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SCOPE

This policy applies to all Charles R. Drew University of Medicine and Science (CDU) faculty, students, staff, affiliates, and others, who is conducting human subject research under the jurisdiction of CDU.

OVERVIEW

During the course of the study and even after study completion, events or outcomes may occur that affects the safety, rights or welfare of the subject. Examples include serious unexpected adverse events, unresolved subject complaints, loss of electronic devices containing identifiable
participant information, FDA warning label, or unapproved changes to the research protocol that resulted in harm to the subjects. Generally, substantive modifications must be made to the research protocol or informed consent process/documents, as well as implementing corrective actions, to safeguard current and future participants. Participants who have withdrawn or completed the study may need to be notified of these serious events and outcomes.

Federal regulations require that the institution (i.e., CDU) have written procedures for ensuring prompt reporting of any unanticipated problems involving risks to subjects or others to the IRB, appropriate institutional officials, and the department or agency head.

The post-approval event or outcome must meet all three criteria to be an unanticipated problem:

1. 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;

2. related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the event or outcome may have been caused by the procedures involved in the research); and

3. suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.

For the purposes of this policy, unanticipated problems are grouped into 3 major categories of events and outcomes: adverse events, protocol deviations and incidents, and updated study safety information and publication.

As seen in the Venn diagram below, not all of the adverse events, protocol deviations and incidents, or updated safety information is an unanticipated problem. The majority of them are not unanticipated problems.
Investigators must report unanticipated problems and other events and outcomes within a specific time frame using the various post-approval report (PAR) forms. The IRB in turn must review and determine whether the event or outcome is an unanticipated problem and if so, promptly report to the federal agencies. The IRB will also determine whether unanticipated problems involving risks to subjects or others is a serious or continuing non-compliance and whether IRB approval should be suspended or terminated.

**REASON FOR POLICY**

The Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) require that institutions have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval [45CFR46.103(b)(5) and 21CFR56.108(b)].

**POLICY STATEMENT**

1. Investigator must submit to the IRB all post-approval reports that meet the submission criteria within the required time frame.
2. IRB must review and make determination whether the research protocol still satisfies the requirements for IRB approval, including
   a. Risks to subjects are minimized
   b. Risks are reasonable in relation to the anticipated benefits (favorable risk/benefit ratio)
   c. Research protocol, consent document, and other applicable documents are adequate;
   d. Participants are provided with the updated information, if necessary;
   e. Adequate safeguards are in place to protect the rights and welfare of the human subjects, including subject privacy and confidentiality of data.
3. Principal Investigator must make changes to the research protocol, informed consent process/documents, other relevant IRB documents, and/or implement corrective actions as required by the IRB.
4. CDU IRB will report unanticipated problems involving risks to subjects or others to the regulatory agencies and institutional official(s).
5. Failure to submit post-approval report involving unanticipated problem is non-compliance and is reportable to the federal government.
PROCEDURES

PI Responsibilities: Submission of the Post-approval Report (PAR) by the Investigator

1. Determine whether the event or outcome is (1) adverse event, (2) protocol deviations and incidents, or (3) updated study safety information and publication. Examples of these categories are found in the Appendix.

2. Assess the event or outcome (from any of the above 3 categories) for the following:
   a. Represents an unanticipated problem involving risk of harm to subjects or others
      i. 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;
      ii. related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the event or outcome may have been caused by the procedures involved in the research); and
      iii. suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.
   b. Occurred under the jurisdiction of CDU (internal) or at other site under another IRB (external) (e.g., multicenter clinical trial)
   c. Occurred during the course of the study, after study completion, or after subject withdrawal or completion
   d. Consequence of the event or outcome
      i. impacts the safety, rights, or welfare of currently or previously enrolled subjects
      ii. alters the risks or the benefit to the subject
      iii. impacts the integrity of the data
      iv. affects the subject’s willingness to participate

3. Use the Table in the Appendix to determine which post-approval reporting (PAR) form, signature requirement, and time frame to submit to the IRB.
   a. Table 1 – Internal and External Adverse Event Reporting to the IRB
   b. Table 2 – Protocol Deviation and Incident Reporting to the IRB
   c. Table 3 – Updated Study Safety Information and Publication Reporting to the IRB
   d. Table 4 – Log of other non-reportable internal and external adverse events, protocol deviations, incidents, and at the time of the continuing review
4. Submit the PAR **within** the required time frame of reporting. Reporting time is counted from the day of discovery or awareness and involves working days (i.e., excludes Saturday, Sunday, and holidays).

