

Conflict of Interest in Research

Research
Misconduct

Topics – Conflict of Interest



Define	Define conflict of interest in research
Describe	Describe policies and regulations related to COI in research
Review	Review reporting and disclosure obligations
Explain	Explain how COI in research is managed

What is Conflict of Interest?



The National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and the National Research Council define a **conflict of interest** as:

"any financial or other interest which conflicts with the service of the individual because it (1) could significantly impair the individual's *objectivity* or (2) could create an *unfair competitive advantage* for any person or organization."

Adapted from CITI Programs, Conflict of Interest Module



Perception is Key

- The possibility that one's actions could be biased is enough to generate a COI.
- A COI exists if an outside observer might possibly think that a person's judgment or objectivity could be biased by the situation.

Does NOT Require Intentional Abuse

- Bias can be introduced either consciously or unconsciously.
- Even if researchers have good intentions, they can still be biased by a financial or personal interest and not be aware of it.





Physician-Industry Relationships

- In a survey of 2,938 randomly selected primary care and specialty physicians,
- 84% reported some type of relationship with industry during the previous year.

**Physician Professionalism and Changes in Physician-Industry Relationships
From 2004 to 2009**, Campbell et al., JAMA Int. Med. 170, 2010

Should the goal be to
completely avoid all possible
conflicts?

Harvard University policy on individual financial conflicts of interest

- [Our] "faculty engage in extramural interactions with industry and other external constituencies. Consultancies, advisory engagements, service on for-profit and not-for-profit boards, translational ventures, and numerous other outside activities **provide opportunities for faculty to direct their expertise and learning to socially useful applications.**
- Faculty members' **collaboration with outside organizations and communities furthers Harvard's mission of societal service** and also benefits the University. Such interactions promote intellectual exchange, enhance professional development, spawn further discovery, and augment and renew the vitality of the University. Accordingly, **Harvard encourages its faculty to engage with the world through outside pursuits.**
- At the same time, the University is cognizant that an individual's relationships with outside enterprises **can engender opportunities for personal gain or financial advantage that may be at odds with the primary obligations the individual assumes as a member of the Harvard faculty"**.

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- **Complete avoidance of conflict is not possible, and might not be desirable.**

Case Study

- Dr. Smith is conducting a research project to test the efficacy of a new drug. The project is sponsored by the company that produces the drug.

- **Is this a conflict of interest for Dr. Smith?**

Case Study

- Dr. Smith is conducting a research project to test the efficacy of a new drug. The project is sponsored by the company that produces the drug. The company has offered to hire Dr. Smith as a paid consultant for a different research study.
 - **If Dr. Smith accepts the consulting position, would this create a conflict of interest?**

Reasons for having and enforcing policies on conflict of interest in research

It's the right thing to do.

- **Protects research from potential bias**
- **Protects the reputations of the investigators and the institution**
- **Protects research participants**

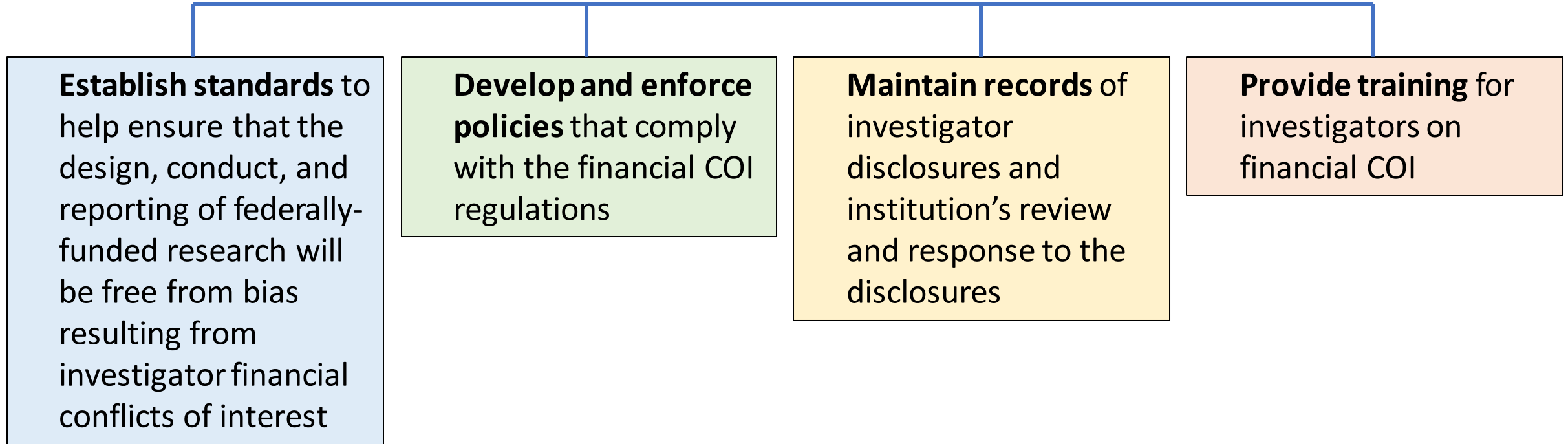
It's the law.

