

March 18, 2015

James Nobles
Legislative Auditor
Room 140 Centennial Building
658 Cedar Street
Saint Paul MN 55155-1603

Dear Mr. Nobles:

The University of Minnesota is now and always has been committed to meeting, upholding and exceeding the highest ethical standards in research practices involving human subjects. While we believed that our current research program reflected this commitment, recent findings from a review by an external independent panel and an Office of the Legislative Auditor (OLA) report demonstrate that we can and must do better.

The loss of Dan Markingson's life is a tragedy. His care team was profoundly saddened by his death, and the University has great sympathy for those closest to him, especially his mother, who lost her son. We at the University have always been dedicated to finding cures and treatments for the most vexing diseases that plague our community, including mental illness. Our goal is to apply the highest standards of ethics and humanity to guide our every interaction with those who entrust themselves to our care.

The Board of Regents has closely followed the work of the external review panel and is aware of OLA's findings. Chair Beeson and Regent Simmons have already created a plan for the Board to take an active role in shaping the University's action plan. The Board will provide ongoing implementation oversight through its Audit Committee to ensure transparency and accountability. I look forward to demonstrating to the Regents our commitment to improve.

To that end we are taking immediate actions:

- Suspending enrollment in all Department of Psychiatry interventional drug studies currently active or awaiting approval, until they have been reviewed by an independent institutional review board (IRB), which will recommend to the University Institutional Official (Dr. Brian Herman) whether or not the suspension should be lifted.
- Creating an Implementation Team to review and prioritize the external panel's recommendations, develop a plan to implement them, and oversee the

implementation. They will report action items and the implementation plan to President Kaler within 60 days (May 15, 2015).

- Using an independent IRB and the University's post approval monitoring process, we will sample additional interventional clinical studies targeting vulnerable populations to guarantee that ongoing activities are appropriate and consistent with approved protocols, and that interactions with human subjects are consistent with the recommendations of the external review panel.
- Appointing a Community Oversight Board, comprised of external experts in human subjects research and research ethics with special emphasis in the area of working with individuals with diminished mental capacity, to make sure that the University's approaches to human subject research are leading practice.
- Visiting leading institutions to learn the best practices followed by their IRBs.
- Implementing new IRB software to enhance the efficiency of the IRB review processes and oversight.

This work has already begun. Before we received the Legislative Auditor and external panel reports, the University committed significant new resources to its Human Research Protection Program (HRPP) and to hire more training and post-approval monitoring staff. We are actively adding more members with relevant expertise to the Institutional Review Board (IRB). We have also established a Research Compliance Advisory Committee that includes nationally recognized experts to consult on strategic risk management in research, including the conduct of human subjects research in individuals with diminished mental capacity.

The University has attempted to address numerous questions about how individuals with diminished mental capacity are engaged in human subjects research. We are sorry that, in particular related to the case of Mr. Markingson, our response has come across as defensive. We want to assure you that our only intent has been to be factual in our responses. The University has relied on the external agencies charged with investigating such matters (the FDA, the Minnesota Board of Medical Practice, and the Hennepin County District Court), to inform us of any deficiencies in our processes and practices and affirm our compliance with laws and regulations.

The University did not influence any of the external reviews and none of those previous reviews reported regulatory violations or alerted us to ethical breaches. If these external reviews were flawed, we were not aware of those shortcomings. We believe that the University's statements were not misleading, but in retrospect, with the recent broader review performed by the external panel and the Legislative Auditor's report, we are now aware that some of our practices have not been above reproach. We regret not identifying our own shortcomings ourselves, and are committed to being transparent and responsive as we move forward.

The independent panel review importantly notes that "the federal human subjects regulations that lie behind and most often animate institutional policy and procedure are all but silent with regard to the protection of individuals with impaired decision making and individuals from populations in which such impairment is lacking." This area of human subject research is

James Noble
March 18, 2015
Page 3

continually evolving and the University is committed to improving our practices and serving as a national model of excellence.

As we move forward, we will use the independent panel's and Legislative Auditor's reports to improve. And we will take an introspective look at ourselves to improve our culture, enhance our policies and practices, make new investments, and reinvigorate our commitment to training, oversight and accountability.

As the independent panel report states there is "much strength in the University's human subjects program and the value of the newly implemented enhancements in policy and practice. The vast majority of faculty and staff demonstrated pride in their work, obvious dedication to the ethical conduct of research, and a desire to improve performance." We have an excellent foundation on which to build.

We appreciate the opportunity to discuss the Legislative Auditor's report with the Senate Higher Education and Workforce Development Committee. We look forward to using this report to improve our human subjects research program and ensure we are beyond reproach.

Sincerely



Eric W. Kaler
President

- cc: Regent Richard Beeson, chair
Regent Dean Johnson, vice chair
Regent Thomas Anderson
Regent Laura Brod
Regent Linda Cohen
Regent Thomas Devine
Regent Michael Hsu
Regent Peggy Lucas
Regent David McMillan
Regent Abdul Omari
Regent Darrin Rosha
Regent Patricia Simmons
Brooks Jackson, dean of the Medical School & Vice President, Academic Health Sciences
Brian Herman, vice president, Research
William Donohue, general counsel
Gail Klatt, associate vice president, Internal Audits