5. Contact the IRB Chair, Vice Chair or physician member, if subjects are at immediate risk, so that interim measures are established to protect the subjects. If an emergent situation arises, the investigators must immediately respond to protect the subject. Upon earliest opportunity, the investigators must contact the IRB Chair, Vice Chair or physician member (for biomedical intervention studies) and submit the post-approval report to the IRB.

6. Submit an amendment at the same time as the PAR form, if the consequences of the event or outcome require changes to the research protocol, consent documents, or other relevant documents.

7. If the amendment is not ready, submit the PAR form first to avoid noncompliance.

8. Investigators must report to monitoring or oversight entities (e.g. research sponsor, coordinating or statistical center, independent medical monitor, DSMB/DMC, biosafety committee), if required under the IRB-approved protocol or institutional policy.

9. If the investigator determines that the event or outcome is not an unanticipated problem, but the monitoring entity subsequently determines that the event represents an unanticipated problem, the monitoring entity should report this determination to the investigator and such reports must be promptly submitted by the investigator to the IRB.

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**Pre-Marketing Investigational Drug (IND) Safety Reports**

If you are conducting IND Studies, and you are both the sponsor and Investigator (i.e., holding IND), you must report any **serious adverse event (SAE)**, whether anticipated or unanticipated, to the FDA Center for Drug Evaluation and Research (CDER) as soon as possible, but no later than 15 calendar days (10 working days) after awareness.

Sponsor/Investigators must also report any **fatal or life-threatening adverse event** as soon as possible, but no later than 7 calendar days (5 working days) after awareness.

- Form FDA 3500A (MEDWATCH)
- Instructions on filling out FDA 3500A
- Regulation: 21CFR320.31(d)(3)

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**IRB Responsibilities: IRB Review**
Initial IRB Review

1. IRB staff will review the post-approval report (PAR) to determine whether the report meets the submission criteria. If not, the staff will send an acknowledgement letter to the investigator.

2. If the PAR meets the submission criteria, staff will assemble supporting IRB documents along with the PAR and send to the IRB Chair for review. In the absence of the IRB Chair, either IRB Vice Chair or a designated committee member will review the report. A physician IRB member must review the PAR for a biomedical intervention study.

3. The supporting IRB documents may include, but not limited to the following:
   a. Research protocol
   b. IRB application
   c. Current approval notice
   d. Current approved informed consent document
   e. Correspondences between study sponsor and investigator
   f. Investigator’s Drug/Device Brochure (if applicable)

4. The IRB Chair will review and determine whether the risk/benefit ratio of the study has changed.

5. The IRB Chair will determine whether the reported event, outcome or information meets the criteria for an unanticipated problem involving risk to subjects or others. The criteria are as follows:
   a. The event is unexpected;
   b. The event is related or possibly related to the research participation; and
   c. Suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.

6. If the IRB Chair determines that the event does not meet the criteria for an unanticipated problem involving risk to subjects or others and requires no further action, the report will be accepted and a letter will be sent to the investigator acknowledged by the IRB Chair.

7. If additional actions are required, a letter will be sent by the IRB Chair to the investigator. The response will be reviewed under the expedited review or full board review upon the discretion of the Chair.

8. If the IRB Chair determines that the event meets the criteria for an unanticipated problem involving risk to subjects or others or cannot make a definitive determination,
the PAR and supporting IRB documents will be reviewed at the next convened IRB meeting.

9. The IRB Chair may request additional information from the Principal Investigator regarding the PAR prior to review at the convened IRB meeting. Information may include, but not limited to:
   a. Updated Progress Report
   b. Log of adverse events, protocol deviations, incidents, subject complaints, updated study safety information
   c. DSMB Report
   d. Monitor Report
   e. Correspondences between investigators, sponsor, federal agencies

10. If the PAR is of the nature that the safety, rights and welfare of subjects are at immediate risk, the IRB Chair will contact the Principal Investigator in order to establish an interim measure to be taken to protect the subjects. The decision and action will be reported at the convened IRB meeting.

11. If the PAR involves noncompliance, the review will also proceed as described elsewhere (see policy on Non-compliance).

Review by a convened IRB meeting (Full Board Review)

1. The PAR and supporting IRB documents will be distributed to the committee members approximately 5 working days prior to the meeting.

