OHRP RESEARCH COMPLIANCE UPDATE: 2023

Laura Odwazny, J.D., M.A.
Office of the General Counsel
U.S. Department of Health and Human Services

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Disclaimer

- *This presentation does not constitute legal advice. The views expressed are the presenter's own, and do not bind the U.S. Department of Health and Human Services or its components.*

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THE COMMON RULE AND OHRP JURISDICTION

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The "Common Rule"

- U.S. Federal Policy for the Protection of Human Subjects – "Common Rule" (1991)
  - Applies to 20 Federal Departments and Agencies
- Research initiated after January 21, 2019 must follow the revised Common Rule (the "2018 Requirements")
  - Research grandfathered under prior version of the Common Rule continues to follow that regulation (the "pre-2018 Requirements")

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Determining Applicability of Common Rule

- **Research involving human subjects conducted or supported by Common Rule department or agency**

- **Non-exempt human subject research covered by a Federalwide Assurance (FWA):**
  - Currently, if research institution voluntarily extends FWA to all research regardless of funding source, OHRP can extend jurisdiction to privately funded research
  - Revised Common Rule preamble states plan to eliminate voluntary extension of FWA, although hasn't happened yet

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Common Rule vs. FDA Regulations: 45 CFR part 46 vs. 21 CFR parts 50 and 56

- Basic requirements for IRBs and for informed consent are congruent
  - 21st Century Cures now allows FDA to implement waiver of informed consent
- Differences in applicability
  - Common Rule based on U.S. Federal Common Rule agency conducting or supporting human subjects research
  - FDA regulations based on use of FDA regulated product: drugs, devices, or biologics

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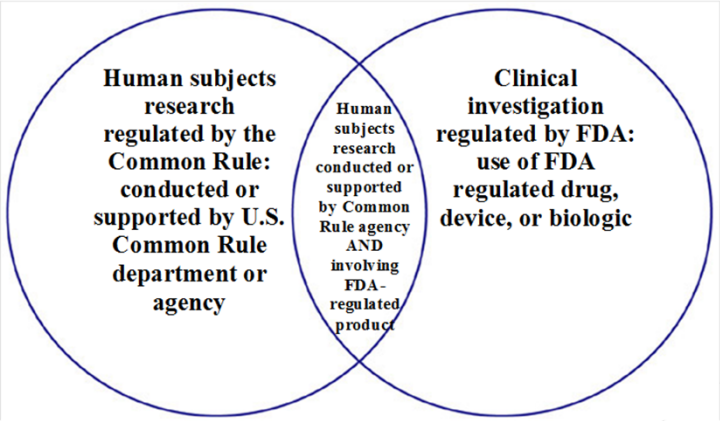
Jurisdiction: Common Rule vs. FDA

- An activity may be regulated under both the Common Rule and FDA informed consent and IRB regulations: e.g., a clinical trial conducted at the NIH Clinical Center that is comparing two FDA-regulated drugs



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Jurisdiction: Institutions and IRBs

- OHRP exerts jurisdiction over institutions, not directly over investigators
- Revised Common Rule codified OHRP's jurisdiction over independent IRBs

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END OF COVID-19 PUBLIC HEALTH EMERGENCY: IMPACT ON REGULATORY FLEXIBILITIES:

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Application of OHRP sIRB Exception-COVID-19

- OHRP sIRB exception –COVID-19 (October 2020)
  - Cooperative research conducted or supported by HHS that is ongoing or initially reviewed by the IRB during COVID-19 public health emergency, as declared by the Secretary of HHS
- 2/10/23 -- OHRP affirmed continued application of the exception:
  - "…as of the date of the conclusion of the public health emergency, the exception will expire and cannot be applied to additional studies. **Research for which the HHS division supporting or conducting the research study has already approved the use of the exception will continue to be excepted from the single IRB requirement**, since the exception applies for the duration of the research." (emphasis added)

https://www.hhs.gov/ohrp/news/announcements-and-news-releases/2023/important-updates-about-the-covid-19-single-irb-exception.html

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GOVERNMENT ACCOUNTABILITY OFFICE (GAO) REPORT:

Institutional Review Boards: Actions Needed to Improve Federal Oversight and Examine Effectiveness


