning, sexual and reproductive health along with general obstetrics and gynecology.

At the October 30, 2019, meeting, the advisory committee will discuss the benefit/risk assessment of a new hormonal contraceptive and provide recommendations on approvability. This meeting raises complicated issues including interpreting effectiveness based on a measure known as the Pearl Index, challenges with assessing venous thromboembolism (VTE) risk, and complexities assessing how the benefits of this product compare to its risks in the context of available therapy. It is critical that the committee include experts who have a depth of understanding about contraception and experience in family planning and contraceptive counseling, like Dr. Eisenberg, to ensure thorough, well-reasoned advice on the challenging issues raised in this application. Based on his qualifications, accomplishments and experiences in

the contraceptive field, we strongly believe Dr. Eisenberg will provide important insights on the benefits and risks of this new contraceptive product in the context of available therapy.

The particular matter is not sensitive.

The meeting topic is not considered sensitive and the FDA Division with responsibility for this product does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial.

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

Unintended pregnancy is a significant public health issue for reproductive aged women. The benefits of contraception to prevent pregnancy was named as one of the 10 great public health achievements of the 20th century by the Centers for Disease Control and Prevention. These benefits are widely recognized and include improved health and well-being, reduced maternal mortality, health benefits of pregnancy spacing for maternal and child health, female engagement in the work force, and economic self-sufficiency for women.[1] Hormonal contraceptive products, which are considered in clinical practice to be an effective contraceptive choice, reduce the risk of pregnancy mainly via suppression of ovulation.

Since hormonal contraceptives were developed, use of lower doses and more convenient dosing schedules have become a priority. The benefits of contraception to prevent pregnancy are weighed against the risk of rare, but serious side effects including heart attack, stroke, and VTE. Epidemiological studies have shown that the use of a combined hormonal contraceptive, whatever the route of administration, increases the risk of VTE, although this risk is lower than when a woman has a pregnancy or is postpartum.

Including Dr. Eisenberg in this meeting will help ensure that the Agency receives thorough, well-reasoned advice on the challenging issues raised in this application. Based on his qualifications, accomplishments and experiences in the contraceptive field, we strongly believe Dr. Eisenberg will provide important insight on the benefits and risks of this new contraceptive product in the context of available therapy.

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

It has been difficult to identify obstetrics and gynecology experts that have significant experience with family planning and contraceptive options. We believe Dr. Eisenberg would be able to make significant contributions to the discussions given his experience in contraception counseling and use. As noted above, Dr. Eisenberg has obtained advanced training in family planning and his area of expertise includes complex contraceptive care. His expertise is directly relevant to the complicated issues raised in this application and is needed to ensure the Agency obtains robust input to inform its regulatory decision.

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[1]Sonfield A, Hasstedt K, Kavanaugh ML, Anderson R. The social and economic benefits of women's ability to determine whether and when to have children. New York (NY): Guttmacher Institute; 2013. Available at: http://www.guttmacher.org/pubs/social-economic-benefits.pdf. Retrieved August 4, 2014.

Accordingly, I recommend that you grant Dr. David Eisenberg, a temporary voting member of the Bone, Reproductive, and Urologic Drugs Advisory Committee, a waiver from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

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.

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

_____ Non-voting

_____ Other (specify):

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_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S
Date: 2019.10.11 08:19:17 -04'00'

Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

October 11, 2019
Date