THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

5th Annual IRB Retreat
February 19, 2020

Morning Agenda

Morning Time	Presentation	Speaker
7:15 -8:00	Registration	
8:00-8:20	Housekeeping	Charlotte Coley, MACT, CIP
8:20-8:30	Welcome	Andy Johns Senior Associate Vice Chancellor
8:30-8:50	State of the Office of Human Research Ethics	Cassandra Myers, CIP, Director Office for Human Research Ethics
8:50 – 9:50	Keynote	Debra Parrish, JD Parrish Law Offices
9:50-10:30	What is RIO's Role?	Eric T. Everett, Ph.D. Professor and Chair, Division of Oral and Craniofacial Health Sciences Professor, Division of Pediatric and Public Health Institutional Research Integrity Officer University of North Carolina at Chapel Hill Associate Editor: European Journal of Oral Sciences
10:30-10:45	BREAK	
10:45 – 11:25	What Is OCT's Role? What is CTQA's Process?	Christine M. Nelson, R.N., B.S.N., MBA/HCM, CCRC, Director OCT Valerie Buchholz, RN, BSN, CCRC, CHRC, Associate Director for QA, OCT
11:25-12:00	Vignettes & Group Discussion	All Presenters

Housekeeping

- WiFi: UNC Guest, NO password needed
- Restrooms just outside the meeting room
- Lunch in Willow Lounge
- Meet your colleagues from other IRBs
- Complete the Retreat evaluation sent to you following today's session.
- Continuing Education Certificate

Welcome

Andy Johns

Senior Associate Vice Chancellor

Cassandra Myers, CIP
Director

Cassandra (Cassie) Myers is the Director for the Office of Human Research Ethics at UNC-Chapel Hill. Myers has over 15 years' experience in IRB administration and healthcare; managing Institutional Review Boards (IRB), developing clinical guidelines, and leading process improvement efforts. Myers is a graduate of The University of Minnesota in Health Management with an emphasis in Biochemistry. She is also a Certified IRB Professional (CIP). Myers came to UNC in 2018 with a breadth of knowledge gained from several organizations in Minnesota, including; Mayo Clinic, ICSI (HealthPartners) and most recently Allina Health in Minneapolis, MN, where she was the IRB Manager.

Office for Human Research Ethics
2020 Member Retreat

Office for Human Research Ethics
Cassandra Myers, CIP

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Topics of Discussion

1. Staffing of the OHRE and Organizational Structure
2. Recruitment of IRB Committee Members
3. Educational Opportunities
4. Educational Outreach
5. Metrics of IRB Activity
6. Refrigerator Opportunities
7. 2019 Achievement Highlights
8. IRBIS Updates

Current OHRE Staffing

There are currently 23 staff members.

New Hires:
Brittane Foy, Marie Grubbs, Alissa (Xuan) Ma, and Jason Zeller (Analysts)

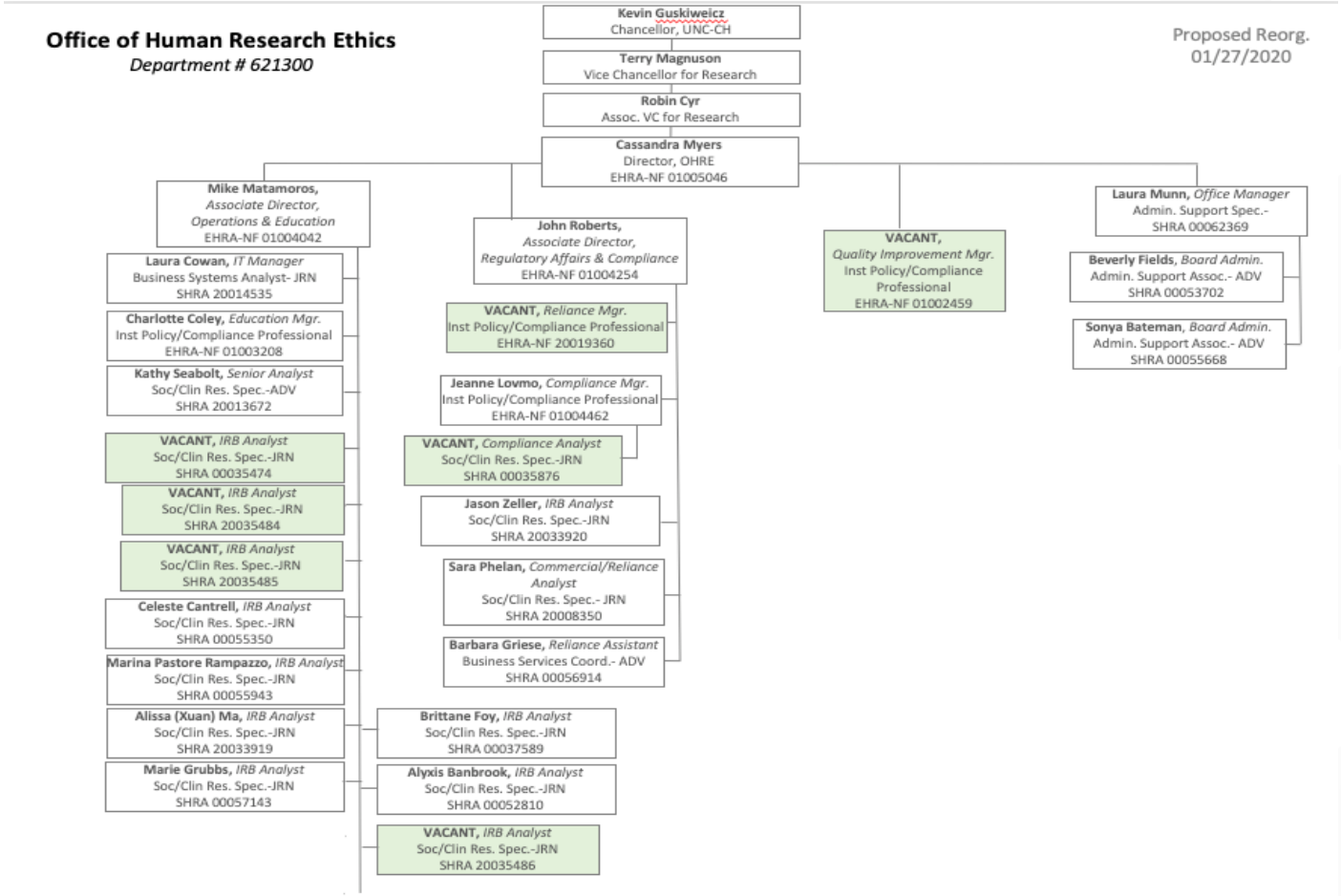
New Positions:
Kathy Seabolt-Senior Analyst
John Roberts- Associate Director, Regulatory Affairs & Compliance
Mike Matamoros- Associate Director, Operations & Education

Searches in Progress: 4 Analysts, 1 Compliance Analyst
Upcoming searches: Quality Manager and Reliance Manager

There are currently 7 staff members who are certified as IRB Professionals (CIP).

- Fall 2019 Session (Sara Phelan)

Organizational Chart



IRB Members

- Continuing to add expertise across all committees
- Support from the OVCR's office to recruit new members through meetings with different schools and groups across campus
- Targeted focus on Nursing participation due to Magnet status
- Trained one new Chair- Dara Barnard, Pharm.D.
- Added 22 new members in the past year
  - Neurology
  - Criminal Justice
  - Nursing
  - Oncology
  - Psychology
  - Pharmacy
  - Social Work

*If you know of anyone interested in joining please have them reach out to Cassandra Myers, OHRE Director at Cassandra.myers@unc.edu

Educational Opportunities

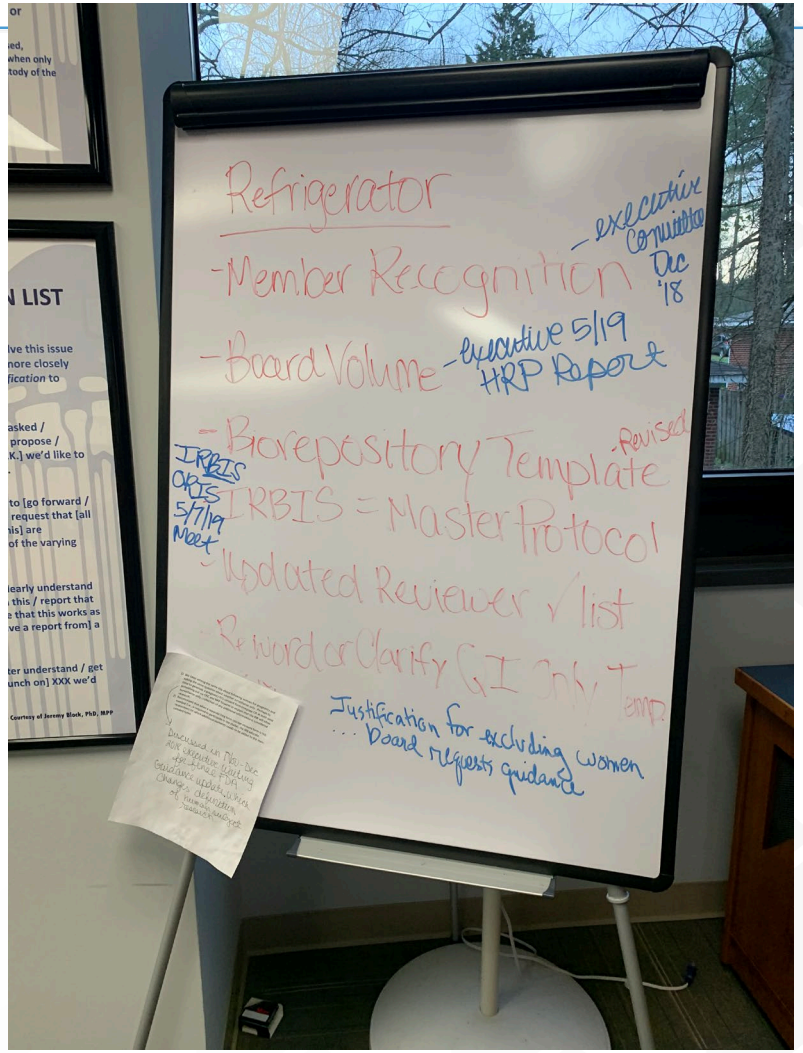
- Board Training at 72 Meetings
- Sent 3 staff to the 2019 national Advancing Ethical Research (AER) Conference (PRIM&R)
- Conducted Chair and Staff Training on Pediatric Risk/Benefit Analysis, including guest speaker (August 2019)
- Participated in numerous webinars from FDA, OHRP, PRIM&R, AAHRPP and others;
  - Planned Emergency Research
  - OHRP Privacy Workshop
  - Subject Injury Language

Educational Outreach

- Presented on Campus Sessions (150% increase):
  - January 15, 2019 “Implementation of the New Common Rule”
  - February 21, 2019 ”Common Rule Update”
  - August 11, 2019 “OSR Symposium-UNC Commercial IRB Utilization”
  - August 27 and September 5, 2019 “UNC Commercial IRB Utilization and Expansion”
  - December 2, 2019 “Administrative Review Update”
- 37 ”Pop-up” sessions on campus with Analysts to provide JIT answers to questions
  - NCTraCS
  - Davis Library
  - CTRC
- Presented at both sessions of New Clinical Research Personnel
- 25+ Group, class and department requests for sessions, topics include:
  - IRB Basics
  - QI vs. Research
  - IRBIS demos

Refrigerator

- Next to Items we worked on**
- Time to clean out the fridge and start fresh:
  - You always need milk, butter and eggs



2020 OHRE Projects

1. Transition to the Revise Common Rule
   - Administrative Review
   - Re-review of Studies
   - New Guidance, SOP's, Algorithm Development, and Training (Board Members, Staff, and Research Community)**

2. Commercial IRB for Multi-Site Industry Sponsored Protocols**
   - Currently working on integration with WIRB system
   - Restructured Process and Documents
   - Board Volume Reduction**

3. Consent Templates Available Online**
   - Next step for bio-repository and other consent form updates

2020 OHRE Projects

3. Board Restructure**
   - Removed Biomed/Non-Biomed Designation
   - Reviewed Safety items at each board meeting
   - Volume Reduction**
     - Went from 21.6 on average to 18.2 items on the agenda
   - Added Additional Expertise
4. OHRE Organizational Restructure
   - Created Two New Positions:
     - Associate Director, Regulatory Affairs & Compliance
     - Associate Director, Operations & Education
   - Received Support for 5 additional positions by the OVCR
5. Jump Start IRB Training for Staff
   - 4 New Analysts
6. OneNote/Internal Guidance
   - Removed regulatory binders that were out of date for staff, one “electronic” gathering place