GAO Highlights

INSTITUTIONAL REVIEW BOARDS

Actions Needed to Improve Federal Oversight and Examine Effectiveness

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GAO Report: Highlights

- GAO was asked to examine independent IRBs, processes used to protect human subjects, and standards of IRB quality.
- Found OHRP and FDA inspect "relatively few IRBs" – annually (on average) OHRP conducts 3-4, FDA 133
- "**OHRP and FDA have not assessed to what extent IRB reviews are effective** in protecting human subjects. This is **because the agencies have not determined the best approaches for doing so.** Evaluating effectiveness is challenging in part due to the absence of validated measures and because IRBs are only one part of the framework of stakeholders responsible for protecting human subjects." (Emphasis added)

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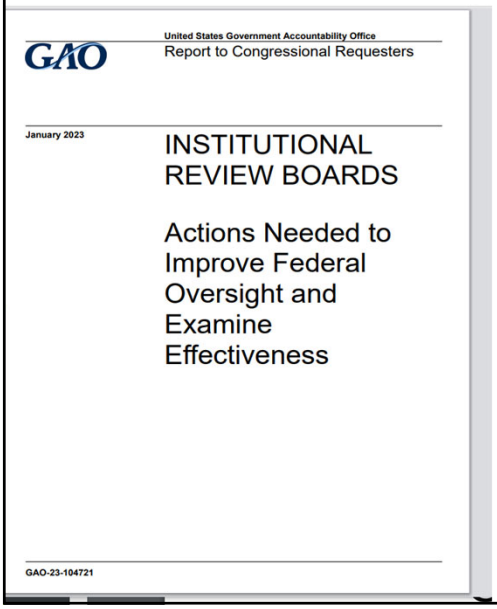
GAO Report – Relevant Recommendations


United States Government Accountability Office
Report to Congressional Requesters

January 2023

INSTITUTIONAL REVIEW BOARDS

Actions Needed to Improve Federal Oversight and Examine Effectiveness

GAO-23-104721

- Conduct annual risk assessment to determine whether OHRP is conducting adequate number of routine IRB inspections and to optimize use of IRB inspections in oversight of IRBs and protection of subjects.
- OHRP/FDA convene stakeholders to examine/implement approaches for measuring IRB effectiveness in protecting subjects. For example:
  - effectiveness measures
  - peer audits of IRB meetings/decisions
  - mock protocols
  - surveys of IRB members, investigators, and human research participants.

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OHRP Response: Charge to SACHRP

Regarding convening HHS stakeholders and measuring IRB effectiveness:

1. What constitutes effectiveness in protecting research participants? This could be defined in terms of avoiding harms, ensuring subjects exercise informed consent, protecting subjects' rights and welfare, treating subjects equitably or fairly, or achieving greater consistency in applying the regulation, or something else. Depending on what is being protected, the IRB's actions could differ and measures of effectiveness would vary accordingly. What definition of IRB effectiveness is the most important to focus on and measure?

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From SACHRP's materials presented at March 2023 meeting-- Possible Standards of Effectiveness

OHRP suggestions to SACHRP:

- Avoiding Harms
- Ensuring subjects exercise informed consent
- Protecting subjects' rights and welfare
- Treating subjects equitably or fairly
- Achieving greater consistency in applying the regulation

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From SACHRP materials presented at March 2023 meeting-- Possible Standards of Effectiveness

OHRP suggestions to SACHRP:

- Avoiding harms
- Ensuring subjects exercise informed consent
- Protecting subjects' rights and welfare
- Treating subjects equitably or fairly
- Achieving greater consistency in applying the regulation

Other possibilities SACHRP noted:

- Compliance with regulatory requirements
- Compliance with Belmont principles
- Compliance with accreditation standards
- IRB member education assessments
- IRB staff education assessments (Certified IRB Professional (CIP) certification)
- Research staff and institutional compliance with IRB requirements
- Public trust in the IRB system
- Human research participant satisfaction with research and IRB's oversight
- Investigator satisfaction

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OHRP Response: Charge to SACHRP (2)

2. SACHRP is one HHS "stakeholder". What other stakeholder groups should HHS convene as part of examining approaches for measuring IRB effectiveness? What factors make an entity an appropriate stakeholder?

