

Research Integrity in Extramural Research at the National Institutes of Health

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Sponsor Influences on the Quality and Independence of Health Research: A Workshop (NASEM)

December 14, 2022



- No relationships to disclose

- Rigor and transparency in applications
- Avoiding bias in funding decisions
- Allegations of research misconduct
- Financial Conflicts of Interest (FCOI)
- Pre-registration and reporting of Clinical Trials
- NIH Data Management and Sharing Policy

Rigor and Transparency in Applications

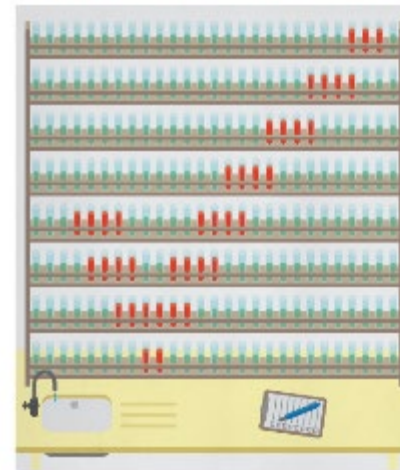


Enhancing Reproducibility through Rigor & Transparency

Four areas of clarification

1. Rigor of the prior research
2. Scientific rigor of the proposed research
3. Relevant biological variables, such as sex
4. Authentication of key biological and/or chemical resources

Started with applications due
on January 25, 2016



NIH plans to enhance reproducibility

Francis S. Collins and Lawrence A. Tabak discuss initiatives that the US National Institutes of Health is exploring to restore the self-sufficiency of preclinical research.

outnumbered by the hundreds of thousands published each year in good faith.

Instead, a complex array of other factors seems to have contributed to the lack of reproducibility. Factors include poor training of researchers in experimental design, increased emphasis on making provocative statements rather than presenting technical details, and publications that do not

Critical experimental design elements

ing, randomization, replication, calculation and the effect of sex. And some scientists reportedly 'strive' to make their experiments and withhold details from full disclosure then only signify to us positive edge'. What hope is the scientists will be able to build in to further biased and increase?

Increasingly, funding agencies and scientific publishing agencies often uncritically favour the publication of research in high-profile journals. Some institutions provide incentives for publication in such journals, including position awards, and in extreme circumstances research⁶

Then there is the problem not published. There are few researchers to publish negative papers that point out serious (or seriously published) work, furthering the problem is the difficulty of unpublished data—and the tailing agencies to establish or verify that research data access.

PRECLINICAL PROBLEMS
Reproducibility is potentially a problem for all disciplines. However, it can be less of a problem in fields where the results are already governed by various physical laws (e.g., physics and chemistry).



Systems with cell lines

However, developing accurate estimates for cell loss inhibition and maintenance would require attention.

Since the 1990s, more than 400 wildlife road kill sites worldwide have been shown to have been underutilized [8, 9]. Originally thought to have been closed from use, these sites have later been found to be

The results of the study showed that the number of road kills was significantly higher than the number of road kills that were reported to the authorities. This suggests that the number of road kills that were reported to the authorities was significantly lower than the number of road kills that actually occurred.

From a different angle, in some cases, even the species of the cell has been identified. A 1991 study of 25 different land and rock cancer cell lines revealed that 50 (98%) were subcloned (4). Analysis of a mixture of these cellular activities and cells used to regenerate for location and storage time late in the United States, Europe, and Asia suggests that at least two of cell lines are available.

Unpublished by author.



NIH to balance sex in cell and animal studies

Francis S. Collins unveils policies to ensure that preclinical National Institutes of Health considers females and males.

calls to action⁷. Publications often continue to neglect sex-based considerations and analyses in preclinical studies¹². Reviewers, for the

stakeholders including publishers. This move is essential, potentially very powerful and need not be difficult or costly.

