# Research Misconduct Framework at USA as part of Good Clinical Practices (GCP)

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## INTRODUCTION:

The text is taken from the requirements of Good Clinical Practices taught at the National Institute on Drug Abuse, an affiliate of the National Institutes of Health, USA.

Public concern about misconduct in research arose in the early 1980s after reports of serious misbehavior by researchers. In one case, a researcher republished dozens of articles under his name that had previously been published by others. In other cases, researchers falsified or made-up research results. Instead of looking into these problems, research institutions sometimes ignored them or covered them up.

Eventually, Congress required federal agencies and research institutions to develop policies on research misconduct. The U.S. Public Health Service created regulations for dealing with research misconduct **(42 CFR 50 Subpart A).** These policies generally have three goals:

- To define research misconduct.
- To establish procedures for reporting and investigating research misconduct.
- To protect both those who report alleged research misconduct and those accused of research misconduct.

This module discusses how federal policy defines research misconduct and provides a brief overview of the U.S. Public Health Service (PHS) processes for responding to allegations of misconduct in PHS-supported research.

### Defining Research Misconduct

Federal regulations define research misconduct as:

"...fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research."

- Fabrication is making up data or results and recording or reporting them.
- Falsification is changing research materials, equipment, or processes or altering or omitting data or results so that the research record does not accurately reflect the research findings.
- Plagiarism is using another person's ideas, strategies, results, or words without giving appropriate credit.

Research misconduct does not include honest error or differences of opinion. Besides, the federal policy on research misconduct does not apply to authorship disputes unless they involve plagiarism.

Research misconduct has a precise meaning in federal regulations. Noncompliance with policies and procedures for the protection of human research subjects, although reportable to an Institutional Review Board (IRB), is not considered to be research misconduct under the federal definition.

To whom does federal policy on research misconduct apply?

Federal policy on research misconduct applies to all federally funded research and all proposals submitted to federal agencies for research funding.

Many research institutions and universities apply the federal policy on research misconduct to all research, whether or not it is federally funded. Besides, many institutions have broadened the federal definition of research misconduct to include other improper practices. Researchers must be familiar with their institutional policies on research misconduct as well as with the federal policy.

Identifying research misconduct

What federal agency oversees investigations of alleged research misconduct?

The Office of Research Integrity (ORI) in the Department of Health and Human Services is responsible for promoting research integrity within the U.S. Public Health Service. ORI oversees investigations of research misconduct allegations and makes final decisions on findings of research misconduct.

Through its Rapid Response Technical Assistance Program, ORI provides technical assistance to any institution responding to an allegation of research misconduct. In addition, researchers may hold informal discussions with ORI about allegations of research misconduct or the handling of research misconduct cases.

Records maintained by ORI during the investigation of an allegation of research misconduct are exempt from disclosure under the Freedom of Information Act to the extent permitted by law and regulation.

Research Misconduct and Other Types of Misconduct

Research misconduct destroys the integrity or honesty of the research record. This sets it apart from other improper activities that may occur in research settings (e.g., financial conflicts of interest, misuse of grant funds, violation of human subject protections, sexual harassment, and discrimination). Although these improper activities are taken very seriously, they are not considered research misconduct because they do not alter the integrity of the research record.

The term *fraud* has often been used to describe dishonesty in research. However, this term is more aptly used to describe illegal, deceptive financial practices. Behavior that destroys the research record's integrity through fabrication, falsification, or plagiarism is most aptly termed *research misconduct*.

All three of the elements below must be present for a finding of research misconduct to be made. Under federal policy, a finding of research misconduct requires that:

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

· The misconduct be committed intentionally, or knowingly, or recklessly; and

· The allegation be proven by a preponderance of the evidence.

- Significant Departure
- Research misconduct must be "a significant departure from accepted practices of the relevant research community." This means that alleged research misconduct should be assessed in the context of practices that are generally understood within a research community, but that may not be written down. Federal policy does not endorse these practices but accepts that they may vary in different research communities.
- Intentionally, or Knowingly, or Recklessly
- Research misconduct must be committed "intentionally, or knowingly, or recklessly." This means that the accused person(s) must have intended to commit research misconduct. However, only *one* of the three characteristics must be shown — that is, the behavior must be shown to be intentional, *or* knowing, *or* reckless.
- A preponderance of the evidence
- An allegation of research misconduct must be proven by "a preponderance of the evidence" (that is, most of the evidence). This is the uniform standard of proof for establishing guilt in most civil fraud cases and many federal administrative proceedings. Non-federal research institutions may apply a higher standard of evidence in internal misconduct proceedings. However, they must use the federal standard as the basis for reporting their findings to the designated federal agency.

Who is responsible for investigating allegations of research misconduct?

Federal policy on research misconduct places the primary responsibility for reporting and investigating allegations of research misconduct with researchers and research institutions. This is consistent with the position, supported by most researchers, that research is a profession that should regulate its conduct.

