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

DATE: April 3, 2023

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

FROM: Byron Marshall
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Meeting Voting Member: **Benjamin Lebwohl, M.D., M.S.**

Committee: Gastrointestinal Drugs Advisory Committee

Meeting date: May 19, 2023

Description of the Particular Matter to Which the Waiver Applies:

Dr. Benjamin Lebwohl is a standing voting member and Chairperson of the Gastrointestinal Drugs Advisory Committee (GIDAC). 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.

On May 19, 2023, the committee will discuss new drug application (NDA) 212833, obeticholic acid 25 mg oral tablets, submitted by Intercept Pharmaceuticals, Inc., for the treatment of pre-cirrhotic liver fibrosis due to nonalcoholic steatohepatitis (NASH). The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

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 $300,000 and $400,000. At the writing of this waiver, specifically, based on the most current publicly available information, this fund contains assets in competing firms: [redacted] (b) (6) These competing firms represent less than 5.9% of the underlying holdings of the fund.

Under the regulatory exemption issued by the Office of Government Ethics (5 CFR § 2640.201(b)), an employee may participate in any particular matter affecting one or more holdings in 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 related funds (specifically, those 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) fund exceeds that amount, he has disqualifying financial interests based on the fund's holdings of the above-mentioned companies.

Basis for Granting the Waiver:

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

Dr. Lebwohl received his medical degree from Columbia University College of Physicians and Surgeons followed by a residency in Internal Medicine and Gastroenterology fellowship. He stayed at Columbia as a fellow in Digestive and Liver Disease, during which time he obtained a Master's Degree in Patient-Oriented Research from the Department of Biostatistics at the Mailman School of Public Health. He was a post-doctoral fellow in a National Cancer Institute-funded Training Program in Cancer-Related Population Sciences under the mentorship of Alfred Neugut. Dr. Lebwohl joined the faculty of the Celiac Disease Center at Columbia University in 2010. He is board certified in internal medicine and gastroenterology. Dr. Lebwohl is currently Associate Professor of Medicine and Epidemiology at Columbia University College of Physicians and Surgeons. He is also an Assistant Attending Physician at New York-Presbyterian/Columbia University Irving Medical Center.

Dr. Lebwohl is President of the Society for the Study of Celiac Disease and is the Director of Clinical Research at the Celiac Disease Center at Columbia University, where he collaborates with investigators in the United States and abroad in epidemiology, patterns of care, natural history, and therapeutics. Dr. Lebwohl's second and related research interest is quality of endoscopy, including improving the detection of colorectal adenomas. He has co-authored more than 300 peer-reviewed publications. His research is supported by the National Institutes of Health, and past research funding includes the American Gastroenterological Association, the Celiac Disease Foundation, and the American Scandinavian Foundation. He is heavily involved in medical education and lectures regularly to trainees on topics including celiac disease, evidence-based medicine, clinical decision making, pseudoscience, diarrhea, and colorectal cancer screening.

Dr. Lebwohl has additional training in epidemiology that most of the members of the committee do not have. His expertise in epidemiology is uniquely suited for a discussion of risks/adverse reactions identified in this NDA. As the Chairperson of the GIDAC he will play an essential role in overseeing the deliberations of this meeting.

The particular matter is considered sensitive.

This topic is considered to be sensitive, as the FDA Division with responsibility for review of this product expects that the meeting may receive significant public interest and non-trade press interest. Fatty liver disease has been more prominent in the press and obeticholic acid is the first drug seeking

approval for this disease.

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

Nonalcoholic fatty liver disease (NAFLD), a condition in which excess fat is stored in the liver, is one of the most common causes of liver disease in the United States (U.S.). It's estimated that about 25 percent of adults in the U.S. have NAFLD and of those about 20 percent have NASH (5% of adults in the U.S.). The reason some people with NAFLD have simple fatty liver and others get NASH is not known, although research suggests that certain genes may play a role.

NASH is the more severe form of NAFLD in which an individual has inflammation of the liver and liver cell damage, in addition to fat in the liver. Inflammation and liver cell damage can also cause fibrosis which leads to permanent liver damage, cirrhosis, and its outcomes. The presence of metabolic syndrome (obesity, dyslipidemia, hypertension, and glucose intolerance) increases the likelihood that a patient has NASH rather than simple steatosis. The pathogenesis of NAFLD is poorly understood but seems to be linked to insulin resistance (e.g., as in obesity or metabolic syndrome). Obeticholic acid is the first drug seeking approval for NASH in the U.S.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Lebwohl will provide for the discussion of the particular matter before the committee.

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

Dr. Lebwohl has been a standing member of the committee since 2017 and Chairperson since 2021. Dr. Lebwohl's expertise in gastroenterology in combination with his training in epidemiology allow him to bring a unique perspective and contribution to the discussion. His diverse collection of professional experiences and previous experiences with AC meetings as a standing member and Chairperson of the GIDAC will be invaluable to a robust and productive discussion of the application coming before the committee.

Accordingly, I recommend that you grant Dr. Benjamin Lebwohl, 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 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: 2023.05.01 09:33:06 -04'00'

May 1, 2023

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

Date