POLICY
Reportable New Information to the IRB for Previously Approved Research

This Policy is Applicable to the following Spectrum Health sites:
Big Rapids (Mecosta County Medical Center), Continuing Care, Corporate, Gerber (Newaygo County General Hospital Association), Ludington (Memorial Medical Center of West Michigan), Outpatient/Physician Practices, Pennock (Pennock Hospital), Priority Health, Reed City (Reed City Hospital Corporation), SH GR Hospitals (Spectrum Health Hospitals), SHMG, United/Kelsey (Spectrum Health United; Spectrum Health Kelsey Hospital), Zeeland (Zeeland Community Hospital)

Applicability Limited to: N/A

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1. **Purpose**
   The purpose of this policy is to establish guidelines for reporting new information/events that arise/occur after initial approval of human subjects research.

2. **Definitions**
   Local Subject: A subject that is enrolled in a clinical research study at a Spectrum Health facility/location or a facility/location that the Spectrum Health IRB (SH IRB) has agreed to serve as the IRB ofRecord for the research in which the event has occurred.

   Protocol Exception: A change in the protocol and/or currently approved research plan, which is made for a single subject or a small group of subjects, which is approved by the Sponsor or funding agency and IRB (and, for device studies, the FDA) prior to implementation. Examples include exceptions to Inclusion/Exclusion Criteria for a single patient, a change in approved study proceduresfor a single patient or small group of patients, etc.

   Non-Compliance: Failure to follow the research regulations, Spectrum Health Policy or the requirements or determinations of the IRB. Note: *In the case of research funded or conducted by the Department ofDefense (DOD), Non-Compliance includes failure to comply with Department of Defense directivesregarding protection of Human Subjects.*

   Continuing Non-Compliance: A pattern of non-compliance (serious or non-serious) that suggests a potential for future non-compliance without intervention; a repeated unwillingness to comply with applicable research standards, regulations or determinations of the IRB; or a persistent lack of knowledge of how to comply on the part of the investigator or a willful lack of commitment by the investigator and study team to protect human participants.

Serious Non-Compliance: Non-Compliance that has or could reasonably be anticipated to have thepotential to, increase a physical, psychological, safety, or privacy risk to, or impair the rights of, Local Subjects.

Reportable New Information: Events/New Information that arises or occurs during the course of research, which are unexpected in nature or scope, potentially adverse, and/or can affect the potential risks or conduct of the research.

Unanticipated: An event is “unanticipated” when it was unforeseeable prior to the time of its occurrence.

Unanticipated Problem (UAP) Involving Risks to Subjects or Others: Any information or event that is (1) unanticipated or unexpected in nature, severity or frequency; (2) indicates that subjects orothers are at increased risk of harm than was previously known or recognized; and (3) related to theresearch. Harm can be physical, emotional/psychological, social, or economic, and can include privacy harms.

Unanticipated adverse device effect or UADE: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, ***if*** that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), **or** any other unanticipated seriousproblem associated with a device that relates to the rights, safety, or welfare of subjects.

3. Policy

While the Principal Investigator (PI) may, as appropriate, delegate some duties for the conduct of the research, the PI retains ultimate responsibility for assuring the reporting of new information and adverse or unanticipated events in accordance with this policy. These must be reported within established timelines.

This policy establishes when and what new, unanticipated, and adverse information related to human subjects' research PI and research personnel must report to the SH IRB after initial approval. It reflects FDA and OHRP regulations and guidance on this topic.

The PI is expected to submit Reportable New Information (RNI) within fine (5) business daysof becoming aware of such information. If the RNI relates to a very serious event, occurrence or information, immediate reporting is encouraged.

The SH IRB will review the new information/event in relation to human subjects’ protections and adherence to federal regulations, state laws, and local policies. The SH IRB will determine if the information or event represents Serious and/or Continuing Non-Compliance, an Unanticipated Problem Involving Risks to Subjects or Others, or the need to Suspend or Terminate IRB Approval due to risk or for cause. If the SH IRB makes one of these determinations, internal and external reporting obligations are triggered. External Reporting must occur within 30 days of initial determination. The IRB will follow standard of work processes to meet these reporting obligations.

Not all events and/or new information that arise/occur during the course of the research must be reported to the SH IRB. The RNI xForm in IRBManager contains detailed examples and additional information that should be reported to the SH IRB.