BETTER WITH A BOON: Certain rigorous studies evaluating the effects of sex differences have been effective in bridging the divide between animal and human work. Two example concerns multiple sclerosis (MS). Women are more susceptible to MS than men are, but develop less-severe forms of the disease. The most widely accepted MS animal model—rhesus experience of autoimmune encephalomyelitis (EAE)—has revealed that sex differences in MS are related to both reproductive and non-reproductive factors. Findings that corticosteroid therapy provided benefits in rhesus EAE

Downloaded from www.rscpub.org on February 4, 2016

PERSPECTIVE:



CELL BIOLOGY

Technologies and policies can improve authentication

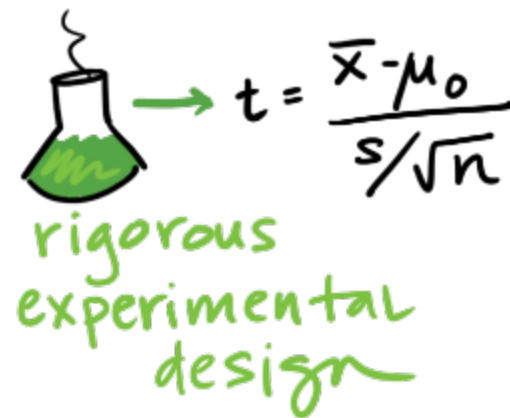
by Jon R. Lunde¹, Francis K. Collins²,
Donald H. Lippman³ and Robert A.⁴

Despite the numerous uses of cell culture in the study of biology and medicine, evidence has accumulated that cell lines are frequently misidentified or contaminated by other cells or microorganisms. This can be a substantial problem in many fields, such as cancer research, where drugs are

PROBLEMS *Armed forces are not always the best way to bring about change.* In the Somali civil war, much more had to be accomplished, and above all, better treatment had to be delivered. (It is in basic principle, not in moralism, that the UN has to be pragmatic.) *Armed forces are not always the best way to bring about change.* Even then,

3493 • J. Neurosci., November 11, 2009 • 29(45):14082–14092 • www.jneurosci.org

- The strict application of the **scientific method** to ensure **robust and unbiased** experimental design, methodology, analysis, interpretation and reporting of results.
- Describe the experimental design and methods proposed and how they will achieve robust and unbiased results.





[Home](#) » [Policy & Compliance](#) » [Rigor and Reproducibility](#) » Enhancing Reproducibility through Rigor and Transparency

POLICY & COMPLIANCE

Policy Topics

Rigor and Reproducibility

Guidance: Rigor and Reproducibility in Grant Applications

Resources for Preparing Your Application

Training and Other Resources

Notices, Blog Posts, and References

Enhancing Reproducibility through Rigor and Transparency

The information provided on this website is designed to assist the extramural community in addressing rigor and transparency in NIH grant applications and progress reports. Scientific rigor and transparency in conducting biomedical research is key to the successful application of knowledge toward improving health outcomes.

Definition

Scientific rigor is the strict application of the scientific method to ensure unbiased and well-controlled experimental design, methodology, analysis, interpretation and reporting of results.

Goals

The NIH strives to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science. Grant applications instructions and the criteria by which reviewers are asked to evaluate the scientific merit of the application are intended to:

FAQs

RELATED RESOURCES

- [For NIH Staff](#)
- Contact: reproducibility@nih.gov

NIH ENHANCING REPRODUCIBILITY GUIDELINES

what you need to know

WHAT ARE THE FOUR ELEMENTS OF RIGOR?

1

RIGOR OF THE PRIOR RESEARCH

2

RIGOR OF THE PROPOSED RESEARCH

3

BIOLOGICAL VARIABLES

4

AUTHENTICATION

Send inquiries to
reproducibility@nih.gov

See also NIH Notice NOT-OD-18-228
<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-228.html>

WHERE IN THE APPLICATION?

1 RESEARCH STRATEGY

The research strategy is where you discuss the significance, innovation, and approach of your research plan. Let's look at an R01, for example:



Introduction to Resubmission and Revision Applications



Specific Aims



Research Strategy



Progress Report Publication List



Vertebrate Animals

The **research strategy** guidelines require that you:

- Describe the strengths and weaknesses in the rigor of the prior research that serves as key support.
- Describe plans to address weaknesses in the rigor of the prior research.
- Describe how your experimental design and methods will achieve robust and unbiased results.
- Explain how relevant biological variables, such as sex, are factored into research designs and analyses.

