Non-compliance: Investigations and Determinations

Purpose

The purpose of this policy is to outline the procedure for reporting and investigating noncompliance with human research protection requirements.

Policy

It is the policy of Boston Children's Hospital to comply with all applicable local, state, and federal regulations in the conduct of clinical research studies. Principal Investigators (PIs) and Department/Division Chiefs or any staff member are:

- Required to report regulatory non-compliance to either the Chair of the Institutional Review Board (IRB), the Director of Clinical Research Compliance, or to the Vice President of Research Administration (Institutional Official) and
- To participate in institutional efforts to address and resolve non-compliance.

The IRB, IRB Chair, Director of Clinical Research Compliance and Institutional Official are responsible for investigating and assessing non-compliance, reporting to the IRB, and requesting further remedies from the IRB itself.

The IRB will make the final determination that an event is non-compliance, serious non-compliance, or continuing non-compliance. For further direction see IRB policy: ***Reportable Events***.

Procedures

Definitions

Non-compliance is defined as any:

- Violation of any regulation that governs human subject research or of any institutional policy for human subjects research,
- Violation of any conditions imposed by the IRB on the approval of the study or conduct of the research, or
- Deviation or departure from an IRB-approved protocol.

Serious Non-compliance is a noncompliant event that has or had the potential to:

- Impact rights, welfare or safety of present, past or future subject(s),
- Increase the risks and/or decrease the benefit for research subjects(s),
- Compromise the integrity of the study data, or

- Affect a subject's willingness to participate in the study.

Continuing Non-compliance is a series of more than one noncompliant event, in reasonably close proximity that indicates the need for evaluation of the methods and systems used to protect human subjects. Continuing non-compliance need not involve a sequence of similar events if the events, taken as a whole, indicate that examination of the methods and systems used is warranted.

Process

Principal Investigators (PIs) are responsible for promptly reporting all suspected incidents of **non-compliance** that could potentially be considered serious or continuing **within 72 hours** of being known. PIs or any other person may make an initial report via email, in person, or verbally, but must follow up with a written report using the ***Reportable Event*** form.

If the report is made outside of CHeRP, then the report should be sent to the IRB Chair, the Director of Clinical Research Compliance, or the Institutional Official.

Any allegation regarding a non-compliant event or any concern about human subject protections will be fully investigated. If at any time during an inquiry or investigation there are concerns regarding scientific misconduct, it will immediately referred to the Vice President of Research Administration, who also serves as the Institutional Official.

Deviations or departures from the IRB-approved protocol that do not have the potential for being considered serious or continuing must still be documented by the investigator as part of their own study records and a summary or list of these events should be submitted to the IRB at the time of continuing review.

If the PI has any question whether a non-compliant event/deviation should be reported, they should contact the IRB.

Deviations that are possibly non-compliant

Deviations, divergences or departures from IRB protocols that are thought to possibly be serious or continuing are submitted using the IRB form: ***Reportable Event***.

1. The Director of Clinical Research Compliance is responsible for screening the event and obtaining any additional information that may be required for initial consideration of the event.
2. The event is then reviewed by the IRB Chair. The IRB chair may request additional information as required and will make a determination as to whether the report should be submitted to the full IRB for a final determination on whether the event meets criteria for serious or continuing non-compliance. Issues such as whether the event was under the control of the investigator will be considered in making this determination.
3. If the event is determined to be serious or continuing non-compliance, the ***Reportable Events*** policy will be followed.

Violation of regulations, institutional policy, or conditions imposed by the IRB

If the event submitted is a violation of:

1. Any regulation that governs human subject research;
2. Any institutional policy for human subjects' research; or
3. Conditions imposed by the IRB on the approval of the study or conduct of the research.

The Director of Clinical Research Compliance is responsible for screening the event and obtaining any additional information that may be required for initial consideration of the event. The IRB Chair and the Director will then discuss the following:

- The incident and the facts presented to date.
- Identification of those individuals involved in the incident or likely to be involved in the investigation and resolution of the incident.
- If necessary, a meeting will be scheduled as soon as possible after the incident is reported (within 72 hours, when feasible) to begin to discuss and resolve the incident. Attendees may include the investigator(s), the investigator's Department/Division Chief, the IRB Chair, the Director of Clinical Research Compliance, the General Counsel, the Institutional Official, and any other staff member thought to be involved in the non-compliance incident and required resolution.
- Whether there are sufficient facts to demonstrate serious or continuing non-compliance that is reportable in accordance with the ***Reportable Events*** policy. If so this will be immediately reported to the IRB who, based on a completed investigation, will make a final determination. If the IRB determines it is serious or continuing non-compliance the ***Reportable Events*** policy will be followed. In most cases, more information will be required before a determination is made that the event is either serious or continuing non-compliance

