Due to the fact that Dr. Gular was unable to attend the meeting, this conflict of interest waiver for Dr. Gular is null and void.

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

DATE: May 5, 2022

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 Standing Member: **Padma Gulur, MD**

Committee: Pharmacy Compounding Advisory Committee

Meeting date: June 8, 2022

Description of the Particular Matters to Which the Waiver Applies:

Padma Gulur, MD, is a standing voting member and Chairperson of the Pharmacy Compounding Advisory Committee (PCAC). 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 June 8, 2022, the committee will discuss bulk drug substances nominated for inclusion on the 503A Bulk List. The nominators of these substances or another interested party will be invited to make a short presentation supporting the nomination. The three bulk drug substances to be discussed relevant to this waiver are ammonium tetrathiomolybdate (uses are evaluated for Wilson disease, use as copper (Cu) chelation therapy for the treatment of breast cancer, kidney cancer, prostate cancer, colorectal cancer, esophageal cancer, and malignant pleural mesothelioma); enclomiphene citrate (to increase serum testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) to normal levels in the treatment of secondary hypogonadism); and ferric subsulfate (for use as an astringent and hemostatic agent during minor surgical procedures).

The three 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 party to the matter for the ammonium tetrathiomolybdate topic. She holds shares of [redacted] stock, valued between $10,000 and $25,000. Under a regulatory exemption issued by the Office of Government Ethics at 5 C.F.R. § 2640.202(a), 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 affected by the matter, if the aggregate market value of the holdings in the securities of all entities does not exceed $15,000. Because Dr. Gulur's financial interest in [redacted] exceeds that amount, she has a disqualifying financial interest. [redacted] is not a party or non-party for the enclomiphene citrate and ferric subsulfate topics.

In addition, Dr. Gulur reported a financial interest in stock in a competing/affected firm for the enclomiphene citrate and ferric subsulfate topics. She holds shares of [redacted] stock, valued between $25,000 and $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 interest in [redacted] exceeds that amount, she has a disqualifying financial interest. [redacted] is not a party or non-party affected by the matter for the ammonium tetrathiomolybdate topic.

Basis for Granting the Waiver:

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

Dr. Padma Gulur 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 Health. Dr. Gulur received her MBBS (Bachelor of Medicine, Bachelor of Surgery) from Bangalore Medical Colle, 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 member of several organizations including International Neuromodulation Society, International Association for the Study of Pain, American Board of Anesthesiology, American Society of Anesthesiologists and 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 and will add valuable insight into discussions on whether the Agency should permit the use of ammonium

tetrathiomolybdate, enclomiphene citrate, and ferric subsulfate in compounding by adding these substances to the 503A Bulks List.

The particular matters are sensitive.

The topics are considered to be sensitive as the FDA Division responsible for review of ammonium tetrathiomolybdate, ferric subsulfate, and enclomiphene citrate does expect that the meeting is likely to receive significant public interest.

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

Section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353a) describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State licensed pharmacy or a Federal facility, or a licensed physician, to be exempt from the following three sections of the FD&C Act: (1) Section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B)) (concerning current good manufacturing practice); (2) section 502(f)(1) (21 U.S.C. 352(f)(1)) (concerning the labeling of drugs with adequate directions for use); and (3) section 505 (21 U.S.C. 355) (concerning the approval of human drug products under new drug applications or abbreviated new drug applications).

One of the conditions that must be satisfied to qualify for the exemptions under section 503A of the FD&C Act is that a bulk drug substance (active pharmaceutical ingredient) used in a compounded drug product must meet one of the following criteria: (1) complies 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, is a component of a drug 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, appears on a list developed by the Secretary through regulations issued by the Secretary (the ''503A Bulks List'') (see section 503A(b)(1)(A)(i) of the FD&C Act).

Copper is an essential microelement that plays an important role in biological processes. When it is imbalanced it can cause abnormalities. Copper is markedly elevated in Wilson disease and is believed to be elevated in cancer cells. Ammonium tetrathiomolybdate is an anticopper drug which acts as a copper chelator to interfere with intestinal uptake of copper when administered with meals and binds plasma copper when taken between meals. It is postulated that ammonium tetrathiomolybdate interferes with angiogenesis and reduces tumor growth.

Enclomiphene citrate is a selective estrogen receptor modulator (SERM) that is thought to compete with estrogen for estrogen receptor binding sites, limiting suppression of release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary and increasing testosterone levels. Secondary hypogonadism stems from a disruption of the hypothalamic-pituitary-gonadal (HPG) axis.

Ferric subsulfate is a hemostatic agent that causes agglutination of surface proteins resulting in

local hemostasis. Local hemostasis induces wound healing targeted to the site of injured vessels and innate wound response following bleeding (blood loss, hemorrhage). Topical hemostatic agents most commonly are used in situations where the use of electrocautery or sutures for hemostatic control of surgical bleeding is not ideal or safe. Different sources define ferric subsulfate as an astringent, hemostatic, or styptic agent.

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.

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

Dr. Gulur's experience in cancer management and assessing the pharmacokinetic properties of study treatments will be invaluable during the advisory committee's discussion of these matters. She has authored numerous publications on cancer-related pain management including related to colorectal cancer and was a faculty mentor at the MD Anderson Cancer Center. Additionally, Dr. Gulur's extensive research background is essential to discussions on whether enclomiphene citrate provides clinically meaningful benefit in the intended patient population. Dr. Gulur has specific expertise related to hematologic function as evidenced by her published research on epidurals in patients on thromboprophylaxis with unfractionated heparin and the value of partial thromboplastin time testing. Dr. Gulur published an article on delayed spinal epidural hematoma with warfarin reinitiation in the Journal of Cardiothoracic and Vascular Anesthesia. Dr. Gulur's expertise in data interpretation and her experiences in pain management and pharmacokinetic data interpretation will provide significant value in the committee's consideration of ammonium tetrathiomolybdate, enclomiphene citrate, and ferric subsulfate.

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:

✓ 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.

Russell Fortney -S Digitally signed by Russell Fortney -S Date: 2022.05.18 07:31:51 -04'00'

May 18, 2022

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

Date