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

DATE: July 19, 2019

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

FROM: Jayne E. Peterson, B.S.Pharm., J.D.
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Member: **Lindsey Baden, M.D.**

Committee: Antimicrobial Drugs Advisory Committee (AMDAC)

Meeting date: August 7, 2019

Description of the Particular Matter to Which the Waiver Applies:

Dr. Baden is the Chairperson of the Antimicrobial Drugs Advisory Committee. The Committee's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of infectious diseases and disorders and make appropriate recommendations to the Commissioner of Food and Drugs.

On August 7, 2019, the committee will discuss supplemental new drug application (sNDA) 208215, supplement 12, DESCOVY (emtricitabine (FTC) 200 mg and tenofovir alafenamide (TAF) 25 mg tablets), submitted by Gilead Sciences, Inc., proposed for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired human immunodeficiency virus (HIV)-1 infection among individuals who are HIV-negative and at risk for HIV. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Baden is Director of Clinical Research in the Division of Infectious Disease, Director of the Center for Clinical Investigations and Director of the Immunocompromised Host Program at Brigham and Women's Hospital. He has identified both a personal financial interest and financial interests of his employer which are imputed to him under federal conflict of interest statute, 18 U.S.C. § 208.

Dr. Baden's employer, Brigham and Women's Hospital, has a contract with (b) (4) (a biopharmaceutical company), a subsidiary of (b) (4) for (b) (4) Dr. Baden is a co-investigator. The study began in 2015 and finished in 2018 with long-term follow up continuing. Dr. Baden's institution will receive between 0 - $50,000 annually for long-term follow up. Dr. Baden does not receive any personal remuneration or salary support for this study.

In addition, Dr. Baden's employer is a clinical research site for the HIV Vaccine Trials Network (HVTN) where Dr. Baden serves as Principal Investigator (PI). The HVTN is a publicly-funded network, with their main funding coming from the National Institute of Allergy and Infectious Diseases (NIAID) of the U.S. National Institutes of Health. Another significant funding source of the HVTN is the Bill & Melinda Gates Foundation. The Network's clinical research sites are located in over 30 cities on five continents. In addition, various pharmaceutical companies collaborate on HIV vaccines through the HVTN. Dr. Baden's institution receives between $1,500,000 and $2,500,000 per year from the HVTN. Dr. Baden receives an estimated (b) (4)% of his salary per year in salary support from this funding. This contract began in 2013 with an anticipated end date in 2020. The following studies are funded through the contract:

• HVTN 106: A Phase 1 randomized , double-blind placebo controlled clinical trial to evaluate the safety and immunogenicity of an HIV-1 vaccine regimen of DNA prime with 3 different HIV-1 envelop inserts (Nat-B env, CON-S env, and Mosaic env) with MVA-CMDR boost in health, HIV-1- uninfected adults. Sponsor: NIAID. Period: December 2014 – September 2020 (NCT02296541)

• HVTN 108: A phase 1/2a clinical trial to evaluate the safety and immunogenicity of HIV clade C DNA, and of MF59®- or AS01B-adjuvanted clade C Env protein, in healthy, HIV-uninfected adult participants. Sponsor: NIAID. Period: December 2016 – February 2020 (NCT02915016)

• HVTN 114: A phase I clinical trial to evaluate the immunogenicity of AIDSVAX® B/E bivalent gp120 vaccine and MVA/HIV62B in healthy, HIV- 1 uninfected adult participants who previously received MVA/HIV62B in DNA/MVA or MVA/MVA regimens in HVTN 205. Sponsor: NIAID. Period: October 2017 – October 2019 (NCT02852005) in follow-up status

• HVTN 120: A phase 1/2a clinical trial to evaluate the safety and immunogenicity of ALVAC-HIV (vCP2438) and of MF59®- or AS01B-adjuvanted clade C Env protein, in healthy, HIV-uninfected adult participants. Sponsor: NIAID. Period: January 2018 – September 2019 (NCT03122223)

• HVTN 127/HPTN087: A phase 1 clinical trial to evaluate the safety and drug levels of a human monoclonal antibody, VRC-HIVMAB075-00-AB (VRC07-523LS), administered in multiple doses intravenously, subcutaneously, and intramuscularly in different dosing schedules to healthy, HIV-uninfected adults. Sponsor: NIAID. Period: February 2018 – July 2021 (NCT03387150)