Regulations Regarding Conflict of Interest in Research

- Federal regulations exist for dealing with **financial** COI in research (2CFR Part 50, Subpart F)
- These regulations apply to institutions that apply for and receive federal research awards
- Goal is “to promote objectivity in research by establishing standards that provide a **reasonable expectation** that the **design, conduct, and reporting** of research will be free from bias resulting from investigator financial conflicts of interest”



Institutional responsibilities under the regulations



Geisinger Research Conflict of Interest Policy

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- • Applies to **all investigators** employed by Geisinger
- Applies to **all research activities**, not just those sponsored by the federal government
- Non-Geisinger employees (e.g. external collaborators) must follow either their home institution's COI Policy or Geisinger's policy
 - Work with OSP to determine the appropriate designation and required documentation
- Is consistent with Geisinger duality-of-interest policies that apply to all employees

- **A 2-step process to deal with potential COI:**

- **identify conflicts** when they occur, and
- **implement Management Plans** to reduce or eliminate bias when conflicts are identified.

Federal Regulations for Investigator Disclosure



1995 regulation

- Significant financial interests
- Related to federally-funded research
- As determined by the **Investigator**

2011 revised regulation

- Significant financial interests
- Related to an investigator's institutional responsibilities
- The investigator's **institution** determines whether the financial interest relates to federally-funded research and if it is a COI

Geisinger policy regarding financial disclosures

- Investigators are to required to disclose all financial interests they have in organizations related to their institutional responsibilities:
 - For the investigator and family members
 - At least annually
 - When there is a significant change
 - For certain kinds of travel payment

Financial interest definitions

A **Financial Interest** includes anything of monetary value, even if the value is not readily ascertainable.

A **Significant Financial Interest** is defined as one or more of the following for the investigator (and family members):

- the aggregated value of remuneration and equity interest in the preceding twelve months exceeds \$5,000;
- equity interest regardless of amount in a non-publicly traded company
- Intellectual property rights and interests (e.g., patents, copyrights) upon receipt of income related to such rights and interests

Financial interest definitions

- Financial Interest (with respect to these policies) **does not** include the following:
 - Remuneration *paid by Geisinger* to investigators employed by Geisinger
 - Intellectual property rights *assigned to Geisinger* and agreements to share in royalties related to such rights
 - Income from investment vehicles, such as mutual funds and retirement accounts, when the Investigator does not directly control the investment decisions made
 - Income from seminars, lectures, teaching engagements, or service on advisory committees or review panels, if sponsored by a government agency, institution of higher education, academic teaching hospital or medical center, or not-for-profit research institute

Travel Disclosures

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- **Travel expenses (including meals) paid for or reimbursed by an outside source must be disclosed*:**
 - For activities related to your professional responsibilities as a GHS employee
 - Applies to family members
 - Includes payments from some types of non-profit institutions
 - *Within 30 days*

*Exclusions for payments from government or academic sources

Physician Payments Sunshine Act









- Part of the Affordable Care Act
- Designed to increase **transparency** around financial relationships between physicians, hospitals and manufacturers of drugs and medical devices
- Requires medical product manufacturers to **disclose to CMS** any payments or transfers of value made to physicians
- The data is published annually in a **publicly searchable database** – the Open Payments Program
- Physicians can review and dispute errors before and after they are made public
- Data in the Open Payments site is reviewed by Geisinger COI staff and compared to financial disclosure information

Case Study

Dr. Smith owns \$20,000 worth of Pfizer stock. He is an investigator on several clinical trials. None of them are sponsored by or test Pfizer products.

