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

DATE: November 14, 2024

TO: Emily Helms Williams
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 Standing Member: **Janet Lee, MD**

Committee: Pharmacy Compounding Advisory Committee

Meeting Date: December 4, 2024

Description of the Particular Matter to Which the Waiver Applies:

Janet Lee, M.D., has been invited to serve as a temporary voting member of the Pharmacy Compounding Advisory Committee (PCAC). Dr. Lee is a special Government employee serving on an advisory committee under the Federal Advisory Committee Act (5 U.S.C. 1001 *et seq.*). The Committee's function is to provide advice on scientific, technical, and medical issues concerning drug compounding under sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act, and, as required, any other product for which the Food and Drug Administration has regulatory responsibility and make appropriate recommendations to the Commissioner of Food and Drugs.

On December 4, 2024, the Committee will discuss a bulk drug substance being considered for inclusion on the 503A Bulks List. The nominator of this substance will be invited to make a short presentation supporting the nomination. The bulk drug substance to be discussed is Thymosin alpha-1 (uses are for hepatitis B, hepatitis C, human immunodeficiency virus (HIV), COVID-19, depressed response to vaccinations; adjuvant to flu vaccines, malignant melanoma, hepatocellular carcinoma (HCC), non-small cell lung cancer (NSCLC), sepsis, infections after hematopoietic stem cell transplantation (HSCT), chronic obstructive pulmonary disease (COPD), myalgic encephalomyelitis and chronic fatigue syndrome (ME/CFS)). The topic is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Lee reported that her spouse holds stock in (b) (6) valued between $25,000 and $50,000, and (b) (6), valued between $0 and $5,000. (b) (6) own marketed products and products in development in the areas where Thymosin is being evaluated and could be financially affected by the discussions of the bulk drug substance at issue.

Under a regulatory exemption issued by the Office of Government Ethics at 5 C.F.R. § 2640.202(b), an employee may participate in any particular matter involving specific parties in which the disqualifying financial interest arises from the ownership of securities issued by one or more entities that are not parties to the matter but that are affected by the matter, if the aggregate market value of the holdings in the securities of all affected entities does not exceed $25,000. Because Dr. Lee's financial interests in (b) (6) exceed that amount, she has disqualifying financial interests.

Basis for Granting the Waiver:

Dr. Janet Lee has unique qualifications and specialized expertise needed for these particular matters.

Dr. Lee is a temporary voting member of the PCAC. She is a Selma and Herman Seldin Distinguished Professor of Medicine, Professor of Pathology and Immunology, and Division Chief, Pulmonary and Critical Medicine at John T. Milliken Department of Medicine, Washington University School of Medicine.

Dr. Lee received her Bachelor of Arts degree in Natural Sciences from the Johns Hopkins University and earned her medical degree from Georgetown University School of Medicine. She completed her residency at University of Alabama at Birmingham followed by a fellowship in Pulmonary and Critical Care Medicine at the University of Washington and a postdoctoral fellowship at the Veteran's Affairs Pulmonary Research Laboratories at the University of Washington.

Dr. Lee is a highly regarded physician-scientist in pulmonary and critical care medicine. She cares for patients requiring intensive care as well as those with advanced lung diseases, including acute and chronic respiratory failure. Her research centers on the host response to severe lower respiratory tract infections and the molecular basis of distinct host-pathogen interactions triggering lung injury. She has previously acted as Director of the Acute Lung Injury Center of Excellence and the Pulmonary Translational Research Core at the University of Pittsburg.

Dr. Lee is a principal investigator on grants from the National Institutes of Health's National Heart, Lung, and Blood Institute, including a grant focused on host protection against pathogen-encoded proteases in acute lung injury and another on host control mechanisms in lung infections. She also leads a grant focused on patient-oriented research in acute lung injury and another on complement components and activity in patients with acute respiratory distress syndrome. She has authored numerous peer-reviewed publications and presented nationally and internationally on her research.

Some of the uses evaluated for Thymosin alpha-1 include COVID-19, sepsis, and COPD. Dr. Lee's vast experience in pulmonary and critical care medicine and understanding of the treatment landscape in these diseases will add valuable insight into discussion on whether the Agency should permit the use of this bulk drug substance in compounding by adding it to the 503A Bulks List.

The particular matters are sensitive.

The topic is considered to be sensitive and the FDA Division responsible for review of the bulk drug substance expects that the meeting is likely to receive significant public interest.

Dr. Lee's expertise in these particular matters is necessary in the interest of public health.

One of the conditions that must be satisfied for a drug product to qualify for the exemptions under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353a) is that the licensed pharmacist or licensed physician compounds the drug product using bulk drug substances (as defined in 21 CFR 207.3) that: (1) comply with the standards of an applicable United States Pharmacopoeia (USP) or National Formulary monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (2) if an applicable monograph does not exist, are drug substances that are components of drugs approved by the Secretary of Health and Human Services (the Secretary); or (3) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under section 503A(c) of the FD&C Act (the 503A Bulks List) (see section 503A(b)(1)(A)(i) of the FD&C Act).

Thymosin alpha-1 (free base) is a N-terminal acetylated 28-amino-acid peptide. It is physiologically present in the human body and originally isolated from thymosin fraction-5 of calf thymus. Chemically produced thymalfasin, which is identical in amino acid sequence to natural Thymosin alpha-1 (free base), is currently used in clinical settings. Thymosin alpha-1 acetate is a salt form of thymosin alpha-1 (free base). Thymosin alpha-1 (free base) and Thymosin alpha-1 acetate have immunomodulatory properties.

Accordingly, in the interest of public health, it is important that the Agency has available the expertise that Dr. Lee 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. Janet Lee's expertise in this matter.

Given the proposed discussion topics that include COVID-19, COPD, and sepsis, the presence of a pulmonary/critical care trained physician would provide needed clinical expertise to the advisory panel. Dr. Lee's background includes editorial responsibilities for many impactful journals, a feature of her background that would assist in the critical review of the literature on Thymosin alpha-1 discussed at the PCAC.

Dr. Lee's spouse's holdings in (b) (6) are each less than 5% of their total financial

holdings. (b) (6) manufactures, markets, and/or distributes more than 52 drugs within the United States. (b) (6) portfolio includes more than 60 medicines and devices worldwide. Therefore, it is not anticipated that this meeting will have a substantial impact on the stock price or overall finances of either company.

Accordingly, I recommend that you grant Dr. Janet Lee, a temporary voting member of the Pharmacy Compounding Advisory Committee, a waiver from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

___X____ 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):

_____

_____

_____ Denied – The individual may not participate.

Emily C. Helms Williams -S

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Emily Helms Williams
Director
Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

Date