PUBLICCITIZEN
1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

May 20, 2014

The Honorable Daniel R. Levinson
Inspector General
U.S. Department of Health and Human Services
330 Independence Avenue, SW
Washington, DC 20201

RE: Senior HHS Officials Allow NIH to Interfere with OHRP's Compliance Oversight Investigation of the Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants: The SUPPORT Study

Dear Inspector General Levinson:

Public Citizen, a consumer advocacy organization with more than 300,000 members and supporters nationwide, and the undersigned individuals are writing to request that your office immediately open a formal investigation to scrutinize the conduct of senior leaders in the Department of Health and Human Services' (HHS's) immediate Office of the Secretary (OS), the Office of the Assistant Secretary for Health (OASH), and other OS components who knowingly allowed the director of the National Institutes of Health (NIH) and other senior NIH officials to interfere with the independence of the Office for Human Research Protections' (OHRP's) ongoing compliance oversight investigation of the SUPPORT study. This interference involved NIH officials reviewing and editing a series of drafts of a pending OHRP compliance oversight determination letter regarding the SUPPORT study, as well as apparently allowing NIH to influence the timing of the release of that letter.

The urgent need for this investigation is based on documents recently obtained by Public Citizen under the Freedom of Information Act (FOIA) which, though heavily redacted, reveal the following:

Over a period of several weeks from April 18 through at least June 4, 2013, numerous senior HHS OS officials, including Deputy Secretary Bill Corr, HHS Chief of Staff Andrea Palm, Assistant Secretary for Health Howard Koh, Principal Deputy Assistant Secretary for Health Wanda Jones, Counselor to the Secretary Caya Lewis, and General Counsel William Schultz, among others, were aware of and, at least passively and in some cases actively, facilitated this interference by NIH.

This occurred despite the fact that NIH — which was involved in the development, approval, funding (at a cost of more than $20 million), conduct, and oversight of the SUPPORT study — had obvious direct conflicts of interest with respect to the investigation of the SUPPORT study by OHRP's Division of Compliance Oversight. Such NIH interference is unprecedented in the

history of OHRP and has seriously compromised the integrity and independence of OHRP's ongoing compliance oversight investigation into the SUPPORT study, fundamentally undermining OHRP's regulatory authority and almost certainly doing long-lasting and possibly irreparable harm to the status of this vitally important regulatory agency, which was established to protect the interests of human subjects.

As you may be aware, in 2000, OHRP — formerly the Office for Protection from Research Risks (OPRR) in the NIH Office of the Director — was administratively relocated from NIH to the HHS OS in large part because of the conflicts of interest that existed between NIH, the largest federal funder of human subjects research, and OPRR, the office responsible for implementing and enforcing HHS human subjects protection regulations (45 C.F.R. part 46). This move was intended to insulate OHRP from exactly the type of NIH interference that has clearly occurred during OHRP's compliance oversight investigation of the SUPPORT study, interference that appears to have culminated in OHRP's decision almost a year ago to indefinitely suspend all compliance activities regarding the study.

A thorough formal investigation by the HHS Office of Inspector General is urgently needed in order to determine the extent to which NIH officials improperly interfered with and were permitted to influence OHRP's compliance oversight activities related to the SUPPORT study.

Below we summarize (a) the long-recognized conflicting interests that exist between NIH and OHRP; (b) NIH's extensive involvement in the oversight and conduct of the SUPPORT study; (c) OHRP's publicly announced compliance oversight actions regarding the study to date; and (d) the documents demonstrating that numerous senior HHS OS officials facilitated NIH's interference in OHRP's ongoing compliance oversight investigation of the study.

I. The long-recognized and well-documented conflicts of interest between NIH and OPRR/OHRP

Substantial conflicts of interest have existed — and always will exist — between NIH and OHRP. They have been well-known for many years and were documented in a series of reports and papers authored by the U.S. General Accounting Office (now the Government Accountability Office), the National Bioethics Advisory Commission (NBAC), scholars commissioned by NBAC, and a review panel convened by a former NIH Director. Detailed pertinent excerpts from each of these reports and papers are presented in Appendix A. We highlight a few of the key comments and conclusions from each of these reports and papers here:

In its March 1996 report, *Scientific Research: Continued Vigilance Critical to Protecting Human Subjects*, the U.S. General Accounting Office noted the following:[1]

> NIH's organizational structure may hamper OPRR's independent oversight and enforcement of human subject protection regulations …

[1] U.S. General Accounting Office. *Scientific Research: Continued Vigilance Critical to Protecting Human Subjects.* March 1996. http://www.gao.gov/assets/230/222250.pdf. Accessed May 6, 2014.

> From a broader organizational perspective, **a potential weakness exists because NIH is both the regulator of human subject protection issues as well as an institution conducting its own human subject research.** The Director of NIH, therefore, has responsibility for both the success of NIH's intramural research program and for the enforcement of human subject protection regulations by OPRR. [Emphasis added]

A few years later, in a paper commissioned by NBAC before OHRP was established, John C. Fletcher at the University of Virginia examined the adverse implications of having OPRR be located within NIH beyond those related to NIH's intramural research program. He concluded the following:[2]

> OPRR's location within the NIH is a structural conflict of missions and incompatibility of functions. This structural conflict gives rise to several troubling and persistent problems—including conflicts of interest—for the professional staff of OPRR and the NIH officials who administer OPRR. …
>
> OPRR's mission is to uphold the primacy of the rights and welfare of [human subjects of research]. This mission is enveloped within the NIH's scientific mission and its powerful interests in funding and conducting research. **This conflict of missions weakens OPRR's authority and stature and engenders conflicts of interest.** [Emphasis added]

In a second paper also commissioned by NBAC, Charles McCarthy, who served as Director of OPRR from 1978 until 1992, cited instances of actual conflicts of interest that had arisen between the leadership of NIH and OPRR during his tenure as director.[3] Some of his key recollections included the following:

> On at least one occasion, the Director, NIH, appeared to be taking a step toward interfering with an OPRR investigation. …
>
> While the Gallo/Zagury investigation [by OPRR] was under way, newly appointed Dr. Bernadine Healy, Director, NIH, sent a strongly worded memorandum to the Director, OPRR, directing him to give her a full accounting of the status of the Gallo investigation. …
>
> The Director, OPRR, responded to Dr. Healy by memorandum stating that briefing her could appear to be a conflict of interest because the investigation concerned alleged

[2] Fletcher JC. Location of the Office for Protection from Research Risks within the National Institutes of Health: Problems of status and independent authority. National Bioethics Advisory Commission. *Ethical and Policy Issues in Research Involving Human Participants. Volume II: Commissioned Papers and Staff Analysis.* August 2001. Bethesda, Maryland. https://bioethicsarchive.georgetown.edu/nbac/human/overvol2.pdf. Accessed May 6, 2014.

[3] McCarthy C. Reflections on the organizational locus of the Office for Protection from Research Risks. National Bioethics Advisory Commission. *Ethical and Policy Issues in Research Involving Human Participants. Volume II: Commissioned Papers and Staff Analysis.* August 2001. Bethesda, Maryland. https://bioethicsarchive.georgetown.edu/nbac/human/overvol2.pdf. Accessed May 6, 2014.

> misconduct by one of her most prestigious employees. The Director, OPRR politely declined to provide the briefing.

Dr. McCarthy concluded:

> OPRR must also be protected against interference by its own supervisors.

In its 1999 report to the NIH Director's Advisory Committee, the Office for Protection from Research Risks Review Panel made the following recommendation based on its findings:[4]

> **OPRR should be administratively relocated from its present location within the NIH.** [Emphasis in original]
>
> … in its present location, as a part of the NIH and reporting to supervisors within the NIH, OPRR is not perceived as an independent office. … This perception of dependence and the concerns about conflicts of interest that arise therefrom compromise the ability of OPRR to function most effectively in providing ethical and regulatory leadership in the arenas of research with human subjects and with animals. …
>
> … the relationship to NIH increases the public perception that OPRR will be biased in the direction of protecting research interests at the expense of protections for human subjects and animals. … This positioning leads inevitably to an appearance of conflict that likely, in specific cases, reflects reality. Even the perception of conflict interferes with a vigorous pursuit of the mission of the office.

