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May 13, 2015

The Honorable Sylvia Mathews Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Secretary Burwell:

Public Citizen, a consumer advocacy organization with more than 350,000 members and supporters nationwide, is writing to express alarm regarding the Office for Human Research Protections' (OHRP) recent decisions (a) not to launch a formal compliance oversight investigation into the human subjects protection program at the University of Minnesota (UM) under the institution's Federalwide Assurance in response to our March 16 complaint letter to the agency (copy enclosed), and (b) not to require UM to suspend enrollment in all ongoing human subjects research, particularly high-risk clinical trials, that had inadequate review by the UM medical institutional review board (IRB) until appropriate re-review by the IRB occurs.

As noted in our complaint letter to OHRP, a recently released report — commissioned by UM through a contract with the Association for the Accreditation of Human Research Protection Programs and prepared by an external review team comprising six experts[1] — documented in detail serious, systemic failures in UM's system for protecting human subjects and signs of widespread violations of Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 C.F.R. Part 46).

Among the most troubling findings of the external review team were the following:

- The UM medical IRB routinely lacked appropriate expertise among its members when reviewing research at convened meetings.

[1] Association for the Accreditation of Human Research Protection Programs. An External Review of the Protection of Human Research Participants at the University of Minnesota with Special Attention to Research with Adults Who May Lack Decision-Making Capacity: Final Report. February 23, 2015. https://www.scribd.com/doc/257152188/AAHRPP-Final-Report-With-Prefatory-Note-and-Cover-Letter. Accessed May 11, 2015.

- When reviewing and approving research, the UM medical IRB failed to ensure that:
  - risks to subjects are minimized and reasonable in relation to potential benefits; and
  - the informed consent of subjects always is obtained under circumstances that minimize the possibility of coercion or undue influence.

The findings of the external review team echo other serious instances of systemic failures of human subjects protections at major academic institutions uncovered by OHRP over the past two decades. Such findings represent an obvious threat to the rights and welfare of human subjects enrolled in medical research studies at UM and, therefore, warrant immediate suspension or restriction of UM's Federalwide Assurance pending implementation of appropriate corrective actions. These actions should include re-review of ongoing human subjects research projects overseen by the UM medical IRB in a manner that fully complies with all requirements of 45 C.F.R. Part 46.

Despite the gravity of the noncompliance documented at UM by the external review team, OHRP informed Public Citizen by email on April 28 that the agency has not opened a compliance oversight investigation of UM's human subjects protection program. Furthermore, OHRP stated:

> [UM] is implementing numerous corrective actions related to these matters and has suspended enrollment in all its Department of Psychiatry interventional drug studies. OHRP is coordinating with [the Food and Drug Administration] on this matter and has requested a follow-up report from [UM].

UM's limited suspension of enrollment in Department of Psychiatry interventional drug studies and OHRP's request for a follow-up report from the university are grossly inadequate actions given that the serious deficiencies identified by the external review team clearly extend well beyond Department of Psychiatry research. As detailed in our complaint letter to OHRP, the external review team identified deficiencies in expertise among UM medical IRB members which extend to the fields of adult hematology, oncology and transplant, cardiology, surgery, and neurology, fields which taken together represent over 300 protocols reviewed by the UM medical IRB from October 1, 2013, through September 30, 2014. Minutes from UM medical IRB meetings revealed little discussion of risks and benefits during most reviews for new biomedical research proposals, proposals in fields not limited to psychiatry. Finally, the length of time allotted for IRB review was alarmingly inadequate given the number of complex items scheduled for review, in areas not limited to psychiatric research.

OHRP's failure to open a formal compliance oversight investigation at UM or to take aggressive enforcement action represents a disturbing abrogation of the agency's responsibility for protecting human subjects. Unfortunately, such relative inaction reflects a continuing pattern of scant compliance oversight action by the agency in recent years.

In closing, Public Citizen urges you to direct OHRP (a) to reverse its decision not to open a formal compliance oversight investigation of UM's system for protecting human subjects, and (b) to mandate that UM suspend enrollment in all ongoing human subjects research, particularly

high-risk clinical trials, that had insufficient review by the UM medical IRB until appropriate re-review by the IRB occurs.

Thank you for your prompt attention to this urgent matter regarding the protection of human subjects.

Sincerely,

Michael A. Carome, M.D.
Director
Public Citizen's Health Research Group

Enclosure

cc: Dr. Karen B. DeSalvo, Acting Assistant Secretary for Health, HHS
Dr. Wanda K. Jones, Principal Deputy Assistant Secretary for Health, HHS
Dr. Jerry Menikoff, Director, OHRP, HHS
Dr. Kristina Borror, Director, Division of Compliance Oversight, OHRP, HHS