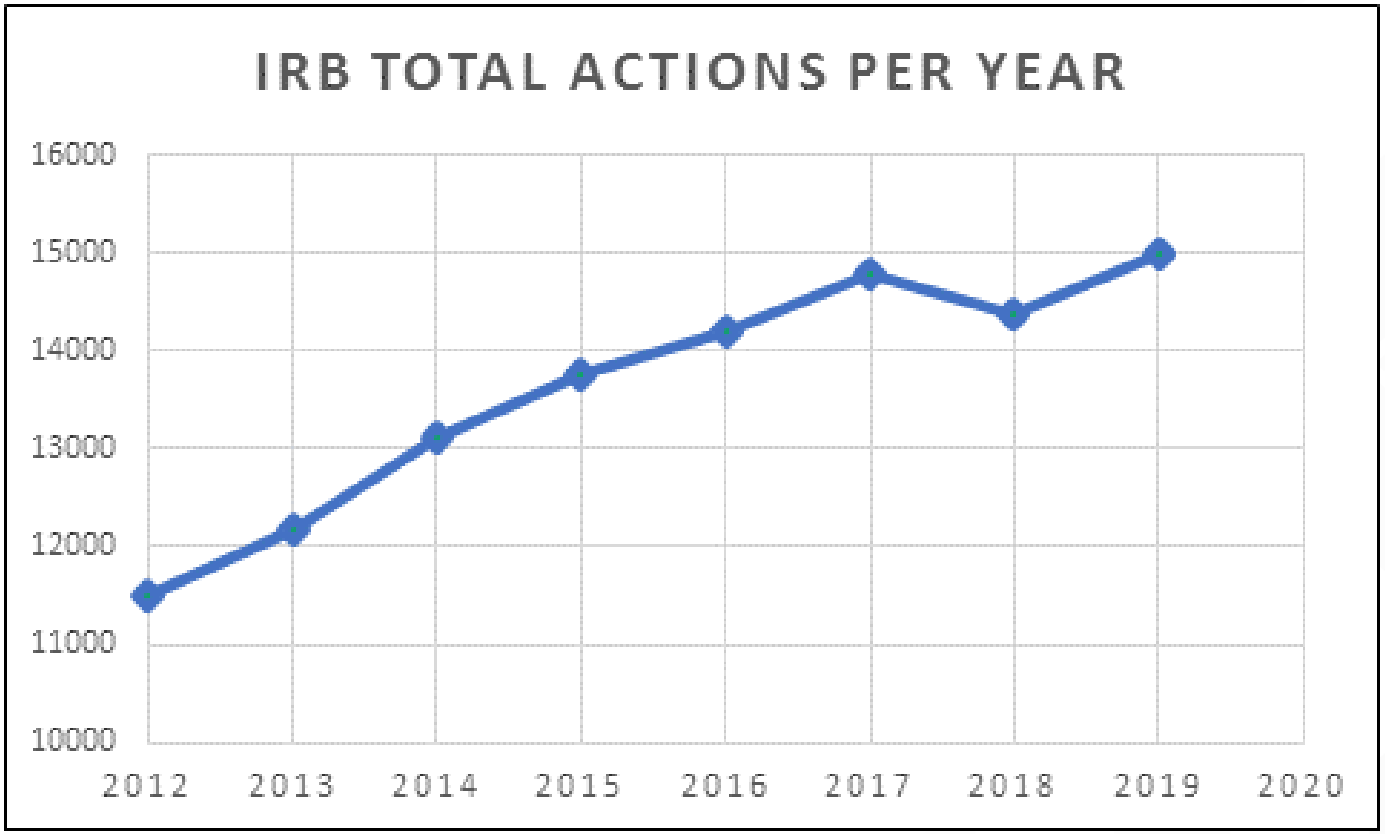
Common Rule Update

- On January 21, 2019:
  - Final revision went into effect.
  - 20 agencies have "signed on"
  - FDA has not harmonized at this time

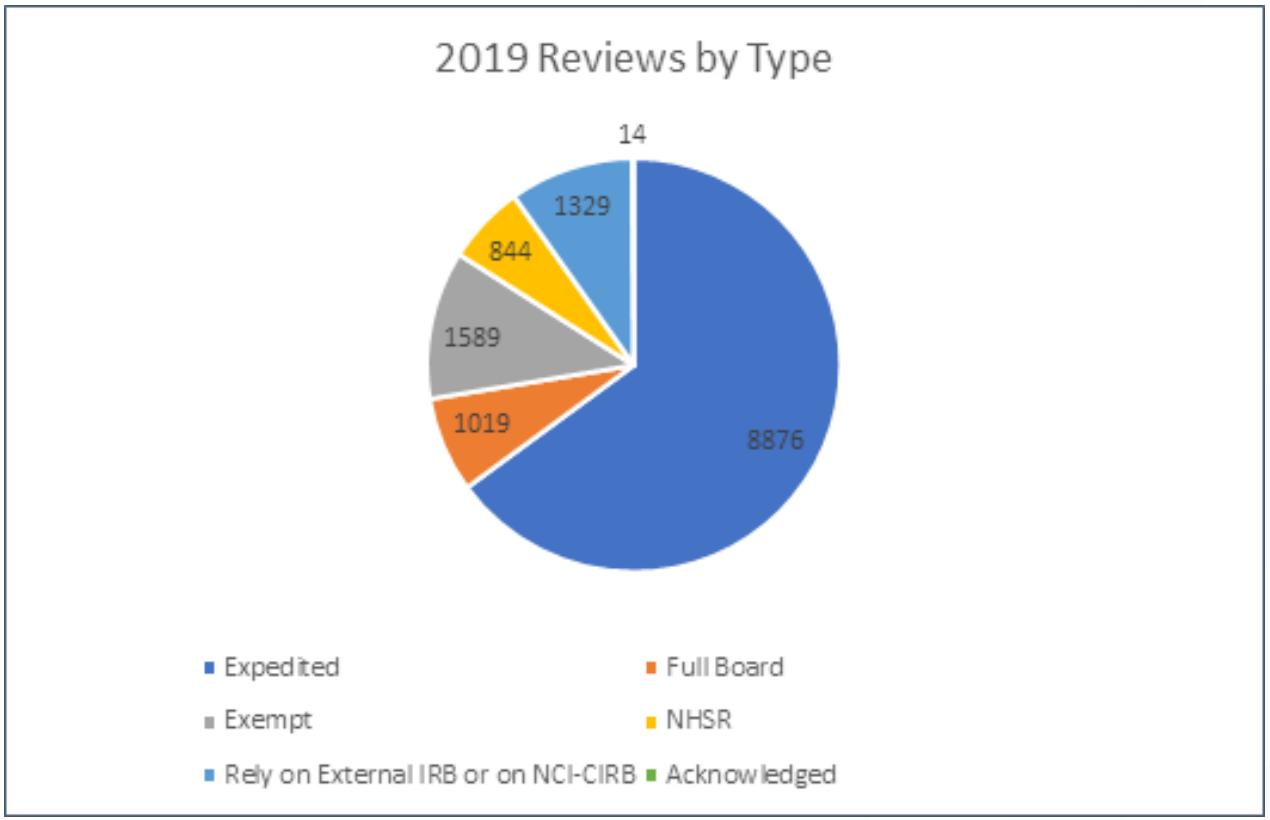
- Largest Change Areas:
  - Exempt Categories
  - Consent Elements
  - Annual Renewal/Continuing Review

- 5027 previously approved studies have been re-reviewed:
  - Over 2400 studies given administrative review
  - 284 studies transitioned to exempt
  - 992 studies initial review were exempt

Total Actions Per Year



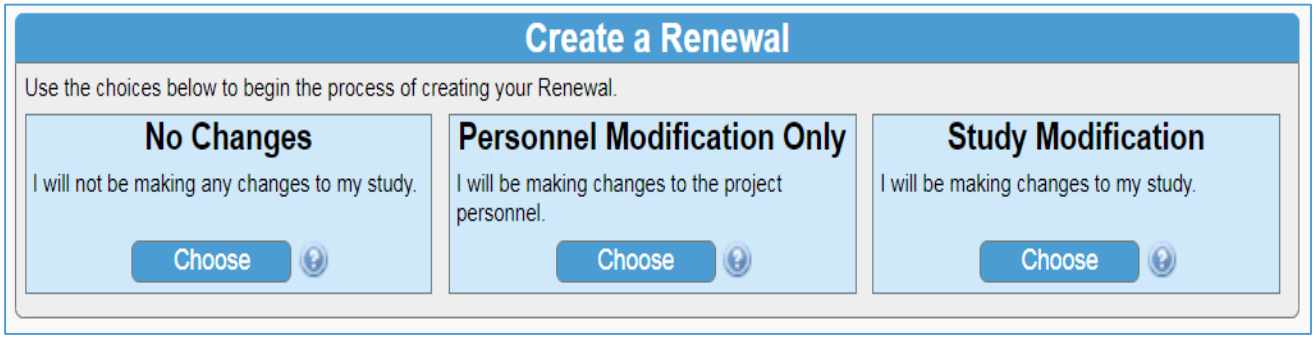
2019 Reviews by Type



IRBIS UPDATES

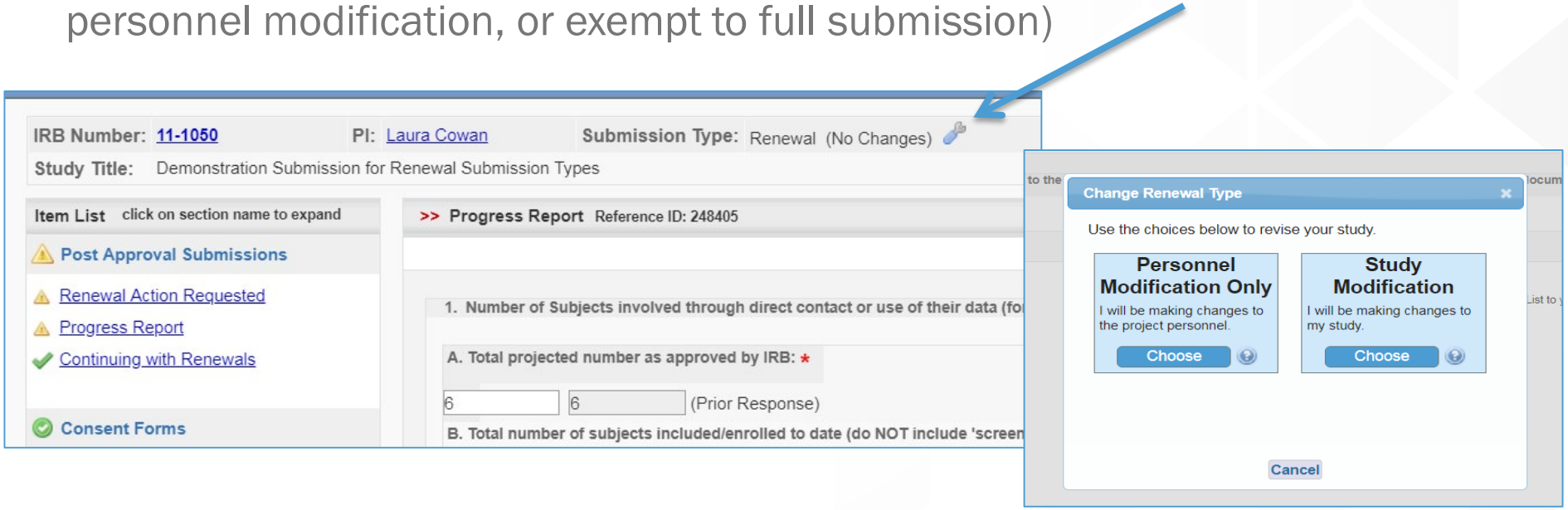
Continuing Review Type- Completed 7/16/2019

- 1st step for several upcoming features:
  - "Study Type Specific Submissions" September 10, 2019
  - Administrative Review Q4 2019
  - Personnel Only Submissions Q4 2019
  - Reduced time looking for non-described modifications**

