Dr. Ami Desai is not attending the meeting; thus, this waiver is null and void.

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

DATE: September 6, 2023

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 Member: **Ami Desai, M.D., M.S.C.E.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: October 4, 2023

Description of the Particular Matter to Which the Waiver Applies:

Ami Desai, M.D., M.S.C.E., is 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 the use in the treatment of cancer and make appropriate recommendations to the Commissioner of Food and Drugs.

On October 4, 2023, the committee will discuss new drug application (NDA) 215500, for eflornithine tablets, submitted by USWM, LLC (doing business as U.S. WorldMeds). The proposed indication (use) for this product is to reduce the risk of relapse in pediatric patients with high-risk neuroblastoma who have completed multiagent, multimodality therapy. The topic is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest(s):

Dr. Desai is employed by the University of Chicago, which is a study site for the clinical trial titled *A Phase 2 Randomized Study of Irinotecan/Temozolomide/Dinutuximab With or Without Eflornithine (DFMO) in Children With Relapsed, Refractory or Progressive Neuroblastoma (ANBL1821, NCT03794349)*. The clinical trial is sponsored by the Children's Oncology Group (COG), and the study drug for ANBL1821 is provided by Cancer Prevention Pharmaceuticals (CPP). At the University of Chicago site, the ANBL1821 clinical trial was initiated on May 28,

2019, and is anticipated to conclude in 2024. Dr. Desai is an investigator for ANBL1821 at the University of Chicago and confirmed that she is not the institutional principal investigator or study chair.

The University of Chicago receives $0 to (b) (4) from COG for each patient enrolled in ANBL1821; the university intends to enroll (b) (4) patients for their clinical trial site, with an estimated total income of $10,000 to $20,000. At the writing of the waiver document, (b) (4) had been enrolled. Dr. Desai does not receive salary support or personal remuneration from the study funding.

Dr. Desai is also an Institutional Principal Investigator/Investigator at the University of Chicago for the clinical trial titled *Phase 1 Study of Difluoromethylornithine (DFMO) and Celecoxib With Cyclophosphamide/Topotecan for Patients With Relapsed or Refractory Neuroblastoma* (*NANT 2012-01, NCT02030964*). The clinical trial is sponsored by New Approaches to Neuroblastoma Therapy Consortium (NANT), and the study drug was purchased through CPP, with manufacture and study distribution through (b) (4)

At the University of Chicago site, NANT 2012-01 was initiated on December 7, 2013, and study accrual was closed on June 22, 2018. The study remains open at her institution until patient follow-up is complete and the study manuscript is published. At the writing of the waiver, according to clinicaltrials.gov the study is estimated to end in December 2023. Dr. Desai did not enroll or oversee active patients on the trial. For her involvement in NANT 2012-01, Dr. Desai received no salary support or personal remuneration. The University of Chicago has received all funding in support of the clinical trial.

Basis for Granting the Waiver:

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

Dr. Desai received a Bachelor of Arts degree from Rutgers University before attending medical school at The University of Medicine and Dentistry of New Jersey (now Rutgers) Robert Wood Johnson Medical School. After graduating from medical school, Dr. Desai completed a pediatric residency at Yale-New Haven Children's Hospital and a pediatric fellowship program at Children's Hospital of Philadelphia, where she focused on pediatric hematology/oncology. Following completion of her fellowship, Dr. Desai received a Master of Science in Clinical Epidemiology at the Perelman School of Medicine at the University of Pennsylvania's Center for Clinical Epidemiology, where her studies focused on Pharmacoepidemiology.

Dr. Desai has certifications with the American Board of Pediatrics for General Pediatrics and Pediatric Hematology/Oncology. Her various academic appointments have focused on pediatrics, oncology, hematology, and stem cell transplantation. She is cited in nearly thirty peer-reviewed publications, with much of her published work focusing on neuroblastoma.

Dr. Desai holds multiple positions with the University of Chicago. These positions include Associate Professor at the Department of Pediatrics' Section of Pediatric Hematology, Oncology, and Stem Cell Transplantation, Clinical Service for the Department of Pediatric

Hematology/Oncology/Stem Cell Transplantation, Outpatient Clinic in the Department of Pediatric Hematology/Oncology, Co-Director of the Pediatric Cancer Risk Program, Co-Director of the I-131 MIBG Program, a member of the Data Safety Monitoring Committee, and Program Leader for Solid Tumors. Dr. Desai is a Steering Committee Member with COG, as well as a Member of COG's Neuroblastoma High-Risk Task Force.

It is particularly important to include Dr. Desai in the upcoming ODAC meeting, given her vast experiences and research in pediatric hematology, oncology, and neuroblastoma. Her unique training in pharmacoepidemiology is of particular importance given the use of an external control in the study forming the primary basis of effectiveness for the application to be discussed.

The particular matter is not sensitive.

This meeting topic is not considered to be sensitive as the FDA Division responsible for review of this product does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial.

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

Neuroblastoma is a term commonly used when describing a spectrum of neuroblastic tumors that arise from primitive sympathetic ganglion cells. They account for 97% of all neuroblastic tumors and widely vary in the clinical presentation, location, histology, and biologic characteristics. They exhibit a broad spectrum of clinical behavior, which ranges from maturation into benign masses, to terminal metastases.

Neuroblastoma is the most common cause of cancer in infants younger than one year of age and the most common extra-cranial solid tumor in children. Annually, there are approximately 700 to 800 new cases of neuroblastoma in the United States, a number that has held steady for many years. Although many children are cured, current data suggests that the 5-year survival rate, depending on risk classification, can range from 50% (high risk) to 95% (low risk). The variables associated with risk classification for patients with neuroblastoma that determine treatment include stage of the disease, patient age, resection findings, tumor genotype and other genetic findings, and the histologic appearance of the tumor. As it relates to patients with high-risk neuroblastoma (HRNB), 20% of patients will have no/mixed response or progressive disease at the end of induction with chemotherapy, and at least 40% will experience disease recurrence after completing multimodal therapy.

The current standard of therapy for HRNB is multimodal treatment that includes an induction, consolidation, and maintenance period. The induction phase includes chemotherapy and surgical resection. The consolidation phase of treatment includes tandem cycles of myeloblative therapy, stem cell transplantation and radiation therapy. The maintenance phase (also known as post-consolidation) includes treatment with dinutuximab with granulocyte macrophage colony-stimulating factor and isotretinoin therapy. Despite improvements in patient outcomes with intensive multimodal therapy, recurrence and death are still common in high-risk patients, and improvement in survival rates in this subgroup is needed.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Desai will provide for the discussion of the particular matter before the committee.

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

It is particularly important to include Dr. Desai in the upcoming ODAC meeting, given her vast experiences in pediatric hematology/oncology and published work in neuroblastoma. Her robust professional and research experience in pediatric oncology, and specifically HRNB, combined with her unique training in pharmacoepidemiology will be invaluable to a robust and productive discussion on the issue coming before the committee.

Accordingly, I recommend that you grant Dr. Ami Desai, 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:

✓ 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: 2023.09.18 14:14:48 -04'00'

September 18, 2023

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

Date