



SMART TALK

A Community Forum to Explore Issues
Surrounding Single IRB Review

Funded by the NIH National Center for Advancing Translational Sciences
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What Is SMART Talk?

An approximately monthly forum with:

- Presentations on topics relevant for single IRB review
- Q&A on topic presented as well as questions submitted when participants register

Open and free to anyone with interest

Upcoming sessions

Getting ready for the 2020 Single IRB requirements, which will include a representative from OHRP

HRPPs and Single IRB: separating institutional responsibilities from those of the IRB

Using the SMART IRB Online Reliance System: pro tips and troubleshooting

Review of Personnel Changes: recommendations from the SMART IRB Harmonization Steering Committee

Single IRB Resources for Researchers

Key SMART IRB Resources at SMARTIRB.ORG

- Master Reliance Agreement
- Implementation Checklist for use of the SMART IRB Agreement
- Online Reliance System (Helps investigators and institutions request, track, and document reliance arrangements for each study)
- SMART IRB SOP Manual
- Communication Plan for Single IRB Review
- Reviewing IRB Instructions for Relying Institution Point(s) of Contact
- Reviewing IRB Instructions for Relying Site Study Teams
- FAQs for Research Teams - Relying on an External IRB
- Overall PI (and Lead Study Team) Checklist
- Relying Site Investigator Checklist
- Grant Applications: Template Description of SMART IRB
- Local Considerations: Institutional Profile
- Local Considerations: Protocol-specific Document

Join us for the next
SMART Talk
September 18, 2019 noon
EDT

*Getting Ready for the
2020 Single IRB
requirements*

Questions?
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REPORTABLE EVENTS

Recommendations for Investigator-initiated Multisite Studies

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Objectives

- Explore:
 - The variation in approach to review of serious and continuing noncompliance
 - The effects of the variation
 - Why harmonization is important in light of single IRB review
- Discuss SMART IRB Harmonization Working Group Reportable Events Recommendations

Why Harmonize?

- Reduce confusion
- Increase or expand efficiencies
- Freedom (for now) to develop best practices
 - Opportunity to engage with peers since everyone is required to use single IRB for non-exempt, federally supported research in 2020
 - There will be implications very soon that we can overcome together

SMART IRB Harmonization Approach

Promoting a more strategic, effective, efficient and cooperative approach to policies, processes and procedures related to single IRB review of multisite studies

Standardize Processes | Increase Compliance | Decrease Burden

The Harmonization Steering Committee and its working groups follow a development cycle guided by content experts, and responsive to public review and comment



Reportable Events Working Group

- Focused on investigator-initiated studies, but with the expectation that recommendations can be generalized
- Concentrates on serious or continuing noncompliance and unanticipated problems rather than
 - noncompliance (including protocol deviations) that is neither serious nor continuing
 - adverse events or serious adverse events that do not meet the definition of unanticipated problems
 - other information study teams might be expected to report to Reviewing IRBs

Protocol deviations

The Reportable Events Working Group endorsed the Recommendation on Protocol Deviations, developed by the Secretary's Advisory Committee on Human Research Protections

Provides an excellent basis from which institutions can implement harmonized approaches at least to protocol deviations.

<https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2012-march-30-letter-attachment-c/index.html>