- **Is this a conflict of interest?**
- **Should Dr. Smith disclose this financial interest?**
- **If it's not a conflict of interest, what could cause it to become one?**

Which of the following are reportable under Geisinger policies?

- Your GHS paycheck if a part of your salary is paid from a federal grant 
- Royalties paid to you by Geisinger for income received on a patent for which you are the inventor 
- Stock you own in a pharmaceutical company 
- An honorarium paid to you for giving a lecture at the University of Pennsylvania 
- A stipend paid to you for service on an NIH study section 
- A fee paid to you by a drug company for giving a talk 
- Travel or meals paid for by a drug company 
- Travel or meals paid for by the American Heart Association 

Considerations for managing conflict when it exists

- The strategy to manage a conflict will depend on its nature and its potential impact
- Some financial interests are difficult to quantify
 - e.g. equity interest in a start-up company could be worth millions or nothing
- COIs relating to human subjects research may require management plans to prevent the research participants from being harmed or exploited.

Geisinger process for managing conflicts

Financial disclosures are reviewed by members of the Geisinger **Research Compliance Office**

Cases of potential COI are evaluated by the **Research COI Committee**¹

If the COI Committee determines that a conflict exists a **Management Plan** is developed

The investigator must agree in writing to follow the plan

The RCO audits and the COI Committee enforces compliance with the Management Plan

¹Includes representatives from research, clinic, finance and legal departments

Possible remedies to manage COI

Most commonly applied remedies:

- Disclose the conflict to co-investigators and collaborators, and in presentations and publications¹
- For research involving human subjects², disclose the conflict to the research participants (e.g. in the informed consent document)

¹Most journals and research associations require financial interest disclosures from all authors or presenters

²The Geisinger IRB requires disclosure of financial interests or an attestation that no conflict exists when a protocol or amendment is submitted for review

Possible remedies to manage COI


Additional remedies that can be applied depending on the nature of the conflict:

- Independent review of research data, analyses, publications, etc.
- Conflicted investigator may not be the Principal Investigator of the project
- Conflicted investigator may not participate in all, or a part of, the research
- Investigator must relinquish their financial interest to remove the conflict of interest

Investigator Training

Financial COI training required

- prior to engaging in research related to any NIH-funded grant
- at least every four years
- immediately under the following circumstances:
 - Changes to Institutional COI policies
 - An investigator new to an institution
 - Noncompliance with institution's policy or management plan.



Research Misconduct

Definition

Consequences

Institutional responsibilities

How research misconduct is reported
and investigated

Definition of Research Misconduct

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

Every phase of the
research enterprise

Definitions

Fabrication

Making up data or results and recording or reporting them

Falsification

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

Appropriation of another person's ideas, processes, results, or words without giving appropriate credit

How Frequent is Research Misconduct?

A survey of reported the following:

- 8.7% of respond2,212 researchers ents had observed or had direct evidence of misconduct over the previous 3 years
- Suspected misconduct was by researchers at all ranks (students to senior Professors)
- More than one-third of incidents were not reported

A 2016 study reported that 3.8% of published papers include “problematic figures”

Titus, et al., *Nature* 453:980-982, 2008

The Research Scandal at Stanford is More Common Than You Think, *New York Times*, July 30, 2023

Stanford President Will Resign After Report Found Flaws in His Research

<https://www.nytimes.com/>

- Dr. Marc Tessier-Lavigne, a prominent neuroscientist, resigned as President of Stanford on August 31, 2023
- This followed a review by an independent panel of scientific papers he co-authored
- Concerns about Dr. Tessier-Lavigne's research were first raised on PubPeer, a crowd-sourced site for scientific publications

The review panel found no evidence that Dr. Tessier-Lavigne personally altered data, but they did conclude that multiple papers had significant errors, including manipulated data and data that were relabeled and reused.

The panel also concluded that Dr. Tessier-Lavigne presided over a research culture that “tended to reward the ‘winners’ (that is, postdocs who could generate favorable results) and marginalize or diminish the ‘losers’ (that is, postdocs who were unable or struggled to generate such data).”

Why Does Research Misconduct Occur?