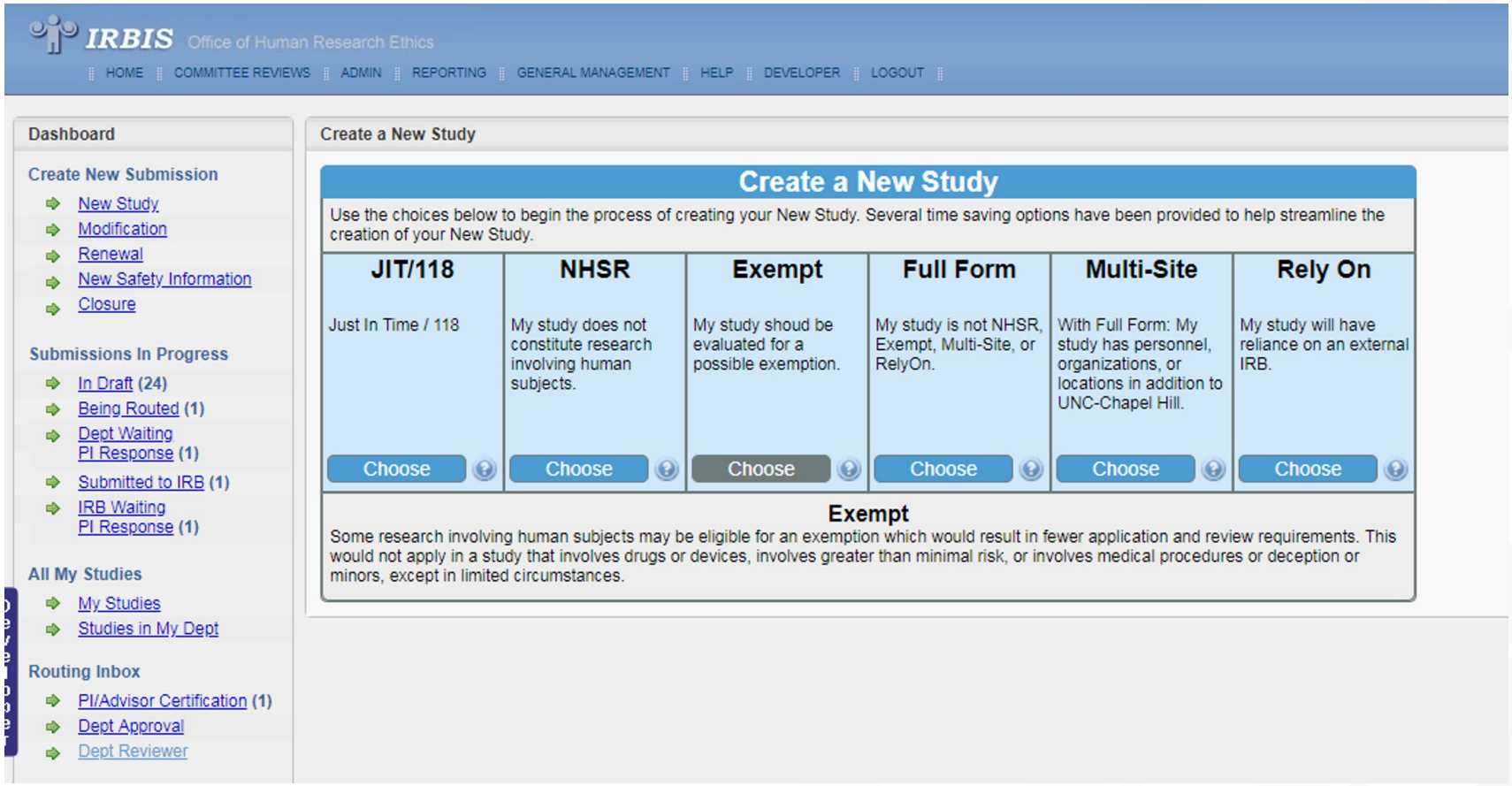


Wrench – Completed 7/16/2019

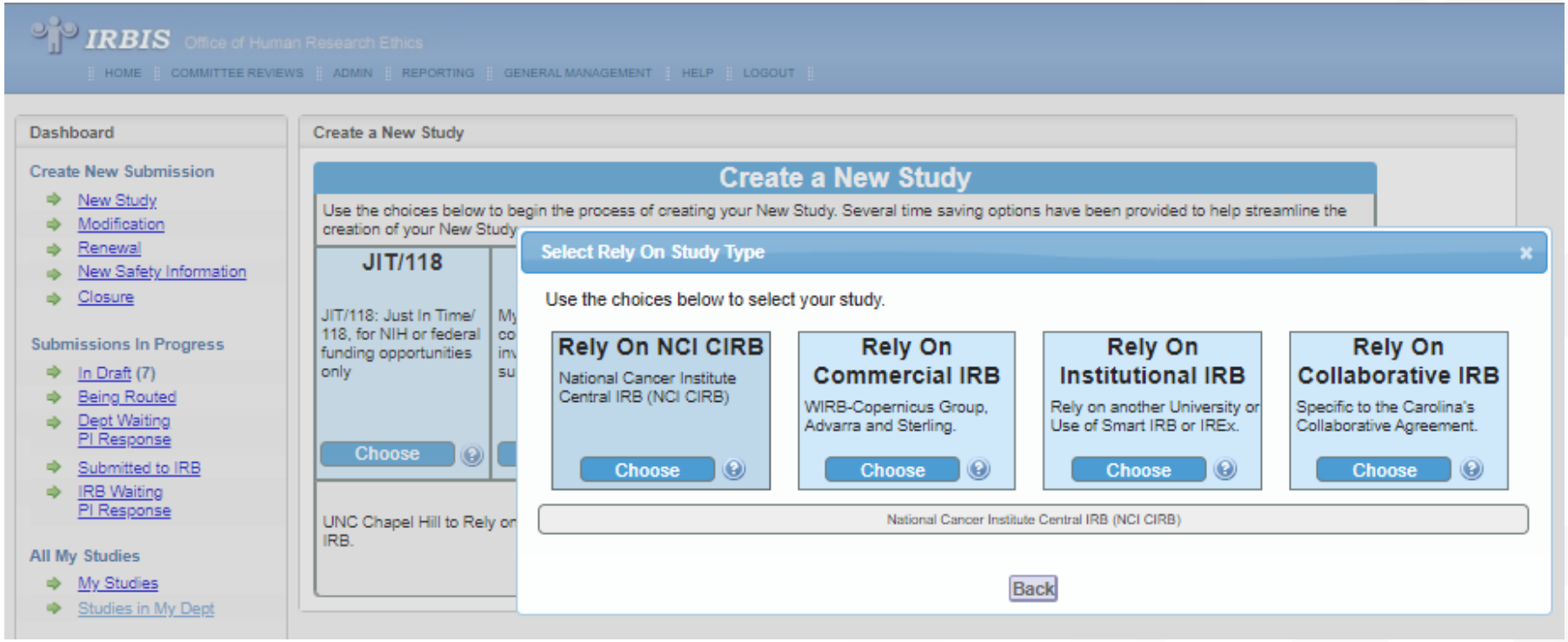
- The “Wrench” feature will be very important for submissions going forward as additional updates are done.
- Allows for a submission change “type” (e.g., Renewal with no changes to personnel modification, or exempt to full submission)



Specific Submission Type-Completed 9/10/2019
Reduced Swim lanes from 1.77 on average to 1.17



Rely On External IRB Submission types – 9/10/2019
50-60% Reduction in Questions

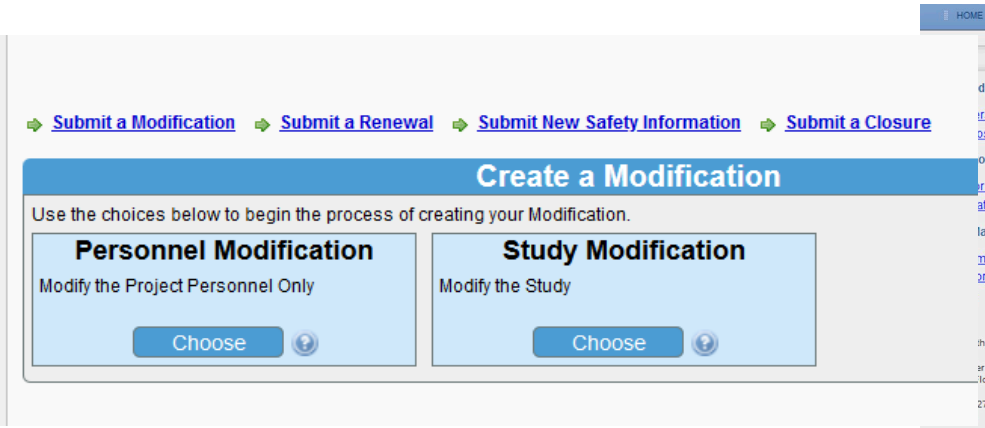


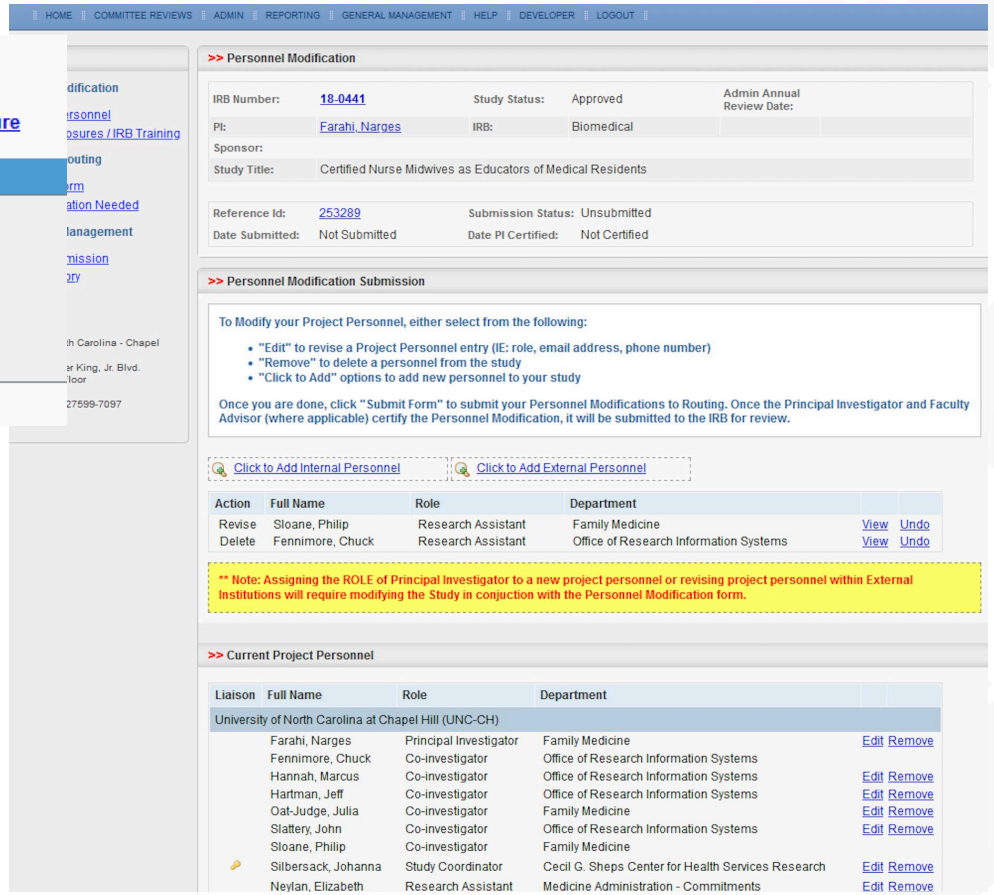
Analyst Assigned– Completed 01/29/2020

If analyst has been assigned

As a reminder the OHRE reviews on a first-in first-out basis and to avoid a bottle neck we assign as an analyst is available.

Next Steps- Personnel Only Modifications

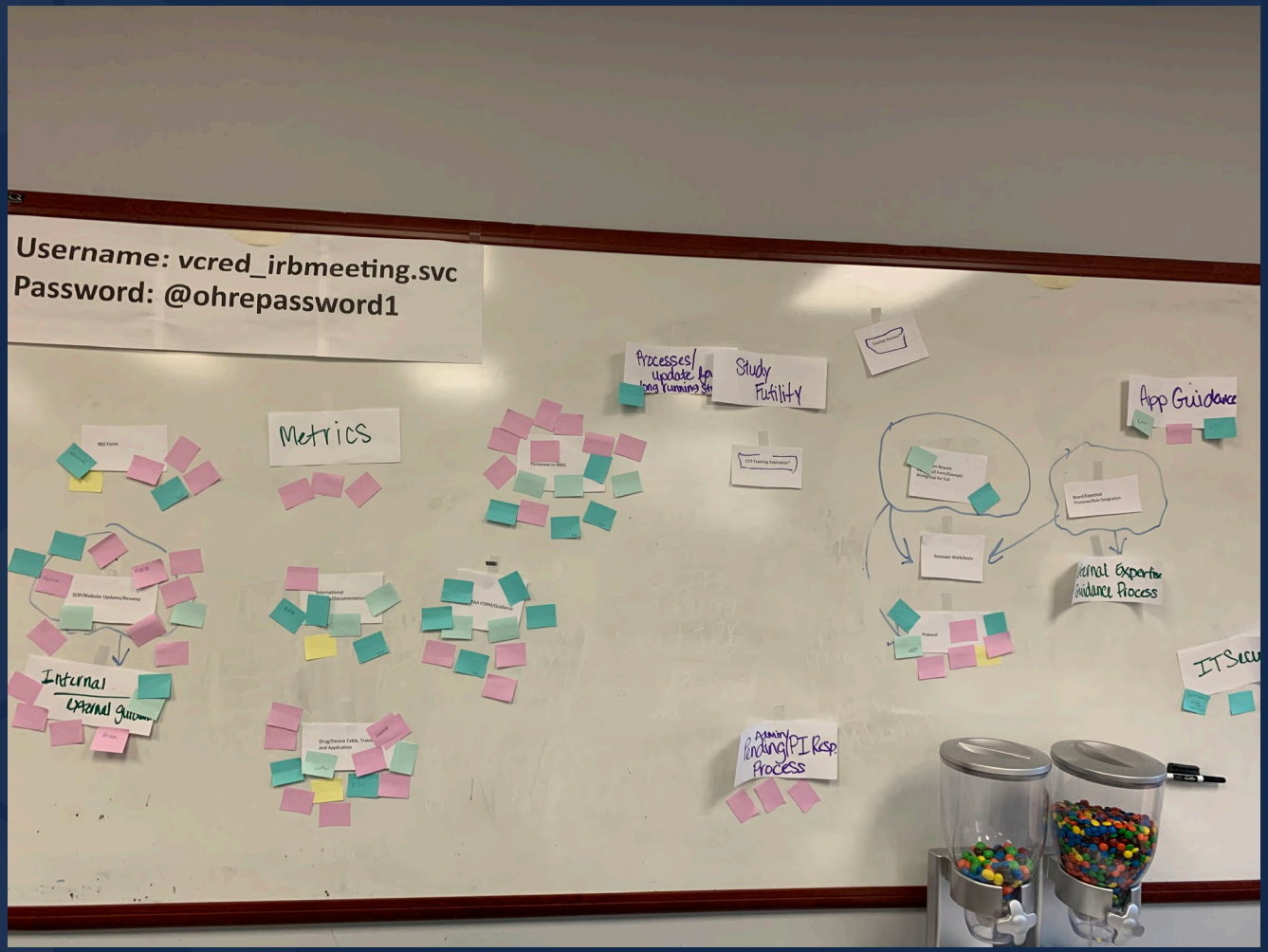




Next Steps - Application Updates

- Similar to the Rely on External IRB applications where ~50% of questions were removed or pre-answered we will be going through the following application types in order to evaluate areas for improvement
  - 118/JIT (Winter/Spring 2020)
  - NHSR (Winter/Spring 2020)
  - Exempt (Summer 2020)
  - Full Form (Fall-Spring 2021)
    - Protocol based submissions

2020 and Beyond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Password: @ohrepassword1
Metrics
Study Futility
App Guidance
Internal
External
Reviewer Worksheets
Protocol

2020 Focus

- IRBIS Updates
  - Further reduction of application as appropriate
  - Protocol based application**
  - Submission Specific Guidance for Common Stips
- Biospecimen and Script Consent Template Revision**
- Further Develop Guidance Documents for Board Review
- Conduct additional sessions on campus
- Drug/Device Table, Guidance, and Education
- NSI Forms

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Debbie Parrish, JD
Parrish Law Offices

Parrish Law Offices is among the top law firms in the United States handling research integrity and misconduct matters. Debra Parrish began handling cases involving research misconduct in 1989, worked with the Department of Health and Human Services' Office of Research Integrity, and has handled numerous cases since returning to private practice.

