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

DATE: June 14, 2017

TO: Janice M. Soreth, M.D.
Associate Commissioner for Special Medical Programs
Office of Medical Products and Tobacco
Office of the Commissioner, FDA

THROUGH: Jeffrey Anderson, MS, RAC
Director (Acting), Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

FROM: Jayne E. Peterson, B.S.Pharm., J.D.
Director, Division of Advisory Committee and Consultant Management
Center for Drug Evaluation and Research

Name of Advisory Committee Member: Adel Karara, Ph.D.

Committee: Oncologic Drugs Advisory Committee Meeting

Meeting date: July 13, 2017

Description of the Particular Matter to Which the Waiver Applies:

Dr. Karara is serving as a temporary voting member of the Oncologic Drugs Advisory Committee (ODAC). 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 cancer and make appropriate recommendations to the Commissioner of Food and Drugs.

During the morning session of the July 13 meeting, the committee will discuss biologics license application (BLA) 761028 for ABP 215, a proposed biosimilar to Genentech/Roche's Avastin® (bevacizumab), submitted by Amgen Inc. The proposed indications/uses for this product are: (1) For the first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with intravenous 5-fluorouracil-based chemotherapy; (2) in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line

ABP 215-containing regimen; (3) for the first-line treatment of unresectable, locally advanced, recurrent or metastatic non-squamous, non-small cell lung cancer in combination with carboplatin and paclitaxel; (4) for the treatment of glioblastoma, as a single agent for adult patients with progressive disease following prior therapy; (5) for the treatment of metastatic renal cell carcinoma in combination with interferon alfa; and (6) in combination with paclitaxel and cisplatin or paclitaxel and topotecan for the treatment of persistent, recurrent, or metastatic carcinoma of the cervix. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Karara reported stock holdings in four potentially competing firms: (b) (4) . The current aggregate value of the stock holdings, at the writing of this waiver, is valued between $25,001-50,000, which exceeds the de minimis amount of the regulatory exemption at 5 CFR § 2640.202(b)(2) for particular matters affecting nonparties.

Basis for Granting the Waiver:

Regulation of biosimilar products is new and is evolving through interpretation of the law and the published FDA guidance. Section 351(i) of the Public Health Service (PHS) Act defines biosimilarity to mean "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product."[1] Evaluation of clinical pharmacology data is critical in addressing "no clinically meaningful difference in safety, purity and potency" between the biosimilar and the US-reference product. As such, clinical pharmacologists will be needed to provide feedback on the non-clinical and clinical studies that the applicant has provided regarding toxicity, pharmacokinetics (PK), and pharmacodynamic (PD) assessments to support the similarity of ABP-215 to US-licensed Avastin® (bevacizumab). It is imperative to have a variety of clinical pharmacology expertise for the overall assessment of biosimilarity.

Dr. Karara is well-versed on the biosimilar regulation, and he participated and advised on two prior biosimilar applications at meetings of the ODAC. Broad pharmacology expertise is needed for this advisory committee meeting to ensure its success.

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

Dr. Karara is Associate Professor of Pharmaceutical Sciences at the University of Maryland Eastern Shore, School of Pharmacy. Dr. Karara received his Ph.D. in 1983 in Pharmaceutical Sciences (Pharmacokinetics), from Washington State University. He received his M.S. and B.Pharm. from Alexandria University in Egypt. He is active in numerous professional organizations, including the American College of Clinical Pharmacology and the American Association of Pharmaceutical Scientists. Dr. Karara is the only clinical pharmacologist with experience in drug development attending this meeting. His knowledge in study design, the conduct of PK and PD trials, and interpretation of data will be unique among the experts at this

[1] Section 7002(b)(3) of the Affordable Care Act, adding section 351(i)(2) of the PHS Act

meeting. Further, he has significant knowledge of biosimilar regulations, an area that is new and still evolving.

There is limited expertise available and it is difficult to locate similarly qualified individuals without a disqualifying financial interest.

There were a total of six special government employees with expertise in clinical pharmacology invited to this meeting, and two were unable to attend due to schedule conflicts. Dr. Karara has work experience in the pharmaceutical industry and is well-versed on regulatory aspects of clinical pharmacology in drug development and drug approval. His industry experience will add valuable expertise to the discussion and will complement the academician perspectives that will be provided by the other three pharmacologists, allowing for a robust discussion of the topic.

The particular matter is sensitive.

The meeting topic is considered to be sensitive. The Agency does anticipate that the meeting is likely to receive significant public interest and (non-trade) press interest, as this will be the first biosimilar monoclonal antibody for cancer indications that will be discussed at an ODAC meeting.

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

The Patient Protection and Affordable Care Act (Affordable Care Act), signed into law on March 23, 2010, amends the PHS Act to create an abbreviated licensure pathway for biological products that are demonstrated to be "biosimilar" to or "interchangeable" with an FDA-licensed biological product. This pathway is provided in the part of the law known as the Biologics Price Competition and Innovation Act (BPCI Act). Under the BPCI Act, a biological product may be demonstrated to be "biosimilar" if data show that, among other things, the product is "highly similar" to an already-approved biological product. A biosimilar product is a biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, known as a reference product, and has no clinically meaningful differences in terms of safety, purity and potency from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products. Biosimilars can provide more treatment options for patients, and possibly lower treatment costs.

Dr. Karara is one of four clinical pharmacologists scheduled to attend this meeting. It is necessary to have several clinical pharmacologists participate, to strive to obtain a diversity of opinions and have a productive meeting. Dr. Karara's participation will allow for a well-rounded discussion; he brings a perspective from his past industry work, as well experience in regulatory aspects of clinical pharmacology and drug development, to enhance committee deliberations in the interest of public health.

The dollar value of the potential gain or loss that may result from participation in the particular matter is small

The current aggregate value of the stock holdings, at the writing of this waiver, is valued between $25,001 - 50,000.

Dr. Karara has served as Temporary Member of the ODAC effectively in the past.

Dr. Karara is well-versed on the biosimilar regulation; he participated and advised on two prior biosimilar applications at ODAC meetings. His knowledge of biosimilar regulations, together with his past service as an ODAC member, makes him a valuable participant in this meeting.

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

In the interest of public health, it is critical for the Agency to review biosimilar products shown to be highly similar to an FDA-approved biological product, and have no clinically meaningful differences in terms of safety, purity and potency from the reference product. Biosimilar products can provide more treatment options for patients, and possibly lower treatment costs. Dr. Karara's clinical pharmacology expertise, knowledge of biosimilar regulations, and past industry work experience make him a critical participant at this meeting, wherein the committee will assess a proposed biosimilar product.

Accordingly, I recommend that you grant Dr. Adel Karara, a temporary voting member of the Oncologic Drugs 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.

Janice M. Soreth -S

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Janice M. Soreth, M.D.
Date

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