- **Professional pressure: winner-takes-all stakes**
 - Academic positions, promotions, grants, etc. are awarded based on publication record
 - Highest value is placed on “high impact” journals that are extremely competitive and place a premium on novelty
 - Authoring a paper in a high impact journal can make or break a scientific career
 - Mentors often take credit for trainees work but fail to take responsibility for errors or mistakes
- **Character issues**
 - Deviant behavior
 - Personal problems



Consequences of Research Misconduct

- Contaminates the scientific literature with false information
- Can lead other investigators to pursue research based on erroneous conclusions
- Wastes time and resources
- Can cause harm to individuals when the false results lead to changes in treatment or behavior
- Erodes public confidence in the scientific enterprise

Criteria for Research Misconduct

- Represents a **significant departure** from accepted practices
 - Has been committed **intentionally, knowingly, or recklessly**
-
- Does not include honest error or differences of opinion



Public Health Service Policies on Research Misconduct – 2005

- Formulated to address growing concerns over the failure of research institutions to investigate allegations of research misconduct
- Outlines **procedures for reporting and investigating misconduct**
- Provides **protection for whistleblowers and persons accused of misconduct**
- Established the Office of Research Integrity (ORI) to monitor and develop policies for dealing with research misconduct

Institutional Responsibilities

Provide education on responsible conduct of research to researchers and trainees

Create and enforce policies and procedures for addressing allegations of scientific misconduct

Develop a "zero-tolerance" climate for scientific misconduct

Report allegations of scientific misconduct and outcomes of inquiries/investigations to the appropriate funding agency (ORI in case of NIH-funded research)



Role of Mentors

- Mentors must ensure that all trainees are aware of the rules governing responsible conduct of research
- Mentors should strive to be **role models** for conducting research responsibly
- Mentors have an obligation to act on and report occurrences of scientific misconduct by their trainees

True or False?

“Research misconduct is rare because science is a self-correcting process; fraudulent work will be identified as other scientists try to replicate the findings”

FALSE

- Most researchers have no interest in trying to repeat work others have reported
- Research studies are often difficult and expensive to replicate
- Very few journals will publish work that is not novel, presents negative results, or is merely an attempt to replicate other work

Case Study

A scientist is collecting data to support her hypothesis that a specific treatment relieves knee pain in runners. The key data come from subjective assessments of pain and mobility in the knee after exercise. She knows which research participants received the treatment when the assessment is made.

Is this research misconduct? If yes, which type?

Case Study

A research assistant is enrolling participants into a research study that involves collecting blood samples for genetic testing. A patient agrees to participate in the research and provides the required samples. After the patient leaves the assistant realizes the patient forgot to sign the informed consent form. The assistant writes the patient's name on the signature line and files the consent form.

Is this research misconduct? If yes, which type?

Case Study

A Professor is writing a paper that describes research conducted in her laboratory. She fails to include as a co-author a student who had conducted some of the experiments included in the paper, because she is unhappy with the student's attitude and work ethic, and wants to teach him a lesson.

Is this research misconduct? If so, which type?

Geisinger Policies on Research Misconduct

- PHS policies apply only to research that receives funding from the Public Health Service (including NIH)
- Geisinger has adopted policies and procedures that are based on the PHS guidelines
- Geisinger has chosen to apply the policy to **all research activities**
 - The exception is that occurrences of misconduct are reported to the PHS Office of Research Integrity only when the affected research received NIH funding

Definitions and roles

Complainant

- The individual who makes a formal allegation of research misconduct
- The **complainant** is protected from retaliation

Respondent

- The individual against whom the allegation of misconduct is directed
- The **respondent** is notified in writing of the allegation and subsequent proceedings, and is allowed to present evidence in their defense

