DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Silver Spring MD 20993

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

DATE: September 28, 2016

TO: Janice M. Soreth, M.D.
Associate Commissioner for Special Medical Programs (Acting)
Office of Medical Products and Tobacco
Office of the Commissioner, FDA

THROUGH: Michael F. Ortwerth, Ph.D.
Director, Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

FROM: Danyiel D'Antonio
Acting Chief, Committee Management Branch
Division of Workforce Management, OM
Center for Devices and Radiological Health CDRH)

Name of Advisory Committee Member: Joanna M. Schaenman, M.D., Ph.D.

Committee: Microbiology Devices Panel of the Medical Devices Advisory Committee

Meeting date: November 9-10, 2016

Description of the Particular Matter to Which the Waiver Applies:

The Division of Microbiology Devices Panel will meet on November 9, 2016, to discuss and make recommendations on the reclassification of quantitative Cytomegalovirus (CMV) viral load assays from Class III (subject to Premarket Approval) to Class II (subject to General and Special Controls). A nucleic acid-based in vitro diagnostic device for the quantitation of CMV viral load, within the context of transplant patient management, is a post-amendment device classified into Class III under section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act. To date, the following product code has been established for CMV viral load devices: PAB (Cytomegalovirus (CMV) DNA Quantitative Assay). This session of the meeting involves consideration of a particular matter of general applicability.

The use of CMV viral load measurements is chiefly for immunosuppressed patients following organ transplantation who are at risk for reactivation of latent infection or new onset primary infection by transmission through blood products. The overall benefit/risk of CMV viral load monitoring for transplant patients is well established and is the standard of care. Hence, it is not the topic for Panel deliberation. For the purpose of obtaining recommendations about possible reclassification, the Panel will be asked to discuss the types of evidence, including clinical evidence, which would be helpful to establish the appropriate controls necessary to mitigate the risks to health and assure the safety and effectiveness of new quantitative CMV viral load assays.

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

Dr. Schaenman is serving as a temporary non-voting member of the Microbiology Devices Panel. The Panel's function is to review and evaluate data concerning the safety and effectiveness of marketed and investigational in vitro devices for use in clinical laboratory medicine including microbiology, virology, and infectious disease, and make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Schaenman's institution, UCLA David Geffen School of Medicine, has a contract to study a (b)(4)., device which is indicated for quantitative Cytomegalovirus (CMV) viral load detection in transplant patients. (b)(4) is an affected entity for this meeting because their device is part of the class of devices under discussion by the Panel. Dr. Schaenman is Assistant Professor of Medicine in the Division of Infectious Diseases. She is a sub-principal investigator for the study, not the awardee or principal investigator. The time period of the study is September 2016 to September 2017. Dr. Schaenman's institution is receiving between $50,001 and $100,000 under this contract; Dr. Schaenman is receiving between $5,001 and $10,000 based on her work as an investigator on the study.

Basis for Granting the Waiver:

There are very few U.S. scientists who have the in-depth expertise necessary for this meeting, i.e., knowledge of the clinical aspects of CMV infection as well as substantive knowledge of the laboratory methods for the measurement of CMV. For the purpose of reclassification, these knowledgeable experts are essential for the discussion of the benefit/risk of reclassification and potential mitigation of risks. How to address variability and non-commutability[1] across tests, and other concerns, through Special Controls, will be a significant aspect of the Committee discussion.

The relatively specialized area that is the subject of this meeting heightens the need for having experts supplement the standing Committee, as there are few standing members with such expertise. One major focus of discussion will be the use of standards as a factor in CMV reclassification. Both FDA-approved CMV viral load assays were developed independent of a newly available WHO international standard. Although having a standard available would superficially appear to support reclassification, significant concerns still remain with commutability across assays. It is essential that the Committee have the relevant expertise on the

[1] Commutability is defined as equivalence of the mathematical relationships between the results of different measurement procedures for a reference material and for representative samples from healthy and diseased individuals. In practical terms, the property of commutability refers to the fact that a calibration material interacts with the test system in a manner similar to patient samples.

Panel for discussion to be productive, as variability and non-commutability across tests is a major issue for reclassification.