• HVTN 128: A Phase I clinical trial to evaluate the safety, pharmacokinetics, and anti-viral

activity of VRC-HIVMB075-00-AB (VRC07-523LS) in the serum and mucosa of healthy, HIV-1 uninfected adult participants. Sponsor: NIAID. Period: January 2019 – May 2020 (NCT03735849)

• HVTN 704/HPTN 085: A phase 2b study to evaluate the safety and efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection among men and transgender persons who have sex with men. Sponsor: NIAID. Period: March 2016 – October 2020 (NCT02716675)

• HVTN 117: A Phase 1/2 study to assess the safety/tolerability of the 2 different vaccine regimens of priming with trivalent Ad26.Mos.HIV and boosting with trivalent Ad26.Mos.HIV and Clade C gp140 plus adjuvant or priming with tetravalent Ad26.Mos4.HIV and boosting with Ad26.Mos4.HIV and Clade C glycoprotein (gp)140 plus adjuvant. Immune responses of the different vaccine schedules will be assessed. Sponsor: Janssen, a subsidiary of Johnson & Johnson. Period: March 2017 – January 2020 (NCT02935686)

• HVTN 118: A Phase 1/2 study to assess safety/tolerability of the different vaccine regimens and to assess envelope (Env)-binding antibody (Ab) responses of the 2 different vaccine regimens. Sponsor: Janssen, a subsidiary of Johnson & Johnson. Period: July 2016 – June 2021 (NCT02788045)

• HVTN 115: A Phase 1 study to evaluate the safety, tolerability, and immunogenicity of EnvSeq-1 Envs adjuvanted with GLA-SE, administered with or without DNA Mosaic-Tre env, in healthy, HIV-uninfected adults. Sponsor: NIAID. Period: August 2017 – January 2022 (NCT03220724)

• HVTN 133: A Phase 1 study evaluating the Safety and Immunogenicity of an HIV-1 gp41 MPER-656 Liposome Vaccine in Healthy, HIV-uninfected Adult Participants. Sponsor: NIAID. Period: July 2019 – June 2021 (NCT03934541)

• HVTN 706: A Phase 3 study to evaluate the vaccine efficacy (VE) of a heterologous vaccine regimen utilizing Ad26.Mos4.HIV and aluminum phosphate-adjuvanted Clade C gp140 and Mosaic gp140 for the prevention of HIV-1 infection in HIV-1 seronegative cis-gender men and transgender individuals having sex with cis-gender men and/or transgender individuals. Sponsor: Janssen, a subsidiary of Johnson & Johnson. Period: June 2019 – June 2023 (NCT03964415)

Basis for Granting the Waiver:

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

Dr. Lindsey Baden, M.D., received his medical degree from Albert Einstein College of Medicine followed by a residency in Internal Medicine at Beth Israel Hospital. He completed a fellowship at the Beth Israel and Brigham and Women's Hospital in infectious diseases and is Board Certified in Infectious Diseases and Internal Medicine. He further pursued a Medical Sciences degree in Clinical Investigation as well as a Master of Science in Epidemiology from Harvard Medical School and Harvard School of Public Health. He is currently an Associate Professor of Medicine at Harvard Medical School as well as Director of Clinical Research in the Division of Infectious Disease, Director of the Center for Clinical Investigations and Director of the

Immunocompromised Host Program at Brigham and Women's Hospital. He is also Director of Infectious Diseases at Dana-Farber Cancer Institute.

His current research interests include HIV vaccine development, novel diagnostics for invasive fungal disease and the impact of infection in the immunocompromised host. He has over 20 years of clinical practice experience and is extensively published in the field of Infectious Disease.

Dr. Baden has been a standing, voting member of the Antimicrobial Drugs Advisory Committee since 2014 and has chaired the committee since 2015. It is particularly important to have Dr. Baden chair the upcoming AMDAC meeting given his broad experience in infectious disease, specifically HIV research and clinical practice, as well as his background in clinical investigation and epidemiology. The combination of his background and experience will be invaluable to the discussion regarding the clinical trial data submitted for Descovy for the HIV PrEP indication.