2. Appropriate review materials may include, but are not limited to the following:
   a. Post-approval report (PAR)
   b. Investigator’s correspondences
   c. Research protocol/grant
   d. Current IRB-approved IRB application
   e. Current IRB approval notice
   f. Current IRB-approved informed consent document
   g. Correspondence between study sponsor and principal investigator
   h. Investigator’s Drug/Device Brochure (if applicable)

3. The convened IRB may request additional detailed information from the principal investigator, sponsor, the study coordinating center, or DSMB/DMC about the adverse event or unanticipated problem in order to facilitate a thorough review before a final determination is made.

4. The convened IRB will consider and make the following determinations, which may include one or more action, but is not limited to the following:
a. The event reviewed constitutes an unanticipated problem
b. The event reviewed constitutes serious and/or continuing noncompliance
c. No further action required
d. Accept and approve the principal investigator’s corrective action plan
e. Modification of the research protocol to minimize risk
f. Modification of the continuing review schedule
g. Modification of the recruitment or informed consent documents
h. Requirement that current subjects re-consent to participation
i. Notification of previously enrolled subjects of new information
j. Notification of currently enrolled subjects of new information, as such information may relate to the subject’s willingness to continue participation in the research
k. Observation of the research or the consent process (i.e., use of a consent monitor)
l. Require additional progress or status reports to the IRB for a specified time period
m. Require prescribed education and training for the investigators and research staff
n. Require IRB audit
o. Notification to other CDU entity, such as institutional official(s), risk management
p. Require corrective action plan
q. Suspension of all or parts of the research (new enrollment, treatment, follow-up or data analysis)
r. Termination of the research

5. The convened IRB may determine that the post-approval reporting involves noncompliance and request further corrective action plan. The policy and procedures for noncompliance is described elsewhere (see policy on Non-compliance).

6. If the convened IRB considers suspension or termination of IRB approval, the review will also proceed as described elsewhere (see policy on Suspensions and Terminations of Previously Approved Research).

7. The outcome and determinations made during the convened IRB meeting will be documented in the correspondence to the principal investigator and the IRB meeting minutes.

8. Written correspondence from the IRB regarding their final action and determination will be forwarded to the Principal investigator within 10 working days of the IRB determination.
   a. The IRB staff will oversee and coordinate with the Chair all written correspondence from the IRB to the principal investigator (PI)
IRB Responsibilities: Reporting Requirements

1. Unanticipated problems involving risks to subjects or others; any serious or continuing noncompliance; and any suspension or termination of IRB approval are reportable to the appropriate federal department or agency head(s) and institutional officials.

2. IRB will make the report according to the policy on “IRB Reporting for Unanticipated Problems, Serious or Continuing Non-compliance, Suspension and Termination”.

<table>
<thead>
<tr>
<th>Form #</th>
<th>Title of the Form</th>
<th>Decision Trees</th>
</tr>
</thead>
<tbody>
<tr>
<td>F-129a</td>
<td>Internal Adverse Event Report</td>
<td>Decision tree for reporting Internal Adverse Event; Internal Subject Deaths</td>
</tr>
<tr>
<td>F-129b</td>
<td>External Adverse Event Report</td>
<td>Decision tree for reporting External Adverse Event</td>
</tr>
<tr>
<td>F-130</td>
<td>Protocol Deviation and Incident Report</td>
<td>Decision tree for reporting Protocol Deviations and Incidents</td>
</tr>
<tr>
<td>F-131</td>
<td>Updated Study Safety Information Report</td>
<td></td>
</tr>
<tr>
<td>F-140</td>
<td>Protocol Deviation and Incident Log for Investigators</td>
<td></td>
</tr>
</tbody>
</table>

DEFINITIONS

Adverse Event: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease (physical or psychological harm) temporally associated with the subject’s participation in the research, whether or not considered related to participation in the research).

Department or Agency Head: The head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

Deviation: Any intended or unintended variance or exception from the IRB approved protocol.

External Adverse Event or Outcome: An event or outcome that is experienced by subjects enrolled at study site(s) (e.g. multicenter clinical trial) under the jurisdiction of other IRBs.

Incident: An undesirable and unintended, although not necessarily unexpected event or outcome involving any aspect of the research study.
**Internal Adverse Event or Outcome:** An event or outcome that is experienced by subjects enrolled at study site(s) under the jurisdiction of the CDU IRB (IRB of record).

**Non-compliance:** Failure to comply with federal regulations, state laws, university policies, and/or the policies, requirements or determinations of the IRB or provisions of the approved research study.

