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Via Email to Francis.Collins@nih.gov and First Class Mail
March 28, 2018

Honorable Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health
Office of the Director
BG 1 Room 118A, 1 Center Drive
Bethesda, MD 20814

RE: Knowledge Ecology International (KEI) March 19, 2018 submission to NIH, regarding four M01 awards to the University of Pennsylvania, and six patents issued to the University of Pennsylvania

Dear Dr. Collins:

I represent The Trustees of the University of Pennsylvania and one of its faculty members, Dr. Daniel Rader, and am responding to KEI's March 19, 2018 submission to the NIH Office of Technology Transfer. KEI cites four M01 awards (see Table 3 in KEI's March 19, 2018 submission), and alleges that the University inappropriately failed to disclose these M01 awards when applying for patents on a dosing method for which the University has obtained six U.S. patents. KEI relies upon inaccurate facts and makes certain incorrect assumptions. As set forth below, the dosing method inventions were conceived and reduced to practice as part of a Phase I/II study funded by the Doris Duke Charitable Foundation, not the federal government. They were not "subject inventions" conceived or first reduced to practice in the performance of a specific research project funded by NIH. Therefore, the University was not required to notify NIH when the inventions were made, or disclose an M01 award in its patent application.

In 2002, Dr. Rader wrote a funding proposal to the Doris Duke Charitable Foundation to conduct a specific research project: a Phase I/II study of the safety and efficacy of pharmacologic inhibition of a microsomal transfer protein (MTP) in patients with homozygous familial hypercholesterolemia (HoFH). The foundation decided to fund this discrete clinical trial, as well as other research projects Dr. Rader proposed, for five years. Study subjects received treatments, and data were collected, from approximately June, 2003 through February, 2004. Dr. Rader's protocol was designed to test a particular dosing strategy for BMS-201038, an MTP inhibitor. Bristol Myers Squibb previously had decided not to commercially develop BMS-201038, because in earlier studies, subjects experienced diarrhea and negative liver enzyme elevations. But Dr. Rader had an idea for a different dosing methodology as a way to minimize these negative side effects, and wanted to study whether changes in the dosing could be safe and effective in patients with HoFH.

M01 awards were infrastructure awards to support a General Clinical Research Center (GCRC) at the Hospital of the University of Pennsylvania, not an award to a specific scientist to conduct a discrete, specified research project (like an R01 award, as one example.) A GCRC was a discrete unit

of research beds within an academic medical center or hospital, separated from general care wards, that the government funded and wanted to be a shared infrastructure resource available to many different scientists, as a way to reduce overall costs for each separate, discrete research project. (For example, it would make no sense for each researcher at Penn to obtain funding for and hire separate nurses, or buy separate blood pressure machines, when these equipment and staff could be shared across projects more efficiently.) M01 awards were used for physical facility renovations to build and maintain the discrete unit within a hospital, and to pay operational expenses such as nurse and other staff salaries, shared equipment, and operating supplies. See NIH's Activity Code definition for M01 awards at: https://grants.nih.gov/grants/funding/ac_search_results.htm?Activity_Code=M01&Search_Type=Indiv

As part of Dr. Rader's Phase I/II study, study subjects received services at Penn's GCRC during June, 2003 to Feb. 2004, such as having their blood pressure, heart rate, and temperature checked, weight measured, and other nursing and dietician services. (Therefore, KEI is wrong to cite three M01 awards to Penn for the periods December, 2000 through November, 2001; from December, 2001 through November, 2002; and from December, 2004 through November, 2005. The dosing methodology claimed in the patent application was not conceived or first reduced to practice during these periods, so the M01 awards to Penn for its GCRC outside of June, 2003 to Feb. 2004 are irrelevant.)

Under Bayh-Dole, the dosing methodology claimed in Penn's patent application, was not a "subject invention" conceived or first reduced to practice in the performance of the M01 award. The dosing methodology was conceived and first reduced to practice in the performance of the Phase I/II clinical trial funded solely by the Doris Duke Charitable Foundation. Therefore, the University of Pennsylvania did not, and was not required to, disclose the dosing methodology invention to NIH as a "subject invention," and the University of Pennsylvania was not required to, and did not, disclose federal funding of its GCRC when Penn filed its patent application.

If NIH has any questions or would like additional information from the University, please contact me directly.

Sincerely,

Robert F. Firestone

Robert F. Firestone
Associate General Counsel
The Trustees of the University of Pennsylvania

courtesy copies to:

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