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From SACHRP's materials presented at March 2023 meeting--**Stakeholders**

- Individuals who volunteer to participate in research
- Patient advocacy groups
- Institutions that conduct research, from Academic Medical Centers to single practitioner sites
- Institutional officials
- IRBs
- Investigators
- Research staff
- Agencies – all Common Rule agencies including FDA
- SACHRP
- Commercial research funders, such as sponsors and CROs
- Bioethicists
- The Consortium to Advance Effective Research Ethics Oversight (AEREO)
- Association for the Accreditation of Human Research Protection Programs (AAHRPP)
- Consultants
- Others?

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OHRP Response: Charge to SACHRP (3)

3. GAO provides several potential effectiveness measures. How do these approaches differ, and what are their benefits and limitations? What approaches should HHS and stakeholders prioritize? Are there other approaches should HHS and these stakeholders consider for measuring IRB effectiveness in protecting human subjects?

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From SACHRP's materials presented at March 2023 meeting-- Measuring Effectiveness

- Surveys and Questionnaires
- Document reviews: IRB minutes, consent forms, etc
- IRB meeting observations
- Event reviews: Unanticipated Problems, investigator non-compliance, participant complaints to the IRB, number of deferrals, etc
- Administrative measurements: Turn around time, error rate
- Attaining AAHRPP Accreditation
- Attaining Certified IRB Professional (CIP) certification

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OHRP COMPLIANCE ACTIVITIES-

2023 NEWS AND WHAT'S ON THE HORIZON

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2022 OHRP Determination Letters

October

October 7, 2022 - University of Arkansas at Little Rock

September

September 7, 2022 - Leland Stanford Junior University

September 7, 2022 - Southern Illinois University

July

July 13, 2022 – Biomedical Research Alliance of New York (BRANY)

March

March 21, 2022 – New York University Grossman School of Medicine

March 8, 2022 – University of Texas Southwestern Medical Center

February

February 28, 2022 - National Jewish Health

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First determination – 45 CFR 46.116(a)(5)(ii) (2018 Requirements)

"In light of the above facts, OHRP determines that these statements in the consent form about the risks and possible benefits of the research did not provide information necessary to satisfy the requirement that the "informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate" (45 CFR 46.116(a)(5)(ii))."

https://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/2022/july-13-2022-biomedical-research-alliance-of-new-york-brany/index.html

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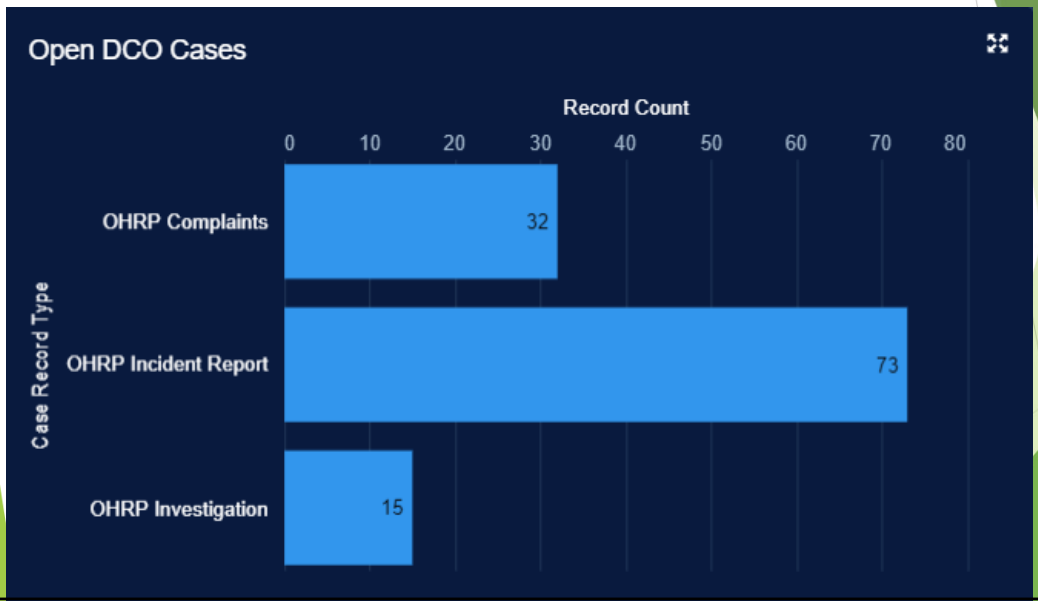
OHRP Open Cases As of May 1, 2023



