

Submitting a Reportable Event When Mayo Clinic Institutional Review Board (IRB) is not the IRB of Record Policy

Scope

Applies to Mayo Clinic Human Research Protection Program when submitting a Reportable event when Mayo Clinic IRB is not the IRB of record.

Purpose

To describe the process and requirements for reporting to the Institutional Official and regulatory agencies (when appropriate) all Unanticipated Problems Involving Risk To Subjects or Others (UPIRTSOs), and non-compliance involving Mayo Clinic personnel or research participants when the Mayo Clinic IRB is not the IRB of Record.

In accordance with the Authorization Agreement between the external IRB and Mayo Clinic and the Mayo Clinic Federalwide Assurance (FWA) registered with the Office for Human Research Protections (OHRP), Mayo Clinic commits to the Department of Health and Human Services (DHHS) that it will comply with the requirements set forth in the Federal regulations 45 CFR 46.103(b)(5) to ensure that investigators promptly report any unanticipated problems involving risk to subjects or others" (UPIRTSO), or any serious or continuing non-compliance, to the Institutional Official and regulatory agencies (when appropriate).

Policy

Reporting Policy

UPIRTSO

- Any UPIRTSO that involves Mayo Clinic personnel or Mayo Clinic research subjects must be reported to the Mayo Clinic Office of Research Regulatory Support (ORRS) **within five working days** of becoming aware of the problem or event, in addition to the reporting requirements of the external IRB.

Protocol Violation/Deviation

- Any MAJOR protocol violation/deviation that affects the rights and welfare of subjects and others, increases risks to subjects and others, decreases potential benefits, compromises the integrity or validity of the research, or represents willful or knowing misconduct, which involves Mayo Clinic personnel or Mayo Clinic research subjects is considered non-compliance and must be reported to the ORRS **within five working days** of becoming aware of the problem. Reporting requirements of the external IRB must also be followed.

Examples of problems and/or events which may meet UPIRTSO Criteria:

- Any accidental or unintentional change to the IRB-approved research protocol that increased risk to subjects or others
- An event that would have implications for the conduct or design of the research project (e.g., requiring a significant, and usually safety-related change in the research project, such as revising inclusion/exclusion criteria or a new monitoring requirement, revised informed consent or revised investigator's brochure).
- Any complaint from a subject that indicates an unanticipated risk, or that cannot be resolved by the research staff
- Problems, events, or new information (e.g. from publications, Data and Safety Monitoring Board [DSMB] reports, interim findings, product labeling changes) that in the opinion of the investigator may adversely affect the rights, safety, or welfare of subjects or others, or which substantially compromise the research data
- Breach of confidentiality (e.g. unapproved Protected Health Information [PHI] disclosure, a stolen, unencrypted laptop containing subject data and identifiers)
- An unexpected hospitalization - new or prolonged
- An unexpected life-threatening adverse experience
- An unexpected death which cannot be attributed to underlying disease
- A newly-developed disability/incapacity - persistent or significant
- An unexpected birth defect/anomaly
- A processing error resulting in a subject receiving a dose of study medication significantly higher than the dose dictated by the IRB-approved protocol, even if the incorrect dosing produces no detectable Adverse Effect (AE)

Examples of problems or events which may meet the definition of Major Protocol Violations/Deviations (non-compliance):

- Enrolling subjects who did not meet inclusion/exclusion criteria on a greater-than-minimal risk study
- Performing study procedures not approved by the IRB
- Performing study procedures before obtaining informed consent
- Failure to obtain and/or document informed consent
- Use of an unapproved consent document
- Changing the protocol without prior IRB approval except when necessary to eliminate immediate harm to a subject
- Breach of confidentiality (i.e. any occurrence of unapproved PHI disclosure)
- Receipt of incorrect treatment or dose by a subject
- Loss or destruction of samples or data
- Over-enrollment of subjects on a greater-than-minimal risk study
- Unauthorized (i.e. not IRB-approved) persons participating in the conduct of a research study

Investigator Reporting Responsibilities

When a UPIRTSO and/or major protocol violation/deviation occurs at Mayo Clinic, but the Mayo Clinic IRB is not the IRB of Record:

- The Investigator must complete reporting according to the requirements of the external IRB.
- The Investigator must report the problem or event to ORRS within five working days of becoming aware of the problem or event by completing the Reportable Event form within the Mayo Clinic IRB electronic (IRBe) system.
- The Investigator must, upon receipt of the external IRB's review and determination regarding the problem or event, submit a copy of that determination to ORRS by:
 - Completing an additional Reportable Event form within the Mayo Clinic IRBe system by selecting "follow-up" in section 3 of the Reportable Event form.

- **Note:** Breach of Privacy/Data for European Union (EU) Residents: Any suspected or actual breach of privacy for a research participant who is a resident of the EU must be immediately reported to the Data Protection Officer at INTLCompliance@mayo.edu. In addition, the investigator must follow all other IRB policies related to reporting of these types of events.

ORRS Responsibilities

When a UPIRTSO and/or major protocol violation/deviation occurs at Mayo Clinic, but the Mayo Clinic IRB is not the IRB of Record, ORRS will:

- Review the submitted Reportable Event form describing the UPIRTSO and/or major protocol violation/deviation.
- Investigate protocol violations and deviations per applicable ORRS procedure. See “Internal Compliance Review of Allegations of Suspected or Actual Noncompliance”.
- Communicate as warranted with the designated IRB of record.
- Notify the IRB Executive Committee, Mayo Clinic Research Compliance Officer, Mayo Clinic Institutional Official, and when required, the applicable federal agencies.