2 ATTACHMENT FOR AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

You must briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies.

These include, but are not limited to:

CELL LINES

ANTIBODIES

SPECIALTY CHEMICALS

OTHER BIOLOGICS

Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.

- ☒ **DO NOT** put experimental methods or preliminary data in this section
- ☒ **DO** focus on authentication and validation of key resources

3 REVIEW GUIDELINES

Here are the additional criteria the reviewers will be asked to use:

- Is the **prior research** that serves as the key support for the proposed project **rigorous**?
- Have the investigators included plans to **address weaknesses in the rigor of prior research** that serves as the key support for the proposed project?
- Have the investigators presented **strategies to ensure a robust and unbiased approach**, as appropriate for the work proposed?
- Have the investigators presented adequate plans to address **relevant biological variables, such as sex**, for studies in vertebrate animals or human subjects?



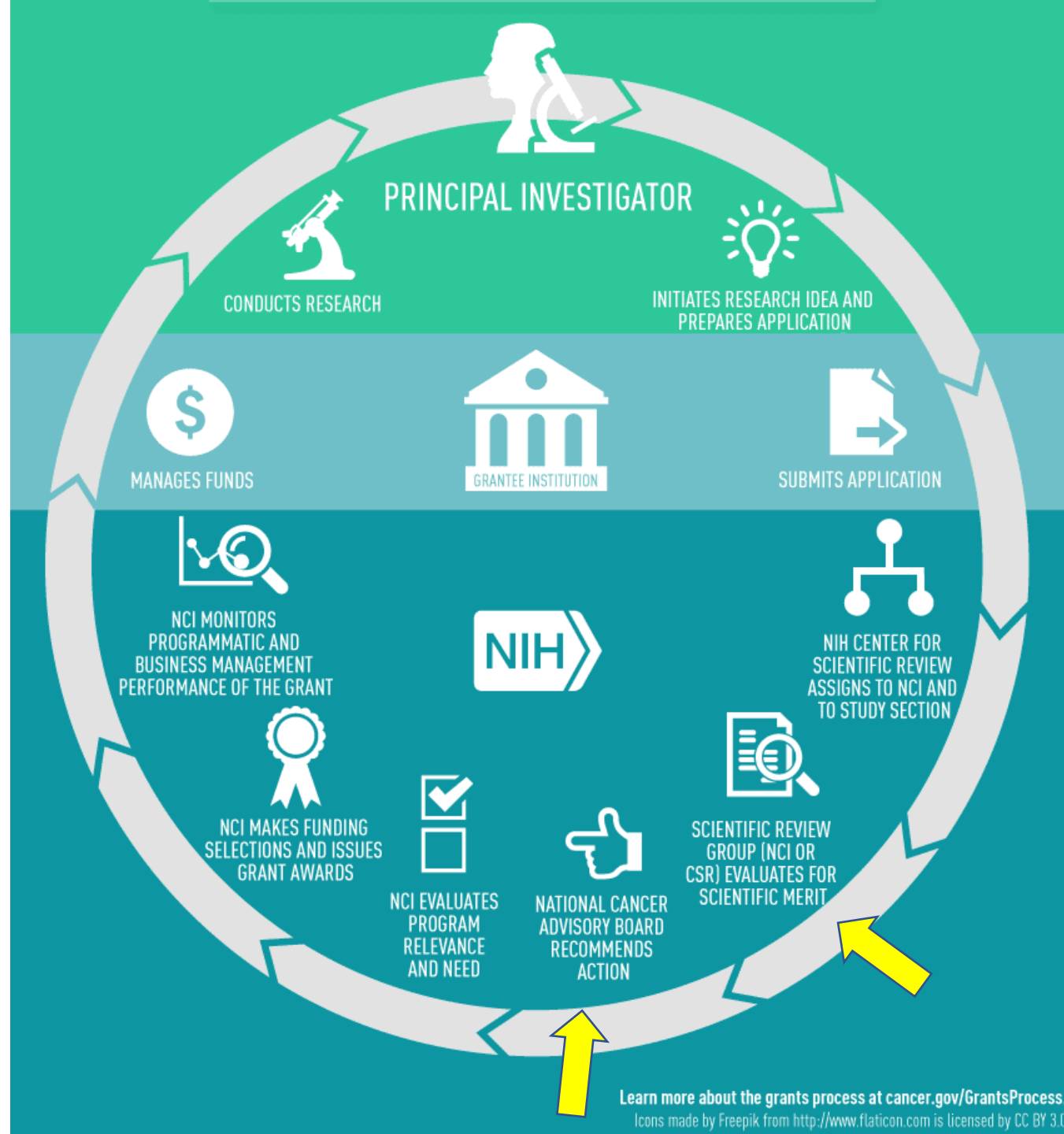
Reviewers will also be asked to comment on that new attachment (see **Update 2**)!