In 2000, then-NIH Director Harold Varmus and then-Secretary of Health and Human Services Donna Shalala concurred with the above recommendations. As a result, effective June 18, 2000, OPRR was removed from NIH, and OHRP was created as a new office within the Office of Public Health and Science (now OASH) and placed under the supervision of the Assistant Secretary for Health.[5]

Finally, in its 2001 report, *Ethical and Policy Issues in Research Involving Human Participants*, NBAC noted the following regarding the new administrative placement of OHRP, presciently anticipating the current conflicts of interest surrounding the SUPPORT study:[6]

> Furthermore, housing an oversight office within a department that conducts or supports human research could create a conflict of interest. Such a potential conflict provided at least part of the reason for the recommendation to relocate [OPRR] from NIH to the [HHS] Office of the Secretary (OPRR Review Panel 1999). **But this degree of**

[4] *Report to the Advisory Committee to the Director, NIH from the Office for Protection from Research Risks Review Panel.* June 3, 1999. http://acd.od.nih.gov/reports/060399b_OPRR_Review_Panel.htm. Accessed May 6, 2014.
[5] 65 FR 37136-37137.
[6] National Bioethics Advisory Commission. *Ethical and Policy Issues in Research Involving Human Participants.* August 2001. Bethesda, Maryland. https://bioethicsarchive.georgetown.edu/nbac/human/overvol1.pdf. Accessed May 6, 2014.

> **separation may still be insufficient, because NIH is part of [HHS], and the new office is still regulating an organization on which it relies for budgetary and other support. The potential conflict of interest is thus attenuated, but not eliminated.** [Emphasis added]

Current staffs within the HHS OS, OHRP, and NIH undoubtedly are aware of the history regarding the conflicts of interest that existed between NIH and OPRR and the fact that such conflicting interests were the major impetus for placing OHRP in the HHS OS.

II. The NIH-funded SUPPORT study

The SUPPORT study involved two simultaneous complex experiments. In one experiment, following delivery, extremely premature infants were randomly divided into two groups that each received different interventions to assist their breathing (specifically, one group received usual care management to ventilate the lungs, and the other received experimental management using a mask placed over the nose to help ventilate the lungs and strict criteria designed to avoid mechanical ventilation).[7] For the second major experiment conducted as part of the SUPPORT study, the infants who had been assigned to each of the two ventilation groups were further randomly divided between a low-oxygen-saturation target group and a high-oxygen- saturation target group, both of which involved experimental interventions.[8]

The fundamental role played by NIH in the SUPPORT study amounts to a clear substantial conflict of interest that NIH has with respect to OHRP's compliance oversight investigation of this study. In particular, we note the following:

(1) The SUPPORT study was conducted by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN).

(2) NICHD; the National Heart, Lung and Blood Institute (NHLBI); and the National Center for Research Resources provided more than $20 million to fund the SUPPORT study.

(3) Rosemary D. Higgins, M.D., Program Scientist for the Neonatal Research Network, Pregnancy and Perinatology Branch, Center for Developmental Biology and Perinatal Medicine, NICHD, helped oversee the development of the SUPPORT study protocol. Dr. Higgins was also listed as an author on the 2010 papers presenting the primary results of the SUPPORT study that were published in *The New England Journal of Medicine*.[9]

---

[7] SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely premature infants. *N Engl J Med.* 2010;362(21):1970-1979.

[8] SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med.* 2010;362(21):1959-1969.

[9] SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med.* 2010;362(21):1959-1969; and SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely premature infants. *N Engl J Med.* 2010;362(21):1970-1979.

(4) The following NIH staff were identified as investigators who participated in the conduct of the SUPPORT study: Dr. Higgins (NICHD); Stephanie Wilson Archer, M.A. (NICHD); Mary Anne Berberich, Ph.D. (NHLBI); Carol J. Blaisdell, M.D. (NHLBI); Dorothy B. Gail, Ph.D. (NHLBI), and James P. Kiley, Ph.D. (NHLBI).[10]

(5) The following NIH staff were identified as members of the Data and Safety Monitoring Committee (DSMC) that monitored the SUPPORT study: Dr. Blaisdell (NHLBI); Dr. Gail (NHLBI); Carl Hunt, M.D., (NHLBI); and Marian Willinger, Ph.D. (NICHD).[11]

(6) Enrollment in the SUPPORT study was temporarily suspended when 247 subjects had been enrolled on the basis of the recommendation of the DSMC and the decision of the NICHD Director.[12] The NICHD Director certainly must have participated in and likely ultimately made the subsequent decision to allow enrollment in the study to resume.

III. OHRP's compliance oversight actions regarding the SUPPORT study

On February 8, 2013, OHRP issued a compliance oversight determination letter to the University of Alabama at Birmingham (UAB), one of the lead institutions for the SUPPORT study, and the Research Triangle Institute (RTI), the data coordinating site for the trial.[13] (A subsequent letter with identical content, except for the deletion of RTI as an addressee, was issued on March 7, 2013, because OHRP determined that RTI was "not engaged in this human subjects research."[14]) In its letter, OHRP determined that the consent forms for the SUPPORT study failed to adequately inform parents of the reasonably foreseeable risks and discomforts of research participation, as required by HHS regulations at 45 C.F.R. § 46.116(a)(2), including risks of blindness, brain injury, and death. NIH officials were copied on OHRP's initial letter to UAB and RTI, but consistent with long-standing precedent, NIH officials apparently had no involvement in the drafting of the letter.

OHRP required that UAB submit a plan that the institutional review board would use to ensure that approved informed consent documents include and adequately address the basic elements of consent as required by the HHS regulations. The enforcement action taken by OHRP was mild and limited in scope relative to the severity of the ethical lapses that OHRP had found.[15]

---

[10] *Ibid*.
[11] *Ibid*.
[12] SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med.* 2010;362(21):1959-1969.
[13] Office for Human Research Protections. Letter to the University of Alabama at Birmingham and Research Triangle Institute. February 8, 2013.
[14] Office for Human Research Protections. Letter to the University of Alabama at Birmingham. March 7, 2013. http://www.hhs.gov/ohrp/detrm_letrs/YR13/mar13a.pdf. Accessed May 6, 2014.
[15] Carome MA, Wolfe SM. Letter to Secretary of Health and Human Services Kathleen Sebelius regarding the SUPPORT study. April 10, 2013. http://www.citizen.org/documents/2111.pdf. Accessed May 6, 2014; Carome M, Wolfe S, Macklin R. Analysis of the complete protocol and consent form for the SUPPORT study: Lack of informed consent and a failure to ensure that risks were minimized. May 8, 2013. http://www.citizen.org/documents/2124.pdf. Accessed May 6, 2014; and Carome MA, Wolfe SM. Letter to

On June 4, 2013, OHRP issued a second determination letter to UAB that strongly reaffirmed the basis for its original findings regarding inadequate informed consent for the SUPPORT study.[16] However, OHRP also informed UAB that it had "put on hold all compliance actions against UAB relating to the SUPPORT case, and [planned] to take no further action in studies involving similar designs until the process of producing appropriate guidance [on informed consent] is completed." This "hold" apparently is still in effect nearly one year later.

What happened between February and June?

Documents obtained under FOIA strongly suggest that NIH — apparently desperate to undo OHRP's compliance oversight determinations — launched an aggressive campaign to undermine OHRP's regulatory authority and regrettably found several willing partners for this campaign at the highest levels of HHS.

IV. Documents obtained under FOIA reveal NIH's interference in OHRP's ongoing compliance oversight investigation of the SUPPORT study

Although heavily redacted, a series of emails recently obtained by Public Citizen in response to a FOIA request provides convincing evidence that, over a period of several weeks, numerous senior HHS OS officials facilitated the interference by NIH in OHRP's ongoing compliance oversight investigation of the SUPPORT study. Among other things, the emails demonstrate that NIH officials were provided multiple opportunities to review and edit drafts of OHRP's June 4, 2013, compliance oversight determination letter to UAB regarding the SUPPORT study and were allowed to directly influence the timing of the final letter's release. Appendix B provides excerpts from key internal HHS emails regarding this matter.

