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

DATE: September 23, 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: **Kathleen Gura, PharmD, BCNSP**

Committee: Pharmacy Compounding Advisory Committee

Meeting Date: October 29, 2024

Description of the Particular Matter to Which the Waiver Applies:

Kathleen Gura, PharmD, BCNSP, FASHP, FPPAG, has been invited to serve as a standing voting member of the Pharmacy Compounding Advisory Committee (PCAC). Dr. Gura 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 October 29, 2024, the Committee will discuss the following 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 four bulk drug substances to be discussed are ibutamoren mesylate (uses are for the treatment of growth hormone deficiency (GHD), osteoporosis, hip fracture, sarcopenia, obesity, and Alzheimer's disease (AD); L-theanine (for the treatment of sleep disorders and anxiety disorders); ipamorelin-related bulk drug substances, ipamorelin acetate and ipamorelin (free base) (for the treatment of GHD and postoperative ileus); and kisspeptin-10 (for the treatment of secondary hypogonadism in men).

The Committee will also discuss a revision FDA is considering to the Withdrawn or Removed List. Specifically, FDA is considering whether to amend § 216.24 to add an entry to the list:

hydroxyprogesterone caproate: all drug products containing hydroxyprogesterone caproate to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous birth. As previously explained in the Federal Register of July 2, 2014 (79 FR 37687 at 37689 through 37690), the list entry may specify that a drug may not be compounded in any form. Alternatively, the list entry may expressly exclude a particular formulation, indication, dosage form, or route of administration from an entry on the list, or a drug may be listed only with regard to certain formulations, indications, routes of administration, or dosage forms. FDA plans to seek the Committee's advice concerning the inclusion of this entry on the list.

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. Gura reported that her spouse 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 value of the holdings in this security is between $25,000 to $50,000.

Additionally, Dr. Gura holds stock in the following competing firms and topics:

- (b) (6), valued between $0 to $10,000, for the kisspeptin, L-theanine, and hydroxyprogesterone topics. (b) (6) is not an affected firm for the ibutamoren and ipamorelin topics.
- (b) (6), valued between $0 to $10,000, for the ibutamoren and ipamorelin topics. (b) (6) is not an affected firm for the kisspeptin, L-theanine, and hydroxyprogesterone topics.
- (b) (6), valued between $0 to $10,000, for the L-theanine topic. (b) (6) is not an affected firm for the kisspeptin, ibutamoren, ipamorelin, and hydroxyprogesterone topics.
- (b) (6), valued between $0 to $10,000, for the ibutamoren, ipamorelin, and L-theanine topics. (b) (6) is not an affected firm for the kisspeptin and hydroxyprogesterone topics.
- (b) (6) valued between $0 to $10,000, for the ibutamoren, ipamorelin, L-theanine, kisspeptin, and hydroxyprogesterone topics.

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. Gura's financial interests in these entities exceed that amount, she has disqualifying financial interests.

Basis for Granting the Waiver:

Dr. Kathleen Gura has unique qualifications and specialized expertise needed for these particular matters.

Dr. Gura is the Pharmacy Clinical Research Program Manager and a clinical pharmacist with the Clinical Nutrition Service at Boston Children's Hospital. She is also an Assistant Professor of Pediatrics at Harvard Medical School and an adjunct member of the faculty at Harvard Medical School, the Massachusetts College of Pharmacy and Health Sciences (MCPHS), Northeastern University, and the University of Connecticut.

Dr. Gura received her B.S. Pharmacy and Doctor of Pharmacy from the Massachusetts College of Pharmacy and Health Sciences in Boston, with high honors. Board certified as a Nutritional Support Pharmacist, Dr. Gura is an active member of the American Society for Health System Pharmacists (ASHP), the American Society for Parenteral and Enteral Nutrition (ASPEN), the Pediatric Pharmacy Association (PPA), and the Massachusetts Society of Health System Pharmacists (MSHP). She served as president of the Massachusetts Society of Health System Pharmacists and is currently serving as the Vice President of ASPEN.

Her professional focus is on academic clinical pharmacy and research, and her topics of expertise include clinical pharmacy and sterile products preparation. Dr. Gura is the author of numerous book chapters on pediatric nutrition and has written more than 140 peer-reviewed articles and other scholarship on topics such as the intestinal failure associated liver disease, clinical practice guidelines for parenteral nutrition, and the use of parenteral nutrition in the neonate. She served as a consultant/subject matter expert for Wolters Kluwer-Kelly (Lexicomp).