Avoiding Bias in Funding Decisions



OVERVIEW OF THE NATIONAL INSTITUTES OF HEALTH AND NATIONAL CANCER INSTITUTE GRANTS PROCESS



The Core Values of NIH Peer Review are:

- | | |
|-----------------------|---------------------|
| (1) Expert assessment | (5) Confidentiality |
| (2) Transparency | (6) Security |
| (3) Impartiality | (7) Integrity |
| (4) Fairness | (8) Efficiency |

<https://grants.nih.gov/grants/peerreview22713webv2.pdf>



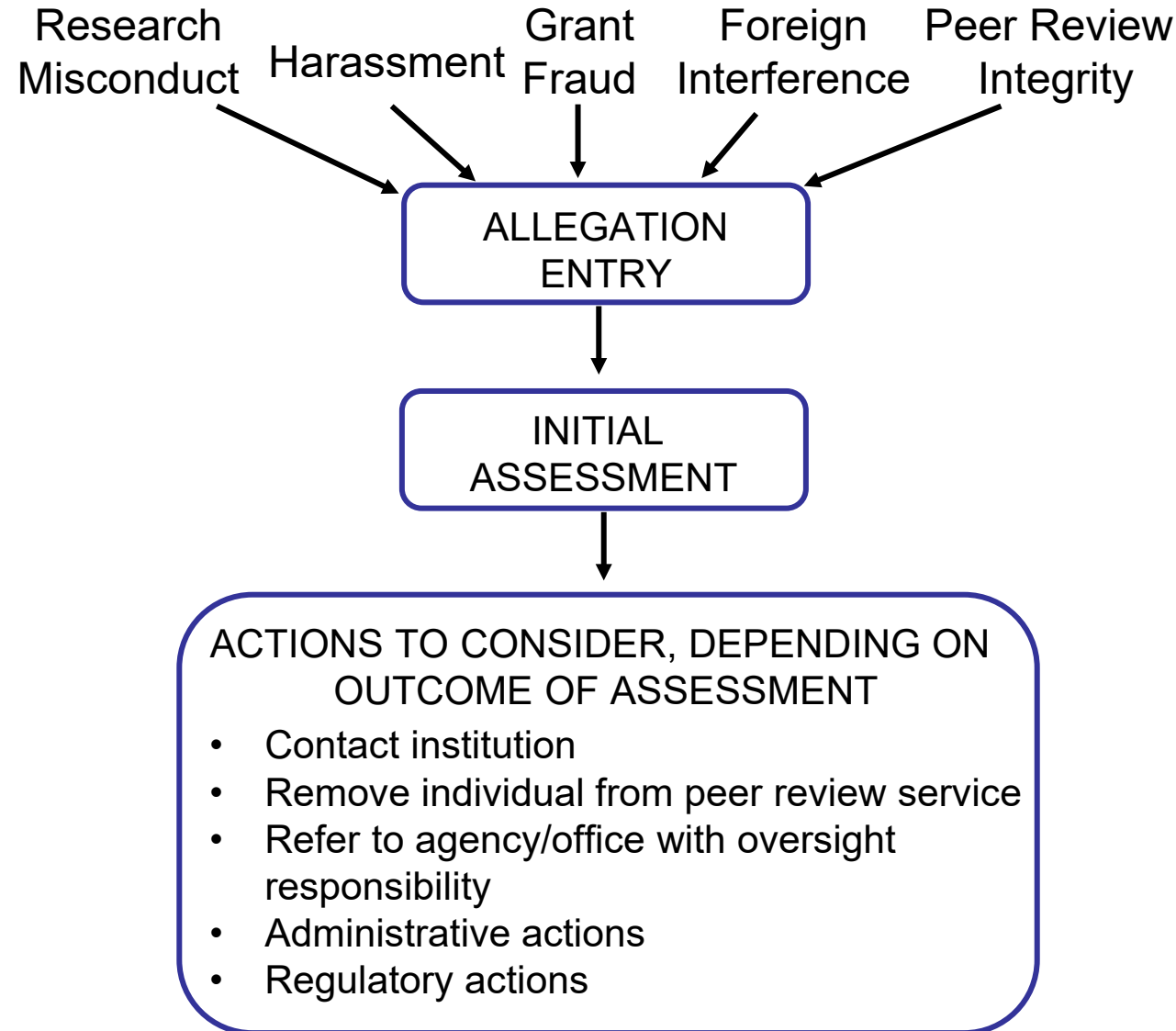
- Manage conflicts of interest, appearance of COI
 - Reviewers certify COI pre- and post-meeting
 - SGEs and Council members adhere also to the Standards of Ethics for Federal Employees
- Lobbyists restricted from serving
- Separation of NIH staff functions (review vs program)
- Policies for managing appeals of initial peer review

