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

DATE: May 22, 2020

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 Temporary Voting Member: **Julia Glade-Bender, M.D.**

Committee: Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee (PedsODAC)

Meeting date: June 17, 2020

Description of the Particular Matter to Which the Waiver Applies:

The Best Pharmaceuticals for Children Act of 2002 (BPCA) expressly charged that the PedsODAC, a subcommittee of the Oncologic Drugs Advisory Committee (ODAC), shall: (A) evaluate and, to the extent practicable, prioritize new and emerging therapeutic alternatives available to treat pediatric cancer; (B) provide recommendations and guidance to help ensure that children with cancer have timely access to the most promising new cancer therapies; and (C) advise on ways to improve consistency in the availability of new therapeutic agents. (Pub. Law 107-109, Section 15(a)(1)).

The role of the Pediatric Subcommittee is legislated by BPCA. Notably, the PedsODAC does not provide advice to FDA with respect to approval of any specific product for any specific pediatric cancer indication. The Office of Oncologic Diseases Products in the Center for Drug Evaluation and Research brings issues related to approval of any product for a cancer indication, including any pediatric cancer indication, to the ODAC, not the PedsODAC.

The cancers of adults and children are very different and although the outcome for children with cancer has improved dramatically during the past several decades, cancer remains the leading cause of death from disease in children. Those children who survive often do so at an enormous cost associated with the long term and late effects of existing therapy, which are frequently debilitating.

Thus, there is an urgent need for new drugs and biologic products for the treatment of childhood cancer.

Pediatric cancer drug development is complex and very different from drug development in other disease areas and is largely dependent upon cancer drug discovery and development in adults. Early consideration of new promising agents for study in children is critical to timely development of new treatments.

On June 17, 2020, during the PedsODAC meeting, information will be presented regarding pediatric development plans for two products that are in development for an adult oncology indication. The subcommittee will consider and discuss issues relating to the development of each product for pediatric use and provide guidance to facilitate the formulation of Written Requests for pediatric studies, if appropriate.

Because pediatric cancer care is very closely integrated with pediatric cancer clinical research and new drug development, all children with cancer are treated at academic centers, and nearly all of these centers are members of a National Cancer Institute-funded clinical trials network. As a result, the experts are invariably researchers at these institutions. The expertise that FDA seeks cannot be found outside of this context. The insights the Agency seeks can be provided only by learned researchers with extensive experience with studies of investigational agents in the pediatric age group. These investigators generally do not derive substantial personal financial benefit from industry grants and contracts to their institutions, and their institutions receive the industry funds necessary to offset institutional costs for patient care and other institutional clinical research costs.

Dr. Julia Glade-Bender is serving as a temporary voting member of the PedsODAC. She has been invited to participate in the June 17, 2020, PedsODAC meeting. The product under consideration for this waiver is SP 2577, application presentation by Salarius Pharmaceuticals, Inc. There is currently one study of SP 2577 in pediatrics in Ewing sarcoma. This topic is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Julia Glade-Bender is Vice Chair for Clinical Research, Department of Pediatrics, Memorial Sloan Kettering Cancer Center (MSKCC). She has not identified any personal financial interests that are likely to be affected by the particular matter to be discussed by the subcommittee. However, she has identified a financial interest of her employer, MSKCC, which is imputed to her under the federal conflict of interest statute, 18 U.S.C. § 208, that can be affected by a particular matter that is the subject of the subcommittee meeting.

MSKCC has a contract for the study titled, Phase I Trial of the LSD1 Inhibitor SP-2577 in Patients with Relapsed or Refractory Ewing Sarcoma [NCT03600649], sponsored by Salarius Pharmaceuticals. This phase 1 study is an open-label, non-randomized dose escalation study of SP-2577. The total funding from Salarius Pharmaceuticals is (b) (4). The study began in September 20, 2019, and is estimated to end August 11, 2020. Dr. Glade-Bender does not receive any personal remuneration or salary support for her role as Co-Investigator.

Basis for Granting the Waiver:

Dr. Glade-Bender has unique qualifications and specialized expertise needed for this particular matter.

Unlike AC meetings focused on a product and indication, this meeting will be a scientific collaboration on the currently available data to gain information that could inform the formulation of a Written Request, if appropriate. Significantly, the advisory committee members will not recommend approval or disapproval of any particular product. Such recommendations would be grossly premature and simply could not be made at this early stage in product development. The majority of oncology products studied in the phase 1 setting in children do not proceed through development to submission and approval of a new drug application. Very few chemical entities in these early stages of evaluation and development ever proceed to a marketing application. Moreover, the role of the PedsODAC is not to provide any advice to the Agency with respect to approval of any specific product for any specific pediatric cancer indication.