Her firm has counseled regional, national, & multi-national companies, educational & research institutions, as well as individual scientists and journal editors and publishers. They have been involved in more than 100 cases of research misconduct, including numerous high-profile cases.

Adjunct Professor, University of Pittsburgh Medical Center, Spring 2016

J.D., Duke University School of Law

B.S.E., Biomedical Engineering, Duke University

M.P.H., Johns Hopkins Bloomberg School of Public Health (expected 2021)

Research Integrity and the IRB

Debra Parrish

February 19, 2020

Overview

- Ethical Frameworks
- History of How We Got Here
  - Human Subjects
  - Research Integrity
  - Conflicts of Interest
  - Responsible Conduct of Research
- Cases

Ethical Framework for RCR

- Values – what is good
- Morals – right from wrong
- Ethics – morals in action
  - Not religion, not feelings, not laws, not culturally accepted norms
- Laws – norms formally promulgated by a political system and enforced through adjudication

Ethical Standards

- Utilitarian – provides the most good and does the least harm – Dr. Spock
- Rights – moral rights – based on human dignity -to make life choices, be told the truth, not be harmed, privacy, etc.
- Fairness/Justice – treat equals equally
- Common good – community approach – police, fire, education, etc.
- Virtue – actions should be consistent with fully evolved human condition – honesty, courage, compassion, generosity, tolerance, fidelity, integrity, fairness, self-control, prudence

Ethical Decision-making

- Could this hurt someone? Is there a good/bad alternative?
- Who has an interest?
- What are my options?
- Evaluate under standards – which option:
  - produces the most good (Utilitarian)
  - Respects the rights of all (Rights)
  - Treats people equally (Justice)
  - Best serves the community (Common Good)
  - Causes me to be the person I want to be (Virtue)

Human Subjects

- WWII
- Declaration of Helsinki
- Human Subject Regulations
- OHRP

Of Mice and Congressmen

US Developmental Events

- 1988/1989 NSF/OSI
- 1992 Office of Research Integrity
- 2000 White House Office of Science and Technology Policy
- 2002 NSF/ORI issues new regulations
- 2005 ORI issues new regulations
- 2010 FDA proposes misconduct regulations

Current US Definition

- Research misconduct means fabrication, falsification, or plagiarism in proposing , performing, or reviewing research, or in reporting research results.
- (a) Fabrication is making up data or results and recording or reporting them.
- (b) Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- (c) Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- (d) Research misconduct does not include honest error or differences of opinion.

Which Definition?

- Institutional
- Agency
- Federal
- Professional
- Journals
- International

RCR

- Human subject, animal welfare, lab practices
- COI – personal, professional, financial
- Mentor/mentee relationships
- Collaborative research including industry
- Peer review
- Data management, acquisition, sharing,
- Research misconduct
- Authorship and publication
- Member of society

Misconduct in Clinical Trials

- Approximately 1/5- 72 cases
- Falsification/fabrication of interview data
- Falsification/fabrication of patient's medical record
- Falsification/fabrication research records
- Failure to follow protocol
- Falsification/fabrication of consent form
- Substitution of specimen

Accusers

- Co-workers
- Replacement scientist
- Study monitors

- PI responsibility
  - Captain of ship
  - King and Lowe (negligence, lack of supervision, inadequate assignment of authority)

Parallel Processes

- Internal – Priv. Termination
- Administrative
  - FDA
  - ORI
- Civil Litigation
- Criminal

Consequences of a Misconduct Finding

- Notice in Federal Register
- Advisory Committee
- Debarment
- Correction of Literature
- Recovery of Funds
- Publicity
- Institutional Sanctions
- FDA/OHRP/ORI
- Congressional inquiry
- Professional license
- Civil litigation

Illustrative Legal Cases

- Fisher - lumpectomy
- Potti - cancer
- Wakefield – MMR
- Kornak – VA case
- Chinese Transplants
- Fals-Stewart

Eric Everett, PhD

UNC Institutional Research Integrity Officer

- Dr. Everett serves as the University liaison to the federal Office of Research Integrity. His responsibilities include evaluating allegations of research misconduct, protecting the rights of complainants and whistleblowers, and providing guidance and support regarding inquires into misconduct allegations. He is a professor in the Department of Pediatric Dentistry.
- Everett earned his M.S. in clinical immunology from the University of Florida College of Medicine, before attending the Medical University of South Carolina for his Ph.D. in molecular cell biology and pathobiology. Following that, Dr. Everett did his postdoctoral work in hematopoiesis and medical genetics at the Indiana University School of Medicine. After spending eight years on the Indiana University faculty, Everett joined the UNC School of Dentistry faculty.
- His research interests include the identification of genes and pathways in the embryonic and postnatal development of craniofacial, oral and dental structures.

"Misconduct in Research: What is the RIO's Role"

Eric T. Everett, Ph.D.
Professor and Chair, Division of Oral and Craniofacial Health Sciences
Professor Division of Pediatric and Public Health
UNC Adams School of Dentistry
Institutional Research Integrity Officer
University of North Carolina at Chapel Hill
Phone: 919-537-3182
Email: research_integrity@unc.edu

5th Annual IRB Retreat: February 19, 2020
IRB Responsibilities for Review & Management of Non-Compliance

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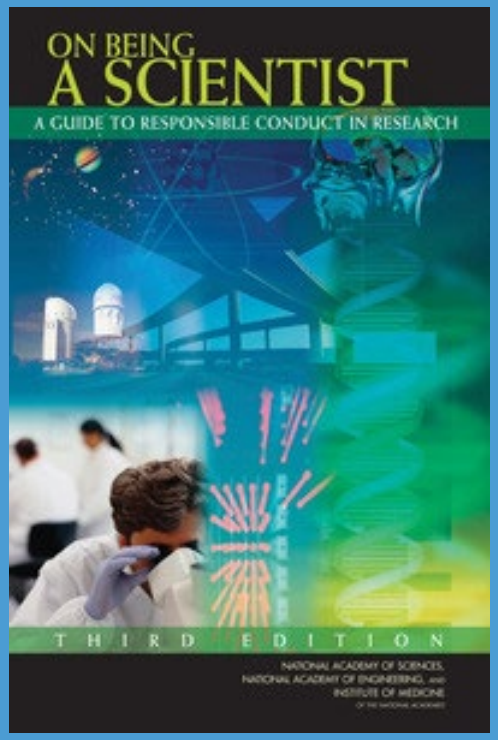
Where the rubber meets the road

"The scientific enterprise is built on a **foundation of trust**. Society trusts that scientific research results are an honest and accurate reflection of a researcher's work. Researchers equally trust that their colleagues have gathered data carefully, have used appropriate analytic and statistical techniques, have reported their results accurately, and have treated the work of other researchers with respect."



The University's Position

"Public trust in the integrity and ethical behavior of scholars must be maintained if research is to continue to play its proper role in our University and society. It is the policy of the University of North Carolina at Chapel Hill (hereinafter "University") that its research be carried out with the highest standards of integrity and ethical behavior."[1]

[1] **Policy and Procedures on Responding to Allegations of Research Misconduct http://policies.unc.edu/files/2014/10/Research-Misconduct.pdf**

It is the responsibility of **all members of the research community** (faculty, students, trainees, postdocs, visiting scholars, technicians and others conducting research at the University) to demonstrate research integrity. The University's policy applies to all **research regardless of funding**.

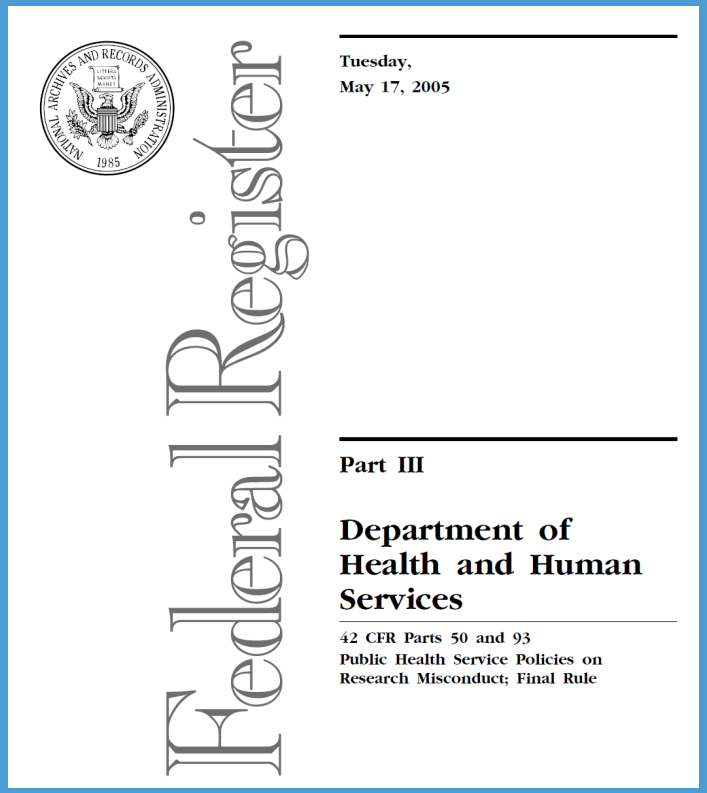
Institutional Responsibility

- Research misconduct involving PHS support is contrary to the interests of the PHS and the Federal government and to the health and safety of the public, to the integrity of research, and to the conservation of public funds.
- The U.S. Department of Health and Human Services (HHS) and institutions that apply for or receive Public Health Service (PHS) support for biomedical or behavioral research, biomedical or behavioral research training, or activities related to that research or research training share responsibility for the integrity of the research process.

Public Health Service (PHS) Policies on Research Misconduct – 42 CFR Part 93 – June 2005

Responsibility and Confidentiality

- Obligation to report concern for possible research misconduct.
  - Report concern to
    - department head (chair)
    - directly to the Research Integrity Officer (RIO) or
    - through a reporting channel i.e. EthicsPoint (anonymous) (https://secure.ethicspoint.com/domain/en/report_company.asp).
- Research misconduct reviews are confidential personnel matters.
- Protection of individuals involved in research misconduct proceedings. Whistleblower protection (PHS) and the University's Retaliation Policy (http://sexualassaultanddiscriminationpolicy.unc.edu/prohibited-conduct/retaliation/and http://policies.unc.edu/policies/research-misconduct/)



Sec 93.103 Research Misconduct

Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

When research is supported by the Public Health Service (PHS), National Science Foundation (NSF), Department of Energy (DOE) and other Federal Agencies the University complies with special reporting requirements found in PHS Policies on Research Misconduct – 42 CFR Part 93 and NSF regulations at 45 CFR 689.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- Research misconduct does not include honest error or differences of opinion.

Public Health Service (PHS) Policies on Research Misconduct – 42 CFR Part 93 – June 2005

- The regulation's purpose is to:
  - Protect the public health and safety
  - To protect the integrity of the scientific research and the research record
  - Conserve public funds
  - Define the responsibilities of the "covered institutions"
  - Define the steps/process for handling allegations of research misconduct
  - Assure notification of ORI of exigent circumstances

Public Health Service (PHS) Policies on Research Misconduct – 42 CFR Part 93 – June 2005

- **§ 93.318 Notifying ORI of special circumstances:**
  - a) Health or safety of the public is at risk, including an immediate need to protect human or animal subjects.
  - (b) HHS resources or interests are threatened.
  - (c) Research activities should be suspended.
  - (d) There is reasonable indication of possible violations of civil or criminal law.
  - (e) Federal action is required to protect the interests of those involved in the research misconduct proceeding.
  - (f) The research institution believes the research misconduct proceeding may be made public prematurely so that HHS may take appropriate steps to safeguard evidence and protect the rights of those involved.
  - (g) The research community or public should be informed.