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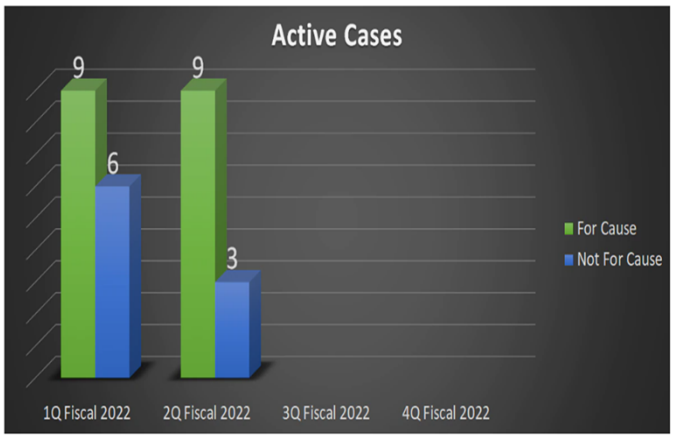
OHRP Division of Compliance Oversight (DCO) Activity Logs FY 2022 - Cases

- For cause: written substantive allegations or indications of noncompliance
- Not for cause: no specific allegations
  - Geographic location
  - Large volume of HHS research
  - Not submitting incident reports
  - Accreditation status
  - Audits of other regulatory agencies
  - Need to evaluate implementation of corrective actions from prior OHRP compliance action



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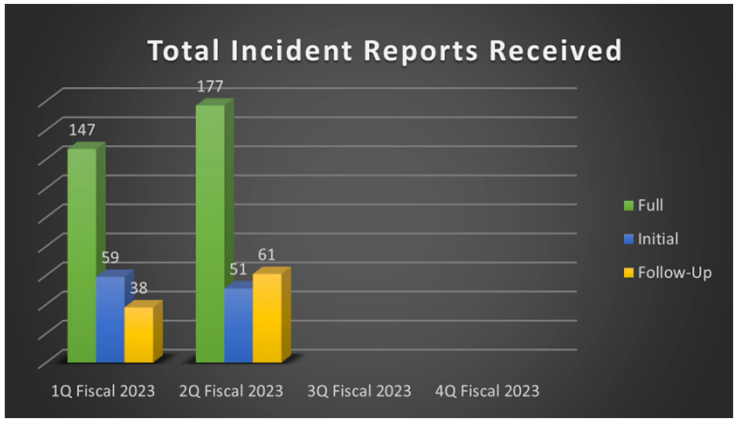
OHRP Division of Compliance Oversight (DCO) Activity Logs FY 2022 -IRPTs



Full reports are complete reports

Initial reports require a follow-up report: the institution has not implemented a corrective action plan or has not completed gathering all information

Unanticipated problems involving risks to subjects or others; serious or continuing noncompliance; suspensions or terminations of IRB approval.

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New OHRP Video: An Overview of OHRP's Compliance Oversight Assessments

- Aid for institutions and IRBs preparing for assessments
- Posted on website 4/20/2023; 1st week viewed ~1200 times
- https://www.hhs.gov/media/3816/modal

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New OHRP Complaints Submission Form- (pending PRA approval)

- Designed to facilitate submission complaints of noncompliance with the Common Rule by using a standardized form
- For compliance with the Paperwork Reduction Act, notice provided in Federal Register for comment until 5/30/2023
- https://www.federalregister.gov/documents/2023/04/27/2023-08880/agency-information-collection-request-30-day-public-comment-request

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On the Horizon…Remodeling OHRP's Compliance Investigation Process

- More virtual site visits
- Incorporation of DEI considerations
  - Focus on awareness of Belmont principle of justice and related considerations, for example:
    - OHRP: examining how institution is asking investigator to ensure appropriate inclusion (consent translation, short form translations, proposed enrollment, local context
    - Institution: reporting difficulty reviewing enrollment data at the time of continuing review for equitable selection after 2018 Common Rule revision removed continuing review for many studies.
- Interview research team members who obtain consent
- Attend multiple IRB meetings rather than just one

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More Possibilities for Remodeling OHRP's Compliance Investigation Process

- Intake form? Might allow institutions to describe aspects of HRPP program, what studies demonstrate implementation of specific provisions of 2018 Requirements
- Self-assessment questionnaire? Might incorporate risk-based process recommended by GAO

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Thank you for your interest in protecting human subjects!

Questions?

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