Dr. Julia Glade-Bender is Vice Chair for Clinical Research and Member, Memorial Hospital, Department of Pediatrics, Memorial Sloan Kettering Cancer Center (MSKCC). She is also Attending Pediatrician, at Memorial Hospital for Cancer and Allied Diseases and Associate Professor of Pediatrics, Columbia University Medical Center. Dr. Glade-Bender earned her medical degree from the University of Pennsylvania School of Medicine and completed her Residency in Pediatrics at Mount Sinai Medical Center. She completed a fellowship and research fellowship in Pediatric Hematology-Oncology at MSKCC. She is board certified in Pediatrics and Pediatric Hematology-Oncology. She specializes in treating children with solid tumors of the bone and soft tissue, including osteosarcoma, Ewing sarcoma, rhabdomyosarcoma, and germ cell tumors.

The particular matter is not sensitive.

The meeting topic is not considered sensitive and the FDA Division with responsibility for the product under discussion does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial. Moreover, the discussion at the meeting will be only one source of information for the Agency's plans related to the submission of a Written Request for evaluating these drugs in children.

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

On June 17, 2020, the subcommittee will meet to discuss SP-2577, which is in early stage development for treatment of Ewing sarcoma. Ewing sarcoma is a rare bone tumor that occurs most often in adolescents; it is a very rare cancer in adults. The National Institutes of Health reports that Ewing sarcoma accounts for about 1.5 percent of all childhood cancers, and it is the second most common type of bone tumor in children. The median age of patients with Ewing sarcoma is 15 years, and more than 50% of patients are adolescents. Approximately 200-250 children and adolescents in the United States are diagnosed with a tumor in the Ewing family of

tumors each year. Treatment options for Ewing sarcoma include chemotherapy, surgery, radiation therapy and high-dose chemotherapy and stem cell transplant. Patients experience side effects of treatment for Ewing sarcoma, including severe delayed late effects from radiation therapy, such as bone growth retardation and secondary cancers. The 5-year survival rate is 76% for children younger than 15 and 60% for adolescents aged 15 to 19. About 30% of patients have a recurrence within the first five years. The same chemotherapy drugs that were used during initial treatment cannot be used again due to toxicity concerns. As a result, physicians must seek alternatives to treatment. The actual context in which the use of this product in Ewing sarcoma is being discussed is in the setting of relapse or recurrent/refractory disease for which there is no curative therapy, highlighting the importance of new drug discovery and development. Dr. Glade-Bender is an expert, internationally recognized in the treatment of bone tumors. Additionally, she is an experienced and accomplished investigator of new drugs for children with cancer which makes her essential to the discussions at this meeting. In the interest of public health, it is critical that FDA have available the unique expertise that Dr. Glade-Bender will provide the committee.

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

The PedsODAC meeting is meant to elicit discussion of the data currently available, and whether there is any pediatric cancer type for which there is an unmet clinical need that this product might address. The advisory committee members will not recommend approval or disapproval of the products under discussion. To meet statutory responsibilities to evaluate and prioritize new and emerging therapeutic alternatives to treat pediatric cancer and to provide recommendations and guidance to help ensure that children with cancer have timely access to the most promising new cancer therapies, this meeting of the PedsODAC requires the participation of experts with a wide and deep knowledge of pediatric oncology and product development. Such experts typically develop their knowledge through their work at centers of excellence for the treatment of pediatric cancers, the very sites where investigational drugs are studied. This is particularly true for experts in rare pediatric cancers; patients frequently must travel to be treated by a physician with experience in a particular rare cancer.

Multiple pediatric oncologists, each with specific sub-specialty expertise and with internationally recognized expertise in pediatric cancer drug development, are needed for this meeting. Dr. Glade-Bender is a leader in developing clinical trials and other treatments for children with cancer that do not respond to standard treatment. She is one of the most active early phase study investigators in the COG Phase 1 Consortium, thus her experience and expertise in study design and conduct are critically important to the committee. She is an internationally recognized clinical trialist in pediatric oncology and accomplished pediatric oncology investigator. Dr. Glade-Bender has the unique combination of expertise in both bone tumors in children and new cancer drug development. Given her extensive experience and background in the specific areas needed for this meeting, any potential for a conflict of interest is significantly outweighed by the need for Dr. Glade-Bender's expertise on this panel.

Accordingly, I recommend that you grant Dr. Julia Glade-Bender, a temporary voting member of the Pediatric Oncology Subcommittee of the Oncology Drugs 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: 2020.06.01 17:37:48 -04'00'

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

June 1, 2020
Date