TITLE: Internal Adverse Event, Protocol Deviation/Violation, Unanticipated Events: Reporting and Review		POLICY/PROCEDURE NUMBER: IRB 15	
Author:	Jana L. Lacera, RN, MSA, CDM	Applicable To:	CHS CIRB
Supersedes:	Reporting of Adverse Events During the Conduct of an IRB Approved Research Study	Issued By:	CHS CIRB
Date Originated:	3/9/99	Date Effective:	6/2020

	CFNI		Community Hospital		St. Catherine Hospital		St. Mary Medical Center
X	Munster, Indiana	X	Munster, Indiana	X	East Chicago, Indiana	X	Hobart, Indiana

POLICY/PROCEDURE STATEMENT:

The Code of Federal Regulations requires the "prompt reporting of any ***unanticipated problems*** involving risks to subjects or others" (Reference Code of Federal Regulations Title 21, Parts 312 and 812, Title 45, Part 46)

PURPOSE

To define the requirements and procedure for the prompt reporting to the Community Healthcare System Central Institutional Review Board (CHS CIRB)

To provide a mechanism for concurrent review of internal adverse events, protocol deviations/violations, unanticipated events and the reports from the monitoring entity (Data Safety Monitoring Board (DSMB)) for those studies approved by the CHS CIRB.

DEFINITIONS

Adverse Event:

1. An adverse event is considered **serious** if:
    - it is fatal or life-threatening;
    - requires or prolongs hospitalization;
    - produces a disability;
    - results in a congenital anomaly/birth defect: or
    - based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed.
2. An adverse event is considered to be of **moderate or greater severity** if:
    - it requires medical evaluation (such as additional laboratory testing) and/or medical treatment; or
    - if it is a serious adverse event.
3. An adverse event is considered to be **unexpected** if:
    - it is not identified in nature, severity or frequency in the current IRB-approved research protocol or informed consent document.
4. An adverse event is considered to be **associated with the research intervention** if:
    - there is a reasonable possibility that the reaction may have been caused by the research intervention (i.e., a causal relationship between the reaction and research intervention cannot be ruled out by the investigator (s).

External adverse events are those events that are experienced by subjects enrolled by investigators at other institutions engaged in multicenter clinical trials and are reported to the principle investigators by the sponsors of an IRB-approved research protocol. There is no requirement by OHRP, FDA or ICH to report external adverse events to the IRB.

Internal adverse events are those events experienced by subjects within the CHS or other research site that falls under the jurisdiction of the CHS CIRB.

Protocol Deviation: An unintended or unapproved change to an IRB approved protocol. Generally does not have a significant effect on the subject's rights, safety, or welfare, or on the integrity of the resultant data. Example: Obtaining a protocol required test one day out of the acceptable "window".

Protocol Violation: Those events that were caused by or could have been prevented by the investigator and which materially affect the study results. Generally affect the subject's rights, safety, or welfare, or the integrity of the data (i.e., the sponsor's ability to use the data) Example: Enrolling a subject who did not qualify for the trial without obtaining the sponsor's permission or repeatedly failing to obtain a protocol required test.

Unanticipated Problem involving risks to subjects or others: Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given all 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 a subject's participation 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) related to the research than was previously known or recognized.

PROCEDURE

Reporting Timelines

Investigators involved in the conduct of CHS CIRB-approved research studies shall report adverse events to the CHS CIRB in accordance with the following timelines:

1. **Internal adverse events** which are unexpected, fatal or life-threatening, and associated with the research intervention must be reported to the CHS CIRB within 24 hours of knowledge of the event. (*Note: It is recognized that the information available during this 24 hour period may not be sufficient to permit accurate completion of the required adverse event reporting forms. However, the CHS CIRB should, at a minimum, be notified of the adverse event during this time frame, with subsequent follow-up submission of a more detailed written report.)*
2. **Internal adverse events** which are unexpected, of moderate or greater severity (but not fatal or life-threatening), and associated with the research interventions shall be reported to the CHS CIRB within 10 calendar days of knowledge of the event.
3. **Protocol Deviations/Violations** The investigator will report those protocol deviations/violations as required by the sponsor. The CHS CIRB should be notified of protocol deviations/violations within 10 calendar days of the date of the event.

Reporting/Review of Adverse Events

1. Internal Adverse Events

Internal adverse events reported to the CHS CIRB in accordance with the requirements addressed above will be reviewed by the Human Protections Administrator within 2 working days of the receipt of the report. All internal adverse events which are serious unexpected, fatal or life threatening will be immediately reported to CHS CIRB Chair for review. The final report will be submitted for full CHS CIRB review at the next convened meeting. The CHS CIRB will notify the investigator in writing of all acknowledgments and/or determinations.