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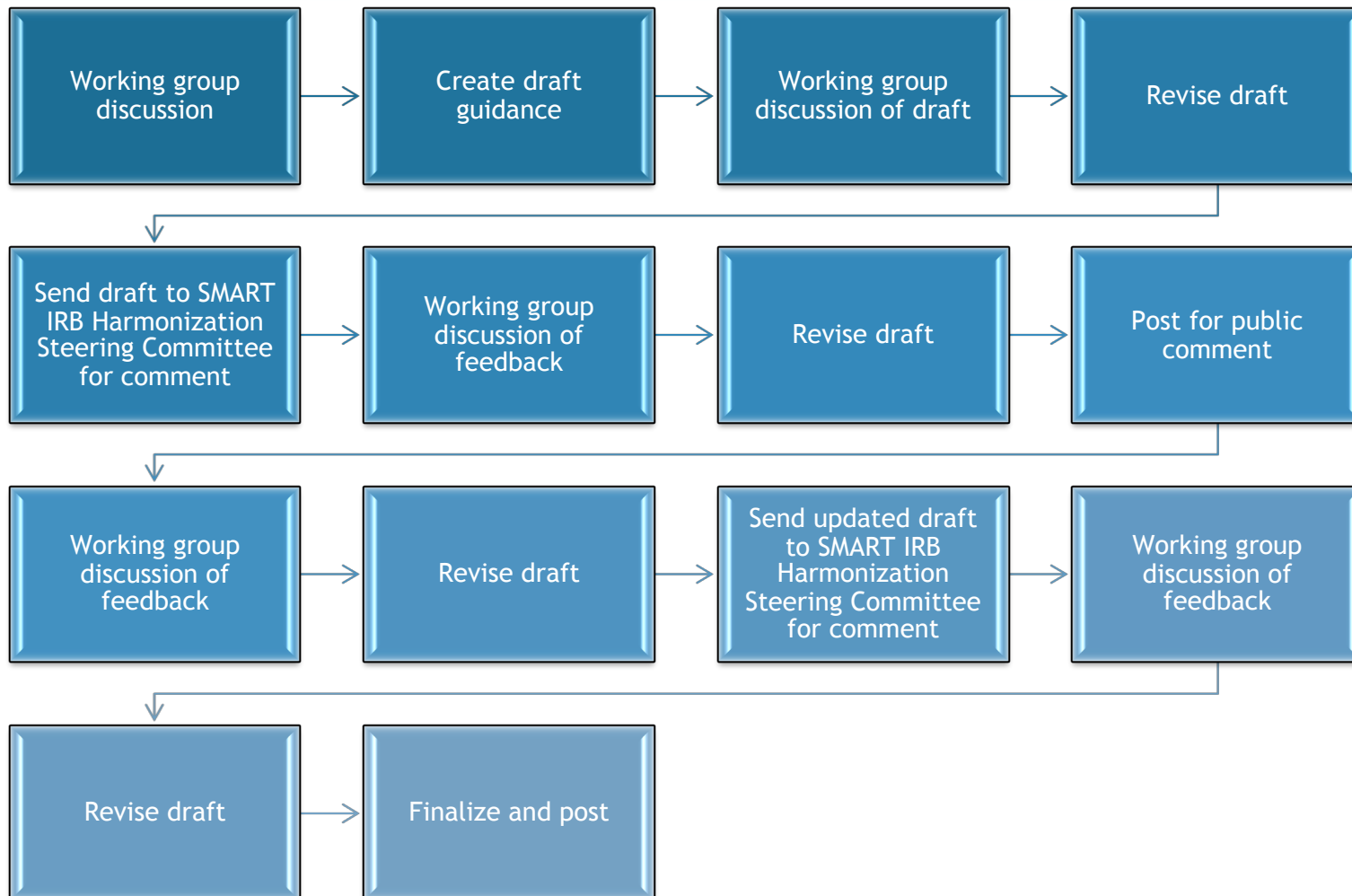
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Guidance development process



How We Vary: Noncompliance and Unanticipated Problems



Definitions

Because the Food and Drug Administration (FDA) and Office for Human Research Protections (OHRP) do not define *noncompliance*, *serious noncompliance*, or *continuing noncompliance* within their regulations, institutions were obligated to develop their own definitions, resulting in significant variation across institutions



Definitions of unanticipated problems tended to follow OHRP guidance

Which events must be promptly reported to the Reviewing IRB

Noncompliance

- Some IRBs require prompt reporting of protocol deviations/noncompliance that do not appear to be either serious or continuing noncompliance
- Others limit reporting to apparent serious or continuing noncompliance

Unanticipated Problems

- Some IRBs require broad reporting of events to assess whether they constitute unanticipated problems
- Others provide triage guidance to investigators and expect them to limit the events submitted to the IRB to potential unanticipated problems

Timeframe for reporting to the Reviewing IRB



Reporting timeframe varies from five days to almost two weeks, with some institutions requiring shorter timeframes for subject deaths.

