



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

DATE: March 25, 2009

TO: Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy
Food and Drug Administration

THROUGH: Vince Tolino 15/
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Michael F. Ortwerth, Ph.D. 15/
Director, Advisory Committee Oversight and Management Staff
Office of Policy, Planning, and Preparedness

FROM: Jayne E. Peterson 15/
Acting Director
Division of Advisory Committee and Consultant Management
Center for Drug Evaluation and Research

Name of Temporary Voting Member: David Harrington, Ph.D.

Committee: Oncologic Drugs Advisory Committee Meeting

Meeting date: March 31, 2009

Description of the Facts on Which the Waiver is Based:

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

Dr. David Harrington is Chair of the Department of Biostatistics and Computational Biology at the Dana Farber Cancer Institute. The department serves as the Statistical Center for the Eastern Cooperative Oncology Group (ECOG). Faculty members in the Statistical Center have subcontracts with [redacted] to provide statistical analysis of data from ECOG studies involving [redacted], for indications [redacted]. Dr. Harrington has no direct involvement in these activities. His only involvement is managerial as chair of the department. He does not receive any personal remuneration or salary support from the funds received.

- Subcontract with [REDACTED] to provide statistical analysis of data from the Eastern Cooperative Oncology Group (ECOG) studies of [REDACTED] for [REDACTED] neoplasms. The project period is [REDACTED]. The magnitude of the interest \$0 - 50,000.
- Subcontract with [REDACTED] to provide statistical analysis of data from ECOG studies of [REDACTED] for [REDACTED] cancer. [REDACTED] is approved for the treatment of [REDACTED] cancer. The project period is [REDACTED]. The magnitude of the interest is over \$300,000.
- Statistical analysis of data from studies of [REDACTED] for [REDACTED] cancer. [REDACTED] is approved for the treatment of [REDACTED] cancer. The project period is [REDACTED]. The magnitude of the interest is over \$300,000.
- Statistical analysis of data from studies of [REDACTED] for [REDACTED] cancer. The project period is [REDACTED]. The magnitude of the funding is \$0 - 50,000.
- Statistical analysis of data from studies of [REDACTED] for [REDACTED] cancer [REDACTED]. The project period is [REDACTED]. The magnitude of the interest is \$0 - 50,000.

Description of the Particular Matter to Which the Waiver Applies:

March 31, 2009, Oncologic Drugs Advisory Committee meeting to discuss supplemental biologic license application (sBLA) 125085/169 of Avastin (bevacizumab), sponsored by Genentech, in collaboration with F. Hoffmann La Roche, proposed indication as single agent, for the treatment of previously treated glioblastoma multiforme.

Additional Facts: none

Basis for Granting the Waiver:

Any decision with respect to Genentech's supplemental application is unlikely to affect the economic stability of [REDACTED], or cause them to prematurely terminate their subcontracts with the Statistical Center. [REDACTED] is a leading [REDACTED] company with a diverse product line. [REDACTED] manufactures and commercializes multiple [REDACTED] products for use in oncology. Total U.S. product sales in 2008 were \$ [REDACTED] an [REDACTED] percent increase from \$ [REDACTED] in 2007.

[REDACTED], it is unlikely to affect the ongoing ECOG studies of [REDACTED] or the Statistical Center's subcontracts. According to [REDACTED] website, "[REDACTED]". Therefore, Dr. Harrington's imputed interests are unlikely to be affected by the outcome of the matter.

Additionally, the subcontracts with [REDACTED] do not represent a substantial portion of the Department's activities or funding. The Department is one of the nation's major statistical centers for carrying out multicenter clinical trials by virtue of being the statistical center of the Eastern Cooperative Oncology Group, the International Breast

Cancer Study Group, the Cancer Care Outcomes Research and Surveillance Consortium, and the Lunenburg Lymphoma Biomarker Consortium. Members of the Department also work closely with the AIDS Clinical Trial Group by leading the coordination of statistics for pediatric AIDS. The department also directs core statistical resources for the Cancer Center Support Grant, six National Cancer Institute-funded Specialized Programs of Research Excellence grants, and many program project grants.