Research institutions that receive federal funding are expected to:

- Foster an environment that discourages all research misconduct.
- Use procedures for receiving and investigating reports of research misconduct.
- Inform scientific and administrative staff of the procedures for responding to allegations of research misconduct and the importance of complying with these procedures.

- Take immediate, appropriate action when research misconduct is suspected or alleged to have occurred at the institution.
- Investigate and rule on suspicions or allegations of research misconduct.
- Report both the start of and the results of a formal investigation (not the initial inquiry) into an allegation of research misconduct to the Office of Office of Research Integrity.
- File an Annual Report on Possible Research Misconduct with the designated federal agency.

Institutional Procedures for Receiving and Investigating Reports of Research Misconduct

In receiving and investigating reports of research misconduct, research institutions must:

- Identify the person(s) whose job is to receive and look into allegations of research misconduct.
- Conduct an initial inquiry to establish whether an allegation has merit.
- If indicated, conduct a formal investigation to reach conclusions about the truth of an allegation.
- Identify a person whose job it is to weigh the conclusions reached in the investigation and take proper action.
- Send reports of the investigation and its findings to the Office of Research Integrity (ORI), the PI, the sponsor, and NIH for NIH-funded or supported research.

INDIVIDUAL RESEARCHERS

Federal policy on research misconduct assumes that research is a self-regulating profession. To be successful, professional self-regulation relies on conscientious participation by all members of the profession. Individual researchers are expected to:

- Maintain a high standard of integrity at all times in all of their research activities.
- Assume responsibility for their actions.
- Take misconduct or alleged misconduct seriously.
- Report apparent misconduct by other researchers.
- Keep confidential at all times information that is relevant to an investigation of alleged misconduct.

Requirements for the Response to an Allegation of Research Misconduct

The federal policy makes researchers and research institutions primarily responsible for reporting and investigating alleged research misconduct. Research institutions' expected tasks in dealing with such allegations are spelled out in 42 CFR P art 50 Subpart A.

Generally, the response to an allegation of research misconduct has three stages.

Inquiry: The inquiry assesses the facts of the allegation and the need for an investigation. An inquiry must be completed within 60 calendar days of its start, unless circumstances require a longer time.

Those accused of misconduct must be informed of the allegation and the inquiry. A written report of the inquiry must be prepared, summarizing the evidence reviewed, and conclusions reached. The accused person(s) must be given a copy of the inquiry report.

Investigation: If the inquiry provides an adequate basis for an investigation, that investigation should begin within 30 days of completion of the inquiry. The decision to begin an investigation must be reported in writing to the Director, Office of Research Integrity (ORI), on or before the date the investigation begins.

The investigation normally will include:

- Examining all documents, including relevant research data, proposals, publications, correspondence, and records of telephone calls.
- Interviewing all informants and all those accused of misconduct and others who may have information about key aspects of the allegation.
- Preparing a report of the investigation's findings and making the report available for comment by all informants and all those accused of misconduct.
- Submitting a final report to ORI, the PI, the sponsor, and NIH for NIH-funded or supported research.

In most cases, the investigation should be completed within 120 days of its start. If the institution decides it cannot complete the investigation within this time, it must submit to ORI a written request for an extension. This request must explain the reason for the delay, report on the investigation's progress so far, and estimate when the investigation will be completed and the final report submitted.

Adjudication: If the investigation concludes that the allegation has merit, the institution may impose

suitable penalties. Besides, the ORI may impose penalties of its own on investigators or institutions.
Institutions must notify the Office of Research Integrity (ORI) immediately if certain circumstances are found during an inquiry or investigation into an allegation of research misconduct.

Responding to Allegations of Research Misconduct in CTN Trials
Every CTN member institution is expected to have an official responsible for investigating complaints of research misconduct, also referred to as the Research Integrity Officer (RIO). When an allegation of scientific misconduct is made in a CTN trial, the Research Integrity Officer of the research institution should be contacted immediately.
The Research Integrity Officer should promptly assess whether the allegation falls under the federal definition of research misconduct and whether sufficient evidence exists to warrant an inquiry. He or she should alert the NIDA Center for the Clinical Trials Network office that an allegation of research misconduct has been made at one or more CTN sites.
Within NIDA, responsibility for oversight of inquiries and investigations into research misconduct rests with the Office of Extramural Affairs.
In addition, if NIDA is the sponsor of a study under an Investigational New Drug (IND), NIDA must promptly report to the FDA any information that any person involved in human subject trials committed research misconduct. If the FDA receives a complaint of alleged trial misconduct, the FDA will independently investigate, separate from the ORI investigation, and proceed with any necessary regulatory actions.
Ensuring Fairness and Timeliness in Responding to Allegations of Research Misconduct
An allegation of research misconduct can have a significant impact on the informant, the accused person(s), and the institution where the alleged misconduct took place. Procedures must be in place to ensure the security of original documents, computers, biological specimens, laboratory notebooks, research, and financial records, and other relevant items that might be altered, lost, or destroyed.
In addition, specific safeguards are necessary to assure all persons concerned with an allegation of research misconduct.
Safeguards for Informants
A whistleblower (informant) is any member of a research institution, including a non-employee, who alleges that the institution or one of its members has engaged in or has failed to respond adequately to an allegation of research misconduct.
The role of the whistleblower is essential to the effort to protect the integrity of research. In good faith, people who report apparent research misconduct must be able to do so in confidence and without fear of retaliation or payback.
Federal policy requires institutions to offer informants the following safeguards:

- Protection of privacy to the extent possible. However, informants cannot remain anonymous.
- Protection against retaliation.
- Fair and objective procedures for examining and resolving research misconduct allegations.
- Diligence in protecting the positions and reputations of informants.