Events and new information that requires reporting the SH IRB includes those that a reasonable person would anticipate could have an effect on the risks, safety, or legal compliance of research activity, such as:

- Information that indicates a new or increased (in frequency or severity) risk.
- Any harm experienced by a Local Subject or other individual which in the opinion of the localinvestigator is unexpected **and** at least probably related to the research **and** suggests that the research places the subjects or others at a greater risk of harm than was previously known or recognized.
- Non-Compliance, including credible allegations, or as established through internal or externalreview.
- Audit, inspection, or inquiry regarding research activities by a federal agency or othergoverning entity.
- Failure to follow the protocol due to the action or inaction of the investigator or human research staff that affects the scientific soundness of the research or the rights, safety orwelfare of human subjects.
- Breach of confidentiality of Local Subject(s) data.
- Change to the protocol taken without prior IRB review to eliminate an apparent immediatehazard to a subject.
- A Local Subject becomes a prisoner while participating in a study that has not been approvedpreviously to involve prisoners.
- Complaints or concerns of a Local Subject that cannot be resolved by the research team.
- Adverse Device Effects (UADE). Note**:** UAPs, Serious or Continuing Non-Compliance, and Suspensions and Terminations of IRB approval, for cause can occur within a study that involves a device. However, the local PI must first assess whether the event is a potential UADE.

A. Unanticipated Adverse Device Effects (UADE):

An UADEs, by definition, must meet all three (3) reporting requirements: Related,Increased Risk and Unexpected. For device studies, regulations require that PI submits a report of an UADE to the sponsor and the reviewing IRB as soon as possible, but in no later than 10 working days after the PI first learns of the event (21 CFR §812.150(a)(1)).

Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after thesponsor first receives notice of the UADE (21 CFR§ 812.46(b), §812.150(b)(1)). This means that Sponsor's evaluation of the UADE is submitted to the participating study PI and the local IRB simultaneously.

The SH IRB expects the local PI to submit the Sponsor's reports via the RNI xForm, noting the appropriate category and describing his/her assessment of the UADE, and Sponsor's report, withinfive (5) days of receiving the report from the Sponsor.

The SH IRB will report to the FDA and sponsoring agency if it makes a determination of Unanticipated Problems (UAP), Serious or Continuing Non-Compliance, or if it decides to Suspend or Terminate IRB approval.

B. Outside Safety Events:

Study related events that occur at sites where the PI **is not** relying on the SH IRB (i.e., not a Local Subject as defined in this policy) are typically **not** considered RNI to the SH IRB *unless*, one or both of the following are true:

1. The outside event provided to the Spectrum Health PI from the Sponsor is determined to be related, unanticipated, and places subjects at a greater risk than previously known. In these instances, the PI should submit a modification to the currently approvedSH IRB protocol to include the Sponsor and/or DSMB's assessment of the event and theSpectrum Health PI's assessment of the event. The modification form should outline the necessary revisions to the SH IRB approved protocol and associated documents to incorporate the event's impact on the risk-potential benefit profile of the study.
2. The investigator relying upon the SH IRB is also the lead PI for a multi-center study and the event occurred at one of the participating sites under their oversight as lead PI. In these instances, the lead PI should submit to the SH IRB a RNI xForm via IRBManager detailing the event and including local IRB determinations, as applicable.

C. Protocol Exceptions:

Protocol Exceptions as defined above, have a regulatory basis in the following areas: DHHS 45 CFR §46.108(a)(3)(iii); FDA 21 CFR §56.108(a)(4); 21 CFR §812.150(a)(4).

Documentation of sponsor, funding agency and/or FDA pre-approval should be submitted to the SH IRB via a modification request for incorporation into the IRB's prior review and approval process. Copies of these approvals for the exception should be maintained in the investigator's researchrecords.

The PI has ultimate responsibility for obtaining prior IRB approval for Protocol Exceptions via a request for modification.

Protocol exceptions/changes that are made without prior SH IRB review to eliminate an apparent immediate harm to a subject should be reported via the RNI xForm indicating this category within the form. The report must include a detailed description of the harm presented, the protocol exception/change made to prevent this harm, and the subject's outcome.

D. Protocol Deviations:

A Protocol Deviation is the failure to comply with the requirements of the Protocol which has been approved by the IRB. The PI is responsible for complying with the Protocol.

Any deviation of the protocol made without prior approval from the sponsor or funding agency, the FDA when applicable, **and** the SH IRB, must be reported to the IRB. Deviations are generally describedas "major" or "minor".

Major deviations are deviations that may potentially have significant impact on the research plan, integrity of the data results and/or subjects' rights, safety or welfare and must be reported to the SH IRBwithin five (5) days of the PI becoming aware of such deviation or impact of such deviation via the RNI xForm. The report must include a description of the deviation, the reason for the deviation, and result or outcome of the deviation and plans to correct or prevent future recurrence if applicable.

Minor protocol deviations that do not significantly impact the research plan, integrity of the data results and/or subjects' rights, safety or welfare, are to be reported to the SH IRB at the time of continuing review via a minor protocol deviation tracking log.

4. Revisions

Spectrum Health reserves the right to alter, amend, modify or eliminate this policy at any time without prior written notice.

5. Policy Development and Approval

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Not Assigned

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Not Assigned

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6. Keywords

Research compliance, research, IRB, RNI, Non-compliance, Unanticipated Problems, reporting, protocol deviation, new information, unanticipated adverse device affects, UADE