| **Title:** Reporting to the Institutional Review Board (IRB) of Adverse Events and Unanticipated Problems Involving Risks to Study Participants or Others  Policy Number: A-COM-0007  **Replaces (supersedes): none**  http://staffnet/Staff/Reference/MarketingandBrandingResources/CHALogoForEveryday.png | **Policy Chronicle:**  Effective Date: 07/21/2020  Date the Original Version of Policy was Effective: (month/year): 04/2003    Most Recent Review (month/year): 07/2020  Owner: (Name/Title)  J. Glover Taylor    Previous Review: 01/2017 |
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| **Area of Operations:**  Research  Institutional Review Board (IRB) | **Regulatory /Accreditation Standard(s)**  JCAHO  Dept. of Health & Human Services/IRB 45 CFR 46  21 CFR 56, 312, 812 |
| **Keyword(s):** Adverse Reaction, Adverse Event, Event Reporting, IRB,  Interventional, Unanticipated Problem | |

**Purpose:** To define Cambridge Health Alliance guidelines, policies, and procedures, in accordance with Federal and Massachusetts law, regarding unanticipated problems involving risks to study participants or others and adverse events and their reporting to the IRB.

**Personnel: All Cambridge Health Alliance Research Staff.**

**Definitions:**

1. Unanticipated problem involving risks to study participants or others: Any incident, experience, or outcome that meets all of the following criteria:

a. 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 form; and (b) the characteristics of the subject population being studied;

a. Related or possibly related to participation in the research (in this policy *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); AND

b. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

2. Adverse Event (AE): Any untoward or unfavorable physical or psychological occurrence in a study participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the volunteer’s participation in the research, whether or not considered related to the volunteer’s participation in the research.

2a. Serious Adverse Events (SAE): (21 CFR 312.32) any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:

a. Results in death;

b. Is life threatening;

c. Results in inpatient hospitalization or prolongation of existing hospitalization;

d. Results in a persistent or significant disability/incapacity or permanent incapacity or substantial disruption of the ability to conduct normal life functions;

e. Results in a congenital anomaly/birth defect; or

f. Based upon appropriate medical judgment may jeopardize the participant’s health and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

2b. Unexpected Adverse Events: Any adverse event occurring in one or more participant in a study protocol, the nature, severity, or frequency of which is not consistent with either:

a. The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the **IRB-approved research** protocol, any applicable investigator brochure, and the current IRB-approved informed consent form, and (b) other relevant sources of information, such as product labeling and package inserts; OR

b. The expected natural progression of any underlying disease, disorder, or condition of the participant(s) experiencing the adverse event and the participant’s predisposing risk factor profile for the adverse event.

Note: Per FDA regulation (21 CFR 312.32), an unexpected adverse event also refers to adverse events or suspected adverse reactions that are mentioned in the investigator brochure as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation.

2c. Unexpected Adverse Device Effect (21 CFR 812.3(s)): 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 or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of the participants.

2d. External adverse event: Adverse events experienced by participants enrolled by an investigator at an institution other than CHA that is engaged in the research.

2e. Internal adverse event: Adverse events experienced by participants enrolled by an investigator at CHA. If a study is only conducted at CHA all adverse events would be considered internal adverse events.

**Policy:**

Adverse event reporting to the Institutional Review Board (IRB) and, in some circumstances, Federal agencies, is required by Federal regulation. Both Federal policy (Common Rule) [45 CFR 46.108(a)(4)] and US Food and Drug Administration regulations [21 CFR 56.108(b)(1); 21 CFR 312.66] require the reporting of unanticipated problems involving risks to study participants or others to the IRB and appropriate institutional officials.

**Procedures:**

A. Submission to the IRB of an internal AE that is NOT an Unanticipated Problem:

1. Any internal event that meets the definition of an AE, but does not meet the definition of an Unanticipated Problem should be summarized and reported to the IRB at the time of Continuing Review,at the time of study termination if prior to the next scheduled Continuing Review, or as part of the annual check-in for research not required to undergo continuing review under the 2018 Revised Common Rule.

NOTE: External AEs that are not serious or are not unanticipated problems do not have to be reported to the IRB.