**Post-approval reporting (PAR):** Reporting of unanticipated problems and other reportable events and outcomes that occurred after IRB approval is obtained. PAR can be submitted through the following forms:
1. Internal adverse event form (F-129a)
2. External adverse event form (F-129b)
3. Protocol deviations and incident form (F-130)
4. Updated Study Safety Information and Publication (F-131)
5. Log of non-reportable adverse events, protocol deviations, incidents to be attached with continuing review form

**Related (possibly related):** There is a reasonable possibility that the event or outcome may have been caused by the procedures involved in the research. The initial assessment is made by the CDU investigator.

**Serious Adverse Event:** Any adverse event that may result in the following: death, is life threatening (places subject at immediate risk of death from the event as it occurred); a required or prolonged hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect, or may require medical or surgical intervention to prevent one of the other outcomes previously listed in this definition. Serious adverse event may be expected or unexpected. If serious adverse event is unexpected, it is also an unanticipated problem.

**Unanticipated Problem:** An event or outcome that meets the following criteria: (1) unexpected; (2) related or possibly related to participation in the research; and (3) suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.

**Unexpected:** The nature, specificity, severity or frequency of the event or outcome is not accurately reflected in the protocol-related documents, such as the IRB-approved research protocol, informed consent document, and investigator brochure, and/or the characteristics of the subject population being studied.

**Unexpected Adverse Event:** Any adverse event where the nature, specificity or frequency of the event is not consistent with either: (1) the known or foreseeable risk associated with the procedures involved in the research that are described in the protocol-related documents (IRB approved protocol, informed consent document, investigator brochure), and relevant sources of information (product labeling/package inserts); or 2) the expected natural progression of any
underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

**REGULATIONS**

DHHS Regulations
- 45CFR46.103(b)(5)(i)
- 45CFR46.103(a)
- 45CFR46.116(b)(5)

FDA Regulations
- 21CFR50.25(b)(5)
- 21CFR56.108(b)(1)
- 21CFR312.53(c)(1)(vii)
- 21CFR312.66
- 21CFR812.150(a)(1)

**REFERENCES**

OHRP, Guidance on Reporting Incidents to OHRP, May 27, 2005
http://hhs.gov/ohrp/policy/procedures for reporting 052505.pdf

OHRP, Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, January 15, 2007

OHRP, Guidance on Written IRB Procedures, January 15, 2007

FDA Guidance for IRBs and Clinical Investigators: Continuing Review after Study Approval – Information Sheet
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126424.htm

FDA Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to IRBs – Improving Human Subject Protection (January 2009)

University of California, Los Angeles, Office of the Human Research Protection Program
Guidance and Procedure: Post-Approval Reporting Requirements (PAR) for Investigators: Reporting of Unanticipated Problems, Including Adverse Events as well as Protocol Violations, Deviations, and Incidents and the Reporting of Updated Study Safety Information
http://ohrpp.research.ucla.edu/file/10098/11-1.pdf
Accessed February 29, 2012

Children’s Hospital of Boston
Human Subjects Protection Update Special Communication
November 2008

**APPENDIX**

**Table 1 – Internal and External Adverse Event Reporting to the IRB**

<table>
<thead>
<tr>
<th>Post-approval reportable events or outcome</th>
<th>Reporting Form*</th>
<th>Signature</th>
<th>Timeframe of Reporting to IRB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject death that is (1) unexpected, (2) related or possibly related to research, and (3) it is an interventional study (includes socio-behavioral studies). <strong>This is an unanticipated problem.</strong></td>
<td>Internal adverse event form (Form 129)</td>
<td>PI or physician co-invest (if PI is not a physician, study physician co-invest must sign)</td>
<td>Within 3 working days of awareness</td>
</tr>
<tr>
<td>Internal (on-site) death that was (1) expected, (2) related or possibly related to the study, and (3) it is an interventional study (include socio-behavioral studies). <strong>This is not an unanticipated problem.</strong></td>
<td>Continuing Review Form (Form 108, Section VI)</td>
<td>PI or co-investigator</td>
<td>Report at the time of continuing review</td>
</tr>
<tr>
<td>Any other internal subject death</td>
<td>N/A</td>
<td>N/A</td>
<td>Do not report</td>
</tr>
<tr>
<td>Internal (on-site) adverse event that is (1) unexpected in nature, severity, or frequency than was previously known or described in the IRB approved informed consent; (2) related or possibly related to the research activity; and (3) serious, placing subjects or others at greater risk of harm than was previously known or recognized. <strong>This is an unanticipated problem.</strong></td>
<td>Internal adverse event form (Form 129)</td>
<td>PI or physician co-invest (if PI is not a physician, study physician co-invest must sign)</td>
<td>Within 5 working days of awareness</td>
</tr>
<tr>
<td>Internal (on-site) adverse event that is not an unanticipated problem</td>
<td>Continuing Review Form (Form 108, Section VI)</td>
<td>PI or co-investigator</td>
<td>Report at the time of continuing review</td>
</tr>
<tr>
<td>External (off-site) adverse event that is (1) unexpected in nature, severity, or frequency than was</td>
<td>External adverse event form (Form 130)</td>
<td>PI or physician co-invest (if PI is not a physician, study physician co-invest</td>
<td>Within 5 working days of awareness</td>
</tr>
</tbody>
</table>
previously known or described in
the IRB approved informed
consent; (2) related or possibly
related to the research activity;
and (3) serious, placing subjects
or others at greater risk of harm
than was previously known or
recognized.
This is an unanticipated problem.

