



Human Subjects Protection Update Special Communication

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COMMITTEE ON CLINICAL INVESTIGATION

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Revised Policies and Procedures for Minor and Significant Deviation and Exception Reporting

The Committee on Clinical Investigation has revised and clarified its policies on reporting “minor” and “significant” deviations to the IRB. The changes were prompted by confusion as to what constitutes a significant and minor deviation and overlap with unanticipated reporting requirements. The following question and answer document will provide information about these changes.

1. Why has there been a change in policy?

The previous guidance document allowed room for inconsistent interpretation. Some investigators reported events that were not “significant” and other investigators did not report events which should come to the attention of the IRB. In addition, there has been considerable confusion as to what constitutes a deviation versus an unanticipated problem or serious/unexpected event. The new policy includes two major changes:

- 1) Specific examples of events that are considered “significant” and “minor” are provided. There is also clarification as to what needs to be reported, how, and within what time frame.
- 2) The separate deviation form has been eliminated. Instead of having separate forms for deviations and unanticipated problems we have merged these into a single form.

Detailed information about these changes follows.

2. What is the difference between a deviation and an exception?

When an investigator anticipates a one time intentional action or process that departs from an IRB approved protocol, he or she may request that a one time **exception** be granted by the IRB. Actions that fail to follow the approved protocol and are noted or recognized after they occur are referred to as **deviations**.

3. Do all deviations and exceptions need to be reported to the IRB?

Not initially. Investigators are required to report **significant** deviations within 72 hours of becoming known and **significant** exceptions to the IRB prior to initiation. Deviations and exceptions that are minor still need to be tracked by the investigator and reported to any sponsor and data and safety oversight committee in accordance with their policies. Minor deviations and exceptions should be compiled and submitted to the IRB at the time of continuing review.

4. What is the definition of “significant”?

Decisions concerning the significance of protocol deviations and exceptions are not based exclusively on actual effects but must be based on both actual and potential effects.

Significant Deviation or Exception meets at least one of the following criteria:

Events that actually or potentially

- i) impact subject safety, welfare or rights
- ii) alter the risks or the benefit to the subject in a more significant, serious or negative way
- iii) impact the integrity of the data
- iv) effect a subject's willingness to participate

5. What are examples of significant and minor deviations or exceptions?

When study deviations or exceptions are identified, it is the responsibility of the Principal Investigator to make an independent determination as to whether it should be classified as minor or significant. Examples of common protocol deviations and exceptions and how they may be classified are provided below. However, based on protocol specific details, sometimes what may be considered minor for one study may be significant in another. This is not an all-inclusive list of potential events. Please contact the IRB office if there are questions

Minor:

1. Missing signed informed consent document but the PI can verify by other methods consent was obtained
2. Inappropriate documentation of informed consent including
 - a. Missing signatures (other than subject and/or parent/legal guardian)
 - b. Copy of consent not given to subject
 - c. Wrong dates
 - d. Wrong signature lines
 - e. Missing documentation of relationship of person providing parental permission (if relationship confirmed to be parent /guardian)
3. Use of invalid consent for a small number of subject as long as the content of the form contains all information that is included in the valid consent
4. Study visits/procedures that are either omitted, conducted outside the visit window or in a different sequence than specified in the protocol as long as this has not potentially impacted the safety and welfare of the subject.
5. Over enrollment of subjects in research that has produced additional data of potential scientific value
6. Study personnel involved in research without appropriate training
7. Use of recruitment materials and processes that include small modifications from those that are approved
8. Assent obtained but not appropriately documented,

Please note, for all these events a single or infrequent occurrence may be considered minor, however, if it is discovered these events have involved a majority of research subjects or the frequency is increasing, this may signify a more systemic problem with the conduct of the research and this could lead to reclassification of the events as significant.

Significant;

1. Failure to obtain informed consent prior to initiating research procedures
2. Informed consent obtained after research procedures are initiated
3. Performing study procedures not approved by the IRB unless to eliminate immediate potential harm to the subject
4. Failure to perform a test approved in the protocol that is important to subject safety or data integrity
5. Drug medication (dosing and dispensing) errors regardless of whether a subject was negatively impacted
6. Failure to follow data and safety monitoring plan
7. Failure to report a serious, unanticipated adverse event that is thought to be possibly or definitively related to research interventions
8. Use of a recruitment process not approved by IRB
9. Enrollment of new subjects after IRB approval has expired
10. Enrolling a subject that does not meet inclusion/exclusion criteria
11. Enrolling an incarcerated youth or a ward of state in a protocol not previously approved to include these populations
12. Parental permission granted by someone other than the parent or legal guardian
13. Assent not obtained when required by IRB
14. Verbal consent obtained when IRB requires written consent

6. What form do I use to submit a Significant Deviation?

THERE IS NO LONGER A SEPARATE DEVIATION FORM. The unanticipated problem form has been revised to include significant deviations as a category. The form may be found on our website. The first question asks the investigator to classify the event being reported. The fifth category is for significant deviations. The form may be found at

http://www.childrenshospital.org/cfapps/research/data_admin/Site2206/Documents/Reportable_Event.doc

7. What form do I submit for a significant exception?

Significant exceptions may continue to be requested by completing the significant exception form that is also found on our website. The form may be found at

http://www.childrenshospital.org/cfapps/research/data_admin/Site2206/Documents/Significant_Exception_Request_Form.doc

8. Will all significant deviation and exceptions be submitted to the full Committee for review?

No, once the form is received in the office it will be reviewed with the IRB Chair to determine whether it should be submitted to the full IRB or whether it can be reviewed administratively. Either way you will get notification upon completion of the review. The IRB Chair or committee may request additional follow-up information or a corrective action plan.

9. Is there a form I can use to internally track minor deviations and exceptions?

The Education and Quality Improvement office has developed 2 different templates that investigators may use to track minor deviations and exceptions. You should feel free to use these templates, adapt them so they are appropriate for your protocol or develop your own. These may be found under study tools and templates at:

http://www.childrenshospital.org/cfapps/research/data_admin/Site2207/mainpageS2207P3.html

There forms may be kept in your regulatory binders and can be attached to the continuing review.

10. What if a sponsor requires that I submit a deviation or exception to the IRB that does not fit under the “significant” category?

The IRB will never refuse to review an event, however we strongly discourage reporting when it is unnecessary. This creates additional paperwork for the investigator and the IRB. One possibility is to provide the sponsor our deviation reporting policy which may be found at:

http://www.childrenshospital.org/cfapps/research/data_admin/Site2206/Documents/cip_p_051_006_modifications.doc

Most sponsors will accept the policy, however if this remain unacceptable you may submit the report and include a note that while the event does not meet the criteria for reporting, the sponsor has required that the event be submitted.

If there are any questions please contact us at 57052