Public Health Service (PHS) Policies on Research Misconduct – 42 CFR Part 93 – June 2005

Current Status: *Active* **PolicyStat ID:** *4512713*

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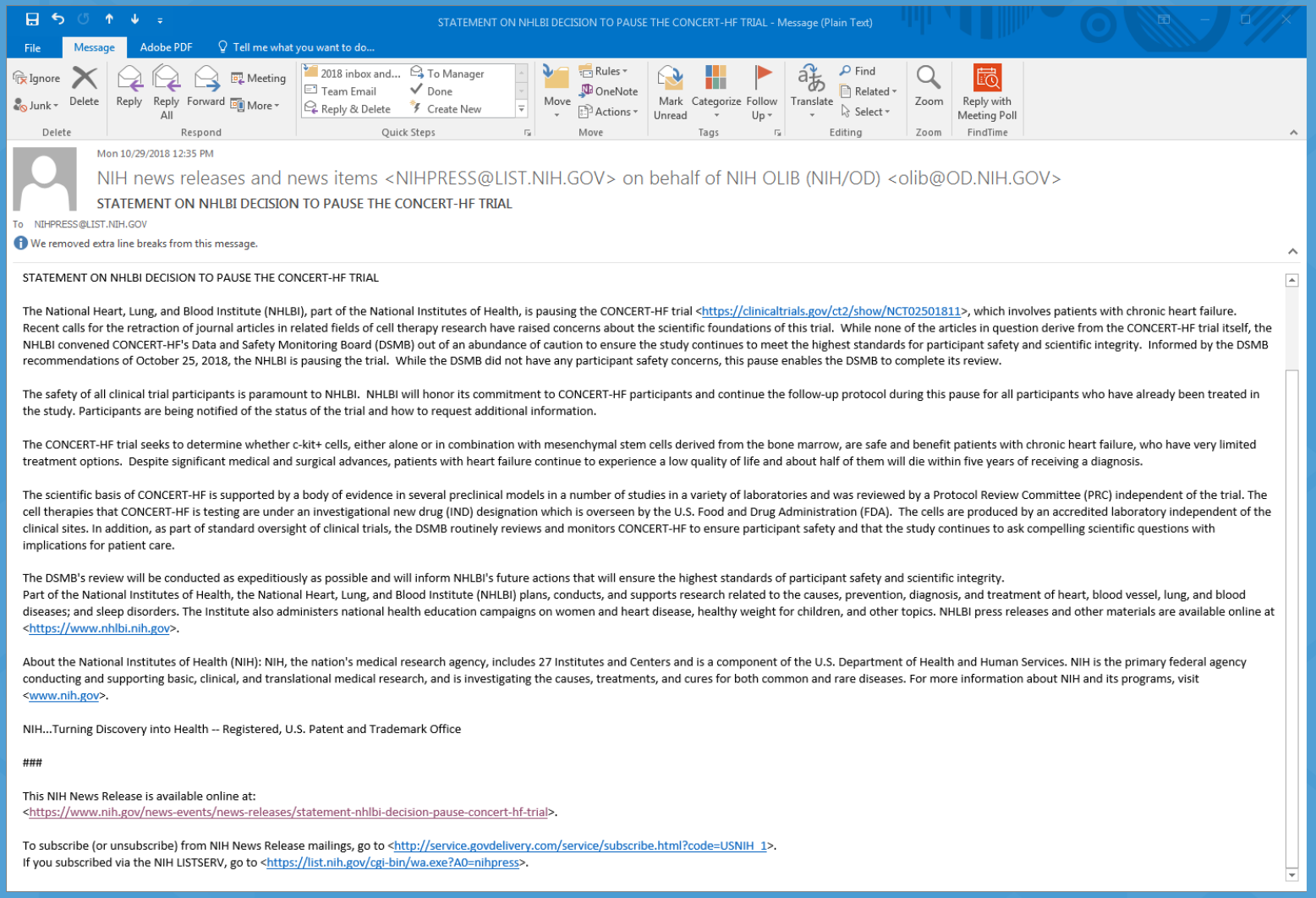
Origination:	*10/7/2014*
Effective:	*10/7/2014*
Last Approved:	*10/7/2014*
Last Revised:	*10/7/2014*
Next Review:	*10/7/2018*
Issuing University Officer:	*Terry Magnuson: Distinguished Professor*
Responsible Unit:	*Research*

University of North Carolina at Chapel Hill Policy and Procedures on Responding to Allegations of Research Misconduct



STATEMENT ON NHLBI DECISION TO PAUSE THE CONCERT-HF TRIAL

The National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health, is pausing the CONCERT-HF trial <https://clinicaltrials.gov/ct2/show/NCT02501811>, which involves patients with chronic heart failure. Recent calls for the retraction of journal articles in related fields of cell therapy research have raised concerns about the scientific foundations of this trial. While none of the articles in question derive from the CONCERT-HF trial itself, the NHLBI convened CONCERT-HF's Data and Safety Monitoring Board (DSMB) out of an abundance of caution to ensure the study continues to meet the highest standards for participant safety and scientific integrity. Informed by the DSMB recommendations of October 25, 2018, the NHLBI is pausing the trial. While the DSMB did not have any participant safety concerns, this pause enables the DSMB to complete its review.

The safety of all clinical trial participants is paramount to NHLBI. NHLBI will honor its commitment to CONCERT-HF participants and continue the follow-up protocol during this pause for all participants who have already been treated in the study. Participants are being notified of the status of the trial and how to request additional information.

The CONCERT-HF trial seeks to determine whether c-kit+ cells, either alone or in combination with mesenchymal stem cells derived from the bone marrow, are safe and benefit patients with chronic heart failure, who have very limited treatment options. Despite significant medical and surgical advances, patients with heart failure continue to experience a low quality of life and about half of them will die within five years of receiving a diagnosis.

The scientific basis of CONCERT-HF is supported by a body of evidence in several preclinical models in a number of studies in a variety of laboratories and was reviewed by a Protocol Review Committee (PRC) independent of the trial. The cell therapies that CONCERT-HF is testing are under an investigational new drug (IND) designation which is overseen by the U.S. Food and Drug Administration (FDA). The cells are produced by an accredited laboratory independent of the clinical sites. In addition, as part of standard oversight of clinical trials, the DSMB routinely reviews and monitors CONCERT-HF to ensure participant safety and that the study continues to ask compelling scientific questions with implications for patient care.

The DSMB's review will be conducted as expeditiously as possible and will inform NHLBI's future actions that will ensure the highest standards of participant safety and scientific integrity.
Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <https://www.nhlbi.nih.gov>.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <www.nih.gov>.

NIH...Turning Discovery into Health -- Registered, U.S. Patent and Trademark Office

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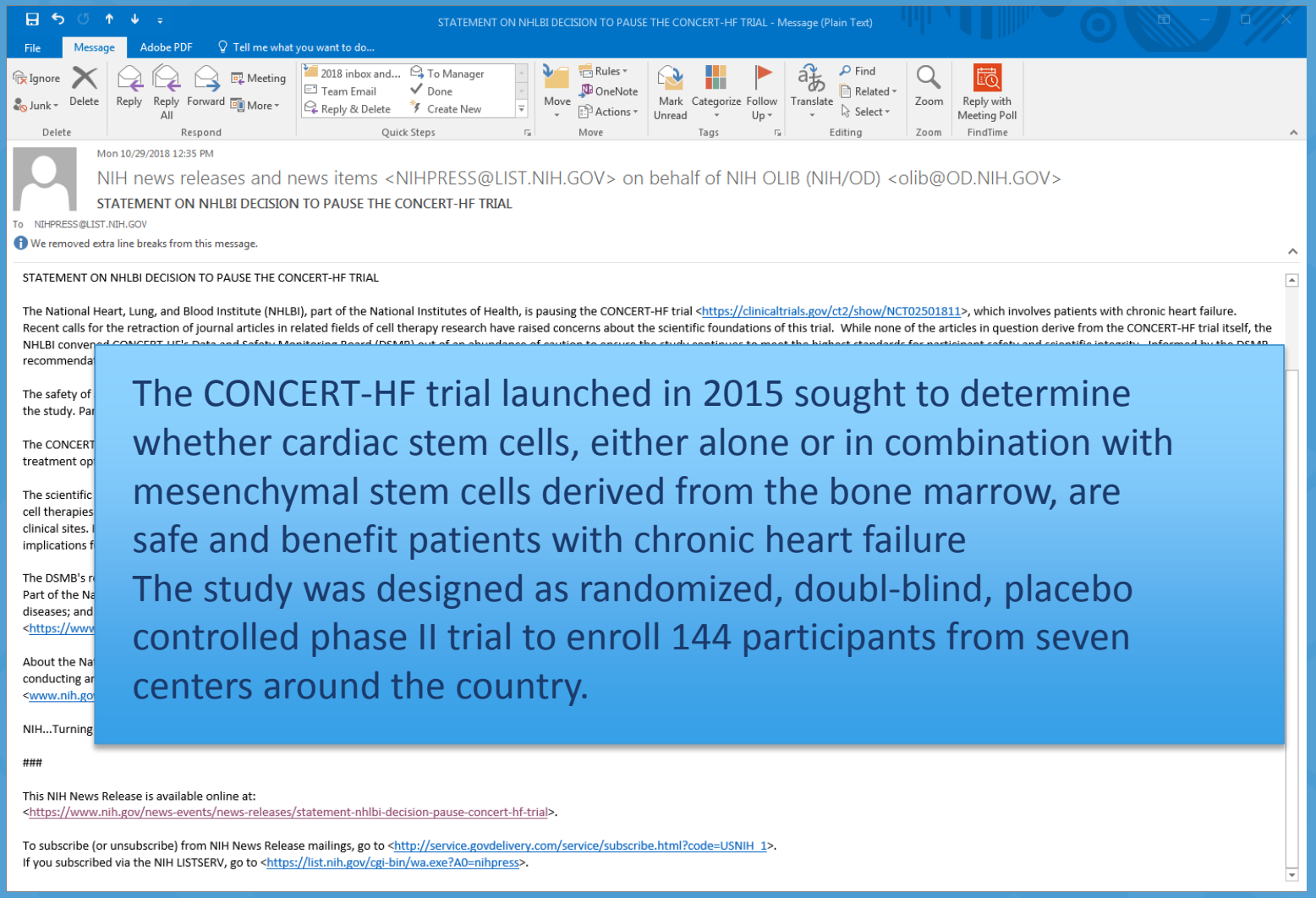
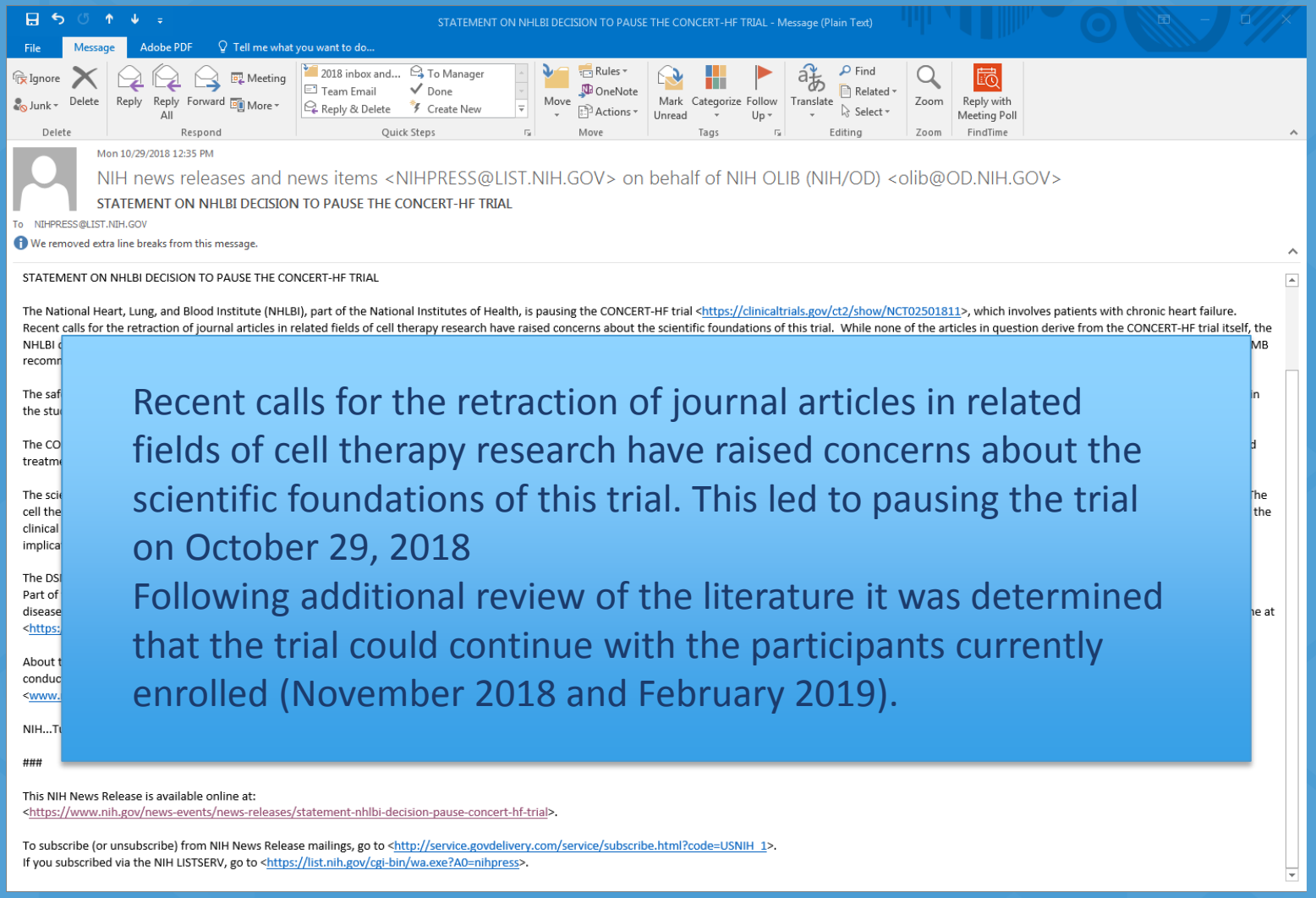
This NIH News Release is available online at:
<https://www.nih.gov/news-events/news-releases/statement-nhlbi-decision-pause-concert-hf-trial>.

To subscribe (or unsubscribe) from NIH News Release mailings, go to <http://service.govdelivery.com/service/subscribe.html?code=USNIH_1>.
If you subscribed via the NIH LISTSERV, go to <https://list.nih.gov/cgi-bin/wa.exe?A0=nihpress>.