The following HHS officials appear to have played key roles and been actively involved in NIH's interference with OHRP's oversight activities, displaying ethical lapses in conduct:

- Bill Corr, Deputy Secretary, HHS
- Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS
- Howard Koh, Assistant Secretary for Health, HHS
- Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS
- Jerry Menikoff, Director, OHRP
- Francis Collins, Director, NIH
- Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH

This list will likely grow once the complete documents, without redactions, are made available for review.

Secretary of Health and Human Services Kathleen Sebelius regarding inadequate safety monitoring of the SUPPORT study. January 27, 2014. http://www.citizen.org/documents/2177.pdf. Accessed May 6, 2014.

[16] Office for Human Research Protections. Letter to the University of Alabama at Birmingham. June 4, 2013. http://www.hhs.gov/ohrp/detrm_letrs/YR13/jun13a.pdf. Accessed May 6, 2014.

Here we highlight just a few of the most revealing emails presented in Appendix B, all of which preceded the release of OHRP's June 4, 2013, compliance oversight determination letter to UAB:

(1) April 24, 2013, 4:06 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[17]

- Addressed to: Howard Koh, Assistant Secretary for Health, HHS.
- Subject: OHRP NIH kerfuffle.
- Attachments: SUPPORT study Protocol.pdf; OHRP Letter to UAB.pdf; NEJM letter to the editor 4-17-13 study researchers.pdf; NEJM 4-17-13 Editorial.doc; AAP 2007 Perinatal Guidelines 6th Ed.pdf.
- Message:

> Hi Howard,
> … I am hoping you might have some time to chat about [Redaction, approximately one-quarter of a line in length] concerning the SUPPORT study.
>
> As you know, NIH believes that OHRP [Redaction, approximately 10 lines in length] If you have not read the protocol, please do so.
>
> This matter needs a rapid resolution. [Redaction, approximately three lines in length]…
>
> And please give me a call to discuss how we can move forward effectively.

(2) May 1, 2013, 02:14 AM email from Francis Collins, Director, NIH:[18]

- Addressed to: Bill Corr, Deputy Secretary, HHS.
- Subject: FW: NIH support summary – nih response.
- Message:

> Hi Bill,
>
> … I have been closely tracking efforts by my staff (Kathy Hudson [Deputy Director for Science, Outreach, and Policy, NIH], Alan Guttmacher [Director, NICHD, NIH], and others) who have been working productively with Howard Koh [Assistant Secretary for Health, HHS] and others in [OASH] and OHRP, to develop a consensus set of statements that OHRP could put forward to clarify the situation with the SUPPORT study. Attached is the most recent version (clocked

[17] Department of Health and Human Services documents released to Public Citizen in response to a Freedom of Information Act request. http://www.citizen.org/documents/support-study-HHS-internal-emails.pdf. Page 302. Accessed May 20, 2014.
[18] *Ibid*. Page 224.

> in at 11:59 PM). I understand that you are meeting with Howard [Koh] in the AM, so I thought you might want to see this.
> [Redaction, approximately one line in length] …

(3) May 3, 2013, 4:54 PM email from Jerry Menikoff, Director, OHRP:[19]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Howard Koh, Assistant Secretary for Health, HHS; Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS; and Kirby Bumpus, OASH, HHS.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.
- Subject: RE: Support study -.
- Message:

  > Kathy,
  >
  > For your weekend enjoyment, **here is the revised version of the SUPPORT letter** … [Emphasis added]

[A three-page attachment was provided that is completely redacted except for OHRP's letterhead on the first page.]

(4) May 12, 2013, 02:10 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[20]

- Addressed to: Howard Koh, Assistant Secretary for Health, HHS, and Jerry Menikoff, Director, OHRP.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.
- Subject: **Suggested correction to OHRP-UAB draft letter**. [Emphasis added]

[An apparent two-page attachment is completely redacted.]

(5) May 31, 2013, 6:04 PM email from Jerry Menikoff, Director, OHRP:[21]

- Addressed to: Bill Corr, Deputy Secretary, HHS; William Schultz, General Counsel, HHS; Howard Koh, Assistant Secretary for Health, HHS; Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; Francis Collins, Director, NIH; Peggy Dotzel, Deputy General Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; Caya

[19] *Ibid*. Pages 206-210.
[20] *Ibid*. Pages 134-136.
[21] *Ibid*. Pages 89-95.

Lewis, Counselor to the Secretary for Science and Public Health, HHS; Andrea Palm, Chief of Staff, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Bradley Wolters; and Kirby Bumpus, OASH, HHS.

- Subject: Draft letter to UAB.
- Attachment: 05 31 13 SUPPORT E clean.docx.
- Message:

> All,
>
> **Here is the latest version of the letter to UAB** … [Emphasis added]

[A six-page attachment is completely redacted except for the header "UAB Letter on SUPPORT study—Page 6" and a "DRAFT" watermark on page 6.]

(6) June 2, 2013, 3:30 PM email from Francis Collins, Director, NIH:[22]

- Addressed to: Bill Corr, Deputy Secretary, HHS; Andrea Palm, Chief of Staff, HHS; Howard Koh, Assistant Secretary for Health, HHS; William Schultz, General Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; Jerry Menikoff, Director, OHRP; Peggy Dotzel, Deputy General Counsel, HHS; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; and Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS.
- Cc to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; and Stephanie Devaney, Office of the Director, NIH.
- Subject: Comments on UAB letter and FRN; Text of NEJM essay.
- Attachment: 05 31 13 SUPPORT E clean NIH.docx; BOOST NZ PI Form-Final-Chch.doc; NEJM SUPPORT_060213.docx.
- Message:

> Hello all,
>
> **Thank you for the opportunity to weigh in on OHRP's letter to UAB** and the Federal Register Notice related to SUPPORT. I have pasted NIH's comments on each of those documents below. [Redaction, approximately three lines in length] [Emphasis added]
>
> We at NIH are grateful for the opportunity to work with such a dedicated team within HHS. We have come a long way, and the outcomes that will be announced on Wednesday will help a great deal. …
>
> **<u>Comments on UAB letter</u>** [Emphasis in orginal]

[22] *Ibid*. Pages 71-78.

[Redaction, approximately 7 pages in length]

(7) June 4, 2013, 3:26 PM email from Francis Collins, Director, NIH:[23]

- Addressed to: Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Sye Tait, Deputy Assistant Secretary for Public Affairs for Public Health, HHS; Howard Koh, Assistant Secretary for Health, HHS; Jerry Menikoff, Director, OHRP; Andrea Palm, Chief of Staff, HHS; Bill Corr, Deputy Secretary, HHS; and Peggy Dotzel, Deputy General Counsel, HHS.
- Cc to: William Schultz, General Counsel, HHS; Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; David Horowitz, Deputy General Counsel, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; Stephanie Devaney, Office of the Director, NIH; and Tom Burklow, Office of the Director, NIH.
- Subject: RE: Last minute logistical challenges.
- Message:

  Hi all,

  Sorry, I have been off line for a few hours at Princeton commencement. This all seems to be coming together well -- thanks for everyone's hard work. NEJM has confirmed that they will post the NIH essay at 5 PM on Wednesday [June 5, 2013]. [Redaction, approximately 10 lines in length] …

The complete set of documents released to Public Citizen is available on our website at http://www.citizen.org/documents/support-study-HHS-internal-emails.pdf.

V. Conclusions and requested actions

The series of email communications among NIH, the HHS OS, and OHRP obtained by Public Citizen documents a truly disturbing picture in which NIH — a conflicted, regulated entity — was allowed to interfere with and improperly influence OHRP's compliance oversight investigation of the SUPPORT study. Most troubling, numerous officials at the very highest levels of HHS facilitated this interference by senior NIH officials, despite the fact that NIH had obvious actual, direct conflicts of interest in the research under investigation.

Dr. Menikoff, and his immediate supervisor, Assistant Secretary for Health Koh, in order to preserve OHRP's independence, should have vigorously refused any requests from NIH to review and modify drafts of OHRP's second compliance oversight determination letter to UAB or to be involved in any other way in this matter, and senior officials in the immediate OS should have backed that refusal. Appallingly, it appears that Drs. Menikoff and Koh willingly capitulated to the demands from NIH that were communicated through the immediate Office of the Secretary and down to OHRP.