Responsible party for submitting reports to the Reviewing IRB

Institutions vary in who they require to submit a report to the Reviewing IRB



Some institutions require the Principal Investigator or members of study teams to submit reports




Others permit direct reports from study auditors or monitors

Who triages and assesses reports of noncompliance

Institutions vary in who reviews reports but tend to require a convened board review of events that appear to constitute unanticipated problems or serious or continuing noncompliance.



At some institutions, IRB staff members review reports to assess likely categorization and then assign it to an IRB chairperson or directly to a convened board.



In other cases, the IRB chairperson assesses reports and refers events that appear to constitute unanticipated problems or serious or continuing noncompliance to the convened board.

Recommendations: Definitions



Source of definitions

The Reportable Events Working Group agreed that definitions should be based upon regulatory language or guidance whenever possible



For example, the use of *apparent* serious noncompliance and *apparent* continuing noncompliance is not within the regulations but used by the VA within its Handbooks/Directives

Definition of prompt reporting

- *Prompt reporting* is defined as an unplanned activity a responsible party performs without delay to initially notify applicable entities of a reportable event (serious or continuing noncompliance or an unanticipated problem) within a specified period of time.

Proposed definition of noncompliance

- ***Noncompliance*** is any failure to follow:
 - Applicable federal regulations, state and local laws, or institutional policies governing human subjects protections, or
 - The requirements or determinations of the IRB, including the requirements of the approved investigational plan (i.e., protocol deviations).
- Noncompliance can result from performing an act that violates these requirements or failing to act when required.

Proposed definition of serious noncompliance

- ***Serious noncompliance*** is any noncompliance that increases risk of harm to subjects; adversely affects the rights, safety, or welfare of subjects; or adversely affects the integrity of the data and research.
- ***Apparent serious noncompliance*** describes an event that *appears* to constitute serious noncompliance, and so requires reporting to an appropriate IRB for consideration, but the IRB has not yet made a formal assessment of the event.

Proposed definition of continuing noncompliance

- ***Continuing noncompliance*** is a pattern of repeated noncompliance which continues **after** initial discovery, including inadequate efforts to take corrective actions within a reasonable timeframe.
- ***Apparent continuing noncompliance*** describes an event(s) that *appears* to constitute continuing noncompliance, and so requires reporting to an appropriate IRB for consideration, but the IRB has not yet made a formal assessment of the event.

Unanticipated problem approach

The Reportable Events Working Group recommends that institutions:

- Follow the OHRP guidance regarding the types of events that constitute unanticipated problems
- Not require reporting of events that do not meet these criteria, such as serious adverse events (SAEs) that are expected or unrelated to study participation
- Follow FDA guidance, for research that falls under FDA purview, to assist with the assessment regarding whether AEs or SAEs also constitute unanticipated problems under the FDA and OHRP guidance.

OHRP definition of unanticipated problems

- OHRP considers unanticipated problems, in general, to include any incident, experience, or outcome that meets **ALL** of the following criteria:
 - Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
 - Related, or possibly related, to participation in the research (in OHRP's guidance document, "possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
 - Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

FDA guidance on unanticipated problems

- FDA believes that only the following adverse events (AEs) should be considered as unanticipated problems that must be reported to the IRB:

FDA AE guidance

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angiodema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome).

FDA AE guidance

- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy).

FDA AE guidance

- Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem.
 - There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus a control).

FDA AE guidance

- An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations.

FDA AE guidance

- A serious AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison).

FDA AE guidance

- Any other AE or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects.

Recommendations: Reporting Timeframes



Reporting timeframes considerations

- When soliciting feedback on our recommendations, the aspect of the draft that received the most comment was in regard to expectations for when events should be reported, both in terms how days are calculated (calendar days vs. business days) and the definition of “prompt.”
- The working group declined to make recommendations for harmonizing the timeframe from when an IRB receives a report to when it makes a determination related to that report, because such timeframes can vary significantly depending on the nature and complexity of the events, as well as other factors.

Recommended timeframe for an initial report to the Reviewing IRB

An investigator (or investigator's designee) or others (e.g., organizational officials) should provide an *initial* report to the Reviewing IRB within 7 calendar days of recognizing apparent serious or continuing noncompliance or an unanticipated problem.

- This recommendation acknowledges that, while a study team (or others) may need more time to evaluate the nature of an event, in certain cases the IRB should be involved in that assessment, in order to help protect the rights and welfare of participants.