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

Dr. Schaenman earned a Ph.D. in Microbiology and M.D. from the University of Virginia, completed an Infectious Diseases fellowship at Stanford University and earned a Master's Degree in Epidemiology from Stanford. She is Assistant Clinical Professor at the David Geffen School of Medicine at UCLA where she serves as a consultant on the in-patient transplant infectious diseases service and out-patient clinic. Dr. Schaenman's research focuses on the older transplant recipient and the immune response to viral infection in immunocompromised hosts. Her clinical experience and laboratory expertise are characteristics highly-valued for this Panel meeting.

Furthermore, Dr. Schaenman is a member of Infectious Diseases Society of America, the American Society of Transplantation, and several other professional societies. She is a recognized expert in transplant infectious disease and serves on FDA's Center for Drug Evaluation and Research Antimicrobial Drugs Advisory Committee. She previously served on the National Institute of Allergy and Infectious Diseases' Division of Microbiology and Infectious Diseases End-Point Committee for CMV studies.

Dr. Schaenman is essential for participation on this Panel because her extensive, specific experience in CMV infection and the additional viral infections to be discussed is invaluable for an informed, productive discussion. Her expertise is amply demonstrated by multiple publications in transplant infectious diseases. Her unique experience and expertise in clinical, laboratory medicine, and epidemiology makes her particularly important for this meeting. Her expertise would be especially difficult to replicate on the Panel in this narrow area.

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

As very few U.S. scientists have expertise in this area, it has been very difficult to locate individuals with the necessary expertise who are free of conflicts to attend this meeting. In the interest of public health, it is critical that Dr. Schaenman participate to ensure fully-informed discussions and recommendations.

Furthermore, representatives of the Infectious Diseases Society of America published a position paper in early 2016 advocating reclassification. This led to a decision by agency management to exclude a number of individuals who might otherwise have been strongly considered for this meeting. The publication of this paper also led to exclusion of two standing Panel members, including the chairperson. These decisions had the effect of shrinking the pool of available experts even further.

In our Panel preparation process, we approached multiple individuals who have experience in these areas, but were unsuccessful in finding the range of expertise to match that of Dr. Schaenman. Other possible Panelists with the relevant expertise who were contacted were ineligible due to financial conflicts or were unavailable due to scheduling conflicts. There is simply no other individual who could be found to replace Dr. Schaenman's expertise for this particular meeting. *The particular matter is not sensitive.*

The particular matter to be addressed by the Panel is not considered sensitive, as it will not change the standard of care for monitoring patients' CMV viral load post-transplantation. The subject of the meeting is whether these devices can be reclassified and Special Controls written, such that, these devices can safely be reclassified to Class II. The Panel discussion is very unlikely to affect current FDA recommendations for requiring clinical studies. FDA policy has evolved significantly since the first approval of a CMV viral load diagnostic test, and this policy is unlikely to be significantly affected by the discussion, as validation studies are likely to be required regardless of whether the regulatory pathway is Class III (subject to Premarket Approval) or Class II (subject to General and Special Controls). The particular matter to be discussed by the Panel may have an impact on the current market, as reclassification may encourage additional manufacturers to enter this market.

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

An evaluation of Dr. Schaenman's financial interest shows that she is a sub-principal investigator (one of several) for a large multicenter study that is involved in blinded comparisons of assays for a well-established clinical use. Because few U.S. scientists have expertise in this area, it is not uncommon that device manufacturers seek out the same experts for conducting studies for CMV diagnostics that FDA would seek for the upcoming Panel meeting. Although investigators participating in large, multi-center clinical studies are evaluating safety and efficacy of these devices for FDA submission, the committee discussion is very unlikely to affect current FDA recommendations for clinical studies. FDA policy has evolved significantly since the first approval of a CMV viral load diagnostic, and this policy is unlikely to be significantly affected by the discussion, as similar validation studies are likely to be required regardless of a Class II or Class III classification status (although in the former case these would be mandated by Special Controls). It should be noted that these studies are often blinded, and they are extremely unlikely to influence the Committee since CMV viral load monitoring is firmly established as the standard of care post-transplantation. This is a general, well known issue and is relevant to all products within the affected class.

Therefore, any conflict of interest created by this interest is greatly outweighed by the need for Dr. Schaenman's expertise in a field where such expertise is limited but imperative to the success of this particular matter.

Accordingly, I recommend that you grant a waiver for Dr. Joanna M. Schaenman, a temporary non-voting member of the Microbiology Devices Panel, from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

____X___ 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/_____ October 21, 2016_____

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