[23] *Ibid*. Pages 26-27.

Among the many astonishing revelations from the recently obtained HHS emails are the facts that (a) a co-investigator for the SUPPORT study, Dr. Higgins, was allowed to review the draft compliance oversight letter to UAB; and (b) the NIH Director sought to have the OHRP letter conveniently issued one day prior to the online publication in *The New England Journal of Medicine* (*NEJM*) of his commentary article co-authored by Drs. Hudson and Guttmacher.[24] Also disturbing is that these NIH leaders essentially leaked to the *NEJM* editors in advance through their manuscript the fact that OHRP soon would be issuing a compliance oversight letter to UAB putting on hold all compliance actions related to the investigation.[25]

Such NIH interference in the conduct of an ongoing compliance oversight investigation appears to be unprecedented in the history of OHRP and likely never occurred even when OPRR was actually part of NIH, despite attempts by some former NIH Directors, as noted by former OPRR Director McCarthy. This interference has seriously compromised the integrity and independence of OHRP's compliance oversight investigation into the SUPPORT study, fundamentally undermining OHRP's regulatory authority and almost certainly doing long-lasting and possibly irreparable harm to the status of this critically important regulatory agency, whose primary mission is to protect human subjects.

NIH's interference in the process and outcome of OHRP's compliance oversight investigation is comparable to a pharmaceutical company's being permitted by senior staff in the FDA Commissioner's office to review and edit a warning letter drafted by FDA Office of Scientific Investigations about violations of the FDA's human subjects protection regulations involving a clinical trial sponsored by that company. Such circumstances obviously would be viewed as grossly unacceptable and, presumably, would never be permitted.

We therefore urge you to immediately launch a formal investigation of this corrupt conduct in order to ensure that all HHS officials who played a role in it are held accountable and that appropriate corrective actions are taken to prevent such improper and unethical interference by NIH in the compliance oversight activities of OHRP from recurring. Among the many important questions that need to be addressed in this investigation are the following:

(1) Which HHS official or officials first proposed giving any person at NIH the opportunity to participate in OHRP's ongoing compliance oversight investigation of UAB and the SUPPORT study, including the opportunity to review and provide edits to OHRP's second compliance oversight letter to UAB regarding the SUPPORT study?

(2) Did the OHRP Director or any other official at OHRP ever voice objections to his or her supervisor, Assistant Secretary for Health Koh, or any other superior (and/or any other person, such as the HHS Inspector General) regarding NIH's interference in OHRP's ongoing compliance oversight investigation of UAB and the SUPPORT study? If so, what was the response from their superiors? If not, why not?

[24] Hudson KL, Guttmacher AE, Collins FS. In support of SUPPORT – A view from NIH. *N Engl J Med*. 2013; 368(25):2349-2351. (Published online June 5, 2013)
[25] *Ibid*.

(3) Did Assistant Secretary for Health Koh ever voice objections to his superiors (and/or any other person, such as the HHS Inspector General) regarding NIH's interference in OHRP's ongoing compliance oversight investigation of UAB and the SUPPORT study? If so, what was the response from his superiors? If not, why not?

(4) Did the HHS General Counsel or any other HHS official advise the Secretary, the Deputy Secretary, the Chief of Staff, the Assistant Secretary for Health, or any other senior HHS official that it was inappropriate to permit NIH to review and edit OHRP's compliance oversight letter to UAB and to influence the time when that letter was to be issued, given NIH's conflict of interest in the matter? If so, when was that advice provided, and what was the response? If not, why not?

(5) Did anyone in the HHS OS consult with the deputy ethics counselor about the propriety of allowing NIH officials, including a co-investigator on the SUPPORT study, to review drafts of OHRP's second compliance oversight letter to UAB?

(6) Did anyone in HHS share any draft of OHRP's second compliance oversight letter to UAB with anyone outside HHS? If so, with whom and when?

(7) Has NIH ever interfered or sought to interfere in any other OHRP compliance oversight investigations or requested an opportunity to review and edit other draft compliance oversight letters related to HHS-funded research? If so, what was the result of those efforts?

(8) How has NIH's interference with OHRP's compliance oversight of the SUPPORT study affected OHRP's other decisions regarding whether to open compliance oversight investigations into other research projects conducted by the NICHD NRN or any other HHS-funded research?

We hope you share our concern regarding these troubling matters, and we look forward to a 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

Larry R. Churchill, Ph.D.
Ann Geddes Stahlman Professor of Medical Ethics
Center for Biomedical Ethics & Society
Vanderbilt University Medical Center
Nashville, TN

Alice Dreger, Ph.D.
Professor of Clinical Medical Humanities and Bioethics
Northwestern University Feinberg School of Medicine
Chicago, Illinois

Rebecca S. Dresser, J.D.
Daniel Noyes Kirby Professor of Law
Professor of Ethics in Medicine
Washington University
St. Louis, Missouri

Carl Elliott, M.D. Ph.D.
Professor
Center for Bioethics
University of Minnesota
Minneapolis, Minnesota

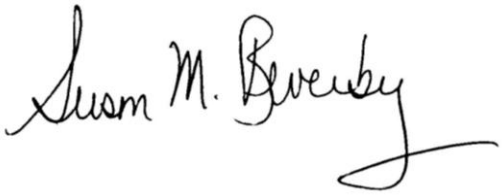
Nancy M. P. King, J.D.
Professor
Department of Social Sciences & Health Policy and Wake Forest Institute for Regenerative Medicine
Wake Forest School of Medicine

Co-Director, Center for Bioethics, Health, & Society and Graduate Program in Bioethics
Wake Forest University
Winston-Salem, North Carolina

Ruth Macklin, Ph.D.
Professor (Bioethics)
Department of Epidemiology & Population Health
Albert Einstein College of Medicine
Bronx, New York

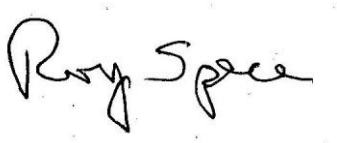
Director, Training Program in Research Ethics in the Americas
Sponsored by the NIH Fogarty International Center

Board of Directors and Past President, International Association of Bioethics



Susan M. Reverby, Ph.D.
Marion Butler McLean Professor in the History of Ideas and Professor of Women's and Gender Studies
Wellesley College
Wellesley, Massachusetts

Lois Shepherd, J.D.
Peter A. Wallenborn, Jr. and Dolly F. Wallenborn Professor of Biomedical Ethics
Professor of Public Health Sciences
Professor of Law
University of Virginia
Center for Biomedical Ethics and Humanities
Charlottesville, Virginia



Roy G. Spece, Jr., J.D.
John D. Lyons Professor of Law
University of Arizona James E. Rogers College of Law
Tucson, Arizona

cc: The Honorable Tom Harkin, Chairman, U.S. Senate Committee on Health, Education, Labor, and Pensions
The Honorable Lamar Alexander, Ranking Member**,** U.S. Senate Committee on Health, Education, Labor, and Pensions
The Honorable Chuck Grassley, U.S. Senate
The Honorable Fred Upton, Chairman, U.S. House of Representatives Energy and Commerce Committee
The Honorable Henry Waxman, Ranking Member, U.S. House of Representatives Energy and Commerce Committee
The Honorable Joe Pitts, Chairman, U.S. House of Representatives Subcommittee on Health, Energy and Commerce Committee
The Honorable Frank Pallone, Jr., Member, Ranking Member, U.S. House of Representatives Subcommittee on Health, Energy and Commerce Committee
The Honorable Jack Kingston, Chairman, House of Representatives Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations
The Honorable Rosa DeLauro, Ranking Member, House of Representatives Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations
The Honorable Darrell E. Issa, Chairman, U.S. House of Representatives Committee on Oversight and Government Reform
The Honorable Elijah Cummings, Ranking Member, U.S. House of Representatives Committee on Oversight and Government Reform