Comments received on recommendation

Some commenters expressed concern that this seven-day timeframe would intimidate study teams who may be unsure of where to submit the report.



This can be addressed by educating study teams regarding single IRB review and ensuring clear communication regarding which IRB has assumed responsibility for a study are critical parts of the transition to single IRB review.

Policy Recommendations



Event reporting requirements

- Policies should describe the reporting requirements for *apparent serious or continuing noncompliance* (i.e., allegation of noncompliance) and *unanticipated problems* taking into consideration how this would occur under a single IRB arrangement.


Prompt reporting expectation

For studies that fall under a single IRB review model, policies should:

- require prompt reporting by the investigator (or investigator's designee) or organizational officials and offices of any apparent serious or continuing noncompliance
- define prompt reporting as the responsible party's initial notification to the Reviewing IRB within 7 calendar days of recognizing apparent serious or continuing noncompliance
- indicate that the prompt reporting requirement is met once initial notification is submitted, even if all of the information is not known at the time of submission

Who can submit reports

Policies should allow flexibility, when possible, regarding who can submit the report to the Reviewing IRB, but with the expectation that the Overall Principal Investigator (PI) for a study and the local investigator at the event site (Site Investigator) are aware of the report submission.



In the case of a report from a whistleblower, the Reviewing IRB would determine which study team members will be informed of the report and when.

Review process

Policies should describe the process by which the IRB:

- Reviews allegations of noncompliance or reports of unanticipated problems
- Determines whether an allegation of noncompliance meets the definition of serious, continuing, or both serious and continuing noncompliance
- Determine whether an event meets the definition of unanticipated problem
- Assesses whether the noncompliance also may constitute an unanticipated problem or an unanticipated problem may also constitute serious or continuing noncompliance

Collaboration with Relying Institutions

Policies should describe a process for alerting Relying Institutions that may be affected by the event and obtaining their input, as appropriate, regarding the event and any proposed corrective actions.

Reporting determinations: When

After the Reviewing IRB makes a final determination of serious or continuing noncompliance, the designated party should promptly report the finding (within 21 calendar days) to

- appropriate institutional officials
- applicable regulatory or oversight agencies
- when appropriate, the sponsor or contract research organization
- when appropriate, other performance sites involved in the research affected by the event

This timeframe includes obtaining feedback from the affected Relying Institution(s) on the planned report

- When the Reviewing IRB (or its institution) is responsible for this reporting, the SMART IRB Agreement requires that relevant Relying Institutions have the opportunity (no fewer than 5 business days, whenever possible) to review and comment on the draft report that is to be sent to the external recipients
- Relying Institutions are expected to promptly provide any comments on the draft report to the Reviewing IRB (or Reviewing IRB Institution), though the Reviewing IRB (Reviewing IRB Institution) is under no obligation to adopt comments of a Relying Institution

Reporting determinations: Who

Policies should:

- Identify the party(ies) responsible for reporting determinations of serious or continuing noncompliance or unanticipated problems to
 - appropriate institutional officials
 - applicable regulatory or oversight agencies
 - when appropriate, the sponsor or contract research organization
 - when appropriate, other performance sites involved in the research affected by the event

This responsibility can be delegated to Relying Institutions, but this delegation should be documented.

Other Considerations: Reviewing IRBs



Align policy definitions with federal regulations

An institution's policies should be based on regulatory requirements and guidance put forth by agencies with statutory authority (e.g., OHRP and FDA), with consideration for the policies and guidance of other federal agencies (e.g., NIH and VA), given their roles in funding and collaboration in human subjects research.



To support harmonization, institutions should use the definitions and terms found within federal regulatory agency regulations and guidance, to the extent possible. The SMART IRB Reportable Events recommendations meet this recommendation.

Accounting for Relying Institutions

An institution that has, or is, an IRB should have policies that take into the account the possibility that an external institution may rely on the institution's IRB.

For example, many institutions have policies that do not require the reporting of external events, which would not be appropriate given that reports from external sites must be reported to that IRB if they are acting as the Reviewing IRB for that site.