- NIH extramural staff trained in how to handle allegations of research misconduct (RM)
- Reviewers and Council members instructed to report allegations directly to the DFO in charge of the meeting
- DFO will report to assigned Research Integrity Officer
- May defer application from review until the proper authorities can deliberate on the situation
- Allegations of RM referred to HHS ORI

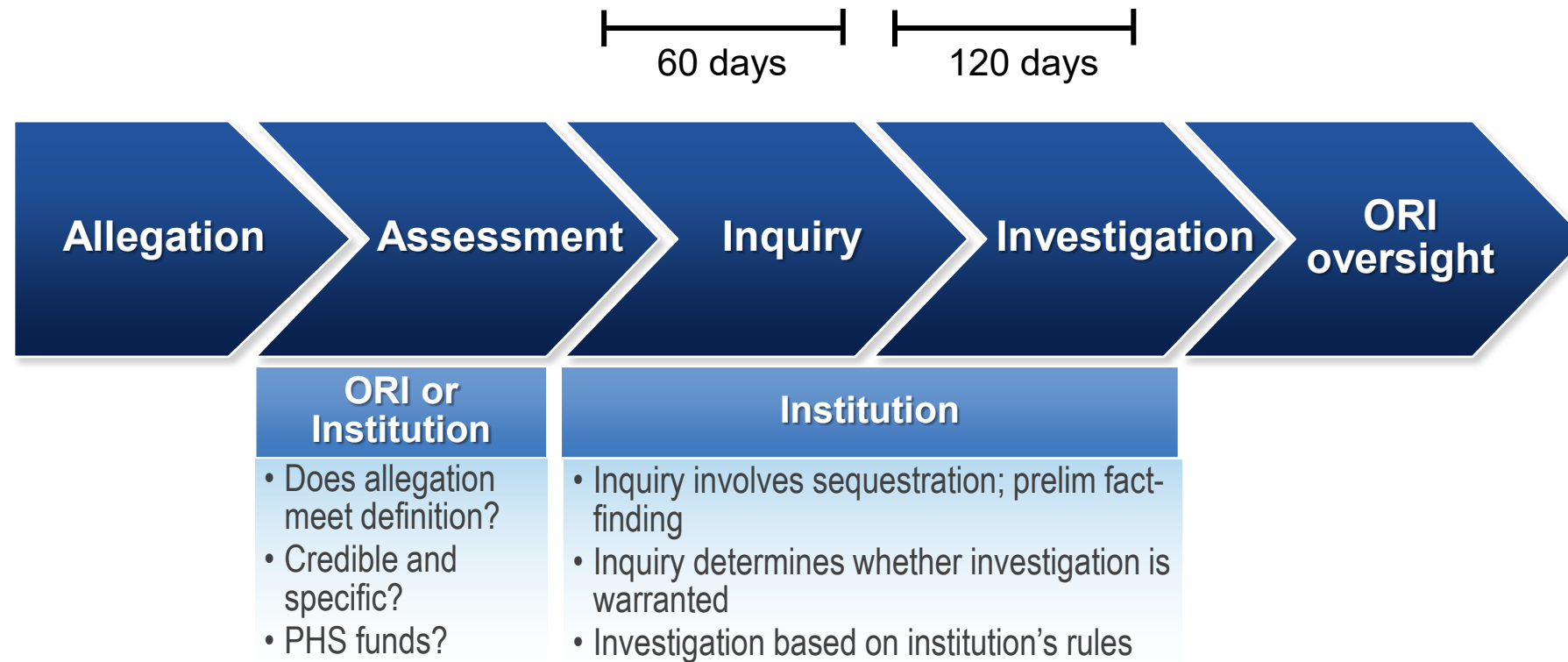
Handling Allegations of Research Misconduct



