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

DATE: November 21, 2017

TO: Rachel E. Sherman, M.D., M.P.H.
Principal Deputy Commissioner
Office of the Commissioner, Food and Drug Administration

THROUGH: Russell Fortney
Director (Acting), Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

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

Name of Advisory Committee Member: A. Michael Lincoff, M.D.

Committee: Bone, Reproductive and Urologic Drugs Advisory Committee

Meeting date: January 9, 2018

Description of the Particular Matter to Which the Waiver Applies:

Dr. Lincoff is serving as a temporary voting member of the Bone, Reproductive and Urologic 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 practice of obstetrics, gynecology, and related specialties, and make appropriate recommendations to the Commissioner of Food and Drugs.

The committee will meet on January 9, 2018, to discuss new drug application (NDA) 206089 (oral testosterone undecanoate capsules) submitted by Clarus Therapeutics, for the proposed indication of testosterone replacement in males for conditions associated with a deficiency or absence of endogenous testosterone: Primary hypogonadism (congenital or acquired) and hypogonadotropic hypogonadism (congenital or acquired). The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Lincoff is Vice Chairman of the Robert and Suzanne Tomsich Department of Cardiovascular Medicine at the Cleveland Clinic, and Director of the Cleveland Clinic Coordinating Center for Clinical Research (C5Research). He does not have any personal financial interests that are likely to be affected by the particular matter to be discussed at the meeting. However, he has identified financial interests of his employer, which are imputed to him under the federal conflict of interest statute, 18 U.S.C. § 208.

The Academic Research Organization, C5Research, at Dr. Lincoff's employer, Cleveland Clinic, has a contract with (b) (4), a competing firm, to perform services related to preliminary startup of the study, (b) (4) This study is a cardiovascular outcomes trial of (b) (4) a competing product, for (b) (4), related to the topic before the advisory committee. This contract pays for C5Research efforts regarding trial design, committee formation, etc. It is anticipated that this contract will transition to the main trial contract by (b) (4), but it is possible that work would continue under another interim temporary work agreement if the main trial budget or contract is not finalized by that point. The study began in (b) (4) and is expected to continue through the end of (b) (4). C5Research will receive between $700,000 - $750,000 total from (b) (4) for this study. Dr. Lincoff's roles in the study are Co-Principal Investigator and managerial. He does not receive any salary support or personal remuneration from this study.

In addition to the preliminary startup contract, C5Research is currently negotiating with (b) (4), for (b) (4) The study is expected to begin in (b) (4) and continue through (b) (4). The funding to C5Research from (b) (4) is anticipated to be between $7,000,000 – $7,500,000 total for this study. Dr. Lincoff's role in the study will be Co-Principal Investigator. He will not receive any salary support or personal remuneration from this study.

Basis for Granting the Waiver:

A key topic of discussion at this advisory committee meeting will be the interpretation of study data on the potential for increased cardiovascular risk related to effects of testosterone undecanoate on blood pressure, serum lipids and/or hematocrit. A fruitful discussion of these matters depends upon having strong expertise in this area and hearing many perspectives. It is particularly important to include someone with Dr. Lincoff's experience in designing and interpreting large cardiovascular outcome trials and his expertise in ischemic cardiovascular disease, which is directly related to one of the major issues being discussed at the advisory committee meeting. In addition, Dr. Lincoff has participated in other FDA advisory committee meetings that involve complex cardiovascular issues demonstrating outstanding judgment, and has productively contributed to the discussions at those meetings and provided important advice for FDA consideration.

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

Michael Lincoff, M.D., received his medical degree from Johns Hopkins University School of Medicine and has been in practice for more than 20 years. He performed fellowships in cardiovascular medicine at the University of Michigan Medical Center and the Cleveland Clinic Foundation, and he performed a fellowship in interventional cardiology at the Cleveland Clinic Foundation. He is Vice Chairman of the Robert and Suzanne Tomsich Department of Cardiovascular Medicine at the Cleveland Clinic. He supervises clinical research activities throughout the Cleveland Clinic as Director of the Center for Clinical Research of the Lerner Research Institute. Dr. Lincoff is also the Director of the Cleveland Clinic Coordinating Center for Clinical Research (C5Research), an academic research organization that plans, coordinates and manages multicenter clinical trials of new therapies. He is a Professor of Medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. He holds the Charles and Charlotte Fowler Endowed Chair for Cardiovascular Research at Cleveland Clinic. His experience in serving as principal investigator or steering committee member of over 15 pivotal trials in ischemic heart disease, enrolling in aggregate over 50,000 patients, provides unique insights into the design and conduct of large cardiovascular outcome trials.

No other current advisory committee member has analogous expertise. Finding another individual with such expertise who has no conflicts is difficult because having consulting or research relationships with entities likely to be impacted by the particular matter before the committee is common in directing a large academic research organization. The review division has indicated that 3-4 cardiologists will be needed for this meeting. As of the writing of this waiver, 16 cardiologists were contacted as potential participants. Six were unable to attend based on scheduling conflicts. Two self-recused based on other conflicts. Six did not respond or are still under consideration. Only one other cardiologist has thus far received final clearance to participate.

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

A productive discussion of the application before the committee at this meeting depends upon having an adequate number of cardiologists attending. The various cardiology experts who were invited to attend this meeting have different and varied expertise. Some experts are sub-specialized within the field of cardiology, such as hypertension, cardiovascular epidemiology, and heart failure. Dr. Lincoff has expertise in ischemic cardiovascular disease, which is directly relevant to the NDA 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 cardiovascular issues being discussed. Dr. Lincoff'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 Clarus Therapuetics' testosterone undecanoate.

The particular matter is sensitive.

The meeting topic is considered to be sensitive. The advisory committee meeting will discuss new drug application for an oral testosterone therapy. If approved, this product is expected to improve patient convenience because the commonly used products are topical gels and injectables. Given the novel route of administration and that testosterone replacement is a high-profile topic of interest in the lay press, there may be some public interest and/or (non-trade) press interest.

Dr. Lincoff'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 testosterone therapy will increase the risk of cardiovascular disease. Millions of middle and older-age men may potentially use this product, many of whom will have underlying cardiovascular disease or cardiovascular risk factors. Understanding the cardiovascular risk associated with this product and ensuring that any such risk can be adequately mitigated will be of major public health importance if this product is approved. Dr. Lincoff's knowledge in the area of cardiology will provide necessary expertise for this important discussion.

Accordingly, I recommend that you grant Dr. A. Michael Lincoff, a temporary voting member of the Bone, Reproductive and Urologic Drugs Advisory Committee, a waiver 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/_____ ___12/18/2017___
Rachel E. Sherman, M.D., M.P.H. Date
Principal Deputy Commissioner
Office of the Commissioner, FDA