As an experienced member and Chair of the AMDAC, it will be essential to have his perspective as well as his leadership at the meeting. He has vast experience running complex meetings which would be complementary to new and less experienced members attending the meeting. Recently, he successfully chaired two complex meetings for the Division of Antiviral Products, one for smallpox and one for rabies. He not only guided the meetings, but also raised important issues that were necessary to fully understand the Division's concerns. Without his extensive background, the Division would not have received the advice that was critical for drug development in these serious and life-threatening infectious diseases.

A key topic of discussion at this advisory committee meeting will be the applicant's strategy to support approval of the PrEP indication for Descovy. In this supplement, the applicant proposes a broad PrEP indication for Descovy (FTC/TAF) to be consistent with that approved for Truvada in 2012, i.e., to reduce the risk of HIV infection in at-risk adults and adolescents. To support the indication, only a single, randomized, double-blind, active-controlled, non-inferiority trial (DISCOVER) was conducted in adult men who have sex with men (MSM) and trans-gender women comparing the safety and efficacy of Descovy to approved Truvada. This trial demonstrated noninferiority of Descovy to Truvada in reducing the risk of HIV-1 acquisition in a population of high-risk MSM.

The effectiveness of Descovy as PrEP, however, has not been clinically evaluated in women or adolescents. While extrapolation of efficacy from the DISCOVER trial can support a PrEP indication in adolescent MSM, the applicant proposes to rely on a bridging strategy to support the indication in women and adolescent girls. Dr. Baden's extensive background in clinical trials and his expertise in infectious diseases, with a focus on HIV are essential for this meeting. He has demonstrated his abilities to handle complex topics, such as rabies and smallpox where the committee had to rely on animal data to support a clinical indication which underscores and supports that it is essential Dr. Baden serves as the Chair of this advisory committee meeting.

The particular matter is not sensitive.

This topic is not considered to be sensitive as the FDA Division with responsibility 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 given that the newsworthy and controversial issues of PrEP were fully addressed 7 years ago at the time of the initial approval of Truvada. PrEP has now been widely embraced as part of a public health strategy to reduce new HIV infections. In addition, Descovy is already approved for the indication of HIV treatment.

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

HIV/Acquired Immunodeficiency Syndrome (AIDS) is a global pandemic. As of 2017, approximately 36.9 million people were infected with HIV globally. More than 1.1 million Americans are currently living with HIV. An estimated 40,000 Americans are being newly diagnosed each year. The U.S. government spends $20 billion in annual direct health expenditures for HIV prevention and care. There is currently no effective cure that exists for HIV but strict adherence to anti-retroviral therapy can dramatically slow the disease's progress and prevent secondary infections and complications, prolonging life.

In February 2019, the U.S. Department of Health and Human Services (HHS) proposed a new initiative to address the nation's HIV epidemic (Ending the HIV Epidemic: A Plan for America) with the goals of reducing the number of incident HIV infections in the U.S. by 75% within 5 years, and by 90% within 10 years. A key component of this strategic initiative is to prevent at-risk individuals from acquiring HIV infection, including the use of PrEP. HHS estimates that increasing PrEP use among high-risk groups could prevent almost 50,000 HIV infections by 2020. If approved for a PrEP indication, Descovy will likely play a direct role in this HHS initiative as the second potential product for this indication. Although efficacy of Descovy and the previously approved Truvada are similar, Descovy may offer some safety benefits in certain subpopulations of people with underlying kidney or bone disease.

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

Dr. Baden has extensive experience in the field of Infectious Disease. His unique expertise, and his ability to chair meetings in which novel and complex issues are points of discussion, make him an ideal participant for this meeting. For example, he chaired two recent AMDAC meetings on complex topics of rabies and smallpox that required a discussion of extrapolation to other populations which is similar to the discussion that will take place at the upcoming AMDAC meeting for Descovy for HIV PrEP. As such, any potential for conflict of interest is significantly outweighed by the need for Dr. Baden's expertise in chairing complex meetings.

Accordingly, I recommend that you grant a waiver for Dr. Lindsey Baden, the Chairperson of the Antimicrobial 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.

Russell Fortney -S Digitally signed by Russell Fortney -S
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Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

July 22, 2019
Date