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Public Citizen: Epilepsy Trial Violated Regulations

Watchdog organization Public Citizen is urging the Office for Human Research Protections, the Food and Drug Administration (FDA) and NIH Director Francis Collins to investigate an NIH-funded trial of epilepsy treatments that enrolled more than 400 subjects at 58 U.S. hospitals. In June 8 letters to the agencies, Michael Carome, M.D., director of Public Citizen's Health Research Group, said the goal of the Established Status Epilepticus Treatment Trial (ESETT) was to assess whether one of three anticonvulsant drugs would "result in better seizure resolution and responsiveness within 60 minutes after initiation of the assigned drug, without additional anticonvulsant medications," in patients who had already been treated with benzodiazepines following a seizure.

During the trial, which ran from November 2015 to December 2018 and enrolled subjects aged one to 94, no consent was obtained because ESETT was conducted "under an exception from the informed consent requirements for emergency research" under FDA regulations. Drugs were administered on a random basis, and there were other marked deviations from usual care, including possible underdosing of subjects over a certain weight, Carome alleged. He also found that "enrollment of subjects who were Black in ESETT was disproportionately high compared with the proportion of patients hospitalized" for this condition. The 60-minute requirement was also "an exceptionally long time," Carome wrote, and may have "potentially deprived clinicians of valuable information that could have been used to guide further anticonvulsant drug therapy." The design of the study precluded "appropriate monitoring to ensure the safety of enrolled subjects," Carome concluded. "As a result of these multiple fundamental flaws in the trial's design, it appears that risks to the subjects enrolled in ESETT were not minimized, nor were they reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge expected to result." Public Citizen asked that the agencies "immediately launch compliance oversight investigations of ESETT and the adequacy of the trial's review and approval by the responsible" institutional review boards, among other issues.

Link to letter to OHRP, FDA