



DEPARTMENT OF HEALTH AND HUMAN SERVICES

OFFICE OF INSPECTOR GENERAL

WASHINGTON, DC 20001



Report of OIG Review of Allegations of Interference in OHRP Compliance Determination for SUPPORT September 2014

This review responds to Congressional, consumer advocacy group, and public requests that the Office of Inspector General (OIG) examine whether officials of the National Institutes of Health (NIH) improperly intervened in the compliance oversight deliberations of the Office of Human Research Protections (OHRP) with respect to the NIH-funded study, Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT). Further, the Congressional request asked that individuals who intervened in the OHRP revised determination letter be held accountable and asked whether OHRP should be relocated from its current location in the Office of the Assistant Secretary for Health to prevent NIH and other interference.

Our review found no indication that NIH or other Department of Health and Human Services (HHS) officials sought to intervene in OHRP's initial determination letter regarding SUPPORT. Our review did confirm that after the initial letter was issued, NIH encouraged OHRP to reverse its determination and that NIH and others in HHS provided input on OHRP's later clarification letter.¹ The emails contained no directive or order to OHRP from NIH or any other official to take a particular policy or scientific position; instead, the NIH emails contained arguments in support of a conclusion different from that reached by OHRP. Our research disclosed no law, regulation, or written policy that prohibits or restricts the kind of consultation that occurred here or would make such consultations improper. That is, no law establishes OHRP's organizational independence (indeed, no statute mentions OHRP by title at all) or prohibits the HHS Secretary from seeking input from other HHS components on OHRP determinations.

If HHS or the Congress were interested in institutionalizing OHRP's independence, there are models elsewhere in the Federal Government. For example, the Inspector General (IG) Act provides both organizational and operational independence. However, even with such a model for independent reviews, Federal OIGs routinely consult with experts in the programs they review. In fact, the Generally Accepted Government Auditing Standards issued by the Government Accountability Office (GAO) specifically provide for such consultation, stating that seeking comment "by responsible officials of the audited entity and others helps the auditors develop a report that is fair, complete, and objective[.]"

Although we confirmed that officials outside OHRP commented on and suggested changes to its revised letter, OIG identified no laws, rules, or policies that were violated by these actions. No

¹ To distinguish this second letter from OHRP's initial compliance determination letter, we here refer to the later correspondence as the "clarification" or "revised" letter.

law mandates OHRP's operational independence. Accordingly, we found no basis for action against the individuals involved.

I. BACKGROUND

A. OHRP

Section 491 of the Public Health Service Act (42 U.S.C. § 289) directs the Secretary of Health and Human Services to establish a process to respond to alleged violations of human subjects protection in research conducted or supported by HHS. The Secretary delegated this responsibility to the newly created OHRP in 2000.² The function was moved from its former organizational location within NIH to the Assistant Secretary for Health within the Office of the Secretary, in part, to minimize the possibility or the appearance of a conflict of interest between a funding agency and the office ensuring protection of human subjects in that funded research. However, neither section 491 nor the delegation to OHRP prohibits OHRP from soliciting, receiving or considering input from other components of HHS, including the funding agencies.

Under the above authority, when OHRP receives an allegation of a violation, it may conduct a for-cause compliance evaluation. OHRP has developed procedures for conducting such an evaluation. In general, OHRP's process includes notifying the institution engaged in the research and requesting that it investigate the allegation, provide a written response with supporting documents, and develop a corrective action plan if any noncompliance is revealed. OHRP evaluates the institution's response and issues a determination letter addressing the allegation of noncompliance. If OHRP identifies noncompliance with human subjects protection regulations, it can (1) require the institution to take corrective measures, such as developing a corrective action plan or improving institutional policies; (2) restrict or suspend research at the institution; and/or (3) recommend that an institution or investigator be debarred from receiving Federal funds for research.³

OHRP has considerable discretion in this process. For example, OHRP is able to determine whether to conduct a for-cause compliance evaluation; how to assess the institution's investigation; whether to consult with experts or conduct a site visit; and what, if any, are appropriate corrective actions.

B. SUPPORT

SUPPORT was a randomized multisite study funded by NIH that enrolled about 1,300 premature infants between 2005 and 2009. One purpose of the study was to determine the appropriate levels of oxygen saturation in infants with extremely low birth weight by comparing lower and higher levels of oxygen saturation in them. The University of Alabama, Birmingham (UAB), was the lead coordinating institution of the 23 sites in the study.

In May 2011, OHRP received a complaint about SUPPORT alleging that the study design was unethical because some infants received "severely reduced" oxygen and the researchers had not

² 65 Fed. Reg. 37136 (June 13, 2000).

