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

DATE: November 13, 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: **Padma Gulur, MD**

Committee: Pharmacy Compounding Advisory Committee

Meeting date: December 4, 2024

Description of the Particular Matter to Which the Waiver Applies:

Padma Gulur, M.D., has been invited to serve as a standing voting member and Chairperson of the Pharmacy Compounding Advisory Committee (PCAC). Dr. Gulur 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 bulk drug substances being considered for inclusion on the 503A Bulks List. The nominators of these substances will be invited to make a short presentation supporting the nomination. The three bulk drug substances to be discussed are AOD-9604-related bulk drug substances (use is for obesity); CJC-1295-related bulk drug substances (use is for growth hormone deficiency); 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 bulk drug substances to be discussed are separate topics, and each topic is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Gulur reported a financial interest in stock in a competing firm for the AOD-9604 and CJC-1295 topics. She holds shares of (b) (6) stock, valued between $25,000 and $50,000. (b) (6) is not an affected firm for the Thymosin alpha-1 topic.

In addition, Dr. Gulur reported that she holds stock in (b) (6) operates pharmacies that provide compounding services for drug products and could be financially affected by the discussions of the bulk drug substances at issue. The market value of the holdings in this security is between $25,000 to $50,000.

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. Gulur's financial interests in (b) (6) exceed that amount, she has disqualifying financial interests.

Basis for Granting the Waiver:

Dr. Padma Gulur has unique qualifications and specialized expertise needed for these particular matters.

Dr. Gulur is a standing voting member and Chairperson of the PCAC. She is a Professor of Anesthesiology and Population Health Sciences at Duke University, Executive Vice Chair of Duke Anesthesiology, and Director of Pain Management Strategy and Opioid Surveillance at Duke University Health Systems.

Dr. Gulur received her MBBS from Bangalore Medical College, Karnataka University. She completed her residency in anesthesiology at Boston Medical Center and fellowship in pain medicine at Massachusetts General Hospital. Dr. Gulur is board certified in anesthesiology and pain medicine and specializes in advanced interventional pain management. She is a Fellow of the American Society of Anesthesiology and a member of several organizations including the International Neuromodulation Society, the International Association for the Study of Pain, the American Board of Anesthesiology, the American Society of Anesthesiologists and the North American Neuromodulation Society.

As a highly regarded physician and researcher, Dr. Gulur has authored numerous peer-reviewed publications on topics such as pain management in adult and pediatric patients, cancer-related pain, and opioid optimization. Additionally, Dr. Gulur has written several chapters in respected books on topics such as pediatric anesthesia, acute pain, trigeminal neuralgia, and rheumatic and arthritic disorders.

Dr. Gulur has developed a unique expertise in interpreting data and medical literature from her extensive clinical and research experience. Dr. Gulur has conducted studies and in-depth analyses on the pharmacology of pain assessment and management that addresses a variety of medications and therapies and utilizes a number of assessment tools. Her extensive research on pain management is published in numerous medication publications. Dr. Gulur's expertise will add valuable insight into discussions on whether the Agency should permit the use of these bulk drug substances in compounding by adding these substances to the 503A Bulks List.

The particular matters are sensitive.

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

Dr. Gulur'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).

AOD-9604 is a hexadecapeptide that is a synthetic fragment of human growth hormone (hGH) (16 amino acids: 177-191) with an additional tyrosine at the N-terminal end. AOD-9604 acetate is an acetic acid salt form of AOD-9604 (free base). AOD-9604 (free base) is a 16 amino acid peptide with a disulfide bond between two cysteines at position 7 and 14.

CJC-1295 (free base) is a synthetic 29 amino acid analogue of GHRH. CJC-1295 acetate is a salt form of a CJC-1295 (free base). CJC-1295 DAC (free base) is CJC-1295 (free base) with an MPA-Lys unit added at the C terminus. Other additional forms of CJC-1295 are CJC-1295 DAC acetate and CJC-1295 DAC TFA. CJC-1295 DAC, CJC-1295 DAC acetate, and CJC-1295 DAC TFA act as growth hormone secretagogues.

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 unique expertise in data interpretation and medical literature that Dr. Gulur will provide for the discussion of the particular matters before the Committee. Dr. Gulur's clinical and research experience will be necessary during the advisory committee's discussion. Dr. Gulur's experience in assessing the pharmacokinetic properties of study treatments will add substantial value to discussions on pharmacokinetic data available to the Committee. Additionally, Dr. Gulur's extensive research background evaluating the efficacy and safety of certain substances on children and adult subjects is essential expertise that will support discussions on whether AOD-9604, CJC-1295, and Thymosin alpha-1 provides clinically meaningful benefit in the intended patient population and whether the Agency should permit its use in compounding by adding it to the 503A Bulks List.

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

Dr. Gulur's extensive experience on the PCAC and as Chair of the PCAC will be invaluable and particularly necessary for the December 4, 2024, meeting. She has been a member of the PCAC since 2014 and Chair since 2018. Dr. Gulur's proven leadership running efficient in-person and virtual meetings with various stakeholders is needed to have a productive discussion on the unique topics coming before the Committee. Dr. Gulur's extensive research background, data analysis, and experience evaluating existing literature related to complex topics will be essential to discussions on whether AOD-9604, CJC-1295, and Thymosin alpha-1 provide clinically meaningful benefit in the intended patient population and whether the Agency should permit its use in compounding by adding it to the 503A Bulks List.

Dr. Gulur's holdings of (b) (6) are less than 5% of her total stock holdings. (b) (6) manufactures, markets, and/or distributes more than 24 drugs within the United States. (b) (6) to the thousands of medications sold through its pharmacies. Therefore, it is not anticipated that this meeting will substantially affect the stock price of either company, if it will affect it at all, or have a substantial effect on (b) (6) overall finances.

Accordingly, I recommend that you grant Dr. Padma Gulur, a standing voting member and Chairperson 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):

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_____ Denied – The individual may not participate.

Emily C. Helms Williams -S

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Emily Helms Williams — Date

Director

Advisory Committee Oversight and Management Staff

Office of the Chief Scientist