| External adverse event is not an
unanticipated problem and all
subjects at the CDU site have
completed study participation,
and the event poses no new risk |
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>N/A</td>
</tr>
<tr>
<td>N/A</td>
</tr>
<tr>
<td>Do not report</td>
</tr>
</tbody>
</table>

**Table 2 – Protocol Deviation and Incident Reporting to the IRB**

<table>
<thead>
<tr>
<th>Post-approval reportable events or outcome</th>
<th>Reporting Form*</th>
<th>Signature</th>
<th>Timeframe of Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol deviations or incidents that is (1) unexpected, (2) related or possibly related to research, and (3) places the participants or others at greater risk or harm than previously known or recognized (i.e. serious). This is an unanticipated problem.</td>
<td>Protocol Deviation or Incident Report Form (Form 131)</td>
<td>PI or co-investigator or investigator familiar with the case</td>
<td>Within 10 working days of awareness</td>
</tr>
<tr>
<td>Protocol deviation or incidents that are not unanticipated problem (include subject complaints that were resolved by the investigators)</td>
<td>Continuing Review form (Form 108, Section V)</td>
<td>PI or co-investigator</td>
<td>Report at the time of continuing review</td>
</tr>
<tr>
<td>Emergent changes to IRB-approved protocol to eliminate any immediate hazard to subjects. This is an unanticipated problem.</td>
<td>Protocol Deviation or Incident Report Form (Form 131)</td>
<td>PI or co-investigator or investigator familiar with the case</td>
<td>Within 3 working days of awareness</td>
</tr>
</tbody>
</table>

**Table 3 – Updated Study Safety Information and Publication Reporting to the IRB**

<table>
<thead>
<tr>
<th>Post-approval reportable events or outcome</th>
<th>Reporting Form*</th>
<th>Signature</th>
<th>Timeframe of Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reporting suspension, hold or termination of study activity initiated by FDA, sponsor, PI, funding agency or by others. This is an unanticipated problem.</td>
<td>Updated Study Safety Information Report Form (Form 132)</td>
<td>PI or physician co-invest. (If PI is not a physician, both PI and study physician co-invest must sign)</td>
<td>Within 3 working days of awareness</td>
</tr>
<tr>
<td>Reporting updated safety information or publication such as FDA Safety Alerts or Safety information from another site if this study is part of a multi-site</td>
<td>Updated Study Safety Information Report Form (Form 132)</td>
<td>PI or physician co-invest. (If PI is not a physician, both PI and study physician co-invest must sign)</td>
<td>Within 10 working days of awareness</td>
</tr>
<tr>
<td>study</td>
<td>Investigator Brochure or Device Brochure</td>
<td>Updated Study Safety Information Report Form (Form 132)</td>
<td>PI or physician co-invest. (If PI is not a physician, both PI and study physician co-invest must sign)</td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
</tr>
<tr>
<td>Data Safety Monitoring Board (DSMB) report or interim study result</td>
<td>Updated Study Safety Information Report Form (Form 132)</td>
<td>PI or physician co-invest. (If PI is not a physician, both PI and study physician co-invest must sign)</td>
<td>Within 10 working days of awareness</td>
</tr>
<tr>
<td>Audit, inspection or monitoring report</td>
<td>Updated Study Safety Information Report Form (Form 132)</td>
<td>PI or physician co-invest. (If PI is not a physician, both PI and study physician co-invest must sign)</td>
<td>Within 10 working days of awareness</td>
</tr>
<tr>
<td>Other safety information or publication that may change the study risk or benefit</td>
<td>Updated Study Safety Information Report Form (Form 132)</td>
<td>PI or physician co-invest. (If PI is not a physician, both PI and study physician co-invest must sign)</td>
<td>Within 10 working days of awareness</td>
</tr>
</tbody>
</table>

### Table 4 – Examples of Protocol Deviations and Incidents

#### Protocol Deviations

The following are some common classification of protocol deviation to assist the investigators. This is not a complete list. Also, depending on the research protocol, some minor deviations could be considered major.

