



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

DATE: May 25, 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, M.S., R.A.C.  
Director, 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: Carola Arndt, M.D.

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

Meeting date: June 21-22, 2017

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 Hematology and Oncology 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 22, 2017, the PedsODAC will meet to discuss two chemical entities in various stages of development for adult cancer indications to assess their relevance for possible development for use in one or more pediatric cancers. The subcommittee will consider and discuss issues concerning possible pediatric cancers and stages of disease to be studied, patient populations to be included, and possible designs of clinical trials to expedite early evaluation to facilitate the development of these chemical entities as potential new drugs for use in pediatric cancer. The discussions may also provide information to FDA pertinent to the formulation of Pediatric Written Requests (PWRs), if appropriate.

Dr. Carola Arndt is serving as a temporary voting member of the PedsODAC. She has been invited to participate in the June 21-22, 2017 PedsODAC meeting. The products under consideration for this waiver are: ASP2215 (gilteritinib), sponsored by Astellas Pharama Global Development, Inc.; and, Olaratumab, application sponsored by Eli Lilly and Company. The topics of this meeting are particular matters involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Arndt reported stock holdings in two potentially competing firms: (b) (6). The current value of the stock holdings, at the writing of this waiver, is \$ (b) (6) and (b) (6), respectively.

Basis for Granting the Waiver:

The PedsODAC meeting is meant to elicit discussion of the data currently available from adult studies and whether there is any pediatric cancer type for which there is an unmet clinical need that these chemical entities might address. The PedsODAC meeting will focus on preliminary discussions and general considerations in pediatrics, including discussions around molecular abnormalities, about potential indications that might be feasible for the drug substances, and about international collaborative efforts. 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. Any

recommendations to FDA with respect to approval of any product for a cancer indication are provided by the ODAC, and not the Pediatric Subcommittee.

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

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.

Carola Arndt, M.D., is Professor of Pediatrics at the Mayo Clinic College of Medicine and Science in Rochester, Minnesota. Dr. Arndt received her medical degree from Boston University, specialty residency training in pediatrics and internal medicine from the Naval Medical Center in San Diego, California, and fellowship training in hematology/oncology from the National Cancer Institute/National Institutes of Health in Bethesda, Maryland.

Further, Dr. Arndt is a member of the Children's Oncology Group's Bone Tumor Committee and the Intergroup Rhabdomyosarcoma Study Group (now Soft Tissue Sarcoma Committee of the COG). She has published over 50 articles on the treatment of various types of sarcoma, and has over thirty years of experience as a research and practicing pediatric hematologist/oncologist, specializing in the treatment of Ewings sarcomas, Osteosarcoma, Rhabdomyosarcoma, and sarcoma. Dr. Arndt's expertise in the rare childhood cancers and experience in the design and conduct of investigational drug trials in children with cancer are critical to the quality of the discussion. She brings a depth of knowledge on the subject matter that would be essential to the meeting discussions.

Dr. Carola Arndt is one of the most senior members of the committee; she is also one of the world's leading experts in the investigation and treatment of bone and soft tissue sarcomas in children. As several of the products under consideration at this meeting may prove to be relevant for evaluation in these types of tumors, her extensive experience and expertise are critical to the deliberations of the committee. She has held important leadership positions in national and international research groups and has published seminal works detailing evolving and current standards of care for bone and soft tissue sarcomas; thus, her opinions would be highly considered by the PedsODAC in advising FDA regarding determinations related to the appropriateness of issuing Written Requests (WR) for the products under discussion. Further, her longstanding role in the leadership of clinical trials in pediatric sarcomas will provide important insights into the practicality and feasibility of any studies to be considered in a WR. Her expertise is critical to the committee as it considers the potential for benefit in studying Gilteritinib and Olaratumab in children. In the interest of public health, it is critical that FDA have available the unique expertise that Dr. Arndt will provide the committee.

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

Given the relative rarity of childhood cancer, collaboration and concentration of expertise are essential. This is particularly true for rare pediatric cancers, which most pediatric oncologists would never see, or may see only once in a lifetime of practice. Although the majority of adult patients with cancer are cared for in the community and enroll in clinical trials at a rate of only

3%, nearly all children with cancer are treated at academic centers, and the vast majority are enrolled in clinical trials. Nearly all of these academic centers are members of the Children's Oncology Group (COG), a National Cancer Institute-funded clinical trials network of more than 230 pediatric institutions throughout the United States, Canada, and other foreign sites.

Pediatric cancer care is very closely integrated with pediatric cancer clinical research and new drug development. The COG and its predecessor cooperative groups have a more than 50-year history. Cooperation and collaboration in the design and conduct of clinical trials over this period of time has changed childhood cancer from a nearly uniformly fatal disease to one where more than 85% are cured. But, despite the dramatic increase in cure rates, cancer remains the major cause of children's death from disease in the United States and other developed countries. Cure often comes at a substantial cost in the form of severe and often debilitating late effects due to toxicity of therapy. Development of new cancer therapies remains a pressing need.

Industry sponsors work closely with investigators and institutional members of the COG, which employ the most expert researchers. In fact, definitive licensing studies, incorporating randomized controlled trial design, are generally only conducted within the COG and its clinical trial infrastructure, which is federally funded for NIH/NCI approved research. Reimbursement for this federally funded infrastructure is provided by industry sponsors in the form of per case reimbursement.

More than 90% of pediatric cancer patients in the United States are treated at COG institutions and most are enrolled in clinical trials. Of the approximately 230 COG institutions, a much smaller number of institutions are involved in early clinical trials of drugs to treat rare pediatric cancers. These institutions employ researchers with the highest levels of expertise in pediatric cancers and drug development, the very experts FDA needs to hear from on the issues before the PedsODAC.

Although efforts were taken to seek out individuals with the least potential for a conflict of interest, for the reasons noted above, finding experts for this meeting has been challenging. Approximately 95% of the experts with the expertise and experience needed are affiliated with COG institutions. Due to their expertise, qualified candidates face many demands on their time.

A productive discussion of the application depends on having a broad contribution of pediatric hematology/oncology experts at the meeting. Multiple experts with diverse pediatric cancer backgrounds are needed in order to have a collaborative scientific discussion of the current available data from the adult studies and whether there are any pediatric cancers in which there is an unmet clinical need that these products might fulfill. In fact, ten other individuals with expertise in Pediatric Oncology and Pediatric Hematology were contacted but were unable to attend due to conflicts of interest, scheduling conflicts and incomplete paperwork.

*The particular matter is not sensitive.*

The June 21-22, 2017, PedsODAC meeting sessions regarding ASP2215 (gilteritinib) and olaratumab are not considered to be sensitive and the Division does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, or congressional 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 evaluation of these drugs for use in children.

Accordingly, I recommend that you grant a waiver for Dr. Carola Arndt, a temporary voting member of the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee, 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):

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Denied – The individual may not participate.

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

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06/01/2017  
Date