STATEMENT ON NHLBI DECISION TO PAUSE THE CONCERT-HF TRIAL - Message (Plain Text)
File
Message
Adobe PDF
Tell me what you want to do...
Ignore
Junk
Delete
Reply
Reply All
Forward
Meeting
More
2018 inbox and...
Team Email
Reply & Delete
To Manager
Done
Create New
Move
Rules
OneNote
Actions
Mark Unread
Categorize
Follow Up
Translate
Find
Related
Select
Zoom
Reply with Meeting Poll
Delete
Respond
Quick Steps
Move
Tags
Editing
Zoom
FindTime
Mon 10/29/2018 12:35 PM
NIH news releases and news items <NIHPRESS@LIST.NIH.GOV> on behalf of NIH OLIB (NIH/OD) <olib@OD.NIH.GOV>
STATEMENT ON NHLBI DECISION TO PAUSE THE CONCERT-HF TRIAL
To NIHPRESS@LIST.NIH.GOV
We removed extra line breaks from this message.
STATEMENT ON NHLBI DECISION TO PAUSE THE CONCERT-HF TRIAL
The National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health, is pausing the CONCERT-HF trial <https://clinicaltrials.gov/ct2/show/NCT02501811>, which involves patients with chronic heart failure.
Recent calls for the retraction of journal articles in related fields of cell therapy research have raised concerns about the scientific foundations of this trial. While none of the articles in question derive from the CONCERT-HF trial itself, the
NHLBI convened
recommenda
The safety of
the study. Par
The CONCERT
treatment op
The scientific
cell therapies
clinical sites.
implications f
The DSMB's r
Part of the Na
diseases; and
<https://www
About the Na
conducting ar
<www.nih.go
NIH...Turning
###
This NIH News Release is available online at:
<https://www.nih.gov/news-events/news-releases/statement-nhlbi-decision-pause-concert-hf-trial>.
To subscribe (or unsubscribe) from NIH News Release mailings, go to <http://service.govdelivery.com/service/subscribe.html?code=USNIH_1>.
If you subscribed via the NIH LISTSERV, go to <https://list.nih.gov/cgi-bin/wa.exe?A0=nihpress>.
The CONCERT-HF trial launched in 2015 sought to determine whether cardiac stem cells, either alone or in combination with mesenchymal stem cells derived from the bone marrow, are safe and benefit patients with chronic heart failure
The study was designed as randomized, doubl-blind, placebo controlled phase II trial to enroll 144 participants from seven centers around the country.


STATEMENT ON NHLBI DECISION TO PAUSE THE CONCERT-HF TRIAL - Message (Plain Text)
File
Message
Adobe PDF
Tell me what you want to do...
Ignore
Junk
Delete
Reply
Reply All
Forward
Meeting
More
2018 inbox and...
Team Email
Reply & Delete
To Manager
Done
Create New
Move
Rules
OneNote
Actions
Mark Unread
Categorize
Follow Up
Translate
Find
Related
Select
Zoom
Reply with Meeting Poll
Delete
Respond
Quick Steps
Move
Tags
Editing
Zoom
FindTime
Mon 10/29/2018 12:35 PM
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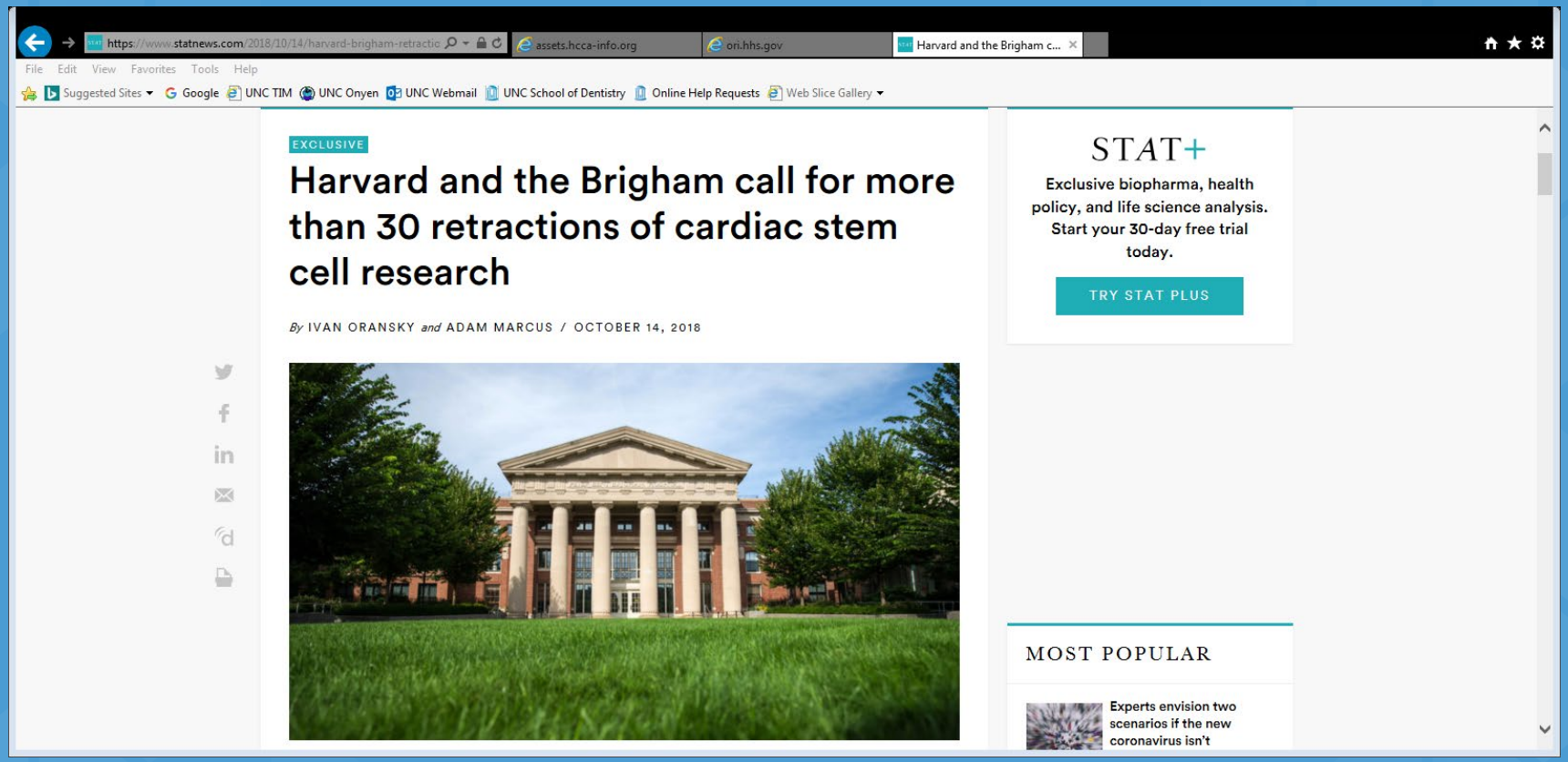
Recent calls for the retraction of journal articles in related fields of cell therapy research have raised concerns about the scientific foundations of this trial. This led to pausing the trial on October 29, 2018
Following additional review of the literature it was determined that the trial could continue with the participants currently enrolled (November 2018 and February 2019).
###
This NIH News Release is available online at:
<https://www.nih.gov/news-events/news-releases/statement-nhlbi-decision-pause-concert-hf-trial>.
To subscribe (or unsubscribe) from NIH News Release mailings, go to <http://service.govdelivery.com/service/subscribe.html?code=USNIH_1>.
If you subscribed via the NIH LISTSERV, go to <https://list.nih.gov/cgi-bin/wa.exe?A0=nihpress>.



https://www.washingtonpost.com/science/2018/10/15/harvard-investigation-finds-fraudulent-data-papers-by-heart-researcher/?utm_term=.50a4c7b0a081

§ 93.223 Research Misconduct Proceeding: Administrative & Confidential Personnel Matter)

"Complainant"
- Journals
- Anonymous
- Proximal to accused (i.e., in lab, collaborator)
- Received from ORI
- Retraction Watch

"Respondent"
- Anyone performing, proposing, reporting
- Can be multiple respondents in a given matter
- All levels of appointment can and have been respondents

Office of Research Integrity
- Jurisdiction over PHS funded work
- Informed when review reaches Investigation
- Waits for institutional finding before own review

§ 93.223 Research Misconduct Proceeding: Administrative & Confidential Personnel Matter)

"Allegation"

(1) falls within the definition of research misconduct in this Policy and applicable federal regulations, including, as applicable 42 C.F.R. § 93.103 and other federal agency guidance, and (2) is sufficiently credible and specific so that potential evidence of research misconduct may be identified. An Inquiry will be conducted if both of these criteria are met.

"Inquiry"

conduct an initial review of the available evidence to determine whether an Investigation is warranted. An Investigation is warranted if: (1) there is a reasonable basis for concluding that the allegation falls within the definition of research misconduct in this Policy and (2) preliminary information-gathering and preliminary fact-finding from the Inquiry indicate that the allegation may have substance.

§ 93.223 Research Misconduct Proceeding: Administrative & Confidential Personnel Matter)

"Investigation"

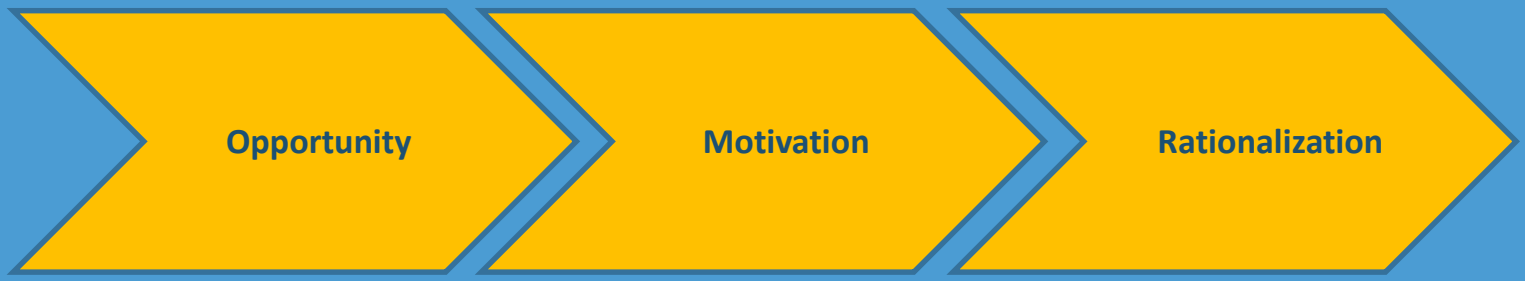
Means the formal development of a factual record and the examination of that record leading to a decision not to make a finding of research misconduct or to a recommendation for a finding of research misconduct which may include a recommendation for other appropriate actions, including administrative actions.

A finding of research misconduct requires that—

(a) There be a significant departure from accepted practices of the relevant research community; and

(b) The misconduct be committed intentionally, knowingly, or recklessly; and

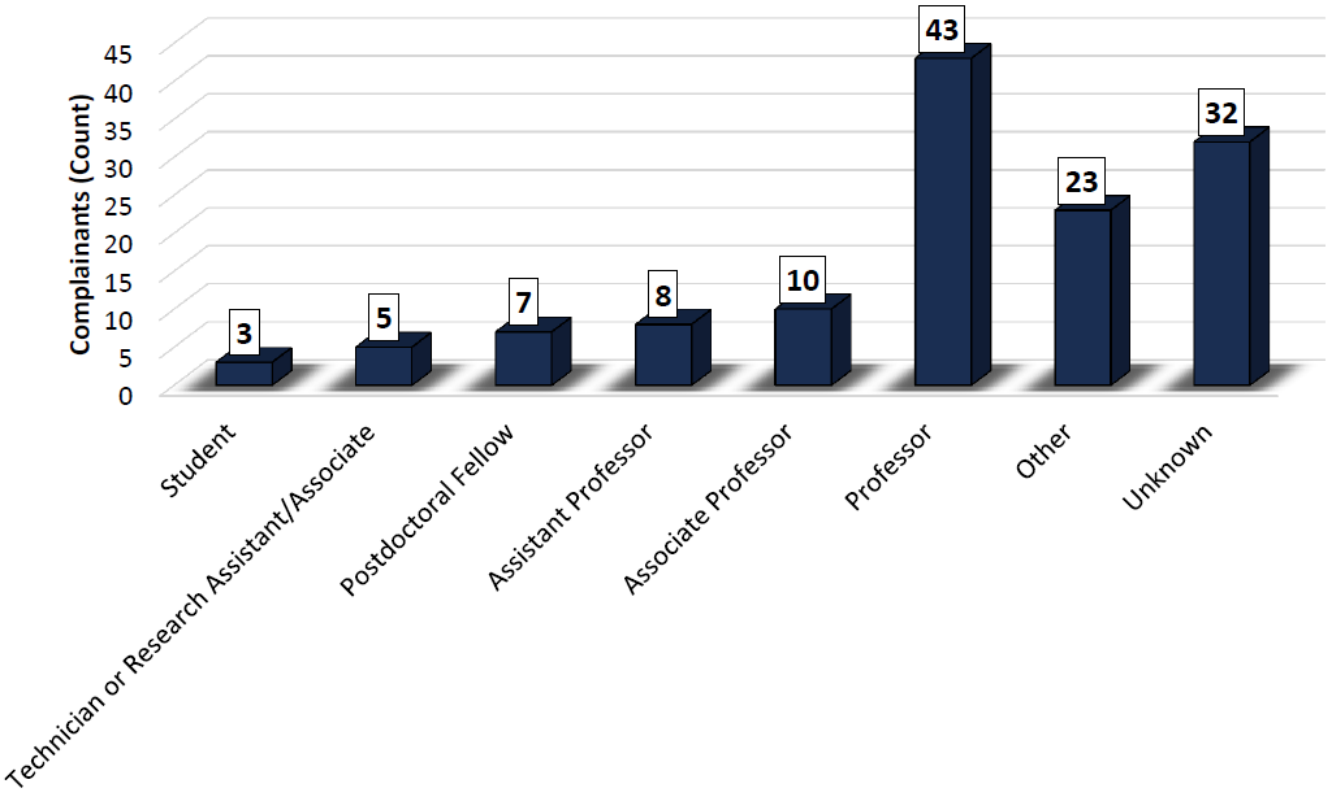
(c) The allegation be proven by a preponderance of the evidence.



