REPORTING OF UNANTICIPATED PROBLEMS, SUSPENSIONS AND TERMINATIONS TO THE APPROPRIATE INSTITUTIONAL OFFICIALS, DEPARTMENTS AND AGENCIES

DESCRIPTION

The Institutional Review Board (IRB) is required by federal state and local laws and regulations, institutional policies, and IRB procedures to communicate certain actions to entities that may have an interest in the status of the research being conducted. The purpose of this policy is to ensure prompt reporting to appropriate institutional officials, funding sources, agency heads, and regulatory agencies.

RESPONSIBILITY

The IRB Chair (or designee) is responsible for ensuring appropriate discussion and corrective and preventative actions are taken regarding unanticipated problems involving risks of harm to participants or others, unexpected adverse event assessments, and investigator serious or continuing non-compliance. The Director of UC’s Office for Research Integrity (UCORI) and the Human Research Protection Program (HRPP) Director are responsible for compliant reporting to internal officials and external regulatory bodies.

DEFINITIONS

Termination: An action initiated by the IRB to permanently stop research procedures.

Suspension: An action initiated by the IRB to temporarily stop research procedures pending future action.

Serious: An event is “serious” if it results in death, a threat to life, hospitalization or prolongation of hospitalization, persistent or clinical significant incapacity, substantial disruption of the ability to conduct normal life functions, or a congenital anomaly or birth defect.

Related: The adverse event is definitely or possibly caused by any drug given to a subject as part of the study, a device used in the study, or a procedure that is carried out as part of the study. It is related when, in the opinion of the investigator or study sponsor, it was more likely than not to be caused by the research procedures.

Unexpected Adverse Event: The adverse event is not an anticipated event for the study drug, device, or procedure and is not explained in the Informed Consent Statement that the study
subject signed.

An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, and informed consent document, or the Investigator Brochure; and (b) the characteristics of the subject population being studied; and

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

The following problems/events represent examples of unanticipated problems involving risks to participants or others. This list is not exhaustive.

- Information that indicates a change to the risks of potential benefits of the research, in terms of severity or frequency. For example:
  - An interim analysis indicates that participants have a lower rate of response to treatment than was initially expected.
  - Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected.
  - A paper is published from another study that shows that an arm of the research study is of no therapeutic value.

- Any adverse event that represents a serious unexpected problem that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome).

- Any adverse event that would cause the sponsor to modify the investigator’s brochure, protocol, or informed consent to assure the protection of human subjects.

- A change in FDA labeling or FDA withdrawal from marketing for safety concerns of a drug, device, or biologic used in a research protocol.

- Change to the protocol taken without prior IRB review to eliminate the apparent immediate hazard to a research participant.

For VAMC Research

For research associated with a Veterans Affairs Medical Center (VAMC) an administrative hold is a voluntary interruption of research enrollments and ongoing research activities by an appropriate VAMC facility official, researcher, or Sponsor (including the Office of Research
Development, ORD, when ORD is the sponsor). The term “administrative hold” does not apply to interruptions of VAMC research related to concerns regarding the safety, rights, or welfare of human research participants, research investigators, research staff, or others. An administrative hold must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by federal agencies, participants, or other research activities (or add the additional information to the UC definition so that it includes both UC and VA stipulations). The terms “suspension” and “termination” apply to interruptions related to concerns regarding the safety, rights, or welfare of human participants, researchers, research staff, or others. Suspensions and terminations do not include: 1) Interruptions in research resulting solely from the expiration of a protocol approval period and 2) Administrative holds or other actions initiated voluntarily by a VA facility official, researcher, or sponsor for reasons other than those described in preceding items.

**PROCESS**

It is the responsibility of the IRB to assure reporting occurs according to the federal regulations, institutional policies, and IRB procedures.

After an unanticipated problem has been investigated, it is the responsibility of the IRB to determine whether an administrative hold, suspension, or termination of an approved study is necessary. The IRB may also impose a directed audit or any other action deemed appropriate for the circumstances. Whatever the outcome, the Director of UCORI shall be fully informed of all actions taken and the final outcome of any investigation, as appropriate. The responsibility for the implementation and coordination of these activities lies with the Director of UCORI or designee. The HRPP Director or designee drafts a report which includes a description of the problem, allegation of non-compliance or complaint and submits it to the IRB Chair for urgent action, when required due to severity of the problem, and for presentation at a convened IRB meeting. After the IRB approves the report and the action taken, the Director of UCORI communicates the report to relevant specific institutional officials (e.g., the Vice President for Research; the Institutional Official; the department head; director of the IRB office), OHRP (for research funded by DHHS), other federal agencies when research is subject to those agencies, to the FDA for FDA-regulated research activities, and to the VAMC Institutional Official with a copy to the Research Compliance Officer (RCO, for VAMC research), the Associate Chief of Staff (ACOS) for Research, the Research and Development Committee, and may include other relevant research review committees.

