REPORTING ATLANTA VAMC PROTOCOL DEVIATIONS/PROTOCOL NONCOMPLIANCE*

*This SOP does not apply to studies using the Central IRB or sponsored by CSP.

I. DEFINITIONS

**Corrective and Preventive Action (CAPA) Plan:** a plan developed by an investigator, with or without the assistance and guidance of the IRB, following an audit into an instance of noncompliance or other problems in the conduct of human subjects research. The CAPA must include measures designed to correct the immediate problem and prevent its recurrence or the recurrence of a similar type of problem. CAPA plans are reviewed and may be modified by the IRB before being approved. Investigators are responsible for implementing CAPAs in a timely manner.

**Continuing Noncompliance:** a persistent failure to adhere to the laws, regulations, or policies governing human research.

**Minor Protocol Deviation:** A deviation from a Research protocol that was approved by the Emory IRB and VA R&D Committee that does not (a) adversely affect the rights, welfare or safety of subjects; (b) adversely affect the integrity of research data; (c) adversely affect the subjects’ willingness to continue participation in the research; or (d) was not undertaken to prevent immediate hazard to a human subject.

**Minor Noncompliance:** Failure by the research study team to follow applicable laws, regulations and/or Emory IRB/VA policies and procedures that does not (a) adversely affect the rights, welfare or safety of subjects; (b) adversely affect the integrity of research data; (c) adversely affect the subjects’ willingness to continue participation in the research; or (d) was not undertaken to prevent immediate hazard to a human subject.

**Noncompliance:** Failure by the research study team to follow applicable laws, regulations and/or Emory IRB/VA policies and procedures that may: (a) adversely affect the rights, welfare or safety of subjects; (b) adversely affect the integrity of research data; (c) adversely affect the subjects’ willingness to continue participation in the research; or (d) not undertaken to prevent immediate hazard to a human subject.

**Protocol Deviation:** A deviation from a Research protocol that was approved by the Emory IRB and VA R&D Committee that may: (a) adversely affect the rights, welfare or safety of subjects; (b) adversely affect the integrity of research data; (c) adversely affect the subjects’ willingness to continue participation in the research; or (d) was undertaken to prevent immediate hazard to a human subject.

**Serious Noncompliance:** a failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as: (1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or (2) Substantively compromising the
effectiveness of a facility’s human research protection or human research oversight programs.

II. POLICY

The two most common types of reviews of research records that take place at the Atlanta are study team self audits and Atlanta VAMC Research Compliance Office (RCO) regularly scheduled audits (annual Informed Consent audit and triennial Regulatory audit).

The type of review (self audit vs. RCO audit) during which a deviation or compliance issue as well as the type of deviation or compliance issue identified will determine what type of reporting will occur.

A. Minor Protocol Deviation/Protocol Noncompliance

A Minor Protocol Deviation/Protocol Noncompliance does not require reporting to the Emory IRB for review unless:

(1) Reporting is required by the research protocol

(2) Reporting is required by the Sponsor or by the protocol or agreement governing the conduct of the research

During a study team self-audit, the PI shall review any instance of a deviation from a research protocol that has not been approved in advance by the Emory IRB or noncompliance with a research protocol to determine if the protocol deviation/protocol noncompliance meets any of the following criteria:

(a) Adversely affects the rights, welfare or safety of subjects.

(b) Adversely affects the integrity of the research data.

(c) Adversely affects the subject’s willingness to continue participation in the research.

(d) Concerns study documentation associated with an FDA-regulated study.

(e) Was a protocol deviation undertaken to prevent immediate hazard to a human subject.