For multisite research involving single IRB review, policies should clearly state that all reports of apparent serious or continuing noncompliance or unanticipated problems should be reported to the Reviewing IRB for any study that involves subjects, data, or specimens and for which the institution's IRB serves as the Reviewing IRB.

Disseminating policies

A Reviewing IRB should have a mechanism in place for informing study teams of their requirements regarding reporting apparent serious or continuing noncompliance and unanticipated problems.



This could be accomplished by describing or linking to the policy in approval letters or including the policy language within an investigator responsibilities document that is distributed to study teams.



A Reviewing IRB could either provide this information to the Overall PI for dissemination to the study teams at each site, or the IRB can directly provide all study teams that it oversees with that information.

Identifying an event-reporting mechanism



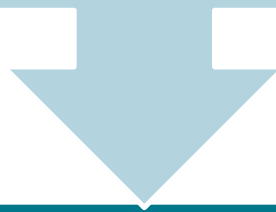
If a Reviewing IRB does not have a mechanism for study teams from Relying Institutions to directly report serious or continuing noncompliance or unanticipated problems to the Reviewing IRB (e.g., within an electronic system that all study teams can access), the Reviewing IRB should make available to study teams information about the process to promptly report these events (e.g., routing the event reporting through an entity such as a coordinating center or designated study team that has access to the Reviewing IRB's electronic system).

Limiting the events reported

Reviewing IRB policies and procedures should ensure prompt reporting of unanticipated problems, but should not require study teams to report events that do not meet this definition, such as events that are expected or unrelated to study participation.

Reporting to OHRP, FDA, and other entities


Under the SMART IRB Agreement, unless an alternate reporting arrangement is agreed upon, the Reviewing IRB is expected to draft any reports regarding a finding of serious or continuing noncompliance or unanticipated problems.



The Reviewing IRB is also expected to provide the involved Relying Institution(s) the opportunity (no fewer than 5 business days, whenever possible) to review and comment on the draft report before the Reviewing IRB (or Reviewing IRB's Institution) sends the report to the external recipients.

Notifying study teams and site personnel of determinations

The Reviewing IRB needs to identify a mechanism for informing study teams and relevant personnel at Relying Institutions (e.g., Points of Contact) regarding findings of serious or continuing noncompliance or of an unanticipated problem that has occurred.



Under the SMART IRB Agreement, the Reviewing IRB is required to promptly notify the Overall PI, Site Investigator(s), and Relying Institution(s) of applicable review decisions as well as any findings and actions. Such notification may be made through the Reviewing IRB's designee.

Triaging events

Institutions should provide sufficient guidance in their policies to allow investigators to make an initial determination regarding whether an event constitutes noncompliance or an unanticipated problem (or both), and develop decision tools to help guide researchers to appropriate determinations.

The Reportable Events Working Group developed examples that could be provided to study teams.

Events to report that may constitute serious noncompliance

- Conducting
 - non-exempt human subjects research without IRB approval
 - human subjects research without obtaining informed consent, when a waiver of informed consent was not approved by an IRB
- Implementing a significant modification to IRB-approved research not needed to eliminate an immediate hazard without prior IRB approval
- Violating any conditions of IRB approval that **could adversely affect subject rights or welfare**
- An event leading to a finding, such as from an audit, inspection, or inquiry by an inspector, that subjects were **placed at increased risk of harm or that the subjects' rights or welfare were adversely affected**
- Failing to
 - adhere to eligibility criteria, such that subjects were **placed at increased risk of harm or their rights or welfare were adversely affected**
 - perform safety assessments within protocol-specific time frames, such that subjects were **placed at increased risk of harm or their rights or welfare were adversely affected**
 - communicate new information to research subjects about study participation **relevant to subject rights or welfare**, such as new risks that could affect subjects' willingness to participate in the study

Events to report that may constitute continuing noncompliance

- A study team repeating the same mistakes on a specific protocol, **after** the initial events were discovered, reported, and a corrective action plan implemented.
- The PI or study team making mistakes on multiple protocols, **after** the initial events were discovered, reported, and a corrective action plan implemented.