The University of Cincinnati reports to the VAMC Privacy Officer any unauthorized use, loss, or disclosure of individually identifiable VAMC patient information of which it becomes aware.
The University also reports to the Cincinnati VAMC Information Security Officer any violations of VAMC information security requirements of which it becomes aware.

For VAMC studies, unauthorized use, loss or disclosure of individually identifiable patient information or portable media must be promptly reported to the employee’s supervisor, VAMC police, VAMC Privacy Officer and RCO.

The IRB can suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to participants. The decision to suspend or terminate the approval of an existing human research study or the determination that the conduct of an investigator constitutes serious or continuous non-compliance or is in direct violation of requirements or determinations made by the IRB is ultimately the responsibility of the IRB.

Recommendations regarding corrective action are drafted by the IRB, reviewed by Legal Counsel, approved by the UCORI Director, and signed by the Institutional Official. The Director will then notify the Vice President for Research, the Investigator’s department head, and the dean of the investigator’s school. When applicable, notification will also be forwarded to the Investigational Drug Service/Hospital Pharmacy, the Office of Sponsored Research Services, the Office of Sponsored Programs Accounting, the faculty advisor, and the appropriate institutional officials at the external sites where the university serves as the IRB of record. Regulatory authorities and sponsors will be notified by the Director of UCORI.

OUTCOMES

a) Compliance: The IRB may determine that the research study under review is in compliance with federal, state and local laws and regulations, institutional policies and IRB procedures, and that no further action is required.

b) Compliance with enhancement: The IRB may determine that the research study under review is substantially in compliance with federal, state, and local laws and regulations, institutional policies and IRB procedures, but may make specific recommendations to improve or enhance the study’s human subjects protections, require additional education, or impose additional oversight of the research.

c) Non-compliance of a non-serious/non-continuing nature: The IRB may determine that the research study under review is not in compliance with federal, state, and local laws and regulations, institutional policies or IRB procedures or the investigator’s response is not adequate to satisfy the committee’s concerns. However, if the incident appears to be isolated, and in essence, is a miscommunication, misunderstanding, or lack of education,
the committee may impose restrictions, require additional subjects protections, additional education, impose additional oversight of the research, or any combination of the above.

d) Non-compliance of a potential serious/continuing nature: In keeping with HRPP Policy VII.03: Non-Compliance in Human Subjects Research and HRPP Procedure 330 Procedures for Investigating Allegations of Non-Compliance the IRB may determine that the Investigator’s failures to comply with federal, state, and local laws and regulations, institutional policies, or HRPP procedures pose such significant risk to participants in the research that the committee may suspend or terminate its approval of the study. A written notice of suspension and the criteria for suspension must be sent to the investigator for each study suspended. Issues of non-compliance must be reported in writing to the Director of UCORI. All investigations/audits for non-compliance are to be reviewed by the assigned IRB Chair and the Director of UCORI.

This reporting will take place within 30 days of the completion of an investigation and/or determination.

Applicable Regulations, Document(s):
21 CFR 56.108(b)
45 CFR 46.103(b)(5)
38 CFR 16.103(b)(5)(1)(i)
21 CFR 312.32
21 CFR 812.60-66: 812.150
HRPP Policy VII.03 Investigating Allegations of Non-Compliance in Human Subjects Research
HRPP Procedure 320 Review of Reportable Events
HRPP Procedure 330 Procedures for Investigating Allegations of Non-Compliance
Veteran’s Health Administration Handbook 1200.5
Veteran’s Health Administration 1605.1
Veteran’s Administration Directive Handbook 6500

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<td>J. Gerlach</td>
<td>Update University reporting responsibilities to the VAMC Institutional Official and Office of Research Development</td>
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Reporting responsibilities to VAMC Institutional Officials and timeframe for reporting loss of PHI to VA officials.

Date Adopted: March 2015  
Signature: ________________  
Signed copy on file: __________________________