Further, according to the review division, Dr. Harrington's participation is essential to this meeting because of his unique expertise. Dr. Harrington serves as Professor of Biostatistics at the Harvard School of Public Health and Chair of the Department of Biostatistics and Computational Biology in the Dana-Farber Cancer Institute. Along with his role as a statistician, Dr. Harrington is also a cancer researcher at the Institute. He is a member of the Institute of Mathematical Statistics and has been elected to the International Statistics Institute. His areas of expertise include: non-parametric methods for survival data and collaborative clinical trials. He has authored or co-authored numerous journal articles with areas of interest such as: non-Hodgkin's lymphoma, leukemia, lung cancer and myeloma.

The committee will discuss supplemental biologic license application for Avastin (bevacizumab) and as such, a current member should be in attendance to provide continuity and consistency of statistical thought.

Dr. Harrington is the only statistician invited to the meeting. One other individual was invited who has a background in Medical Oncology, Epidemiology, Hematology, and Biostatistics. However, Dr. Harrington's main area of expertise is in statistics/biostatistics and Dr. Harrington is the standing statistician on the Oncologic Drugs Advisory Committee (ODAC). Although this application does not present unusual statistical problems or issues, the ODAC needs a statistician who provides his expertise to the other committee members with regard to interpretation and commentary on statistical analyses performed by the applicant and by FDA.

Dr. Harrington, as the sitting statistician member of the Oncologic Drugs Advisory Committee (ODAC), has a unique expertise for this meeting. Dr. Harrington's expertise in the statistical considerations for studies of cancer therapies and other types of drug development is critical for this advisory committee discussion as he is the only expert on the ODAC regarding analysis and interpretation of statistical analysis, including descriptive statistics from the studies to be presented as well as potential input on the confirmatory trial which the applicant has initiated. Dr. Harrington's expertise is exemplified by his extensive experience as lead statistician for a National Cancer Institute-funded Cooperative Group program and knowledge of clinical trials for a variety of cancer types, including rare cancers such as glioblastoma multiforme. In addition, Dr. Harrington has specific expertise in the analysis and problems with small clinical trials, as discussed in his publication entitled, "The tea leaves of small trials," an editorial published in the *Journal of Clinical Oncology*. This expertise has special applicability to the advisory committee discussion because both of the clinical studies of Avastin for the treatment of glioblastoma multiforme are "small trials" that are historically controlled. The use of small historically-controlled trials for drugs seeking

accelerated approval is a common in cancer drug approvals but not in other clinical disciplines, thus requiring a statistician with expertise in the standards applied by FDA to accelerated approval for cancer drugs. Dr. Harrington has the necessary expertise through many years of service as an ODAC member and special Government employee to the Office of Oncology Drug Products in FDA. Dr. Harrington has unparalleled expertise in statistics and his unique perspective on "small trials" will provide irreplaceable insight.

The division feels strongly that Dr. Harrington has the background and expertise to lead an appropriate and stimulating discussion during the meeting. He has been a sitting member of the ODAC for the past 3 1/2 years and has had experience on the committee in analyzing data presented to the committee. His knowledge of clinical trial design and his experience as a biostatistician and cancer researcher will bring a wide range of knowledge to this meeting.

As described above, we believe that the interest of the Government in Dr. Harrington's participation outweighs the concern that a reasonable person may question the integrity of the Agency's programs and operations.

Thus we are requesting a waiver for David Harrington, Ph.D., a member of the Oncologic Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a) .

Certification:

X The individual may participate – The need for the Special Government Employee's services outweighs the potential for a conflict of interest.

X The individual may participate – The individual's participation is necessary to afford the advisory committee essential expertise.

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/
Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy

3/27/09
Date