Related Procedures

[Internal Compliance Review of Allegations of Suspected or Actual Non-compliance](#)

Related Documents

[IRB Electronic Reportable Event Form - Sample Application](#)

[Privacy Breach Notification Policy](#)

[General Data Protection Regulation Compliance Policy](#)

Definitions

Reportable Event: Reportable Event is a type of event that requires reporting to the IRB within 5 working days: The investigator must follow the process (with an associated IRB form) to report any problem or event or other act or omission to the IRB that in their opinion is a UPIRTSO.

Federalwide Assurance (FWA): A formal, written, binding attestation in which an institution commits to the Department of Health and Human Services (DHHS) that it will comply with applicable regulations governing research with human subjects.

IRB of Record: A reviewing IRB that assumes IRB responsibilities for another organization and is designated to do so through an approved Federalwide Assurance (FWA) on file with the Office for Human Research Protections (OHRP).

Note: Commercial IRBs will not have FWAs, but must be registered with the OHRP.

ORRS: The Office of Research Regulatory Support (ORRS), as part of the Mayo Clinic Human Research Protection Program (HRPP), investigates alleged non-compliance and coordinates reporting to the Institutional Official and/or external authorities as appropriate.

UPIRTSO: Unanticipated Problem Involving Risk to Subjects or Others is any problem or event which, in the opinion of the local Investigator, meets all three of the following criteria:

- **Serious:** Serious problems or events that result in significant harm (which may be physical, psychological, financial, social, economic, or legal), or places subjects or others at a greater risk of harm than was previously known or recognized. Note that actual harm need not have occurred for there to be a change in the risk/benefit ratio.
- **Unanticipated:** A problem or event is "unanticipated" when it was unforeseeable at the time of its occurrence and is:
 - Not already described as a potential risk in the approved informed consent
 - Not already described as a potential risk in the approved protocol
 - Not listed in the Investigator's Brochure
 - Not part of an underlying disease
 - Occurred at an increased frequency or at an increased severity than expected
- **Related:** A problem or event is "related" if it is possibly related to the research procedures.

Protocol Violation/Deviation: Any change, divergence or departure from the study design or research procedures that has not been approved by the IRB. Most protocol violations/deviations are considered non-compliance.

- **Major Protocol Violation/Deviation:** Any change that affects the rights and welfare of subjects and others, increases risks to subjects and others, decreases potential benefits, compromises the integrity or validity of the research, or represents willful or knowing misconduct (see list of potential major protocol violation/deviations on page four of this document).
- **Minor Protocol Violation/Deviation:** Any change that did not increase the risk or decrease the benefit or significantly affect the subject's rights, safety or welfare and/or the integrity of research data (e.g. a routine lab missed at a visit and re-drawn, shortening the duration between a planned study visit, using an outdated Health Insurance Portability and Accountability Act [HIPAA] form or consent form when there are no differences between the two forms other than the approval date).

Non-compliance: An act or omission in the conduct or oversight of human subject research that represents a failure to follow: 1) federal, state or local regulations; 2) institutional policies relevant to human subject research; 3) the approved research plan; and/or 4) the determinations of the IRB.

Serious Non-compliance: Any non-compliance that results in, or has the potential to: a) substantially compromise the rights and welfare of subjects; b) substantially impact the integrity and validity of the study data; and/or c) compromise the integrity and effectiveness of the Mayo Clinic Human Research Protection Program.

Continuing Non-compliance: Continuing non-compliance is a pattern of non-compliance that continues to occur after a report of non-compliance and a corrective action plan have been reviewed and approved by the IRB. Continuing non-compliance may also be a pattern of non-compliance that continues to occur after the IRB has directed the investigator to correct the issue(s).

Refer to the list of definitions in [General Data Protection Regulation Compliance Policy](#) and [Privacy Breach Notification Policy](#).

References

[Association for the Accreditation of Human Research Protection Programs \(AAHRPP\)](#)

[45 CFR Part 46 Protection of Human Subjects](#)

[21 CFR Part 56 Institutional Review Boards](#)

[FDA Guidance for Clinical Investigators, Sponsors, and IRBs - Adverse Event Reporting to IRBs - Improving Human Subject Protection](#)

Owner

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Revision History

Date	Synopsis of Change
10/18/2021	Revision outside of scheduled review. Owner and Contact updated. Minor formatting edits.
10/21/2019	Updated Owner and to include GDPR content.
10/27/2017	Changed IRB Compliance Unit (IRCU) to Office of Research Regulatory Support (ORRS)
10/22/2017	Updated glossary term Continuing non-compliance.
9/6/2017	Minor revision. Updated the following definitions per Glossary review: Federalwide Assurance (FWA), IRB of Record, Protocol Violation/Deviation, and Reportable Event.
12/29/2016	Scheduled Review, updated to new template added hyperlinks and changed reviewer.
01/18/2016	"10 times" changed to "significantly"
12/04/2015	Revised the definitions for non-compliance, serious non-compliance, and continuing non-compliance to match the definitions in the glossary

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