Research Misconduct:

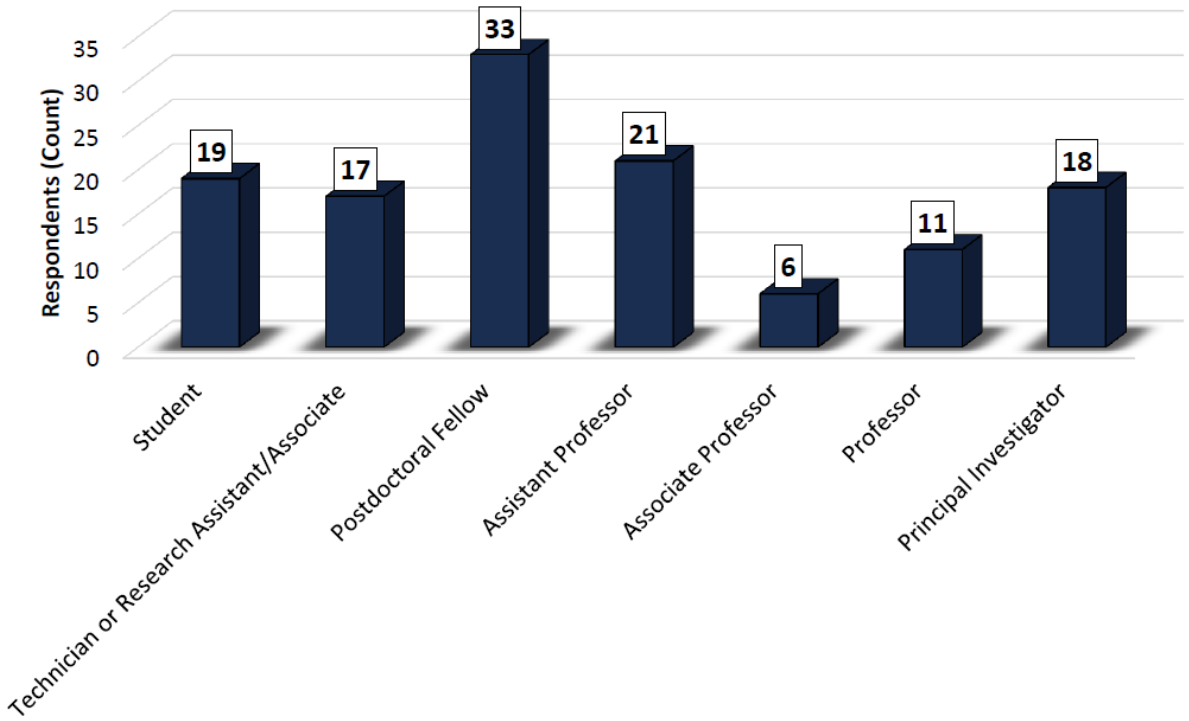
- can be committed by any member of the research team
- may occur at any stage of the research

Rank of Complainants in Cases with Findings of Research Misconduct, 2006 - 2015



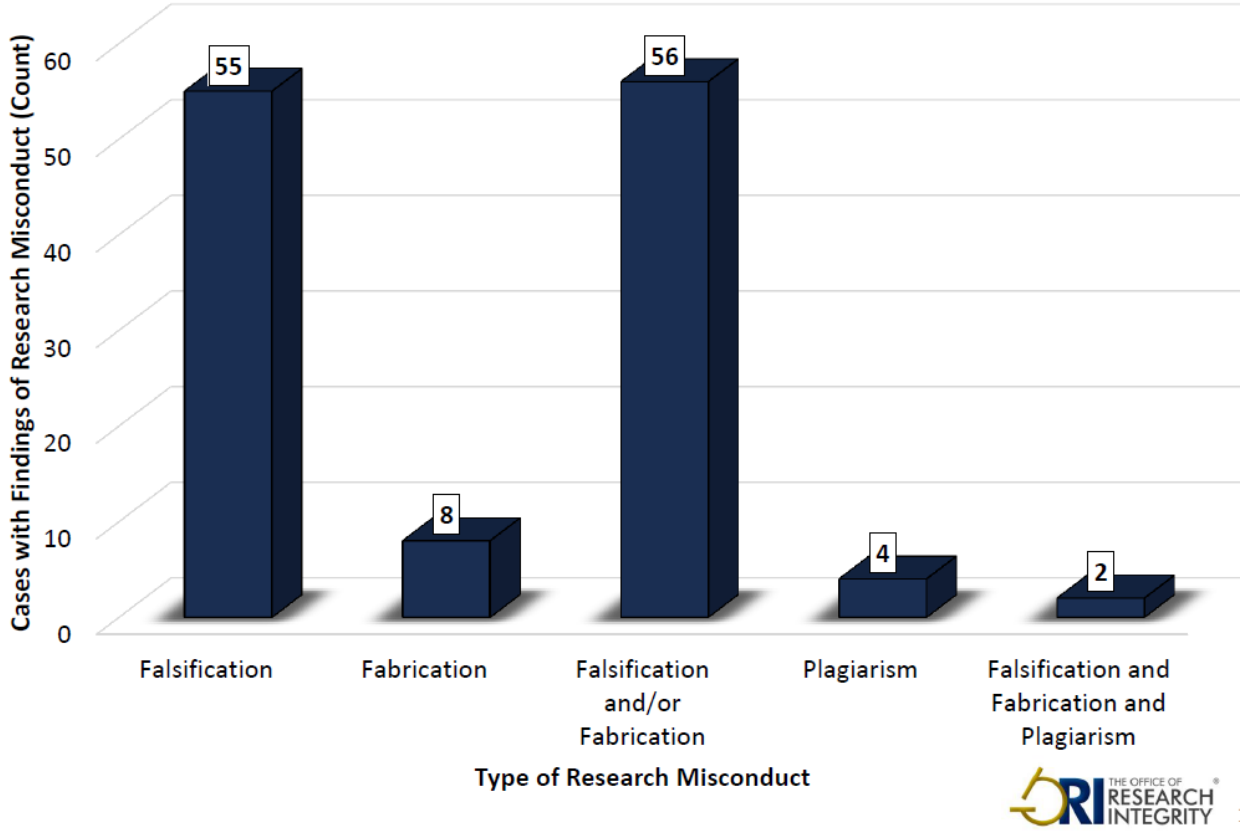
THE OFFICE OF RESEARCH INTEGRITY

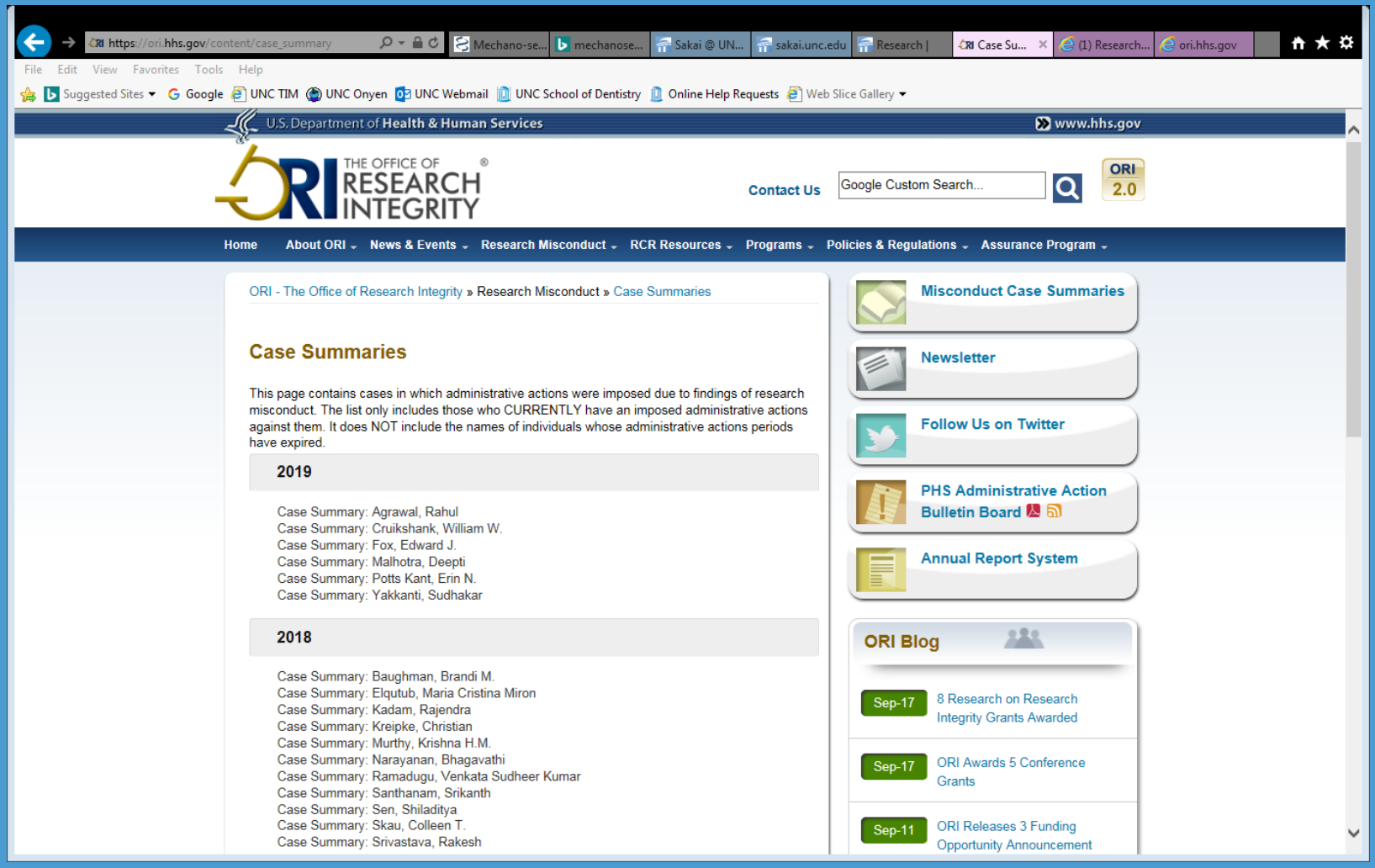
Rank of Respondents in Cases with Findings of Research Misconduct, 2006 - 2015

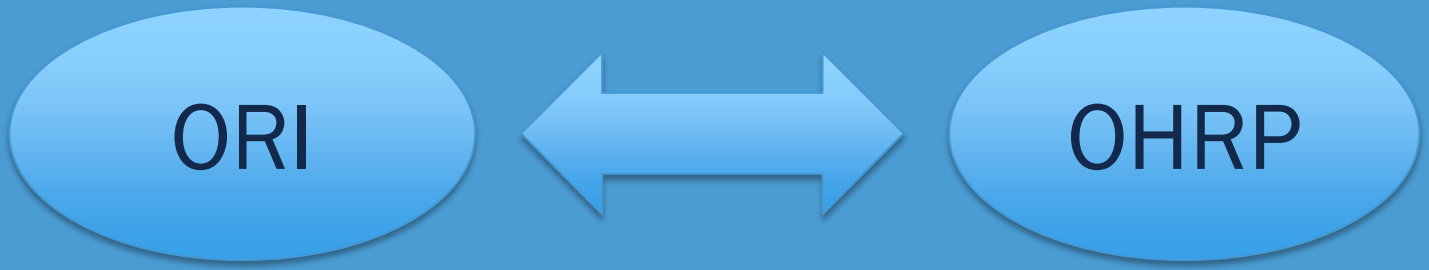


THE OFFICE OF RESEARCH INTEGRITY

Types of Misconduct in Cases with Findings of Research Misconduct, 2006 - 2015




https://ori.hhs.gov/content/case_summary
Mechano-se...
mechanose...
Sakai @ UN...
sakai.unc.edu
Research |
Case Su...
(1) Research...
ori.hhs.gov
File Edit View Favorites Tools Help
Suggested Sites
Google
UNC TIM
UNC Onyen
UNC Webmail
UNC School of Dentistry
Online Help Requests
Web Slice Gallery
U.S. Department of Health & Human Services
www.hhs.gov
THE OFFICE OF RESEARCH INTEGRITY
Contact Us
Google Custom Search...
ORI 2.0
Home
About ORI
News & Events
Research Misconduct
RCR Resources
Programs
Policies & Regulations
Assurance Program
ORI - The Office of Research Integrity » Research Misconduct » Case Summaries
Case Summaries
This page contains cases in which administrative actions were imposed due to findings of research misconduct. The list only includes those who CURRENTLY have an imposed administrative actions against them. It does NOT include the names of individuals whose administrative actions periods have expired.
2019
Case Summary: Agrawal, Rahul
Case Summary: Cruikshank, William W.
Case Summary: Fox, Edward J.
Case Summary: Malhotra, Deepti
Case Summary: Potts Kant, Erin N.
Case Summary: Yakkanti, Sudhakar
2018
Case Summary: Baughman, Brandi M.
Case Summary: Elqutub, Maria Cristina Miron
Case Summary: Kadam, Rajendra
Case Summary: Kreipke, Christian
Case Summary: Murthy, Krishna H.M.
Case Summary: Narayanan, Bhagavathi
Case Summary: Ramadugu, Venkata Sudheer Kumar
Case Summary: Santhanam, Srikanth
Case Summary: Sen, Shiladitya
Case Summary: Skau, Colleen T.
Case Summary: Srivastava, Rakesh
Misconduct Case Summaries
Newsletter
Follow Us on Twitter
PHS Administrative Action Bulletin Board
Annual Report System
ORI Blog
Sep-17 8 Research on Research Integrity Grants Awarded
Sep-17 ORI Awards 5 Conference Grants
Sep-11 ORI Releases 3 Funding Opportunity Announcement


ORI
OHRP

Be prepared to check the box

serve as guarantor of the work you performed, had full access to all the data for the work you performed, and take responsibility for the integrity of the data and the accuracy of the data analysis.

