Embargoed Until: 7:00 a.m. EST Wednesday, Mar. 9, 2016

Contact: Angela Bradbery, abradbery@citizen.org, (202) 588-7741
Karilyn Gower, kgower@citizen.org, (202) 588-7779

New Evidence Validates Call for Unethical Trial to Be Investigated, Suspended

Study Forces Hundreds of Resident Doctors Nationwide to Work Dangerously Long Shifts, Placing Them and Their Patients at Risk of Serious Harm

WASHINGTON, D.C. – Newly obtained government documents regarding a highly unethical clinical trial that forces many first-year medical residents to work dangerously long shifts provide further evidence that the trial violates basic ethical principles and federal regulatory requirements for the protection of human subjects, Public Citizen and the American Medical Student Association (AMSA) said in a letter today.

The letter was sent to the U.S. Department of Health and Human Services' (HHS) Office for Human Research Protections (OHRP). In November and again in February, Public Citizen and AMSA called on OHRP to investigate two highly unethical trials – iCOMPARE and FIRST – both compelling many first-year medical residents to work shifts of 28 consecutive hours or more – nearly twice the current maximum number of hours allowed for such residents. Public Citizen and AMSA also urged OHRP to suspend the ongoing iCOMPARE trial. OHRP failed to launch an investigation of either trial or suspend the ongoing iCOMPARE trial, which involves internal medicine residents at 63 residency training programs across the country.

"It is urgent that the iCOMPARE trial be suspended and investigated given that residents and their patients continue to be put at risk," said Dr. Michael Carome, director of Public Citizen's Health Research Group. "The newly obtained documents show overwhelming evidence of egregious ethical and regulatory lapses regarding the design, conduct and oversight of the trial. iCOMPARE epitomizes a human subjects protection system that has failed dismally at all levels."

Public Citizen recently obtained the documents from the National Institutes of Health (NIH), one of the funders of the iCOMPARE trial, under a Freedom of Information Act request. Some significant findings include:

- At least 56 of the 63 internal medicine training programs participating in the iCOMPARE trial, either: (1) did not have the required institutional review board (IRB) review because the trial was found — incorrectly — not to involve human subjects research or to involve

only exempt human subjects research; or (2) did have the IRB review occur, but the IRBs reviewed the trial using an expedited review procedure, even though the trial did not qualify for such a review procedure. An expedited review procedure typically involves a single IRB member. However, it is highly doubtful that a single individual would have had sufficient breadth of expertise, training and background to make the complex regulatory and ethical determinations required for IRB review of the iCOMPARE trial.

- Nearly three months ago, OHRP received the same records from NIH documenting the serious failures regarding IRB review of the iCOMPARE trial, but has yet to take action to intervene to protect human subjects by opening an investigation or suspending the trial.
- Documents, which appear to have been created more than three months after the iCOMPARE trial began, support Public Citizen and AMSA's previously stated contention that the research involves greater than minimal risk for the resident subjects enrolled at institutions randomized to the experimental group. In particular, the documents indicate that the iCOMPARE researchers recognized that the trial's experimental intervention could be exposing the resident subjects to increased risks of motor vehicle accidents, needle-stick injuries that can expose the residents to bloodborne pathogens, and depression due to sleep deprivation. These events needed to be carefully monitored during the trial to ensure the safety of the resident subjects. But there is no evidence that the IRBs that reviewed the trial were informed of these risks and the details of the monitoring plan.
- The NIH's National Heart, Lung and Blood Institute required that a Data and Safety Monitoring Board (DSMB) be established to collect and monitor serious adverse events in the subjects of the iCOMPARE trial, including the residents. One key role of any DSMB is to monitor the safety of subjects while the trial is ongoing. However, the iCOMPARE DSMB didn't convene for the first time until more than three months after the trial began. Failing to have a fully functioning DSMB and monitoring plan prior to the start of such a high-risk trial represents an additional failure to ensure iCOMPARE subjects' risks are minimized.

"In light of the increasingly overwhelming evidence of widespread, serious ethical and regulatory violations related to the iCOMPARE trial, a decision by OHRP to not initiate a formal for-cause compliance oversight evaluation of all institutions participating in this unethical trial would constitute an unacceptable abuse of the agency's discretion and an abrogation of its fundamental responsibility to protect human subjects," the letter concludes.

Public Citizen and AMSA also sent a letter to the HHS Acting Assistant Secretary for Health, Dr. Karen DeSalvo, who is the immediate supervisor of the OHRP director, requesting an urgent meeting.

Read the letter to OHRP. Read the letter to the HHS Assistant Secretary for Health.

###