Neither research institutions nor individual researchers may penalize persons who, in good faith, the report alleged research misconduct. Even if the allegations are not sustained, as long as they are made in good faith, informants must be protected because they play a vital role in professional self-regulation.
Safeguards for Accused Persons
Most allegations of research misconduct are not substantiated. Persons accused of research misconduct must be assured that the mere filing of allegations will not bring their research to a halt or be the basis for other disciplinary action without compelling reasons. Additional safeguards for accused persons include:

- Timely written notification of allegations made against them.
- A description of all allegations.
- Reasonable access to the data and other evidence supporting the allegations.
- The opportunity to respond to allegations, supporting evidence, and any proposed findings of research misconduct.

- Confidential treatment to the maximum extent possible.

Objectivity and Expertise of Investigators

The persons selected to investigate allegations of research misconduct must have the appropriate expertise and no unresolved conflicts of interest.

Timeliness

Reasonable time limits must be set for the response to an allegation of research misconduct. Extensions of time may be allowed when necessary.

Confidentiality

Knowledge of the identities of both subjects and informants involved in research misconduct investigations should be closely held to the extent possible. However, the accused person is entitled to know the identity of the informant.

Alleged misconduct in a clinical trial that could threaten trial participants' health or safety must be reported immediately to the principal trial investigator, the federal agency sponsoring the trial (NIDA in the case of CTN studies), and the Office of Research Integrity (ORI). The name(s) of the accused person(s) should remain confidential, but steps must be taken to ensure trial participants' safety.

Possible Penalties for Research Misconduct

Research institutions may penalize researchers who are found to have committed research misconduct by terminating their employment or by requiring supervision of future research activities.

When a grantee institution upholds a finding of research misconduct by anyone working on an NIH-funded research project, the grantee must assess the effect of the finding on that person's ability to continue working on the research project. In addition, the grantee must promptly obtain approval from the sponsor and NIH for any intended change of principal investigator or other key personnel involved in the research project.

The Office of Research Integrity (ORI) may also impose penalties for research misconduct. Penalties are determined by the severity of the misconduct. Factors that ORI may consider in choosing a penalty may include the degree to which the misconduct:

- Was committed in a knowing, intentional, or reckless manner.
- Was an isolated event or part of a pattern.
- Had a significant impact on the research record, research subjects, other researchers, institutions, or public welfare.

The Office of Research Integrity (ORI) may impose a variety of penalties when a finding of research misconduct is upheld. These penalties may include:

- Correction of the research record.
- Letters of reprimand.
- Suspension or termination of a research grant.
- Suspension or debarment from receiving federal funds.

When administrative actions are imposed by ORI (or the FDA, who has their bulletin boards for debarred and disqualified investigators), the names of the individuals will be made public.

If the ORI believes that research misconduct may have involved criminal or civil fraud, it will refer the matter promptly to an investigative body such as the Department of Justice or the Office of the Inspector General, Department of Health and Human Services.

ICH GCP and Research Misconduct

ICH GCP was put together and became operational after a public outcry of research misconduct that had occurred over the years. Following the ICH GCP guideline assists in preventing fraud and misconduct. So research misconduct is also a form of non-compliance to ICH GCP.

Summary of Key Points

- The federal policy defines research misconduct as "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results." This definition does not include honest error or differences of opinion, or authorship disputes unless they involve plagiarism.
- Federal policy on research misconduct applies to all federally funded research and all proposals submitted to federal agencies for research funding.
- The Office of Research Integrity (ORI) in the Department of Health and Human Services oversees investigations of research misconduct allegations and makes final determinations on findings of research misconduct within the U.S. Public Health Service.
- The federal policy places the primary responsibility for reporting and investigating

research misconduct allegations with researchers and research institutions.

- Generally, the response to an allegation of research misconduct has three stages:
- Inquiry (to assess the facts of the allegation).
- Investigation (if the inquiry provides an adequate basis for one).
- Adjudication (imposing of suitable penalties if the allegation is found to have merit).

Penalties for research misconduct may include termination of employment, suspension or termination of a research grant, and suspension or debarment from receiving federal funds.

**REFERENCES:**

1. NIDA. National Institute on Drug Abuse, USA
2. ICH. International Council for Harmonization