The IRB Chair may also:

- Determine that the incident does not meet potential criteria for serious or continuing non-compliance and require either no further action or compliance with a corrective action plan that is acceptable to the Chair and agreed upon by the investigator.
- Require that preliminary steps be immediately taken to further investigate and begin to correct the noncompliant incident and report to the IRB.
- Determine the incident to represent serious or continuing non-compliance and recommend to the IRB that the protocol be suspended or terminated in whole or in part. This step may be taken as a final measure or as an interim measure where investigatory conclusions, although incomplete, are conclusive enough in pertinent part to just IRB action.

IRB Chair and Director of Clinical Research Responsibilities

Institutional Review Board Responsibilities

The IRB is responsible for making a final determination as to whether serious or continuing non-compliance has occurred. The IRB is to receive notification of any instance where the IRB Chair has determined that a potential incident of serious or continuing non-compliance exists. This should occur at the earliest possible time which is usually the next scheduled meeting.

The IRB should be advised by the Director of Clinical Research Compliance or the IRB Chair about the actions taken thus far and determine further actions to be taken. All members will be given information known to date of the incident and important supporting documents. The IRB, directly or through a delegate, such as the Director of Clinical Research Compliance or a subcommittee formed for the purpose, may request any documents it deems necessary to conduct the investigation.

As determined by the specifics of the situation, the IRB reserves the right to conduct any type of investigation deemed necessary in order to obtain the required information. Moreover, the IRB may delegate any component of the investigation to those individuals best suited to perform the functions of the investigation. At any time during the investigation, the IRB may take any one or more of the following actions:

- Suspend or terminate the protocol.
- Designate an individual or a subcommittee to review and investigate the incident and provide information and recommendations for resolution back to the IRB.
- Require additional information.
- Require modifications to the protocol and/or consent form.
- Require that subjects currently or previously on protocol be notified of the non-compliance when such information might relate to their willingness to continue to take part in the research.
- Require that subjects be re-consented.
- Modify the continuing review schedule.
- Require remedial education.
- Require oversight by a senior investigator.
- Monitor the informed consent process.
- Require immediate or periodic audits by the Education and Quality Improvement Program (EQuIP).
- Referring concerns or findings to areas of the organization that administer other policies, laws, and regulations implicated by the non-compliance
- Any other action deemed necessary by the IRB

The IRB will be continually updated as information becomes available until final resolution. If it determined the incident represents serious or continuing non-compliance the ***Reportable Events*** policy will be followed.

In the case of non-compliance due to IRB administrative operations, the IRB chair will ensure that all IRB administrative operations staff is recused from IRB members' discussion and/or determinations made about serious or continuing non-compliance.

Investigator Responsibilities

Investigators are responsible for reporting non-compliance that could potentially be considered serious or continuing in their protocols.

Investigators may choose to voluntarily initiate a suspension or termination until the potential issue is investigated and/or resolved.

Investigators will also be informed, in writing, when allegations of non-compliance are made on their protocols. Investigators are required to fully cooperate with any fact finding and subsequent investigation, and maintaining all potentially useful records pending investigation, even if regulations or other policies would otherwise permit destruction of those records. The investigator is responsible for responding promptly, in writing, to all issues and questions raised. This may include an explanation of the non-compliance event, answers to questions raised by the IRB, and a plan of action to ensure that similar incidents do not occur in the future. Investigators are responsible for complying fully with all directives of the IRB, whether investigatory or remedial. If the IRB has determined that subjects must be contacted with regards to the non-compliance incident, the investigator will be responsible for doing so if the IRB so directs.

For deviations or departures from approved protocols that do not have the potential for being considered serious or continuing, investigators are still required to track these events and submit them with the next continuing approval. Sample templates for tracking are available on the ***EQuIP website***.

Institutional Official Responsibilities

The Institutional Official is responsible for submitting a report on behalf of the institution in accordance with the ***Reportable Event*** policy.

The Final Report

For incidents determined to be serious or continuing non-compliance, the ***Reportable Event*** policy will be followed. A file of the non-compliance incident, regardless of the ultimate determination, will be maintained in the IRB office.

Related Content

IRB Policy

Reportable Event

IRB Form

Reportable Event

Document Attributes

Title	**Noncompliance: Investigations and Determinations**		
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