Events to report that may constitute unanticipated problems

Identification of a new or increased risk, which could include:

- An event occurs adversely affecting subject safety, which results in premature study closure.
- Identification of a new risk (e.g., one not described in the protocol, consent documents, package inserts, investigational drug brochure, or device information). Identification of an increased risk, including a known risk that is occurring more frequently or with greater severity than previously expected.
- Occurrence of an event within the study that indicates an increased risk of harm and requires a change to the protocol or consent document.
- Event that results in a withdrawal, restriction, or modification for safety reasons of a marketed approval of a drug, device, or biologic that is used in a research protocol.
- An event leading to a finding, such as from an audit, inspection, or inquiry by a federal agency that subjects were placed at increased risk of harm.

Events to report that may constitute unanticipated problems

- Malfunction of a device used as part of the research that increases risks or resulted in harm to subject(s).
- Incorrect imaging scan performed for research purposes that results in increased exposure of subject(s) to radiation or radiopharmaceuticals that would not have otherwise occurred.
- Protocol deviation that harmed a subject or placed subject at risk of actual harm or significantly increased the risk of actual harm, which could include:
 - Missed study tests or study visit(s) that could affect subject safety.
 - Enrollment of a subject who did not meet all eligibility criteria.
 - Failure to follow safety-monitoring plan.
 - Prescribing, dispensing, or administration error that results in a subject receiving an incorrect drug or dose.

Events to report that may constitute unanticipated problems

- An event that leads to a protocol deviation to eliminate an immediate hazard to a subject made without prior IRB approval.
- Breach of confidentiality, where one or more research records containing private identifiable information about a subject was disclosed to persons not authorized to have access to the information.
- A stolen laptop or thumb drive with private identifiable information, if the device is not encrypted or password protected.
- Suspension of an investigator's privileges to conduct research by the researcher's institution or suspension of a physician researcher's medical license.

Events to report that may constitute unanticipated problems


- Unresolved research-related complaints concerning the safety or welfare of the participant.
- Unexpected pregnancy on a study that could expose a fetus to harm.
- Errors in research-related laboratory reports that increased risks to participants.
- Instances in which subject(s) experienced physical abuse as a result of others becoming aware of their participation in the research.
- Unexpected violence by participants in a group counseling session.

Other Considerations: Relying Institutions



Providing or having input on corrective action plans

When an event(s) that may constitute serious or continuing noncompliance or an unanticipated problem occurs at a Relying Institution, the institution should have processes in place to help formulate the corrective action plan(s) that will be presented to the Reviewing IRB as part of its consideration of the event(s).



In addition, the Relying Institution should be prepared to provide input on corrective actions proposed by the Reviewing IRB in connection with the ceded research.

Ensuring events are reported to the Reviewing IRB

- When a Relying Institution identifies (e.g., through a QA/QI audit) apparent serious or continuing noncompliance or an unanticipated problem on a ceded study conducted by its own research team, or when an institution takes actions that could extend to ceded research and therefore affect oversight by an external IRB (e.g., restricting research personnel privileges), the Relying Institution should have processes in place to ensure the event and any relevant corrective actions are communicated to the Reviewing IRB.

Promptly providing feedback on external reports

- When the Reviewing IRB is responsible for reporting determinations of serious or continuing noncompliance or unanticipated problems to regulatory agencies (e.g., OHRP, FDA), sponsors, funding agencies, or other oversight authorities, the Relying Institution should have processes in place to provide prompt feedback on the draft communication.

Other Considerations: Research Teams



Triaging and assessing events

FDA guidance notes that in a multisite study, sponsors typically have more experience and expertise with the study agents than an individual investigator and, therefore, the sponsor is in a better position to process and analyze the significance of event information from multiple sites and to make a determination about whether an event is an unanticipated problem.



In the absence of such a sponsor, research teams should have mechanisms in place to ensure events are reviewed in a timely manner (such as by the Overall PI, which may include input from a local site investigator or data monitoring entity), and to advise regarding whether an event related to a study intervention constitutes an unanticipated problem.

Reporting events

Study teams should be aware of:

- The Reviewing IRB's requirements for reporting noncompliance (including protocol deviations) and unanticipated problems, including how the Reviewing IRB defines these events, and the timeframe they require for reporting.
- The process for local site submission of event reports to the Reviewing IRB.