Appendix A

Excerpts of Reports and Commissioned Papers Documenting the Conflicts of Interest Between NIH and OPRR/OHRP

U.S. General Accounting Office, *Scientific Research: Continued Vigilance Critical to Protecting Human Subjects*, March 1996[26]

> In addition, NIH's organizational structure may hamper OPRR's independent oversight and enforcement of human subject protection regulations, although we found no specific instance in which this occurred. Although OPRR is located within the Office of Extramural Research, OPRR is responsible for enforcing compliance with human subject protection regulations for research conducted or supported by both the Office of Intramural Research and the Office of Extramural Research. Under this structure, the OPRR Director reports to the Deputy Director for Extramural Research, who, in turn, reports to the Director of NIH. Because the Deputy Director for Intramural Research also reports to the Director of NIH, OPRR has no direct authority over the research conducted by the intramural program. As a result, when OPRR cited NIH's Office of Intramural Research in 1991 for compliance violations, for example, OPRR had to depend on that office's good will and professional conduct to implement the corrective action plan proposed by OPRR, since OPRR did not have direct authority to require NIH to correct violations. According to OPRR, NIH will complete implementation of the plan by April 1996, 5 years after the problems were noted.
>
> From a broader organizational perspective, a potential weakness exists because NIH is both the regulator of human subject protection issues as well as an institution conducting its own human subject research. The Director of NIH, therefore, has responsibility for both the success of NIH's intramural research program and for the enforcement of human subject protection regulations by OPRR.

John C. Fletcher. Location of the Office for Protection from Research Risks Within the National Institutes of Health: Problems of Status and Independent Authority. National Bioethics Advisory Commission. *Ethical and Policy Issues in Research Involving Human Participants. Volume II: Commissioned Papers and Staff Analysis.* August 2001. Bethesda, Maryland[27]

> **Executive Summary and Major Findings**
>
> **A. On the Location of OPRR in Government**
>
> 1) OPRR's location within the NIH is a structural conflict of missions and incompatibility of functions. This structural conflict gives rise to several troubling and

[26] http://www.gao.gov/assets/230/222250.pdf. Accessed May 6, 2014.
[27] https://bioethicsarchive.georgetown.edu/nbac/human/overvol2.pdf. Accessed May 6, 2014.

persistent problems—including conflicts of interest—for the professional staff of OPRR and the NIH officials who administer OPRR.

The report's arguments are based on these points and findings:

■ OPRR's mission is to uphold the primacy of the rights and welfare of [human subjects of research]. This mission is enveloped within the NIH's scientific mission and its powerful interests in funding and conducting research. This conflict of missions weakens OPRR's authority and stature and engenders conflicts of interest.

■ The most compelling evidence of conflict of interest is that OPRR is far more effective and authoritative in regulating grantee institutions than [HHS] agencies.

■ The NIH is in the implausible position of regulating itself. Internally, the NIH leadership suffers from institutional blindness to the structural problem and the issue of conflict of interest. Externally, the NIH suffers a credibility problem. Others, such as the General Accounting Office (GAO), the Human Research Ethics Group, and this observer, clearly see a conflict of missions that lead to conflicts of interest. The NIH leadership neither acknowledges nor moves to remedy the situation. In that the NIH is an agency of the [HHS] and part of the Executive Branch of government, the White House and [HHS] have the ultimate responsibility for the problems that weaken OPRR and its mission in [human subjects research].

■ An inappropriate location for OPRR imposes burdens that weaken the entire system, e.g., reduced status and lack of respect, political pressure from the NIH requiring problematic compromises, and inordinate time and effort to correct noncompliance and other significant problems …

Despite the wish of Dr. Shannon [former Director, NIH] and others, the OPRR, if not a bureau of ethics, is the sole official voice and continuing presence within government with a priority of protecting [human subjects of research]. The OPRR is inadequate, for several reasons, to do this task within its current mandate. Problems arising from location contribute to this condition. The NIH exercises a dual role to promote and regulate [human subjects research]. Although the NIH's problem is far less dangerous, there is a historical analogy in the Atomic Energy Commission's (AECs) failure from 1951–1973 to hold together both the promotion of nuclear energy and regulation of its uses. [HHS] and Congress should face and resolve a persistent conflict of missions and interests between the NIH and OPRR. …

III. Location of OPRR: Impact on its Mission
A. Historical Background on [Human Subjects Research] and the NIH

The argument in this report is that structural conflicts of mission between OPRR and the NIH engender conflicts of interest for OPRR's staff and NIH officials. How does this report use the term "conflicts of interest?" In his discussion of this topic in the context of health care, Erde first describes an "artificially narrow account" of a conflict of interest,

i.e., "conflicts of interest occur when and only [when] a [physician] strays or is tempted to stray from...role mandated duties for the sake of...economic benefit." Erde goes on to discuss a much broader range of causes (e.g., motives, situations, and structures) that may or may not influence conflicts of interests. This report seeks an understanding of conflicts of interest informed by Erde's broader discussion, e.g., in this situation—for regulators (at OPRR) and for funders and sponsors of [human subjects research] (at the NIH)—conflicts of interests are either "motives that … [regulators or funders/sponsors] have and/or situations in which we could reasonably think ... [their] responsibilities to observe, judge, and act according to the moral requirements of their role are or will be compromised to an unacceptable degree." The next several parts of the report provide historical background and data to support the argument. …

B. Problems and Conflicts Linked to OPRR's Location
1. OPRR's Authority and (NIH's) Institutional Blindness to Conflicts of Mission and Interests

A recent report of the Human Ethics Research Group of the University of Pennsylvania recommended that "the placement and role of the (OPRR) in the regulatory system should be reassessed." The report stated:

> The primary mission of the federal regulations is to protect research subjects. One important obstacle to reform in this area is structural: The agency charged with enforcing and interpreting the regulations, the OPRR, is part of a larger bureaucracy that is also its major client and one of the nation's leading sources of research funding, the NIH. As a matter of principle, the agency should not be located within the structure of any government funder, and its charter should specify that it is independent. Obviously, the agency would have to continue to be accountable to the professional and lay constituencies which its [sic] serves, and a suitable reporting structure would have to be devised.

Dr. Harold Varmus, NIH Director, denied any conflict of missions or institutional interests. He wrote in response to the GAO report, "In fact, the OPRR oversees and interacts with the NIH just as with any extramural institution." Dr. Varmus argued that there was no weakening of OPRR's independent oversight and authority, because "the lines of authority of the NIH Deputy Director for Intramural Research and the OPRR Director do not cross within NIH." He also attributed the five-year span to resolve the violations to "the complexity of fully implementing the corrective actions rather than a function of weakness in the OPRR's ability to enforce human protection regulations within the NIH organizational structure." Dr. Varmus did not discuss the nature of the "complexity" or address the proposition that the NIH was demonstrating by its behavior the basic conflict of institutional interests. His answer to GAO's critique was essentially that it was resolved internally as a matter of lines of authority. The GAO report rightly reiterated before closing, "We disagree with NIH's conclusion and believe that a potential weakness exists in OPRR's ability to enforce human subject protection regulations within NIH." …

Charles McCarthy. Reflections on the organizational locus of the Office for Protection from Research Risks. National Bioethics Advisory Commission. *Ethical and Policy Issues in Research Involving Human Participants. Volume II: Commissioned Papers and Staff Analysis.* August 2001. Bethesda, Maryland[28]

