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

DATE: August 22, 2018

TO: Rachel Sherman, M.D., M.P.H.
Principal Deputy Commissioner
Office of the Commissioner, Food and Drug Administration

THROUGH: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

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 Member: **Benjamin Lebwohl, M.D., M.S.**

Committee: Gastrointestinal Drugs Advisory Committee (GIDAC)

Meeting date: October 18, 2018

Description of the Particular Matter to Which the Waiver Applies:

Dr. Benjamin Lebwohl is a standing voting member of the Gastrointestinal Drugs Advisory Committee. The Committee's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of gastrointestinal diseases and make appropriate recommendations to the Commissioner of Food and Drugs.

The committee will meet on October 18, 2018, to discuss new drug application (NDA) 210166, for prucalopride tablets for oral administration, submitted by Shire Development, LLC, proposed for the treatment of chronic idiopathic constipation (CIC) in adults. The topic of this meeting is a particular matter involving specific parties.

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

Dr. Lebwohl reported a financial interest in [redacted] (b) (6), a healthcare sector mutual fund. The value of his holding in this fund is between $200,000 - $300,000. At the writing of this waiver, this fund contained assets in three competing/affected firms: [redacted] (b) (6)

(b) (6). The top 25 holdings of the fund include (b) (6), representing approximately 5.11% of the underlying value of the fund. (b) (6) are not in the top 25 holdings; each representing less than 1.44%.

Under a regulatory exemption issued by the Office of Government Ethics, an employee may participate in any particular matter affecting one or more holdings of a sector mutual fund where the disqualifying financial interest in the matter arises because of ownership of an interest in the fund and the aggregate market value of interests in all funds in which there is a disqualifying financial interest and which concentrate in the same sector does not exceed $50,000. Because Dr. Lebwohl's financial interest in the (b) (6) exceeds that amount, he has disqualifying financial interests based on the fund's holding of the above-listed companies.

Basis for Granting the Waiver:

The primary issue for discussion at this meeting will be the benefit/risk profile of the use of prucalopride, given the potential cardiovascular risks associated with this class of products. The proposed population for treatment of prucalopride to the market is supported by data from clinical trials and epidemiologic data. Therefore, a productive discussion and assessment of the data depends on having experts with a strong expertise in clinical gastroenterology, with experience treating adult patients with IBS-C and chronic idiopathic constipation (CIC), combined with an understanding of how to interpret epidemiological data. Dr. Lebwohl has unique qualifications and specialized expertise needed for the evaluation and interpretation of the type and nature of clinical trial and especially epidemiologic data that will be presented. Dr. Lebwohl's background in these areas will allow for valuable contribution to the discussion.

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

Benjamin Lebwohl, M.D., M.S., received his medical degree from Columbia University College of Physicians and Surgeons and later received his Masters of Science in Biostatics from Columbia University, Mailman School of Public Health. He is an Assistant Professor of Medicine and Epidemiology at Columbia University College of Physicians & Surgeons; Director of Clinical Research, Celiac Disease Center at Columbia University and an Assistant Attending at New York-Presbyterian/Columbia University Medical Center. Dr. Lebwohl was awarded a two-year fellowship at NIH, where he studied colorectal cancer prevention. Dr. Lebwohl was a Gerstner Scholar (2014-2017) at Columbia, studying the impact of gluten exposure on the microbiome in patients with celiac disease and non-celiac gluten sensitivity. He is also the recipient of the American Gastroenterology Association Research Scholar Award (2014-2017), collaborating with the Channing Laboratory at Harvard to study risk factors for celiac disease and the health effects of gluten in large cohort studies.

His current areas of clinical expertise include upper endoscopy, GI endoscopy procedure, colonoscopy, colon and rectal disease, colon cancer screening and prevention, and celiac disease. Dr. Lebwohl collaborates with Columbia University – Celiac Disease Center and abroad in the areas of the epidemiology, patterns of care, and natural history of celiac disease. His second related research interest is quality of endoscopy, including bowel preparation prior to colonoscopy,

improving the detection of colorectal adenomas, and improving the diagnostic yield of biopsy of the small intestine. Since 2011, Dr. Lebwohl has been involved with the Screening Colonoscopy Report Cards program at the NYC Department of Health and Mental Hygiene. He helped to develop a system for the measurement of colonoscopy quality indicators, including the adenoma detection rate, which is widely regarded as the most important process measure in screening colonoscopy.

In addition to his expertise in gastroenterology, Dr. Lebwohl's background in epidemiology and biostatistics will be valuable to the advisory committee discussion centering on aspects of the adequacy and strength of the efficacy data for prucalopride to support potential approval, and in providing thoughtful evaluation of the risk/benefit profile for this product and broader public health considerations. Furthermore, as an experienced member of the GIDAC, it will be essential to have his perspective, complementary to other members who may be participating for the first time in a GIDAC meeting.

Multiple experts are needed.

Multiple gastroenterologists were invited to attend this meeting to allow for a diverse panel of experts that would include those who treat adults and pediatric patients; this would help provide a balanced assessment of the acceptability of the known and anticipated risks associated with the proposed treatment with prucalopride. Although there are a number of gastroenterologists scheduled to attend this meeting, Dr. Lebwohl is the only invited expert with a combination of expertise in adult gastroenterology, biostatistics, and epidemiology. His expertise in this area allows him to bring a unique persepective and contribution to the discussion. Having a diverse collection of professional experiences represented on the panel would provide an opportunity for a robust and productive discussion of the meeting topic.

The particular matter is not sensitive.

The meeting topic is not considered to be sensitive. The Division does not expect that the meeting is likely to receive significant broad public interest, (non-trade) press interest, or congressional interest.

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

CIC is one of the two most common functional gastrointestinal disorders worldwide. CIC has a global prevalence of 14%, affecting more commonly females, older adults, and those of lower socioeconomic status. Chronic constipation significantly impairs patients' quality of life, most notably among the elderly. Doctors do not know what causes CIC, and there is no known cure. First line treatment in most cases includes non-prescription options such as fiber products (psyllium) or nondrug interventions. Over-the-counter (OTC) therapies and nondrug interventions are not specifically approved for CIC. Following OTC options, only three prescription drugs are approved: lubiprostone, linaclotide and plecanatide. No one medication works for all patients suffering from chronic gastrointestinal disorders. With availability of new therapies, if this product is approved, patients and their doctors can select the most appropriate treatment for their condition. In the interest of public health, it is important that the agency have available the unique expertise that Dr. Lebwohl will provide for the discussion of the particular matter before the committee.

Accordingly, I recommend that you grant Dr. Benjamin Lebwohl, a standing voting member of the Gastrointestinal 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 Special Government Employee's Ability to Act:

_____ Non-voting

_____ Other (specify):

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_____

_____ Denied – The individual may not participate.

Russell Fortney -S

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Date: 2018.09.25 09:54:16 -04'00'

for Rachel Sherman, M.D., M.P.H.
Principal Deputy Commissioner
Office of the Commissioner, Food and Drug Administration

September 25, 2018
Date