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NIH accused of interfering in ethics probe

E-mails suggest agency was allowed to influence an external investigation of one of its clinical trials.

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When US government investigators determined last year that a trial funded by the US National Institutes of Health (NIH) violated human-subject protections, the agency did something unusual — it disputed the finding. But internal e-mails released today by a watchdog group suggest that the NIH had a role in drafting the investigators' report.

The controversy stems from a multi-site, NIH-funded trial to study the effects of supplemental oxygen in premature infants. Such treatments can improve the chances of survival in these infants, but doses that are too high can cause blindness.

The trial tested high and low oxygen doses in 1,300 infants. Both doses tested fell within the normal range of care that the infants would have received had they not been enrolled in the trial, but in March 2013, the Office of Human Research Protections (OHRP) at the US Department of Health and Human Services (HHS) — which oversees the NIH — said that parents were not adequately informed of the study's risks. The OHRP also threatened to sanction the study's lead investigators.

The NIH pushed back against the findings. In a June 2013 commentary in the *New England Journal of Medicine*, agency director Francis Collins and other officials disputed the OHRP's findings, arguing that the trial was ethically designed and that investigators could not have foreseen the risks. Earlier that month, the OHRP said in a letter to the lead trial site that it had backed off its plans to sanction the study's researchers.

Subsequently, the HHS promised to revise and clarify its rules on informed consent in trials that fall within normal standards of care. The agency says that those rules are still being drafted.

But according to e-mails obtained by the non-profit watchdog organization Public Citizen in Washington DC, NIH officials corresponded extensively with OHRP investigators before the June letter was released, and were allowed to edit its drafts. The documents are highly redacted, making it hard to determine what changes, if any, the NIH sought. But they do show Collins thanking HHS investigators for the opportunity to "weigh in", and suggest that the NIH delayed the letter's release.

Asked about the correspondence, an HHS spokesperson said that the "OHRP regularly works with entities such as the NIH, [institutional review boards] and others to ensure the protection of human subjects in research."

But Michael Carome, director of health research at Public Citizen, calls the situation "unprecedented". He notes that the OHRP was designed to be independent of the NIH. "It's almost irrelevant whether any changes were made to the letter. It compromises the integrity of the OHRP by even giving the NIH the opportunity to look at the letter, much less review serial drafts," he adds.

Public Citizen and US Representative Rosa DeLauro have both sent letters to the HHS inspector general calling for an investigation into the officials' actions.

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