> The fact that OPRR reported to the Deputy Director for Extramural Research [at NIH], who was ultimately responsible for all research awards, placed OPRR in a position of potential conflict with its own supervisor. So long as Dr. Lamont-Havers served in that position, the system worked well. As will be seen, conflict arose some four years later. …
>
> When Dr. Malone was appointed Deputy Director, NIH, he continued to ask OPRR to report to him. However, when Dr. Malone was replaced by Dr. William Raub as Deputy Director, Raub ordered OPRR to report to the new Associate Director for Extramural Research, Dr. Kathryn Bick. The legal advisor to the PHS advised Dr. Raub at the time that to return to the previous arrangement in which OPRR reported directly to the Deputy Director for Extramural Research was to risk a conflict of interest. The reasoning of the Office of General Counsel was clear. Since OPRR was to exercise oversight authority over research projects that bore the stamp of approval of its immediate supervisor—the Deputy Director for Extramural Research—OPRR was placed in a position where it might have to overrule or criticize actions taken by its boss.
>
> Dr. Bick had previously been employed as Deputy Director of the Neurology Institute (NINDS) which funded several animal studies that were discontinued by OPRR for their lack of compliance with the PHS Policy on Humane Care and Use of Laboratory Animals. The Neurology Institute had been severely criticized in the public media for funding these studies.
>
> Shortly after Dr. Bick was named Deputy Director for Extramural Research, she froze personnel hiring in OPRR, cut its travel budget, and dramatically reduced its education budget. Her deputy was Dr. George Galasso, who succeeded her as Acting Deputy Director for Extramural Research. Dr. Galasso continued Dr. Bick's policies of constraint of OPRR. …
>
> D. On at least one occasion, the Director, NIH, appeared to be taking a step toward interfering with an OPRR investigation. In the same case, a member of Congress urged punishment for the accused before all of the evidence was evaluated. Dr. Robert Gallo, a prominent NIH intramural scientist, was credited by many with discovering HIV. (Crediting Gallo with this finding was disputed by French scientists who claimed Gallo stole their findings.) ...
>
> While the Gallo/Zagury investigation was under way, newly appointed Dr. Bernadine Healy, Director, NIH, sent a strongly worded memorandum to the Director, OPRR, directing him to give her a full accounting of the status of the Gallo investigation. She sent a similar memorandum to the Office of Research Integrity (ORI), which was

[28] https://bioethicsarchive.georgetown.edu/nbac/human/overvol2.pdf. Accessed May 6, 2014.

examining the French claims that Dr. Gallo had "stolen" the credit for discovering the HIV virus from French scientists.

The Director, OPRR, responded to Dr. Healy by memorandum stating that briefing her could appear to be a conflict of interest because the investigation concerned alleged misconduct by one of her most prestigious employees. The Director, OPRR politely declined to provide the briefing. The Director of ORI gave Dr. Healy the requested briefing. Subsequently Dr. Healy was severely criticized in a congressional hearing by Rep. John Dingell (D. MI) for interfering with the investigation carried out by ORI …

In an exit interview several years after the Gallo/Zagury case, Dr. Healy acknowledged that she regarded OPRR's failure to brief her as an act of defiance that infuriated her. Only after she was criticized by Mr. Dingell for interfering with the ORI investigation did she come to believe that OPRR's action was in the public interest …

OPRR must also be protected against interference by its own supervisors …

V. Findings

… 3. The present setting of OPRR constitutes an apparent conflict of interest. As noted above, on a number of occasions in the past this appearance manifested itself as a reality. Potential conflict surfaces as a concern each time OPRR forwards its proposed budget request to the agency that it regulates. OPRR should not regulate the agency within which it is located and to whom it looks for funding, personnel, promotions, and staff honors and bonuses.

Report to the Advisory Committee to the Director, NIH, from the Office for Protection from Research Risks Review Panel. June 3, 1999[29]

I. OPRR should be administratively relocated from its present location within the NIH.

Interviews with knowledgeable persons, both within and outside of government … confirmed the position, previously expressed in contract papers prepared for NBAC, that in its present location, as a part of the NIH and reporting to supervisors within the NIH, OPRR is not perceived as an independent office. … This perception of dependence and the concerns about conflicts of interest that arise therefrom compromise the ability of OPRR to function most effectively in providing ethical and regulatory leadership in the arenas of research with human subjects and with animals. After considering the advantages and disadvantages of OPRR's current location, the Review Panel concluded that relocating OPRR was the only way to address these perceptions and concerns and to ensure OPRR's independence and maximize its effectiveness.

[29] http://acd.od.nih.gov/reports/060399b_OPRR_Review_Panel.htm. Accessed May 6, 2014.

A. Conflicts of Interest Arising from OPRR Location Within NIH

> OPRR is perceived to be affected by conflicts of interest because of its position in the hierarchy of the NIH and its concomitant obligation to review research conducted by NIH researchers. … the relationship to NIH increases the public perception that OPRR will be biased in the direction of protecting research interests at the expense of protections for human subjects and animals. … This positioning leads inevitably to an appearance of conflict that likely, in specific cases, reflects reality. Even the perception of conflict interferes with a vigorous pursuit of the mission of the office. Both the appearance and the actuality of a conflict of interest are of concern to the Review Panel.

National Bioethics Advisory Committee, *Ethical and Policy Issues in Research Involving Human Participants*, August 2001. Bethesda, Maryland[30]

> Furthermore, housing an oversight office within a department that conducts or supports human research could create a conflict of interest. Such a potential conflict provided at least part of the reason for the recommendation to relocate the Office for Protection from Research Risks from NIH to the [HHS] Office of the Secretary (OPRR Review Panel 1999). But this degree of separation may still be insufficient, because NIH is part of [HHS], and the new office is still regulating an organization on which it relies for budgetary and other support. The potential conflict of interest is thus attenuated, but not eliminated.

[30] https://bioethicsarchive.georgetown.edu/nbac/human/overvol1.pdf. Accessed May 6, 2014.

Appendix B

Email Correspondence Among NIH, the HHS OS, and OHRP Documenting NIH's Interference in OHRP's Ongoing Compliance Oversight Investigation of the SUPPORT Study

April 18, 2013, 8:43 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[31]

- Addressed to: Bill Corr, Deputy Secretary, HHS; Sally Howard, then-Chief of Staff, HHS; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Andrea Palm, then-Counselor to the Secretary for Science and Public Health, HHS; and Marc Smolonsky, Associate Deputy Secretary, HHS.
- Cc to: Francis Collins, Director, NIH; Lawrence Tabak, Principal Deputy Director, NIH; and Stephanie Devaney, Office of the Director, NIH.
- Subject: Materials for SUPPORT Study.
- Attachments: SUPPORT study Protocol.pdf; Alabama, SUPPORT Consent, 2008-06-04.pdf; NEJM Support Study 2010.pdf; OHRP Letter to UAB.pdf; UAB Response to OHRP 032213.pdf; and OHRP Media Quotes_Statement_TP_QA klh.doc.
- Message:

  Thanks so much for your time this afternoon. [Redaction].

  Attached are the following materials related to the SUPPORT study: …
  Let me know if you have any questions.

April 19, 2013, 10:11 AM email from Sally Howard, then-Chief of Staff, HHS: [32]

- Addressed to: Jerry Menikoff, Director, OHRP; Francis Collins, Director, NIH; Howard Koh, Assistant Secretary for Health, HHS; Marc Smolonsky, Associate Deputy Secretary, HHS; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; David Horowitz, Deputy General Counsel, HHS; Peggy Dotzel, Deputy General Counsel, HHS; and Sye Tait, Deputy Assistant Secretary for Public Affairs for Public Health, HHS.
- Cc to: Bill Corr, Deputy Secretary, HHS, and others.
- Subject: RE: SUPPORT research.
- Message:

  The meeting will need to be at 10:45. We will be sending a conference call number as well

[31] Department of Health and Human Services documents released to Public Citizen in response to a Freedom of Information Act request. http://www.citizen.org/documents/support-study-HHS-internal-emails.pdf. Page 304. Accessed May 20, 2014.
[32] *Ibid*. Page 303.

April 24, 2013, 4:06 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[33]

- Addressed to: Howard Koh, Assistant Secretary for Health, HHS.
- Subject: OHRP NIH kerfuffle.
- Attachments: SUPPORT study Protocol.pdf; OHRP Letter to UAB.pdf; NEJM letter to the editor 4-17-13 study researchers.pdf; NEJM 4-17-13 Editorial.doc; AAP 2007 Perinatal Guidelines 6th Ed.pdf.
- Message:

> Hi Howard,
> … I am hoping you might have some time to chat about [Redaction] concerning the SUPPORT study.
>
> As you know, NIH believes that OHRP [Redaction] If you have not read the protocol, please do so.
>
> This matter needs a rapid resolution. [Redaction] …
>
> And please give me a call to discuss how we can move forward effectively. …

April 24, 2013, 11:45 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[34]

- Addressed to: Bill Corr, Deputy Secretary, HHS.
- Subject: NIH two pager SUPPORT 042413 11PM.
- Attachments: NIH two pager SUPPORT 042413 11PM.docx
- Message:

> I note that [Francis Collins, Director, NIH] has engaged you tonight on this issue so I wanted to include you on the communication below.
>
> Please let me know how I can be helpful.