Possible Workflow for Event Reporting & Review



Study team becomes aware of an event that may require reporting to the Reviewing IRB and:



takes prompt action to eliminate any apparent immediate hazards to subjects when needed



reports event within required timeframe(s) to:



the Reviewing IRB through the established process (e.g., directly to the Reviewing IRB vs. through a Lead Study Team or coordinating center)

- promptly consults with Reviewing IRB if unsure whether event meets reporting requirement
- provides a preliminary report if gathering additional information or the time needed to develop a corrective action plan would exceed Reviewing IRB's requirements for event reporting
- provides additional information to the Reviewing IRB through the established mechanism upon request



others if the event suggests subjects were placed at increased risk of harm or their rights or welfare were adversely affected; others could include:

- Overall PI
- Lead Study Team
- Relying site study teams
- coordinating center
 - study sponsor
 - local IRB/HRPP
 - FDA
- data monitoring board/committee

After receiving the report, the Reviewing IRB:

triages event to determine level of review needed and assesses whether additional information is required to assess the event

takes prompt action to eliminate any apparent immediate hazards to subjects when needed

identifies which site(s) may be affected by the event(s) reported

if the event(s) might be determined to be serious noncompliance, continuing noncompliance, or an unanticipated problem or the Reviewing IRB suspended (or will suspend) the research, reaches out to IRB/HRPP point of contact at relying institution(s) to alert them regarding the event and actions

consults with the IRB/HRPP point of contact at relevant relying institution(s) regarding proposed corrective action plan

When the Reviewing IRB finalizes determinations related to the event and corrective action plan:

communicates determinations regarding the event(s) through the established mechanism to

Overall PI

relevant site investigators

relevant relying institution points of contact

drafts and sends correspondence to applicable regulatory or oversight agencies (e.g., OHRP, FDA, VA ORO) and the study sponsor or contract research organization (when appropriate), if the Reviewing IRB determined an event(s) constituted serious noncompliance, continuing noncompliance, and/or an unanticipated problem or suspends or terminates a study

before sending final correspondence to applicable regulatory or oversight agencies, obtains input on draft from relevant relying institutions

provides a copy of final correspondence to regulatory or oversight agencies (e.g., OHRP, FDA, VA ORO), study sponsors, or contract research organizations to relevant relying institution(s) and relevant study teams

Scenarios for Discussion



Scenario 1

- A Relying Institution conducts an audit of a federally supported and FDA-regulated study that has been ceded to an external IRB and discovers potential serious noncompliance...
 - What is reported to the Reviewing IRB?
 - Who reports any findings to the Reviewing IRB?
 - Should any reporting occur locally?
 - Who develops the corrective action plan?
 - Who ensures the corrective action plan is implemented and effective?
 - Who reports to federal agencies? Sponsors?

Scenario 2

- The Reviewing IRB reviews a report of potential noncompliance that occurred at a single relying site. The Reviewing IRB determines that serious noncompliance occurred...
 - The study is federally funded
 - Who reports the finding of serious noncompliance to OHRP?
 - Who should be informed of this finding at the Relying Institution and who is responsible for the communication?
 - Is there a role for the Overall/Lead PI in addressing the noncompliance and creating a corrective action plan?

Scenario 3

- A Reviewing IRB reviews a report of a potential unanticipated problem that occurred at a single study site for an FDA-regulated oncology study and determines that, based on its policies, the event does not meet the definition of an unanticipated problem. The study team reports the event to a group in its local HRPP and that group thinks that the event suggests an increased risk to study participants and recommends study suspension until additional actions are taken to mitigate this risk....
 - Who has the authority to suspend the study?
 - What communications should occur with the Reviewing IRB?
 - Can the Relying Institution make an independent finding of an unanticipated problem and make a report to the FDA or other federal authorities?

Scenario 4

- An Institution is aware that an Investigator has had consistent compliance challenges. The Investigator will be participating in a multi-site study supported by an NIH grant, which requires single IRB review. The Reviewing IRB will not be this investigator's home institution.
 - What is the Relying Institution's obligations to the Reviewing IRB in terms of disclosing information about potential concerns about the investigator's performance?
 - Should the Relying Institution put additional measures in place to monitor the Investigator's performance?
 - How do institutions track for noncompliance or performance issues across studies?

Questions and Discussion

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