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

DATE: July 29, 2021

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

FROM: Prabhakara Atreya, Ph.D.
Director, Division of Scientific Advisors and Consultants
Center for Biologics, Evaluation, and Research (CBER)

Name of Advisory Committee Meeting member: **Charles Vite, B.S., DVM, Ph.D. Diplomate, ACVIM (neurology)**

Committee: Cellular Tissue and Gene Therapies Advisory Committee (CTGTAC)

Meeting dates: September 2-3, 2021

Description of the Particular Matter to Which the Waiver Applies:

D. Charles Vite, B.S., DVM, Ph.D., a special government employee, has been invited to participate in the September 2-3, 2021, CTGTAC meeting as a temporary voting member (TVM). The committee will meet in open session to discuss the evaluation of the toxicity risks in the context of vector design and quality, non-clinical and clinical studies, and the long-term monitoring of human recipients of AAV gene therapies. The committee will hear presentations and discuss topics on genotoxicity, hepatotoxicity, thrombotic microangiopathy, dorsal root ganglion (DRG) toxicity, and magnetic resonance imaging (MRI) findings in the brain.

The topic of this meeting is a particular matter of general applicability. The CTGTAC will discuss more than one general scientific topic and many invited speakers from the field will give presentations. No specific marketing applications will be discussed. The discussion will not focus on approval, ongoing approval, or conditions of approval of any specific product, and it is a non-voting meeting. The particular matter will affect entities that make, or are seeking to make, AAV vector-based gene therapy products.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Charles Vite is a Professor of Neurology for the Department of Clinical Sciences at the University of Pennsylvania. He is invited to serve as a TVM for the September 3, 2021, CTGTAC meeting, Session 5: Neurotoxicity: Brain MRI Findings and Session 4: Neurotoxicity:

Dorsal Root Ganglion Toxicities. Dr. Vite cumulatively owns between (b) (6) worth of stock holdings in affected firms (b) (4) . Accordingly, the matter before the committee involving AAV gene therapies will have a direct and predictable effect upon Dr. Vite's financial interests.

In addition, Dr. Vite is a Principal Investigator on a study entitled (b) (4) (b) (4) that began on (b) (4) , with an anticipated end of (b) (4) . The University of Pennsylvania, Dr. Vite's employer, is the primary site for the study, which is funded by (b) (4) . The institution anticipates receiving between (b) (4) per year for this study, and Dr. Vite anticipates receiving (b) (6) per year in salary support.

Basis for Granting the Waiver:

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

Dr. Vite earned his B.S. degree from Cornell University, his D.V.M. from Purdue University, and his Ph.D. from the University of Pennsylvania. He is a board-certified veterinary neurologist and professor of neurology in the Section of Neurology & Neurosurgery Department of Clinical Sciences and Advanced Medicine at the University of Pennsylvania, School of Veterinary Medicine. His research focuses on the characterization and treatment of neurological disorders by studying naturally occurring nonrodent models of human diseases, including rare diseases such as Krabbe disease and Niemann-Pick, type C disease. He has published extensively on biomarkers and functional outcomes of neurological disorders in animals and the administration of AAV vector-based products in different animal species and disease models. He was also an invited participant at the National Institutes of Health meeting on *Next Generation Strategies for Gene-Targeted Therapies of Central Nervous System Disorders* in 2019. In addition to his experience with the specific product class (AAV-vector based products) being discussed at this CTGTAC meeting, his understanding of ante-mortem disease markers and methodologies, including imaging techniques, to evaluate the neurodegenerative process is highly relevant to two meeting topics that are focused on AAV vector-associated neurotoxicity in animals (i.e., DRG toxicities in nonrodent species and MRI findings in the brains of animals and humans). His expertise in this particular subject matter and his contribution to the committee's discussion will be highly valued and is necessary in the interest of public health.

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

It has been challenging to identify similarly qualified individuals without a disqualifying financial interest. This is because most academic scientists are involved in product development given that AAV vector-based gene therapy products show great promise in the clinic and the technology is rapidly developing towards translation. Several other prospective participants have already been recused due to conflicting financial interests.

The particular matter is not sensitive.

The meeting topic for this session is not sensitive; however, the meeting may still receive significant public interest or (non-trade) press interest due to the discussions involving various toxicity risks noted in the pre-clinical and clinical studies, and the long-term monitoring of human recipients of AAV gene therapies.

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

Dr. Vite is well known and is recognized as an accomplished scientist/researcher with extensive experience in feline and canine models of neurodegenerative diseases and canine epilepsy. He is also experienced with the administration AAV vector-based gene therapy products in these animal species/models.

Given his exceptional scientific background, Dr. Vite's participation in this meeting will bring the benefit of his expertise in multiple fields that are critical to the CTGTAC's deliberations.

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

The strong need for Dr. Vite's demonstrated expertise and diverse perspective that he can bring to this matter before the committee greatly outweighs any potential for a conflict of interest.

Accordingly, I recommend that you grant Dr. Charles Vite, a temporary voting member of the Cellular Tissue and Gene Therapies 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):

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_____ Denied – The individual may not participate.

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

August 17, 2021
Date