[The attachment was redacted, except for the following:] "**NIH's Concerns about OHRP's Complaint**" [emphasis in original]

April 24, 2013, 9:54 PM email from Francis Collins, Director, NIH:[35]

- Addressed to: Bill Corr, Deputy Secretary, HHS.
- Subject: SUPPORT study issue still unresolved.

[33] *Ibid*. Page 302.
[34] *Ibid*. Pages 295-299.
[35] *Ibid*. Page 294.

- Importance: High
- Message:

> Hi Bill,
>
> [Redaction]
>
> Do you have a few minutes early tomorrow to discuss this? …
>
> Thanks, and sorry to trouble you …

April 25, 2013, 10:26 AM from Francis Collins, Director, NIH:[36]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH.
- Subject: Fwd: SUPPORT study issue still unresolved.
- Message:

> Spoke with Bill, he's on it. [Redaction] …

May 1, 2013, 02:14 AM email from Francis Collins, Director, NIH:[37]

- Addressed to: Bill Corr, Deputy Secretary, HHS.
- Subject: FW: NIH support summary – nih response.
- Message:

> Hi Bill,
>
> … I have been closely tracking efforts by my staff (Kathy Hudson [Deputy Director for Science, Outreach, and Policy, NIH], Alan Guttmacher [Director, NICHD, NIH], and others) who have been working productively with Howard Koh [Assistant Secretary for Health, HHS] and others in [OASH] and OHRP, to develop a consensus set of statements that OHRP could put forward to clarify the situation with the SUPPORT study. Attached is the most recent version (clocked in at 11:59 PM). I understand that you are meeting with Howard [Koh] in the AM, so I thought you might want to see this.
>
> [Redaction] …

[36] *Ibid*. Page 294.
[37] *Ibid*. Page 224.

May 3, 2013, 4:54 PM email from Jerry Menikoff, Director, OHRP:[38]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Howard Koh, Assistant Secretary for Health, HHS; Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS; and Kirby Bumpus, OASH, HHS.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.
- Subject: RE: Support study -.
- Message:

  Kathy,

  For your weekend enjoyment, here is the revised version of the SUPPORT letter. …

[A three-page attachment was provided that was completely redacted except for OHRP's letterhead on the first page.]

May 4, 2013, 03:27 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[39]

- Addressed to: Jerry Menikoff, Director, OHRP; Howard Koh, Assistant Secretary for Health, HHS; Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS; and Kirby Bumpus, OASH, HHS.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.
- Subject: RE: Support study -.
- Message:

  Thanks for taking the time to chat on a spring Saturday afternoon. Here are the edits we discussed. …

May 4, 2013, 3:36 PM email from Jerry Menikoff, Director, OHRP:[40]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Howard Koh, Assistant Secretary for Health, HHS; Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS; and Kirby Bumpus, OASH, HHS.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.

[38] *Ibid*. Pages 206-210.
[39] *Ibid*. Page 206.
[40] *Ibid*. Page 206.

- Subject: RE: Support study -.
- Message:

> Thanks again, Kathy, to you and Alan and your colleagues for the collegial manner in which we reached this point. And we will welcome similar discussions that you mentioned that will be needed as we move forward. …

May 12, 2013, 02:10 PM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[41]

- Addressed to: Howard Koh, Assistant Secretary for Health, HHS; and Jerry Menikoff, Director, OHRP.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.
- Subject: **Suggested correction to OHRP-UAB draft letter**. [Emphasis added]

[An apparent two-page attachment is completely redacted.]

May 13, 2013, 10:16 AM email from Jerry Menikoff, Director, OHRP:[42]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH.
- Cc to: Howard Koh, Assistant Secretary for Health, HHS; Alan Guttmacher, Director, NICHD, NIH; Rosemary Higgins, Program Scientist for the Neonatal Research Network, NICHD; Francis Collins, Director, NIH; and other NIH staff.
- Subject: RE: Suggested correction to OHRP-UAB draft letter.
- Message:

> Kathy,
>
> At the moment, we aren't contemplating quoting anything that hasn't already been made public. We certainly appreciate your pointing all of this out to us, and we would hope to make appropriate clarifications to our letter …

May 14, 2013, 9:20 PM email from Jerry Menikoff, Director, OHRP:[43]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH.
- Cc to: Alan Guttmacher, Director, NICHD, NIH; Stephanie Devaney, Office of the Director, NIH; Howard Koh, Assistant Secretary for Health, HHS; and Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS.
- Subject: RE: Suggested correction to OHRP-UAB draft letter.

[41] *Ibid*. Pages 134-136.
[42] *Ibid*. Page 132.
[43] *Ibid*. Page 128.

- Message:

  Kathy,

  [Redaction]

  Thus, after these changes, footnote 2 would read as indicated below. …

  Here is what the revised footnote 2 would say:

  [Redaction]

May 16, 2013, 9:47 AM email from Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS:[44]

- Addressed to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH.
- Subject: RE: Suggested correction to OHRP-UAB draft letter.
- Message:

  Kathy, thanks again for your continued work with us on this letter; it's been positive and productive, and I think as hard as it's been, we're in a better place on this.

  [Redaction] …

May 16, 2013, 11:31 AM email from Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH:[45]

- Addressed to: Wanda Jones, Principal Deputy Assistant Secretary for Health, HHS.
- Subject: Suggested correction to OHRP-UAB draft letter.
- Message:

  [Redaction]

  Any word from Caya [Lewis, Counselor to the Secretary for Science and Public Health, HHS] or Andrea [Palm, Chief of Staff, HHS] about the status of the letter?

May 17, 2013, 4:17 PM email from Howard Koh, Assistant Secretary for Health, HHS:[46]

- Addressed to: Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Bill Corr, Deputy Secretary, HHS; Andrea Palm, Chief of Staff, HHS; William

[44] *Ibid*. Page 127.
[45] *Ibid*. Page 127.
[46] *Ibid*. Page 112.

Schultz, General Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; and Peggy Dotzel, Deputy General Counsel, HHS.

- Cc to: Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; Sye Tait, Deputy Assistant Secretary for Public Affairs for Public Health, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; and Kirby Bumpus, OASH, HHS.
- Subject: RE: Next steps on SUPPORT study.
- Message:

> Caya and colleagues
>
> Attached is the final updated draft letter from OHRP.
> It accepts all the changes communicated from you in the earlier message/draft this morning, and in addition, makes one slight change in the direct citation for footnote 2, as was recommended by you.
>
> The proposed next steps then would be:
>
> 1) To send this letter early next week- Monday or Tuesday.
> 2) To post this letter on the OHRP website one day after sending …
>
> In the meantime, OASH/OHRP Communications is working [with the Assistant Secretary for Public Affairs] Communications on tps. …

May 23, 2013, 8:46 AM email from Francis Collins, Director, NIH:[47]

- Addressed to: Andrea Palm, Chief of Staff, HHS; and Bill Corr, Deputy Secretary, HHS.
- Cc to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; and Alan Guttmacher, Director, NICHD, NIH.
- Subject: Draft of essay for NEJM on SUPPORT.
- Attachment: NEJM draft – support statement 5-23-13.docx.
- Message:

> Hi Andrea and Bill,
>
> It was very helpful to speak to Andrea last night about next steps in the debate about the SUPPORT study, and the larger implications for studies that investigate variations in the standard of care. …

May 31, 2013, 6:04 PM email from Jerry Menikoff, Director, OHRP:[48]

- Addressed to: Bill Corr, Deputy Secretary, HHS; William Schultz, General Counsel, HHS; Howard Koh, Assistant Secretary for Health, HHS; Jarel LaPan, Chief of Staff to

[47] *Ibid*. Page 104.
[48] *Ibid*. Pages 89-95.

the Deputy Secretary, HHS; Francis Collins, Director, NIH; Peggy Dotzel, Deputy General Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Andrea Palm, Chief of Staff, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Bradley Wolters; and Kirby Bumpus, OASH, HHS.