If the PI determines that none of the aforementioned criteria listed under (a) – (e) are met, then the PI may consider the protocol deviation/protocol noncompliance to be Minor Protocol Deviation/Protocol Noncompliance and reporting of the matter to the Emory IRB is not required, unless mandated by Sponsor, protocol or contract. The PI and study team should correct the issue as allowable and document the issue and any corrections in the regulatory binder’s Minor Protocol Deviation/Protocol Noncompliance log sheet. The log sheet will also capture the PI’s review of the protocol deviation/protocol noncompliance and reasons for the determination of a Minor Protocol Deviation/Protocol noncompliance.
Minor Protocol Deviations/Protocol Noncompliance noted during an RCO audit will be discussed with the PI and study team. The PI and study team should correct the issue as allowable and document the issue and any corrections in the regulatory binder’s Minor Protocol Deviation/Protocol Noncompliance log sheet. The log sheet will also capture the review of the protocol deviation/protocol noncompliance and reasons for the determination of Minor Protocol Deviation/Protocol Non-Compliance.

B. Protocol Deviation/Protocol Noncompliance

Protocol Deviation/Protocol Noncompliance requires reporting to the Emory IRB for review. During a study team self-audit, the PI shall review any instance of a deviation from a research protocol that has not been approved in advance by the Emory IRB or noncompliance with a research protocol to determine if the protocol deviation/protocol noncompliance meets any of the following criteria:

(a) Adversely affects the rights, welfare or safety of subjects.*

(b) Adversely affects the integrity of the research data.

(c) Adversely affects the subject’s willingness to continue participation in the research.

(d) Concerns study documentation associated with an FDA-regulated study.

(e) Was a protocol deviation undertaken to prevent immediate hazard to a human subject.

*If the rights, welfare or safety of research subjects is affected, the VA Reportable Event Form should be completed (rather than the protocol deviation/violation section of eIRB) for the issue to be evaluated as a potential Unanticipated Problem. Please refer to the policy for Reportable Event Reporting for VA for instructions on the AREF website.

If the PI determines that one or more of the aforementioned criteria listed under (a) – (e) are met, then the PI must consider the issue to be a protocol deviation/protocol noncompliance and report the matter to the Emory IRB within 10 days.

The PI and study team should self-report the issue in eIRB under the Reportable Events tab. The type of event would be a Protocol Deviation/Violation.

Deviations/Protocol Noncompliance noted during an RCO audit will be discussed with the PI and study team. The PI and study team should self-report the issue in eIRB under the Reportable Events tab (if necessary note that VA Research Compliance Office is requires reporting). The type of event would be a Protocol Deviation/Violation.

Contents of Protocol Noncompliance Report: The PI’s report should specify: (a) protocol requirement and/or the VA policy or procedure or law or regulatory requirement that was not followed; (b) description of manner in which actions taken deviated from or failed to comply with the requirement including date and time of event; (c) effect of Non-Compliance, including any effect on Human Subjects; (d) reason for deviation/failure; and (e) any action that will be taken in terms of modifying or amending Research
protocol or process/procedure to be put in place to ensure that Noncompliance does not occur again.

The IRB Chair, Director, or qualified IRB staff (analyst, Team Lead) shall perform an initial review of all reports received.

C. **Apparent Serious or Continuing Noncompliance Found Outside of Human Research Audit**

All reports or allegations of noncompliance will be investigated, and if confirmed, appropriate corrective actions will be taken. Corrective actions will be appropriate to the nature and the degree of non-compliance.

A Research Compliance Officer or Auditor identifying apparent serious or continuing noncompliance (as defined in examples provided in VHA Handbook 1058.01) during an informed consent or regulatory audit must perform an investigation and prepare a written report of the noncompliance to the IRB within 5 business days of discovery.

The IRB Compliance Oversight Review Team (CoRe) will make a preliminary determination of whether the issue is noncompliance, serious or continuing. If the issue is determined by CoRe to be noncompliance, that is potentially serious and/or continuing noncompliance, the issue will be referred further to IRB Committee Q convened meeting for final determination.

Apparent serious or continuing noncompliance found during a human regulatory audit that is determined to be neither serious or continuing by the CoRe Team will be provided a CAPA plan (with a timeline) which is proposed by the RCO and approved by the CoRe Team. The CoRe Team determination and CAPA plan will be presented to the R&D Committee. The RCO will report the noncompliance to ORO as a follow-up report to the initial report. Additional reporting may be required to outside entities.

The IRB Committee Q, in a convened meeting, will determine if the noncompliance is serious noncompliance and/or continuing noncompliance.

