Reviewer Guide for Reportable Events & Notifying the IRB

Office of Research Integrity & Compliance | Version 2
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This document to help IRB members during their review of *Notify IRB* assignments, such as deviations, adverse events, and UPIRTSOs. If further assistance or clarification is required, please contact the ORIC at 304-293-7073, or at IRB@mail.wvu.edu.

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Notify IRB

The PI needs to submit all substantial deviations and adverse events:

1. Within five (5) working days of the occurrence; OR
2. Within five (5) days since the occurrence has come to the attention of the PI

These submissions are done via the *Notify IRB* action in the protocol.

Reportable Events

Adverse events (AE)

Defined as any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article.

Only Adverse Events that meet the following criteria need to be reported within 5 working days:

1. Adverse events involving direct harm to participants which in the opinion of the principal investigator meet the criteria for an unanticipated problem involving risk to subjects or others.
2. An unanticipated event related to the research that exposes participants to potential risk but that does not involve direct harm to participants.
3. An unanticipated event related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk.

Note: Any other adverse events may be reported with the next continuing review submission.

Deviations

Depending on the nature and risk of the deviation, are classified in two ways:

1. **Minor deviations** re an administrative departure from the IRB-approved protocol procedures and were made without prior IRB, and sponsor (if applicable), approval. It is an accidental or unintentional change, or non-compliance, with the research protocol that neither:
    a. Increases the risk, not decreases benefit, to the participant(s)
    b. Significantly affects the subject's rights, safety or welfare and/or the integrity of the research data

Examples of minor deviations include:

i. A protocol visit scheduled outside the protocol window
ii. Bloodwork drawn outside the protocol window
iii. Participant unable to come in for a visit on time,
iv. Consent forms are not dated, and/or the participant did not initial each page

Note: Any actions that the Primary Investigator (PI) considers to be minor deviations, according to the criteria listed above, may be reported upon the protocols next submission or renewal.

2. **Major deviations** are a departure from an approved protocol that:
    a. Has caused harm or posed a significant risk to an individual associated with the research
    b. Has compromised the scientific integrity of the data collected for the study
    c. There is evidence of willful or knowing misconduct on the part of the investigator(s)
    d. Continuing non-compliance with federal, state, and/or local research regulations

Note: Investigators are required to report major deviations to the WVU IRB, as defined above, and occur at WVU's research site(s) to the IRB within five (5) working days of their occurrence, or within five (5) days of the investigator becoming aware of their occurrence.

Related events arise and can linked to one of the protocol procedures if the procedure increases the risk of the event occurring, or the procedure and event affects the rights and welfare of current participants.

Serious events are anything that results in one of the following: death, is life-threatening, requires hospitalization or prolongation of hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Unanticipated Adverse Device Effects (UADE) are defined as "any serious effect on health or safety or any life-identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects" (21 CFR 812.3(s)). A violation is an accidental or unintentional change to, or non-compliance with the IRB-approved procedures without prior sponsor and IRB approval.

Unanticipated event is a broad term to include research related events that occurred unexpectedly. This can also occur when the frequency, severity, or specificity is not consistent with the current investigator brochure, protocol, consent form, package insert, or label of a drug.

Unanticipated Problem Involving Risk To Subjects or Others (UPIRTSO) is a term used when an unanticipated problem(s) presents risk to the subject, multiple subjects, or others:

1. Is unexpected or unanticipated at the time of its occurrence and is not already described as potential risks in the approved research protocol or consent document, not listed in the Investigator Brochure, not due to an underlying disease, and does occurs at an increased frequency or increased severity than what is expected.
2. Is related or possibly related to participation in the research.
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Violations generally increase risk and/or decrease the benefit; affect the subject's rights, safety or welfare and/or the integrity of the research data. This term is not defined by The Common Rule or FDA Regulations.

Reviewing a *Notify IRB* Submission

Once the PI or coordinator submits one of these actions, the system will send a notification to the IRB that the Notify IRB action was submitted. The action will display in the *History* section of the protocol with the date it was submitted and the form(s) attached with associated comments entered.

Once the IRB staff receives the email notification, the submission is reviewed in the *Protocol History* and then assigned to a Board member for review. The Board member receives an email notification the will have "FYI" in the subject line.

The reviewer should:

1. Go to the *Protocol History*, where the notification and required attached documents will be available for review.
2. If it is a deviation, SAE or UPIRTSO a form should be attached from our website.
    a. If it is an "Other" there should be an attachment explaining why the event is brought to the Board's attention. These may be DSMB letters, updates on the study that are not amendments and do not need to be attached in the attachments. Often they are documents from the study sponsor.

Note: All notifications must be accompanied by an attachment.

3. Determine if the information is sufficient and can be acknowledged or if further information is needed.
4. Enter their comments in the *Online Review* page and click "Review Complete."
    a. If the reviewer is requesting additional information the request will be given the PI and upon resubmission will be sent back to the reviewer for determination.
    b. The request and responses will be tracked in the Protocol History section of the protocol.

Once the action is acknowledged by the reviewer, IRB staff will acknowledge the action in the protocol, which will be recorded in the *Protocol History* section.

Requests to Close Enrollment

Although these are reviewed by staff, members should be aware that when a PI states in an amendment or continuing review that their study is closed to enrollment, this does not affect the status of the protocol in the system. The consent forms will still be watermarked with approval dates.

The PI must submit a close to enrollment action in order to change the status. The status can be seen in the left upper hand table of each page of the protocol. Once a close to enrollment action is taken and acknowledged, the status will change to Closed to Enrollment in the table. Also all pdfs in the attachments will be watermarked closed to enrollment and can no longer be used to enroll subjects.

Request to Close an Approved Protocol

The completion or termination of the study, whether premature or not, is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Once the IRB staff receives the email notification, the *Protocol History* is opened to see if the Closure Report Form from the ORIC website is included. If it is, the protocol is assigned to a Board member for review.

The reviewer should:

1. Determine if the information is sufficient and can be acknowledged or if further information is needed.
2. Enter their recommendation and any comments on the *Online Review* page, click 'Review Completed' and close out the study.

If you are requesting additional information the request will be given the PI and upon resubmission will be sent back to the reviewer for determination.

The request and responses will be tracked in the Protocol History section of the protocol.

Once the action to Close is acknowledged, the PI may not conduct any actions on this study.