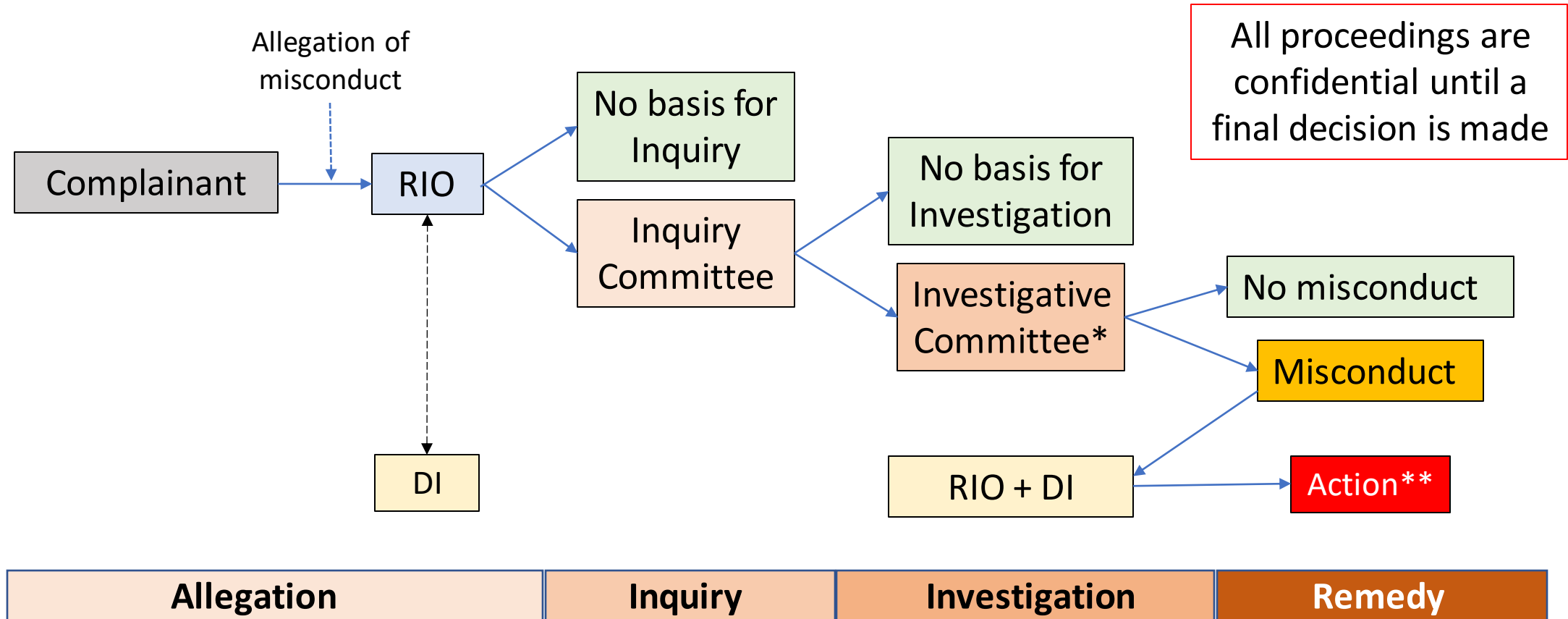
Research Integrity Officer (RIO)

- The individual responsible for overseeing the institution's research integrity policies and procedures, and to whom formal allegations of misconduct are reported

Deciding Official

- A senior administrative official who, along with the RIO, makes decisions regarding Inquiries, Investigations and Remedies for findings of misconduct

A multi-step process for reporting and addressing allegations of research misconduct

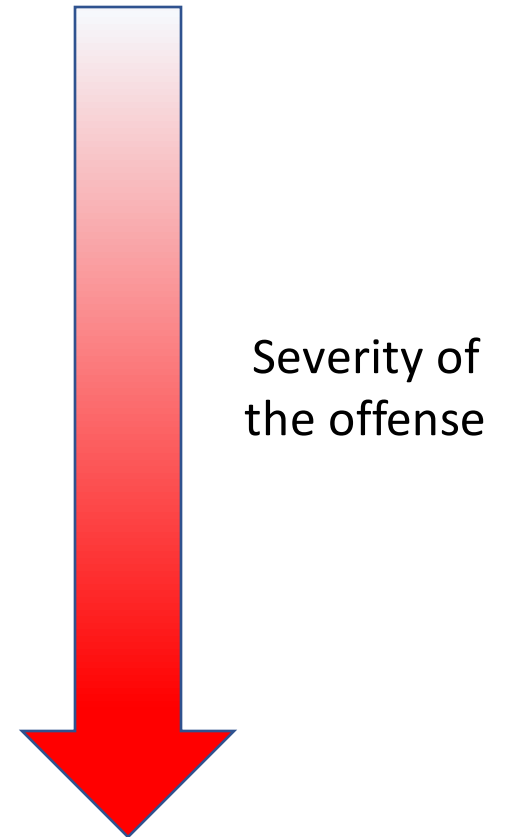


*preponderance of evidence standard of proof

**if PHS funded research ORI must be notified; ORI can require additional actions and publicly disclose a misconduct finding

Possible Consequences of a Finding of Research Misconduct

- Additional training and/or research oversight
- Retraction or correction of publications affected by the misconduct
- Termination of research funding
- Prohibition from future funding
- Restitution of funds
- Termination of employment
- Criminal charges



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