<table>
<thead>
<tr>
<th>Common minor protocol deviations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Missing signed informed consent document but the PI can verify by other methods consent was obtained</td>
</tr>
<tr>
<td>• Inappropriate documentation of informed consent including</td>
</tr>
<tr>
<td>• 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</td>
</tr>
<tr>
<td>• 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.</td>
</tr>
<tr>
<td>• Over enrollment of subjects in research that has produced additional data of potential scientific value</td>
</tr>
<tr>
<td>• Study personnel involved in research without appropriate training</td>
</tr>
<tr>
<td>• Use of recruitment materials and processes that include small modifications from those that are approved</td>
</tr>
<tr>
<td>• Assent obtained but not appropriately documented.</td>
</tr>
<tr>
<td>• Any lapse in study approval where there is a continuation of research activities (i.e., recruitment, enrollment, procedures, data analysis)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Common major protocol deviations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Failure to obtain informed consent prior to initiating research procedures</td>
</tr>
<tr>
<td>• Informed consent obtained after research procedures are initiated</td>
</tr>
<tr>
<td>• Performing study procedures not approved by the IRB unless to eliminate immediate potential harm to the subject</td>
</tr>
<tr>
<td>• Failure to perform a test approved in the protocol that is important to subject safety or data integrity</td>
</tr>
<tr>
<td>• Drug medication (dosing and dispensing) errors regardless of whether a subject was negatively impacted</td>
</tr>
<tr>
<td>• Failure to follow data and safety monitoring plan</td>
</tr>
</tbody>
</table>
- Failure to report a serious, unanticipated adverse event that is thought to be possibly or definitely related to research interventions
- Use of a recruitment process not approved by IRB
- Enrollment of new subjects after IRB approval has expired
- Enrolling a subject that does not meet inclusion/exclusion criteria
- Enrolling an incarcerated youth or a ward of state in a protocol not previously approved to include these populations
- Parental permission granted by someone other than the parent or legal guardian
- Assent not obtained when required by IRB
- Verbal consent obtained when IRB requires written consent

**Other types of deviations**
- Any emergent deviation from the IRB protocol made without prior IRB review to eliminate apparent immediate hazard to a research subject
- Any unintended or intended deviation from the IRB approved protocol that involves potential risks or has the potential to recur
- Any lapse in study approval where there is a continuation of research activities (i.e., recruitment, enrollment, procedures, data analysis)
- Any identified noncompliance with federal regulations, state laws, University policies and/or requirements or determinations of the IRB or provisions of the approved research study
- Any event that requires prompt reporting according to the protocol or the study sponsor

**Incidents**
- Any complaint of a study subject that indicates an unexpected risk or the complaint cannot be resolved by the research staff
- Any breach of confidentiality or privacy
- Computer data security breach (i.e. lost or stolen computers/laptops and/or removable media used as storage devices, such as a flash drive or CD) on which personally identifiable information may have been or be acquired by an unauthorized person
- Incarceration of a study subject in a medical study not approved to enroll prisoners
- Loss of adequate resources to support continued research activities
- An unexpected natural disaster, such as an earthquake, that destroys records or disrupts scheduling

**Table 5 – Examples of Updated Study Safety Information and Publication**

<table>
<thead>
<tr>
<th>Updated Study Safety Information and Publication</th>
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</thead>
<tbody>
<tr>
<td>- Data Safety Monitoring Board (DSMB) Report</td>
</tr>
<tr>
<td>- Audit, inspection, or monitoring report</td>
</tr>
<tr>
<td>- Interim study results</td>
</tr>
<tr>
<td>- FDA Safety Alerts</td>
</tr>
<tr>
<td>- Publication in the literature or other findings</td>
</tr>
<tr>
<td>- Revised Investigator’s Drug/Device Brochure</td>
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<tr>
<td>- Notification of any change in study status</td>
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<tr>
<td>- Changes in the FDA labeling or withdrawal</td>
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<tr>
<td>- Any information that requires prompt reporting</td>
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</tbody>
</table>

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