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May 1, 2019

Jerry Menikoff, M.D., J.D.
Director
Office for Human Research Protections
U.S. Department of Health and Human Services
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

RE: Project Title: Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis Trial
Sponsor: National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health
Principal Investigator: David A. Schoenfeld, Ph.D., Massachusetts General Hospital, Clinical Coordinating Center for the NHLBI-funded Clinical Trials Network for the Prevention and Early Treatment of Acute Lung Injury (PETAL Network)
ClinicalTrials.gov Identifier: NCT03434028

Dear Dr. Menikoff:

As you are aware, *The Wall Street Journal* (*WSJ*) on April 28 reported that senior National Institutes of Health (NIH) officials, including Principal Deputy Director Lawrence A. Tabak,[1] explicitly forbade Drs. Charles Natanson and Peter Eichacker — two senior scientists at the NIH Clinical Center — from communicating with the Office for Human Research Protections (OHRP) about serious ethical and regulatory lapses involving the ongoing NIH-funded Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis **(**CLOVERS) trial that were presented in Public Citizen's August 28, 2018, letter to the OHRP, despite a direct request from your office to interview these scientists about these issues.

In light of these disturbing revelations, Public Citizen urges the OHRP to immediately (a) cease its ethics-undermining subservience to the NIH, invoke its authority under the U.S. Department of Health and Human Services (HHS) human subjects protection regulations at 45 C.F.R. Part 46.103(c), and suspend the CLOVERS trial until the NIH allows these scientists to speak to your staff and your office has completed its compliance oversight evaluation of the trial; and (b) demand that the HHS Inspector General immediately launch a formal investigation to scrutinize the conduct of senior NIH officials in this matter. The OHRP should have taken such actions months ago.

The OHRP is the chief regulatory agency charged with implementing and enforcing the HHS human subjects protection regulations. Among the agency's core responsibilities is to conduct compliance oversight evaluations of substantive allegations of noncompliance with these regulations that involve research funded by the NIH and other HHS agencies.

[1] Burton TM. NIH blocks two doctors from speaking out to investigators. *The Wall Street Journal*. April 28, 2019. https://www.wsj.com/articles/nih-blocks-two-doctors-from-speaking-out-to-investigators-11556456520. Accessed April 30, 2019.

It is our understanding that OHRP, in evaluating our complaint, sought input from Drs. Natanson and Eichacker regarding the adequacy of revisions to the CLOVERS protocol that were made subsequent to our complaint to OHRP.

The reported efforts by senior NIH officials, as described by the *WSJ*, to muzzle Drs. Natanson and Eichacker and thereby effectively interfere in the OHRP's compliance oversight evaluation of the alleged serious ethical and regulatory lapses involving CLOVERS constitute gross misconduct and corruption at the highest levels of the NIH, tantamount to an obstruction of ethical justice for the subjects of the CLOVERS trial. Such misconduct demonstrates that senior NIH officials are more interested in protecting the organization from public criticism and avoiding potential embarrassment than in protecting the rights and welfare of human subjects.

As you know, the OHRP — formerly the Office for Protection from Research Risks (OPRR) in the NIH Office of the Director — was administratively relocated from the NIH to the HHS Office of the Secretary in large part because of the conflicts of interest that existed between NIH, the largest federal funder of human subjects research, and the OPRR. Consistent with the main purpose of that relocation, NIH cannot be allowed to have any role in determining with whom OHRP staff speak when conducting compliance oversight evaluations of NIH-funded research.

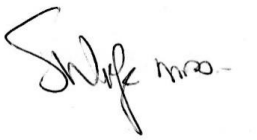
It is imperative that any NIH employee who has concerns about ethical or regulatory violations related to the protection of human subjects in any NIH-funded (or other) clinical trial be free to communicate with the OHRP about those concerns without fear of reprisal. The unconscionable actions of the NIH leadership to prohibit such communications with OHRP undermine the protections for human subjects who are enrolled in NIH-funded research and, ultimately, public trust in NIH.

Likewise, the fact that OHRP has not already leveraged its regulatory authority by suspending the CLOVERS trial in response to the intransigence of NIH leadership represents a serious failure of leadership by the OHRP and erodes public trust in your agency.

We hope you share our concern regarding this troubling matter, and we look forward to an appropriate, favorable response to our urgent request. Please contact us if you have any questions or need additional information.

Sincerely,

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



Sidney M. Wolfe, M.D.
Founder and Senior Adviser
Public Citizen's Health Research Group

Enclosure

cc: The Honorable Alex Azar, U.S. Secretary of Health and Human Services
ADM Brett P. Giroir, M.D., Assistant Secretary for Health, HHS