B. Submission to the IRB of an internal or external AE that is an Unanticipated Problem:

1. Any internal or external event that meets the definition of an AE **AND** meets the definition of an Unanticipated Problem is to be reported to the IRB within 5 business days of discovery.

2. The Principal is responsible for reporting the event to the IRB on the Unanticipated Problem/Adverse Event form.

C. Submission to the IRB of an internal or external SAE:

1. Any internal or external event that meets the definition of a SAE is to be reported to the IRB within 5 business days of discovery.

2. The Principal is responsible for reporting the event to the IRB on the Unanticipated Problem/Adverse Event form.

D. Submission to Sponsor or other applicable agency of an AE or an Unanticipated Problem

The Principal Investigator is to submit reports of unanticipated problems and AEs in accordance with the requirements of the sponsor and other applicable agencies (*e.g.,* FDA).

E. Submission to the IRB of an event that is not an AE, but requires reporting to the IRB:

1. Certain events, while not AEs, do need to be e reported to the IRB within 5 business days of discovery. Examples of such events include, but are not limited to:

a. Breach of confidentiality.

b. Suspension or early termination of the research study by the Sponsor or other agency.

c. Incarceration of a research participant enrolled into the study.

d. Medication error, regardless of whether participants experienced harm.

e. New information (*e.g.,* interim analysis, safety monitoring report, publication, or other finding) that suggests that there are new or increased risks to participants or others

f. A complaint by a research participant or others that suggests that rights, welfare, or safety of a participant has been adversely affected.

g. Any event or problem that is unanticipated (in terms of nature, severity, or frequency), related or possibly related, and suggests that there is an increased risk to subjects or others than was previously known.

a. Any other problem that suggests that the research places participants or others at an increased risk of harm or adversely affects the rights, welfare, or safety of participants or other.

2. The Principal Investigator is responsible for reporting the event to the IRB on the Unanticipated Problem/Adverse Event form.

3. See above section “D. Submission to Sponsor or other applicable agency of an AE or an Unanticipated Problem."

B. Submission of reports to CHA Risk management

Submission of reports to the IRB does not fulfill the requirement of submission of incident reports to CHA Risk Management. Those reports are required and are to be reported per CHA incident reporting policy.

IRB Review:

1. The CHA IRB Administrator receives and screens Unanticipated Problem/Adverse Event form for completeness. If information is missing, the IRB Administrator will request the missing information from the Principal Investigator.

2. The IRB Administrator will forward the completed report form to the IRB Chair, Vice-Chair, or designee for review.

3. The IRB Chair/Vice-Chair/designee will determine whether the event meets the definition of an unanticipated problem involving risks to subjects or others.

4. If the event:

a. Does not meet the definition of an unanticipated problem involving risks to subjects or others, then the IRB Chair/Vice-Chair/designee may review the submission via expedited review procedures.

b. Does meet the definition of an unanticipated problem involving risks to subjects or others, it will be referred to the convened IRB for review and determination.

If the IRB Chair/Vice-Chair/designee is unable to determine if the event is an unanticipated problem involving risks to subjects, it will be referred to the convened for review and determination.

5. The IRB Reviewer or convened IRB, as the case may be, will review the report and determine whether the event meets the definition of an unanticipated problem involving risks to others and further action needs to be taken. Potential action may include:

• Modification to the protocol.

• Modification to the consent form or consent process.

• Past or current participant notification.

• More frequent continuing review.

• Monitoring of the research and/or the consent process.

• Placing the study on temporary hold to new enrollment and/or study procedures are discontinued.

• Suspension or involuntary termination of the study (see IRB Operations Manual for policies).

6. The Principal Investigator will be notified in writing of the review and whether any modifications or actions are required. A copy of the notification is sent to the Department Chief.

**Attachments:** Algorithm for reporting to the IRB of Adverse Events and Unanticipated Problems

**This policy has been reviewed and approved electronically by:**

| **Approver** | **Title** | **Initials** | **Date** |
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| J. Glover Taylor | Sr. Director, Sponsored Research | JGT | 07/21/2020 |
| Lior Givon, MD | Chair, Institutional Review Board | LG | 07/23/2020 |
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