³ OHRP, *Compliance Oversight Procedures for Evaluating Institutions* (Oct. 14, 2009), <http://www.hhs.gov/ohrp/compliance/evaluation/>.

obtained informed consent.⁴ In response, OHRP conducted a for-cause compliance evaluation of SUPPORT at UAB. OHRP issued a determination letter to UAB on March 7, 2013,⁵ in which it set out background information on the retinopathy of prematurity and its association with oxygen levels provided to premature infants, summarized SUPPORT, and analyzed the SUPPORT experimental protocol and its consent form template. OHRP determined the consent form did not meet regulatory requirements for informed consent. OHRP required UAB to provide a corrective action plan to its Institutional Review Board to ensure that its approved informed-consent documents include the elements of 45 CFR § 46.116(a). OHRP notified NIH prior to initiating its compliance evaluation, and NIH provided OHRP with SUPPORT study documents.

SUPPORT and OHRP's initial determination letter received significant attention in the media and in professional publications. The letter triggered a public debate among prominent scholars, physicians, and bioethicists concerning informed consent requirements in research testing treatments within a standard of care; whether SUPPORT was such research; and the state of knowledge of reasonably foreseeable risks at the start of SUPPORT, among other issues.

In response to the concerns of the research community and NIH, OHRP issued a clarification letter to UAB on June 4, 2013.⁶ OHRP reaffirmed its decision that UAB's informed consent document for SUPPORT was inadequate, but acknowledged the difficulty in defining reasonably foreseeable risks in research involving interventions considered to be within the standard of care. OHRP put on hold compliance actions against UAB relating to SUPPORT and committed to providing guidance on this topic. Later that month, HHS announced a public meeting on how human subjects protection regulations should be applied to research on interventions within the standard of care. This public meeting was held on August 28, 2013.

II. DISCUSSION

OIG has been asked to determine whether officials of NIH inappropriately influenced OHRP's revised determination letter regarding SUPPORT. A request to OIG from a Member of Congress referenced redacted emails that HHS had produced for a consumer advocacy group pursuant to a request under the Freedom of Information Act. OIG obtained the same set of emails; however, we reviewed those emails without redactions. We also reviewed additional documentation and researched applicable law and policies governing OHRP operations.

Our review confirmed that NIH provided input on OHRP's clarification letter regarding SUPPORT.⁷ There were numerous emails in which NIH officials disagreed with aspects of OHRP's initial determination letter and encouraged OHRP to revise it. Generally, arguments and counterarguments were made to senior officials in the chain of command for OHRP. In some instances, NIH positions apparently prevailed; in others, OHRP arguments did. As is evident from the two determination letters, OHRP did not alter its determination that UAB's informed consent for SUPPORT was in violation of human subjects protection regulations. Emails also acknowledged that the ultimate decision on the content of its determination letter was OHRP's.

⁴ OIG received an earlier Congressional request to conduct a review to determine whether OHRP followed its procedures in its compliance evaluation of SUPPORT. This review is available at <https://oig.hhs.gov>.

⁵ http://www.hhs.gov/ohrp/detrm_lettrs/YR13/mar13a.pdf.

⁶ http://www.hhs.gov/ohrp/detrm_lettrs/YR13/jun13a.pdf

⁷ The emails we reviewed did not indicate that NIH provided input on OHRP's initial determination letter (though it did receive a copy prior to issuance).

The emails contained no directive or order to OHRP from NIH or from senior officials in HHS to take any particular policy or scientific position.

Senior level officials of HHS were involved in the discussions between OHRP and NIH regarding SUPPORT. The emails indicate that this was prompted by the publicity and controversy surrounding SUPPORT, correspondence from bioethicists on both sides of the issue, and correspondence from a consumer advocacy group. These senior officials were generally in the direct line of supervision of OHRP; their goal seemed to be to resolve a disagreement—primarily a scientific disagreement—between two components within HHS.

Occasionally, OHRP and NIH sought input from the Office of the General Counsel and staff of relevant public affairs and communications offices. Many of these emails discussed responses to public inquiries generated by both of OHRP's determination letters.

A. OHRP Legal Authorities

To determine whether the interactions disclosed in internal SUPPORT-related emails violated Federal rules, we researched OHRP's authorizing statutes, implementing regulations, and policies. Specifically, we looked for any prohibitions on interference in OHRP compliance activities or OHRP consultation with other HHS components. Further, we examined the applicable authorities to determine whether OHRP was granted organizational independence from other agencies in making compliance determinations. Following is a brief summary of those authorities and our findings.

OHRP's authority to act derives from 42 U.S.C. § 289(b)(2). It reads in full:

The Secretary shall establish a process for the prompt and appropriate response to information provided to the Director of NIH respecting incidences of violations of the rights of human subjects of research for which funds have been made available under this [Act]. The process shall include procedures for the receiving of reports of such information from recipients of funds under this [Act] and taking appropriate action with respect to such violations.

The statute does not name OHRP or its predecessor, the Office for Protection from Research Risks (OPRR). It does not stipulate any particular office in HHS that must take on the responsibility for human research subjects protection. Until 2000, responsibility was assigned to various offices in NIH, lastly to OPRR in the Office of the Director at NIH. In 1999, the Director convened a review panel to study both the sufficiency of the authorities exercised by OPRR and its organizational location. That panel recommended that OPRR be moved from NIH to the Office of the Secretary and that it report to the Assistant Secretary for Health or the Surgeon General. One reason for this recommendation was that OPRR was perceived to be affected by conflicts of interest because it was located within NIH, but was tasked with reviewing research conducted by NIH staff and grantees. The Secretary agreed and in 2000, the OPRR function was transferred to the Office of the Secretary and OHRP was created.⁸ As recommended, OHRP reports to the Assistant Secretary for Health.