- Subject: Draft letter to UAB.
- Attachment: 05 31 13 SUPPORT E clean.docx.
- Message:

  All,

  Here is the latest version of the letter to UAB. …

  [A six-page attachment is completely redacted except for the header "UAB Letter on SUPPORT study—Page 6" and a "DRAFT" watermark on page 6.]

June 2, 2013, 3:30 PM email from Francis Collins, Director, NIH:[49]

- Addressed to: Bill Corr, Deputy Secretary, HHS; Andrea Palm, Chief of Staff, HHS; Howard Koh, Assistant Secretary for Health, HHS; William Schultz, General Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; Jerry Menikoff, Director, OHRP; Peggy Dotzel, Deputy General Counsel, HHS; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; and Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS.
- Cc to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; and Stephanie Devaney, Office of the Director, NIH.
- Subject: Comments on UAB letter and FRN; Text of NEJM essay.
- Attachment: 05 31 13 SUPPORT E clean NIH.docx; BOOST NZ PI Form-Final-Chch.doc; NEJM SUPPORT_060213.docx.
- Message:

  Hello all,

  Thank you for the opportunity to weigh in on OHRP's letter to UAB and the Federal Register Notice related to SUPPORT. I have pasted NIH's comments on each of those documents below. [Redaction]

  We at NIH are grateful for the opportunity to work with such a dedicated team within HHS. We have come a long way, and the outcomes that will be announced on Wednesday will help a great deal. …

  Comments on UAB letter [Emphasis in orginal]

[49] *Ibid*. Pages 71-78.

[Redaction]

June 3, 2013, 8:28 AM email from Howard Koh, Assistant Secretary for Health, HHS:[50]

- Addressed to: Francis Collins, Director, NIH; Bill Corr, Deputy Secretary, HHS; Andrea Palm, Chief of Staff, HHS; William Schultz, General Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; Jerry Menikoff, Director, OHRP; Peggy Dotzel, Deputy General Counsel, HHS; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; and Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS.
- Cc to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; and Stephanie Devaney, Office of the Director, NIH.
- Subject: Comments on UAB letter and FRN; Text of NEJM essay.
- Attachment: 06 03 13 SUPPORT Letter Draft.docx.
- Message:

  Colleagues,

  We now enclose comments/updates on 1) OHRP letter to UAB, 2) the [Federal Register Notice] and 3) the proposed NEJM Perspective.

  1) Regarding the **OHRP Letter,** attached is the updated version. There are some slight changes that accept and implement NIH's first suggestion. [Redaction]. …

  3) **NEJM piece**

  We are appreciative of the professional tone of this piece, and NIH has written this carefully and professionally.

  We have 2 quick suggestions. We would like to raise [Redaction]

  Thank you for the opportunity for this dialogue. …

  [Emphasis in original]

June 3, 2013, 10:38 PM email from Francis Collins, Director, NIH:[51]

- Addressed to: Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; William Schultz, General Counsel, HHS; Bill Corr, Deputy Secretary, HHS; Howard Koh, Assistant Secretary for Health, HHS; Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; Jerry Menikoff, Director, OHRP; Peggy Dotzel, Deputy General

[50] *Ibid*. Page 62.
[51] *Ibid*. Page 54.

Counsel, HHS; David Horowitz, Deputy General Counsel, HHS; and Andrea Palm, Chief of Staff, HHS.
- Cc to: Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; and Stephanie Devaney, Office of the Director, NIH.
- Subject: Last minute logistical challenges.
- Message:

> Dear colleagues,
>
> We submitted the revised essay to NEJM this evening, and the editors are excited and gratified about the progress reflected in the changes. [Redaction] …Would this be possible.
>
> [Redaction]
>
> Can this plan work for all parties?
>
> Thanks again, for everyone's hard work and flexibility in getting this information in front of the public as soon as possible. …

June 4, 2013, 6:59 AM email from Jerry Menikoff, Director, OHRP (sent from iPhone):[52]

- Addressed to: apparently those individuals who received the preceding email from Francis Collins, Director, NIH.
- Message:

> We are looking into this on the OHRP end. I am hopeful that the letter can be released and posted consistent with the described timing. I will let everyone know when I have more information.

June 4, 2013, 02:22 PM email from Howard Koh, Assistant Secretary for Health, HHS:[53]

- Addressed to: Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Jerry Menikoff, Director, OHRP; Andrea Palm, Chief of Staff, HHS; Bill Corr, Deputy Secretary, HHS; and Peggy Dotzel, Deputy General Counsel, HHS.
- Cc to: Francis Collins, Director, NIH; William Schultz, General Counsel, HHS; Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; David Horowitz, Deputy General Counsel, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; Stephanie Devaney, Office of the Director, NIH; and Sye Tait, Deputy Assistant Secretary for Public Affairs for Public Health, HHS.
- Subject: RE: Last minute logistical challenges.

[52] *Ibid*. Page 44.
[53] *Ibid*. Page 28.

- Message:

Hi, here are the next steps, as we see them:

5) OHRP Letter to UAB-
c) Send today Tuesday afternoon
d) Post Letter on OHRP Website tomorrow Wednesday at 5 PM.

6) NIH NEJM Perspective- Post tomorrow Wednesday 5 PM
7) OHRP Web Posting Announcing the Public Meeting
a) Post at 5PM tomorrow Wednesday …

Let us know if this timetable works and that one word change is ok. …

If so, OHRP will then proceed with Step 1A, ie, to send the OHRP Letter to UAB today.

June 4, 2013, 3:26 PM email from Francis Collins, Director, NIH:[54]

- Addressed to: Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Sye Tait, Deputy Assistant Secretary for Public Affairs for Public Health, HHS; Howard Koh, Assistant Secretary for Health, HHS; Jerry Menikoff, Director, OHRP; Andrea Palm, Chief of Staff, HHS; Bill Corr, Deputy Secretary, HHS; and Peggy Dotzel, Deputy General Counsel, HHS.
- Cc to: William Schultz, General Counsel, HHS; Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; David Horowitz, Deputy General Counsel, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; Stephanie Devaney, Office of the Director, NIH; and Tom Burklow, Office of the Director, NIH.
- Subject: RE: Last minute logistical challenges.
- Message:

Hi all,

Sorry, I have been off line for a few hours at Princeton commencement. This all seems to be coming together well -- thanks for everyone's hard work. NEJM has confirmed that they will post the NIH essay at 5 PM on Wednesday. [Redaction] …

June 4, 2013, 3:44 PM email from Howard Koh, Assistant Secretary for Health, HHS:[55]

- Addressed to: Francis Collins, Director, NIH; Caya Lewis, Counselor to the Secretary for Science and Public Health, HHS; Sye Tait, Deputy Assistant Secretary for Public Affairs

[54] *Ibid*. Pages 26-27.
[55] *Ibid*. Page 26.

for Public Health, HHS; Jerry Menikoff, Director, OHRP; Andrea Palm, Chief of Staff, HHS; Bill Corr, Deputy Secretary, HHS; and Peggy Dotzel, Deputy General Counsel, HHS.

- Cc to: William Schultz, General Counsel, HHS; Jarel LaPan, Chief of Staff to the Deputy Secretary, HHS; David Horowitz, Deputy General Counsel, HHS; Kathy Hudson, Deputy Director for Science, Outreach, and Policy, NIH; Alan Guttmacher, Director, NICHD, NIH; Stephanie Devaney, Office of the Director, NIH; and Tom Burklow, Office of the Director, NIH.
- Subject: RE: Last minute logistical challenges.
- Message:

  Thanks everyone, to recap the:

  1) OHRP Letter to UAB
     a) Will send now
     b) Post Letter on OHRP Website tomorrow Wednesday at 5 PM

  2) NIH NEJM Perspective- Post tomorrow Wednesday 5 PM
  3) OHRP Web Posting Announcing the Public Meeting
     Will Post at 3-4PM tomorrow Wednesday, with the one word change noted …