UNC-CH

Eric T. Everett, Ph.D.
Institutional Research Integrity Officer
University of North Carolina at Chapel Hill
Office: 919-537-3182
Email: research_integrity@unc.edu or eric_everett@unc.edu

THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

15-Minute Break

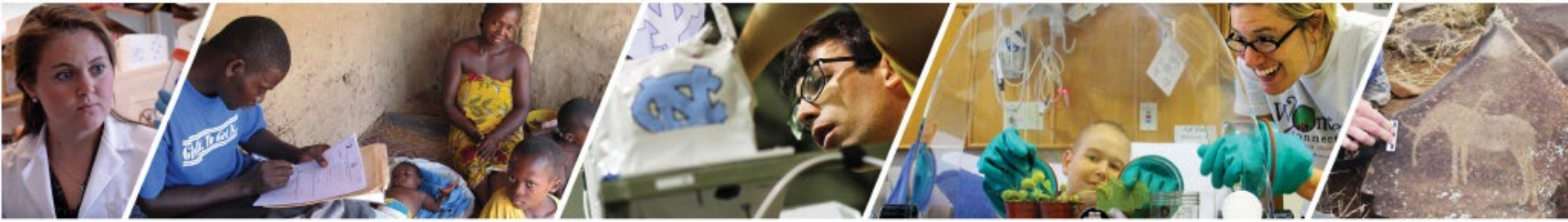
10:30 – 10:45 AM

Christine M. Nelson RN, BSN, MBA, CCRC
Director, Office of Clinical Trials

Chris has been at UNC just under 6 and ½ years. She came to Chapel Hill from Hawaii working at the largest healthcare system in the state and partnering with the University of Hawaii. Chris' background is ER, trauma and flight nursing. She began her career in research when asked if she would be willing to take on the Research Institute at Hawaii Pacific Health. As you can imagine it was a big change from the emergency room as she had no real background in research.

While at UNC she has had the opportunity to roll out the Clinical Trials Quality Assurance and billing Compliance programs. Christine is committed to improving research processes within UNC and by her retirement hopes to tear down as many silos as possible.

Office of Clinical Trials



Christine Nelson, Director Office of Clinical Trials

UNC RESEARCH

Office of Clinical Trials

The core purpose of the Office of Clinical Trials (OCT) to ensure compliance with federal, state and institutional requirements.

- Serving as the point of contact for questions or issues related to clinical trials
- Developing and implementing programs and initiatives to enhance the quality of clinical research and support regulatory compliance, through the implementation of the OnCore clinical trials management system enterprise wide.
- Our office is available for education, consultation and guidance on the conduct of clinical trials.

Human Subjects Research Protection Program

Supporting the Human Research Protection Program (HRPP)by conducting post IRB approval of clinical studies through the Clinical Trials Quality Assurance (CTQA)program.

FY 2019:

Total - 56

Routine review – 11

Requested reviews – 4

Lineberger Comprehensive Cancer Center (LCCC) Data Safety Monitoring plan reviews – 25

LCCC Multisite when UNC/LCCC is the coordinating site – 16

Research Billing Compliance

Ensure correct clinical trial billing of research subjects through the Research Billing Compliance Program.

- Education
- Billing audits
- Billing Coverage Analysis

Clinical Research Billing

Routine audits completed

protocols - 14

- # subjects - 220

Special projects audits completed

- # protocols - 14
- # subjects-

ClinicalTrials.gov

Ensure compliance with the ClinicalTrials.gov registration and results reporting

- DHHS regulation and NIH policy affecting registration and results reporting for clinical trials became effective on January 18, 2017. The DHHS regulation, known as the Final Rule, describes requirements for registering and submitting summary results information for certain Applicable Clinical Trials to ClinicalTrials.gov. A complementary NIH policy applies to all clinical trials funded by NIH, regardless of whether they are subject to the Final Rule
- Possible non-compliance consequences include the following if required registration and results reporting cannot be verified:
  - Suspension, termination, or retraction of grant (or contract) funding;
  - Consideration of the non-compliance in future funding decisions;
  - Civil monetary penalties to the “Responsible Party” (i.e., Principal Investigator) of up to $12,000/day.

Scientific Review Committee

Coordinate the Scientific Review Committee and serve as a resource for protocol development for the research community

- All clinical research conducted at the University of North Carolina at Chapel Hill involving **greater than minimal risk** must undergo scientific review. Scientific review is a process that evaluates the scientific merit of a clinical trial protocol. The review must be completed and approved by the Scientific Review Committee (SRC) or Oncology Protocol Review Committee prior to IRB submission.
- The Protocol Review Committee conducts scientific review of all oncology trials

Compliance Checks

- Good Clinical Practices training
- Completed coverage analysis
- IRB approval
- Fully executed agreement
- Ensure compliance by reviewing the billing coverage analysis, fully executed agreement and IRB approved consent form for congruency and accuracy

Compliance Checks

FY 2019

Using the contract management system (ALICE) compliance with GCP training, IRB approval, completion of the billing coverage analysis (BCA), COI is confirmed and consistency between the clinical trial agreement, IRB approved informed consent and BCA on all industry sponsored clinical trials is confirmed prior to being forwarded to the Office of Sponsored Research for account set up.

<u>Compliance Reviews:</u>

Number of BCA new submissions reviewed - 245

BCAs finalized - 260

More numbers

Regulatory Inspections

The CTQA team assists investigators and study teams with FDA, DEA and Sponsor audits. Upon notification of an audit the CTQA with work with the investigator and team by reviewing study documents, providing education on interaction with inspectors/auditors.

Number of FDA inspections supported:

FY 2019 - 3

FY 2018 - 3

Number of DEA inspections supported:

FY 2019 – 0

FY 2018 - 1

ClinicalTrials.gov

OCT has **one** dedicated staff member monitoring ClinicalTrials.gov, reaching out to investigators before results are due and assisting with the complicated task of results reporting in the CT.gov system. She also assists investigators in responding to questions from CT.gov.

OCT is **100%** compliant with results reporting in ClinicalTrials.gov

Subject Injury Language

As of April 2018 the UNC has approved standard subject injury language for our ICFs

- The Industry Contracting team in OSR is required to obtain certain subject injury language in the CTA with industry sponsors, this is based on the MOU in place with the UNC HC system
- Language can be slightly modified to maintain congruency between the CTA and ICF.
- Language is modified for PI initiated and Federally or non-profit funded clinical trials
- The “official” letter approving the SIL is generated by OCT. Saved on a shared drive.

Additional services/projects

Assisting when a subject injury does occur

CRO and Sponsor Liaison

Single Submission project

Protocol Builder

Payments to study subjects

Consultation

Educational Activities

Operational Excellence

CRSO planning

CTMS – OnCore

Rate Cards

REDCap Cloud

NRP

Questions?

Valorie A. Buchholz
RN, BSN, CCRC, CHRC

Associate Director for Quality Assurance

Office of Clinical Trials

THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

Clinical Trial Quality Assurance Program (CTQA)

Valorie Buchholz

Associate Director, CTQA Program

CTQA

- Program development began January, 2014

- Designed to support investigators in ensuring research is conducted in accordance with federal, state, and institutional regulations

- Goal: to review 10-15% clinical trials each year

First Routine Review: November 2014

First Directed Review: October 2014

	FY 2016	FY 2017	FY 2018	FY 2019
Routine	3	43	39	37
Directed (For Cause)	12	10	4	2
External Inspections (FDA, DEA, Other Countries)	2	2	6	3

Which regulations inform our review process?

- ❑ 45CFR46
- ❑ 45CFR164
- ❑ 21CFR50
- ❑ 21CFR312
- ❑ 21CFR812
- ❑ ICH GCP – E6(R2) - includes biomedical as well as social/behavioral research
- ❑ OHRE SOPs
- ❑ Other regulations as applicable

Selection Criteria for Routine Reviews

(not exhaustive)

- Investigators holding an IND/IDE inclusive of those who are the PI when UNC holds the IND/IDE
- Studies which are open to enrollment or have subjects still undergoing intervention
- Phase 1 studies
- High enrollment
- Vulnerable Populations
- Studies which have multiple NSI reports
- Federally funded studies without external monitoring
- Studies with significant number of protocol deviations

Reports

Observation Category	# of Observations
1-Subject Accountability	
2-Informed Consent	
3-Site Regulatory Administration	
4-Staff Qualifications	
5-Protocol Compliance	
6-Subjects Records	
7-Data Management	
8-Documentation Practices	
9-Subject Protection and Adverse Events	
10-Investigational Product	
11-Facilities and Equipment	
12- Other Area(s) Observations	
13- Clinical Trials Disclosure (CTD)	
TOTAL	

Example

1. Informed Consent/Assent/HIPAA Forms

1.1	**Telephone Screening/Oral Consent information used prior to IRB approval**	
	Description:	Questions related to whether subjects had history of [redacted] were asked of 4 parents prior to IRB approval of that question on the telephone screening script. Information on the Oral Consent regarding an email link to non-parent providers and the ability of the study team to contact those non-parent providers was provided to the parents. (See attached tables – Telephone Screening used before IRB approval – update included [redacted] question **AND** Oral Consent. Information highlighted in yellow on the tables).
	Regulatory Reference:	45CFR46; ICH GCP 4.8.2; OHRE SOP 701
	Rationale:	Represents a major deviation from or deficiency in compliance with applicable regulations, guidelines, protocol, standard operating procedures (SOPs) and/or policies.
	CAPA Plan:	Please submit this finding to the IRB as a new safety information (NSI) report. Per IRB procedures, NSI reports must be submitted within 7 calendar days of becoming aware of the event. **Please submit the CAPA plan directly to the IRB with this NSI report.**

Routine Review Report Distribution

Division Chief (if applicable)
Department Chair
Research Compliance Officer
Office of University Counsel – Research Liaison
OHRE Director
OHRE QI/QA Manager
OCT Director

(If SOM PI – Director, Compliance and Research Integrity)

Directed Reviews

Studies reviewed in response to a directive by:

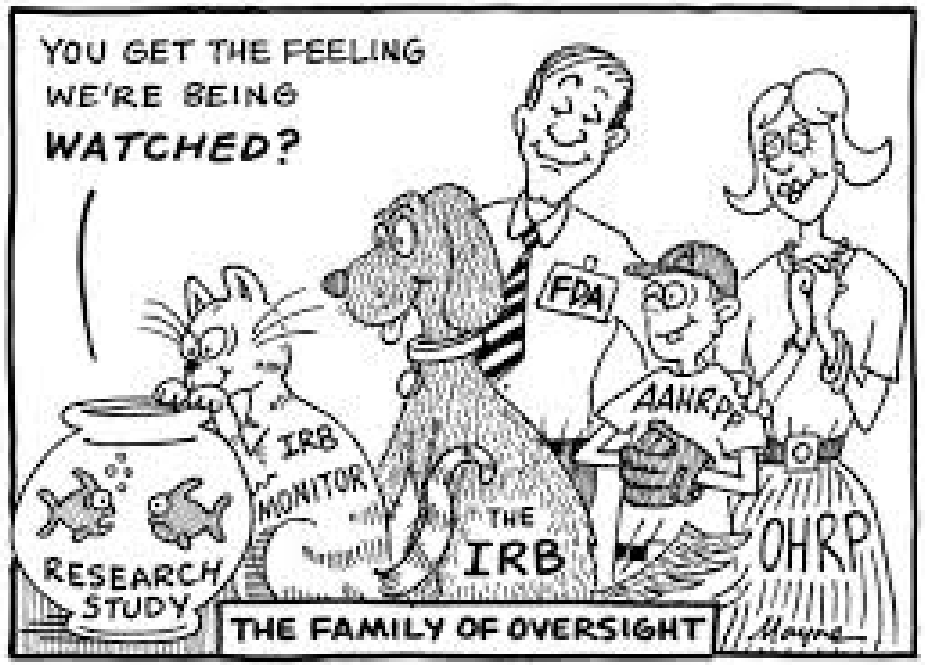
- Institutional Official
- OHRE Director/IRB Chairs

Directed Review Report Distribution

Dependent on Office requesting the review

PI does not receive a copy from the reviewers

- reviewers will discuss findings with PI


YOU GET THE FEELING WE'RE BEING WATCHED?
FDA
AAHRPP
IRB MONITOR
THE IRB
OHRP
RESEARCH STUDY
THE FAMILY OF OVERSIGHT

Questions?


UNC
RESEARCH

Vignettes & Group Discussion

Acknowledgements for the Scenarios

- Ernest Prentice, PhD,

  Former Assistant Vice-Chancellor

  University of Nebraska Medical Center

- Bruce Gordon, MD

  Assistant Vice-Chancellor for Regulatory Affairs

  Executive Chairman, Institutional Review Boards

  Professor, Pediatrics

  University of Nebraska Medical Center

Lunch in Willow Lounge

12:00 – 1:00PM