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

DATE: February 11, 2019

TO: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

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

Name of Advisory Committee Member: **William B. Messer, M.D., Ph.D.**

Committee: Vaccines and Related Biological Products Advisory Committee

Meeting Dates: March 6-7, 2019

Description of the Particular Matter to Which the Waiver Applies:

Dr. William B. Messer will be serving as a temporary voting member of the Vaccines and Related Biological Products Advisory Committee (VRBPAC). The Committee reviews and evaluates data concerning the safety, effectiveness, and appropriate use of vaccines and related biological products which are intended for use in the prevention, treatment, or diagnosis of human diseases, and, as required, any other products for which the Food and Drug Administration has regulatory responsibility.

On March 7, 2019, the committee will meet in open session to discuss and make recommendations on the safety and effectiveness of a Dengue Tetravalent Vaccine (Live, Attenuated) [Dengvaxia] manufactured by Sanofi Pasteur. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Messer has identified financial interests of his employer which can be affected by the particular matter before the committee. These financial interests are imputed to him under the federal conflict of interest statute, 18 U.S.C. § 208.

Dr. Messer's employer, the Oregon Health Science University (OHSU), has two contracts with (b) (4) to conduct two studies related to Dengue Fever:

1. (b) (4) – The study ended in January 2019, but OHSU has not yet received all funds for the study, which can be impacted by the particular matter before the advisory committee; OHSU is expected to receive between $150,000 - $200,000, including approximately (b) (6) in salary support for Dr. Messer.

2. (b) (4) – If approved, this product would compete with the product under review by the committee. It is anticipated the contract will end in (b) (4) and all work will end at that date. OHSU will receive between $700,000 and $800,000 from the (b) (4) funded study. Dr. Messer's role in the study will be principal investigator. He will not receive any salary support or personal remuneration from the study.

Basis of Granting the Waiver:

A key topic of discussion at this advisory committee meeting will be the interpretation of data on the safety and effectiveness of a Dengue Tetravalent Vaccine (Live, Attenuated) [Dengvaxia] manufactured by Sanofi Pasteur. The advisory committee will discuss the clinical development of a vaccine (Dengvaxia) against dengue disease caused by dengue virus serotypes 1, 2, 3, and 4 to be administered to individuals 9 through 45 years of age with laboratory-confirmed previous dengue infection and living in endemic areas. A fruitful discussion of these matters depends on having strong expertise in this area and hearing many perspectives. It is particularly important to include someone with Dr. Messer's expertise specifically in the relationship between flavivirus genetic variability and human antibody-mediated neutralization of the dengue disease, which is directly related to the major issues to be discussed at the advisory committee meeting. Dr. Messer has participated in National Institutes of Health study sections and has productively contributed to the discussions at those meetings and provided important advice for federal government considerations.

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

Dr. William Messer, M.D., Ph.D. received both his medical and doctoral degree from the University of North Carolina and has been in practice fifteen years. He performed fellowship at the University of North Carolina in molecular virology where he co-designed a panel of robust DENV serotype 1, 3, and 4 molecular clones to manipulate components of the DENV genome. During medical school and residency, he helped develop a high throughput flow-cytometry based DENV neutralization assay and developed protocols for characterizing DENV infection in primary human dendritic cells. He is an Assistant Professor in the Department of Microbiology and Immunology. He is also the consulting attending physician in the Division of Infectious Diseases at the OHSU School of Medicine and he lectures at the OHSU School Medicine on virology, hemorrhagic viruses, and fundamentals of HIV. He is an invited expert for the

Biomedical Advanced Research and Development Authority (BARDA), the Infectious Disease Society of Oregon, the Global Center for Infectious Diseases in Seoul Korea and the University of Puerto Rico. His experience in serving as principal investigator on nine studies on dengue virus immunity provides unique insights on safety and efficacy of dengue vaccines.

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

No other current advisory committee member has expertise comparable to Dr. Messer's. Finding another individual with such expertise who has no conflicts is difficult because having consulting or research relationships with entities on studies likely to be impacted by the particular matter before the committee is common among large academic research organizations. The review division has indicated that 3-4 researchers with expertise in dengue will be needed for this meeting. As of the writing of this waiver, 5 researchers were contacted as potential participants. One had a financial conflict with the meeting sponsor and the remaining three are federal employees with direct supervisory reporting relationships within the federal government. Dengue is considered a rare disease by the National Organization of Rare Diseases and its research community is very small.

A productive discussion of the application before the committee at this meeting depends upon having an adequate number of dengue experts attending. The various dengue experts who were invited to attend this meeting have different and varied expertise. Some experts are subspecialized within the field of virology, such as rare disease, and geographic specific dengue infections. Dr. Messer has expertise in dengue disease immunity, which is directly relevant to the topic being discussed at the advisory committee meeting. Being able to draw upon a diverse set of competencies and knowledge is essential if the committee is to successfully address the complex dengue vaccinology issues being discussed. Dr. Messer's participation in the committee's discussions will ensure the level of expertise and scientific objectivity required to provide expert advice and recommendations to the Agency regarding the safety and effectiveness of a Dengue Tetravalent Vaccine (Live, Attenuated) [Dengvaxia].

The particular matter is sensitive.

The meeting topic is considered to be sensitive. The advisory committee meeting will discuss a new drug application for preventing dengue virus infections that can cause Dengue fever, a debilitating disease that typically leads to prolonged fever and severe joint pain. Dengue infection can also progress unpredictably to a life-threatening form of the disease called Dengue Haemorrhagic Fever. According to CDC, more than one-third of the world's population live in areas at risk of dengue infection and associated disease, sometimes with fatal consequences. Dengue is caused by any one of four related viruses transmitted by mosquitoes. If approved, this product before the committee is expected to help prevent such disease in the US, its territories, and in other countries. Given the significance and global impact of Dengue disease and the possible availability of the vaccine, this may be a high-profile topic of public interest and/or non-trade press interest.

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

It is critical for the Agency to determine, with input from outside experts, whether this dengue vaccine will increase the immunogenicity to dengue disease. Dr. Messer has a strong clinical background in the evaluation of flavivirus infections in human clinical trials as well as a background in flavivirus virology and immunology. He has a keen understanding and strong scientific background with regard to viral, host and immunologic factors causing flavivirus diseases including dengue disease.

Accordingly, I recommend that you grant Dr. William B. Messer, a temporary voting member of the Vaccines and Related Biological Products 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.

_____ /s/ _____ February 15, 2019_

Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

Date

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