Overview of OER Allegation Review Process



Research Misconduct Proceedings



42 CFR § 93



NIH Interim Actions for Integrity Concerns

- Protect public, research participants, research, research process, and public funds
- Interim actions include, but not limited to:
 - Specific award conditions
 - Additional supervision
 - Certification of data
 - Request change of PI
 - Restrict funds
 - Suspend or Terminate award
- Also, referral to HHS Office of the Inspector General



Financial Conflicts of Interest (FCOI)



- HHS regulation [42 CFR Part 50 Subpart F](#), Promoting Objectivity in Research (FCOI regulation)
 - establishes standards that provide a reasonable expectation that the design, conduct, or reporting of NIH-funded research will be free from bias resulting from any Investigator's conflicting financial interest
- Investigator reports SFI to recipient institution, recipient institution assesses for FCOI and provides management plan to NIH for approval

Registration and Reporting of Clinical Trials



Dissemination of NIH-Funded Clinical Trial Information

- All NIH defined CTs to register and report results in [ClinicalTrials.gov](https://clinicaltrials.gov)
- Regardless of:
 - Study Phase
 - Type of intervention
 - Subject to regulation
- [NIH Grants Website regarding CT Registration and Results Reporting](#)

[NOT-OD-16-149](#)
[FDAAA](#)
[42 CFR Part 11](#)



CT Registration and Results Reporting Policy requires:

- Plan in the application outlining compliance with the policy; becomes part of Terms and Conditions
- Statement in the CT consent forms regarding posting of CT information at ClinicalTrials.gov
- REGISTERING in ClinicalTrials.gov no later than 21 days after enrolling the first participant
- REPORTING summary results ClinicalTrials.gov no later than one year after primary completion date

Data Management and Sharing Policy

NIH has a longstanding commitment to making the results of NIH-funded research available. Responsible data management and sharing has many benefits, including accelerating the pace of biomedical research, enabling validation of research results, and providing accessibility to high-value datasets.

[About the Data Management and Sharing Policy →](#)



Planning & Budgeting for Data Management and Sharing

Find out what NIH expects in a Data Management & Sharing plan and what costs are allowed in a request.



Data Management

Proper data management is crucial for maintaining scientific rigor and research integrity. Learn about best practices for scientific data management.



Sharing Scientific Data

Under the NIH Data Management & Sharing Policy, investigators are empowered to choose the most appropriate methods for sharing scientific data. Learn more about methods for

THANK YOU!

NIHResearchIntegrity@mail.nih.gov



National Institutes of Health
Office of Extramural Research