Dr. Gura has decades of experience in sterile compounding (e.g., parenteral nutrition) and pediatrics. Parenteral nutrition is often compounded and is a sterile intravenous (IV) solution that is administered through a catheter into a vein to provide nutrients to patients who can't use their gastrointestinal tract. She has worked in children’s hospitals since 1982 in a variety of roles including as a clinical pharmacist, sterile products manager, and manager of clinical research. She served on the United States Pharmacopeia’s (USP) Parenteral Nutrition Safety Expert Panel and on the Boston Children’s Hospital Parenteral Nutrition Safety Task Force, Neonatal Intensive Care Unit (NICU) Committee, and NICU Parenteral Nutrition Task Force. Dr. Gura has also served on the Institute for Safe Medication Practice’s Expert Advisory Panel at the Sterile Compounding Technology Safety Summit. She has taught, written, and lectured extensively on sterile compounding, parenteral nutrition, and pediatrics in a variety of forums, including internationally.

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. Gura’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).

Ibutamoren mesylate is the mesylate salt of a non-peptide small molecule that binds to and activates ghrelin receptors. Acting as a ghrelin receptor agonist, ibutamoren (the active moiety of the salt) can induce growth hormone release from the anterior pituitary gland in vitro and in vivo. Ibutamoren mesylate acts as a growth hormone secretagogue, a class of drugs that consists of a variety of synthetic peptide or non-peptide agents that stimulate endogenous GH release.

L-theanine is a non-proteinogenic amino acid present almost exclusively in the tea plant (Camellia sinensis). Oral L-theanine was determined to be Generally Recognized as Safe (GRAS) and is marketed in the United States as an ingredient in fruit juices and drinks, non-herbal teas, sports beverages, specialty bottled waters, chocolate bars and chews, hard candies, and breath mints, and chewing gum. L-theanine may be used as a dietary supplement, food, or drug product.

Ipamorelin (free base) is a pentapeptide hormone containing non-proteinogenic amino acids while Ipamorelin acetate is a salt form of a peptide consisting of five amino acids. Ipamorelin (free base) and ipamorelin acetate act as growth hormone secretagogues.

Kisspeptin-10 is a synthetic peptide consisting of ten amino acids. Kisspeptin is an upstream regulator of GnRH secretion. The pulsatile secretion of GnRH initiates puberty, coordinates ovulation, and maintains overall reproductive function.

One of the conditions that must be satisfied for the compounded drug to qualify for the exemptions under section 503A or section 503B of the FD&C Act is that the drug that is compounded does not appear on a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (Withdrawn or Removed List) (see sections 503A(b)(1)(C) and 503B (a)(4) of the FD&C Act). The Withdrawn or Removed List is codified at 21 CFR 216.24.

Makena (hydroxyprogesterone caproate injection, 250 mg/mL), NDA 021945, was approved in 2011 under the accelerated approval pathway to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous birth. However, the postmarketing confirmatory trial failed to verify the clinical benefit of Makena and the available evidence demonstrated that Makena was no longer shown to be effective under its conditions of use. FDA concluded that the statutory standard in section 506(c) of the FD&C Act for expedited withdrawal was met, and that approval should be withdrawn. On April 6, 2023, the FDA Commissioner and Chief Scientist issued a decision withdrawing the approval of Makena and the ANDAs that referenced Makena.

Accordingly, in the interest of public health, it is important that the Agency has available the combined expertise in pediatrics and sterile compounding that Dr. Gura will provide for the discussion of the particular matters before the committee. Dr. Gura's decades of expertise in sterile products preparation and pediatrics are directly relevant given the topics for discussion at this PCAC meeting. Three of the four bulk drug substances on the agenda for discussion at the October 29, 2024, PCAC meeting were nominated and evaluated for, among other routes of administration, intramuscular (IM) or subcutaneous (SC) routes. In addition, the discussion of the proposal for an entry on the "Withdrawn or Removed List" involves an injectable product for SC or IM administration to reduce the risk of preterm birth. Medication used in the IM and SC routes must be sterile for safety reasons. In addition, all of the nominated bulk drug substances could be prescribed for pediatric patients. Both pediatric patients and pregnant women are considered high risk populations.

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

Dr. Gura's demonstrated experiences will provide significant value in the committee's consideration of these topics. Dr. Gura's strong foundation in sterile products compounding, clinical trials and her vast experiences as a clinical pharmacist, educator, and clinical researcher are essential to the committee's enhanced and in-depth discussion. In addition, Dr. Gura has specialized expertise in pediatric patient populations that other members of the committee do not possess.

Dr. Gura's holdings of the six affected stocks are, taken together, less than 5% of her total financial holdings. Furthermore, it is not anticipated that this meeting will substantially affect the stock price of any of these six companies since they are large and diverse. (b) (6) selling hundreds of different drugs, and the other five firms are all large drug companies offering a wide range of drugs, and it is not anticipated that this meeting will meaningfully affect their overall finances.

Accordingly, I recommend that you grant Dr. Kathleen Gura, a standing 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):

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_____

_____ Denied – The individual may not participate.

Emily C. Helms Williams -S

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_____ October 10, 2024

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