Investigator must complete and submit the following:

- *CHS CIRB Adverse Event Report Form*

2. External Adverse Events

External Adverse Event Reports: (i.e. external sponsor generated safety reports) may be reported to the CHS CIRB if required by the sponsor, however, the CHS CIRB will not formally review these reports. The Adverse Event Report form will be stamped as "received" with the date and a copy will be returned to the investigator. The original Adverse Event Report Form and the Summary of External Adverse Event Reports Form will be filed in the appropriate study binder. .

If submitting, the Investigator must complete and submit the following for the external adverse events reported by the sponsor:

- *CHS CIRB Adverse Event Report Form*
- *Summary of External Adverse Event Reports Form*

The Investigator *will not submit* the sponsor generated adverse event report forms to the CHS CIRB

Reporting/Review of Internal Adverse Events at Continuing Review

To submit a research protocol for renewal, the investigator must complete:

1. *Request to Renew a Research Study*
2. *Summary of Clinical Trial Adverse Events for each subject.*
    - Only those Internal Adverse Events that can be categorized as Definite or Probable, or Serious Unexpected need to be reported again during the process of renewal or closure.
    - A detailed summary of the adverse events which includes information about the nature of each event; the date of the event; the site at which the event occurred; causality considerations; and any outcome or follow-up information to the event.
3. There is no requirement to submit External Adverse Events from the sponsor.

***Note**: The CHS CIRB may request additional subject-specific information (e.g., final outcomes, clarification of causality determinations) related to the adverse events. Possible delays in research protocol renewal may be avoided by including additional details with the initial renewal report; especially if the reported adverse events would raise a concern regarding a change in the benefit-to-risk ratio study participation.*

Reporting/Review of Adverse Events of a Non-Local IRB Approved Protocol

1. The investigator remains responsible for notifying the CHS CIRB of all Internal Adverse Events as outlined above.
2. The CHS CIRB will review all Internal Adverse Events as outlined above.
3. The CHS CIRB will not review External Adverse Event reports.
4. The investigator remains responsible for reviewing all adverse event information and submitting/maintaining the documentation required by the sponsor.
5. The investigator will alert the CHS CIRB of any information that may affect the continuation of the protocol at the local level.
6. The CHS CIRB will notify the investigator in writing of all acknowledgments and/or determinations.

Reporting/Review of Protocol Deviation/Violation

1. The investigator must submit a *Protocol Deviation/Violation Form* within 10 calendar days of knowledge of the event.
2. The submission will be reviewed within 2 working days of the receipt of the report. All Protocol Deviations/Violations which are serious unexpected, fatal or life threatening will be immediately reported to the CHS CIRB Chair for review. The final report will be submitted for full CHS CIRB review at the next convened meeting.
3. The CHS CIRB will notify the investigator in writing of all acknowledgments and/or determinations.

SUMMARY OF REPORTING PROCESS

Internal Adverse Events – Process is the same for CHS CIRB and Non-Local IRB approved studies	**External Adverse Events**
Definition: • Occurred to a subject enrolled in a CHS CIRB-approved research protocol • Is associated with the research intervention • Event classification is Serious Unexpected • Causality is Definite or Probable	**Definition:** • Occurred at an external site and is reported to investigators of a CHS CIRB-approved research protocol by external sponsors of multicenter studies
Reporting Process: Complete and submit *Adverse Event Report Form* : Unexpected, life-threatening *within 24 hours of knowledge of the event*. Unexpected, of moderate or greater severity within *10 calendar days of knowledge of the event.*	**Reporting Process if required by sponsor:** Complete and submit within 30 days of their receipt by the investigator: • *Adverse Event Report Form* • *Summary of External Adverse Event Reports Form* • Do not attach Sponsor generated report forms **Note: the CHS CIRB will stamp the Report Form as "Received" and return a copy to the PI.**
Reporting Process at Time of Renewal: Complete and submit: • *Request to Renew a Research Study* • *Summary of Clinical Trial Adverse Events Form*	**Reporting Process at Time of Renewal:** **NONE**
Protocol Deviation/Violation	**Non-Local IRB Approved Protocol**
Submit as required by the sponsor. Complete and submit *within 10 calendar days of knowledge of the event.* *Protocol Deviation/Violation Form*	**Reporting Process:** **NONE**

REFERENCE:

21 CFR Part 56.108 (b)
Part 312.53 (c)(1)(vii)
Part 312.66
45 CFR 46.103

ACCEPTED BY:

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DATE REVISED: 4/05, 8/2007, 1/2009, 7/2009

REVIEWED AND ACCEPTED by the Community Hospital IRB 3/99

REVIEWED AND ACCEPTED by the CHS CIRB 6/05, 9/07, 1/09, 3/2013, 4/2016, 11/2017, 6/2020

Date	Initials
1/2009	JL
7/2009	JL
3/2013	JL
3/2016	JL
11/2017	JL
6/2020	JL