⁸ 65 Fed. Reg. 37136 (June 13, 2000).

OHRP is responsible for developing, monitoring, and providing compliance oversight for HHS regulations for the protection of human subjects in research conducted or supported by HHS. These rules are housed at 45 CFR Part 46. OHRP's compliance oversight division has issued compliance oversight procedures it follows when conducting evaluations and recommending corrective actions. The current version of this policy is OHRP's *Compliance Oversight Procedures for Evaluating Institutions* updated in 2009.⁹

Finally, the HHS Grants Policy Statement and NIH Grants Policy Statement discuss OHRP's responsibility for oversight of grantee compliance with the HHS human subjects' regulations. It includes OHRP's compliance oversight evaluations and corrective actions.

None of the above statutes, regulations, or policy documents bars HHS components from expressing opinions on proposed OHRP compliance findings or prohibits OHRP from consulting with NIH or other components in HHS. In fact, such professional consultation seemed to be contemplated by the 2000 OPRR Review Panel report that recommended moving the function out of NIH and into the Office of the Secretary. That report explicitly discussed the benefits of such consultation:

Once OPRR is not in the line of authority within NIH, it should be more comfortable in engaging NIH in discussions on difficult issues knowing that if consensus eludes the process, the differences of opinion will be presented to the Secretary for discussion.

In short, we found no Federal legal authority that proscribes the interactions in the emails we reviewed or directs that OHRP have organizational independence. Thus, there is no basis for OIG to recommend action against the individuals involved.

B. Requirements as to Organizational or Operational Independence

As noted above, OHRP legal authorities do not mandate that it be independent. If HHS or the Congress were interested in providing OHRP organizational or operational independence, there are models in Federal law where functions or offices are granted this type of independence. One of the most extensive grants of independence is to the statutory Inspectors General, who report only to their Secretaries¹⁰ and even they may not "prevent or prohibit" the IGs from undertaking or completing particular inquiries. (Other examples we found in a cursory statutory search included: explicit grants of organizational independence (Office of Research Integrity, 42 U.S.C. § 289(b)(1); directions that an entity report solely to a particular official (Office of Child Support Enforcement Audit Division, 42 U.S.C. § 652(a)); authorization to communicate views to agency officials without prior approval (Director of Operational Test and Evaluation in the Department of Defense (10 U.S.C. § 139); and prohibitions on intervention in enforcement actions (Office of the Comptroller of the Currency, 12 U.S.C. § 1(b)).¹¹

⁹ OHRP, *Compliance Oversight Procedures for Evaluating Institutions* (Oct. 14, 2009), <http://www.hhs.gov/ohrp/compliance/evaluation/>.

¹⁰ The Secretary may delegate this authority to the next ranking official – at HHS, the Deputy Secretary – but to no other official of the Department. (IG Act, § 3(a), 5 U.S.C. App. § 3(a)).

¹¹ We have not examined how these statutory grants of independence operate in the particular agencies; we offer them only as examples of statutory language addressing independence. Further, because we have not conducted an OIG evaluation of vulnerabilities in OHRP structure, we express no opinion on the appropriateness of statutory or administrative independence for OHRP.

Note, though, that even if an OIG-type model of independence were adopted, OIG auditors, inspectors, and evaluators routinely consult with experts in the programs they review. OIG benefits from program staff's technical and programmatic expertise. In fact, the Generally Accepted Government Auditing Standards issued by GAO explicitly provide for such consultation. Specifically, the GAO "Yellowbook" at Chapter 7.2 directs that auditors "should obtain and report the views of responsible officials of the audited entity concerning the findings, conclusions and recommendations included in the audit report" GAO further states that providing the audited entity with a draft for review and comment "by responsible officials of the audited entity and others helps the auditors develop a report that is fair, complete, and objective Obtaining the comments in writing is preferred, but oral comments are acceptable." Consultation is also incorporated into the reporting provisions of the *Quality Standards for Inspection and Evaluation*, issued by the Council of the Inspectors General on Integrity and Efficiency.

III. CONCLUSION

OIG confirmed that, after OHRP issued its original compliance determination letter to UAB in March 2013, NIH officials disagreed with the conclusions in that letter and urged OHRP to revise them. Officials outside OHRP, including NIH officials, also suggested edits to drafts of a clarification letter sent by OHRP to UAB regarding SUPPORT. We found no legal authority that prohibits such consultation.

The emails contained no directive or order to OHRP from NIH or from senior officials in HHS to take any particular policy or scientific position. Although in this case we found no evidence that OHRP was directed to reach a particular conclusion, we also found no legal authority that would bar the Secretary of HHS from doing so. Because we found no violation of law or rule, we found no basis for action against the individuals involved.