A CAPA will be provided by IRB Committee Q in the convened meeting with a timeline for completion. If IRB Committee Q determines that serious and/or continuing noncompliance occurred, then the IRB Chair or designee must report this determination to the Facility Director, ACOS-R and R&D Committee within 5 business days. The Facility Director must report to ORO RO within 5 business days after notification (or if previously reported, provide a follow-up. Additional reporting to outside entities may be required, such as OHRP.

In instances of serious and/or continuing noncompliance as determined by the IRB, the Noncompliance Review Committee (NCRC), which is a subcommittee of the R&D Committee, will meet to review the case and either accept the IRB Committee Q’s CAPA or suggest additional actions to the R&D Committee. Consideration will be given to the nature of the deficiency or issue, its impact on the safety of the human subjects, and the investigator’s compliance history.
The RCO will present the final CAPA plan (after NCRC input) to the R&D Committee. The R&D Committee will review and approve the final CAPA plan.

The RCO will follow-up on all elements of the CAPA to ensure all have been completed. Follow-up reports will be provided to ORO as requested.

A final report will be provided to R&D Committee and ORO when all elements of the CAPA have been completed.

D. **Apparent Serious or Continuing Noncompliance Found During a Human Research Audit**

All reports or allegations of noncompliance will be investigated, and if confirmed, appropriate corrective actions will be taken. Corrective actions will be appropriate to the nature and the degree of non-compliance.

An RCO/RCA identifying apparent serious or continuing noncompliance (as defined in examples provided in VHA Handbook 1058.01) during an informed consent or regulatory audit must perform an investigation and prepare a written report of the noncompliance to the Facility Director, the ACOS/R, the R&DC Chair and IRB within 5 business days of discovery. The Facility Director reports apparent serious or continuing noncompliance within 5 business days after notification to the ORO Regional Office, ORD, and VISN leadership. The apparent serious or continuing noncompliance will be reported in writing (on the agenda) for the next RD&C meeting.

The IRB Compliance Oversight Review Team (CoRe) will make a preliminary determination of whether the issue is noncompliance, serious or continuing. If the issue is determined by CoRe to be noncompliance, that is potentially serious and/or continuing noncompliance, the issue will be referred further to IRB Committee Q convened meeting for final determination.

Apparent serious or continuing noncompliance found during a human regulatory audit that is determined to be neither serious or continuing by the CoRe Team will be provided a CAPA plan (with a timeline) which is proposed by the RCO and approved by the CoRe Team. The CoRe Team determination and CAPA plan will be presented to the R&D Committee. The RCO will report the noncompliance to ORO as a follow-up report to the initial report. Additional reporting may be required to outside entities.

The IRB Committee Q, in a convened meeting, will determine if the noncompliance is serious noncompliance and/or continuing noncompliance.

If no serious or continuing noncompliance occurred, then a final report to the R&D Committee and follow-up to ORO to is required. A CAPA will be provided by IRB Committee Q in the convened meeting with a timeline for completion. The RCO will provide follow-up report to ORO and any other relevant entities as required.

If the RB Committee Q determines that serious and/or continuing noncompliance occurred, then the IRB Chair or designee must report this determination to the Facility
Director, ACOS-R and R&D Committee within 5 business days. The Facility Director must report to ORO RO within 5 business days after notification (or if previously reported, provide a follow-up. Additional reporting to outside entities may be required, such as OHRP.

In instances of serious and/or continuing noncompliance as determined by the IRB, the Noncompliance Review Committee (NCRC), which is a subcommittee of the R&D Committee, will meet to review the case and either accept the IRB Committee Q’s CAPA or suggest additional actions to the R&D Committee. Consideration will be given to the nature of the deficiency or issue, its impact on the safety of the human subjects, and the investigator’s compliance history.

The RCO will present the final CAPA plan (after NCRC input) to the R&D Committee. The R&D Committee will review and approve the final CAPA plan.

The RCO will follow-up on all elements of the CAPA to ensure all have been completed. Follow-up reports will be provided to ORO as requested.

A final report will be provided to R&D Committee and ORO when all elements of the CAPA have been completed.