REPORTABLE EVENTS POLICY

I. PURPOSE

To provide guidance to George Washington University (GWU), Medical Faculty Associates (MFA) and GWU Hospital faculty, staff, and students regarding the reporting of certain events related to human subject research. Pursuant to federal regulations and this GWU IRB policy, any unanticipated problems involving risks to subjects or others, any serious or continuing noncompliance with 45 CFR Part 46, 21 CFR Part 56 (as applicable) and conditions of IRB approval, and any suspension or termination of IRB approval shall be reported to the following individuals/organizations:

a. GWU Committee on Human Research, Institutional Review Board (GWU IRB);

b. Appropriate GWU officials (such officials will vary depending on the reportable event, e.g., Dean, department chair, etc.);

c. Relevant federal department or agency heads for federally funded research or the sponsor for non-federally funded research; and/or the FDA for research studies involving drugs, devices, biological agents or FDA-regulated diagnostic products;

d. Non-federal study sponsors; and

e. The Office of Human Research Protections (OHRP), via the GWU Office of Health Research, Compliance, and Technology Transfer (OHRCTT).

This reporting responsibility extends to principal investigators (PIs) as well as any GWU, MFA and/or GWU Hospital faculty, staff, or student who becomes aware of the occurrence of a reportable event associated with a human subject study. Such faculty, staff, or students need not be associated with the human subject study in which the reportable event occurred in order to make such a report. The reporting requirements outlined below are mandatory for PIs that become aware of the occurrence of a reportable event associated with his/her study. The reporting requirements outlined below are voluntary for all other GWU, MFA or GWU Hospital faculty, staff, or students, i.e., individuals not associated with a study in which a reportable event has occurred.

As a general matter, all events that must be reported to the NIH, FDA, or other Federal agencies must also be reported to the GWU IRB (in accordance with this policy) and the study sponsor (in accordance with the study specific protocol).

II. DEFINITIONS

Adverse Event means any undesirable experience concerning the health of a participant occurring during human subject research, whether or not it is considered related to the study.
intervention. **Undesirable events/activities that are existent at baseline i.e., activities occurring prior to study enrollment, are not generally considered adverse events; however, undesirable events associated with such baseline activities are generally considered adverse events.**

**Disability** means a substantial disruption of a person’s ability to conduct normal life functions.

**Expected Adverse Event** means any adverse event that occurs with the same frequency or severity as expected or described in the investigator brochure, package inserts, protocol and/or informed consent form.

**Protocol Deviation** refers to a deviation from the IRB approved investigational plan.

**Relationship to Study Intervention** includes the following:

- **definite** – adverse event is clearly related to the intervention;
- **probable** – adverse event is likely related to the intervention;
- **possible** – adverse event may be related to the intervention; and
- **unrelated** – adverse event is clearly not related to the intervention.

**Serious Adverse Event (SAE)** means any adverse event that results in death, a life-threatening adverse drug experience, **inpatient** hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

**Unanticipated adverse device effect** means 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 serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

**Unexpected Adverse Event** means any adverse event that occurs with more frequency or greater severity than expected or described in the investigator brochure, package inserts, protocol and/or informed consent form.

**III. REPORTABLE EVENTS**

What follows is a list of events that are reportable to the GWU IRB as well as the prompt-reporting timeframe associated with each reportable event. The term prompt reporting is not defined by regulation, thus different timeframes have been established depending on the degree of severity and probability of recurrence of each reportable event. If submitting a report as a PI, the timeframes outlined below must be met. If submitting a report in any other capacity (e.g., voluntarily reporting as a GWU, MFA or GWU Hospital faculty, staff, or student not associated with a study in which a reportable event has occurred) the timeframes outlined below do not need to be met. However, please keep in mind that the sooner a report is submitted, the sooner it can be investigated.
The timeframes associated with reporting events to non-federally funded sponsors must occur in accordance with the study specific protocol and/or GWU IRB required timeframes.

A. Unanticipated Problems Involving Risks to Subjects or Others

The GWU IRB has interpreted unanticipated problems involving risks to subjects or others to include: certain serious adverse events (SAEs), unexpected adverse device effects, unexpected adverse events, failure to obtain informed consent/research subject authorization prior to use of an intervention in a study, complications & complaints, certain protocol deviations, and investigational device recalls or destructions. If unanticipated problems are encountered in the course of a study, or if new information becomes available that could change the perception of a favorable risk vs. benefit ratio, the PI is responsible for informing the GWU IRB so that the IRB can review the information to determine if the study should be continued as approved, modified, or discontinued.

1. Serious Adverse Events

As a general matter, any SAE that must be reported to the NIH, FDA, or other Federal agencies must also be reported to the GWU IRB. Such SAEs include all SAEs involving GWU enrolled subjects, certain SAEs involving non-GWU enrolled subjects, all deaths, and Data Safety Monitoring Board (DSMB) Reports, when applicable. If an SAE occurs and the SAE is expected as natural progression of disease, the GWU IRB will simply acknowledge receipt of the SAE, but take no action on the SAE report unless otherwise requested/indicated.

a. SAEs Involving GWU Subjects. All SAEs involving GWU subjects (i.e., subjects enrolled into a study with a GWU Informed Consent Form (ICF)) must be reported to the GWU IRB as soon as possible, but no later than 48 hours after the PI becomes aware of the event, regardless of whether the SAE was study related. SAEs that occur to subjects enrolled with a GWU ICF are considered top priority for review by the GWU IRB regardless of whether the SAE was expected or unexpected. In order to report such an event involving a GWU subject, the PI must complete a SAE Notification Form for GWU Subjects. This form is available at http://www.gwumc.edu/research/forms.htm. Please keep in mind that SAEs involving GWU subjects may require protocol and/or ICF modifications; therefore a proposed modified protocol and/or ICF should accompany the SAE Notification Form when deemed necessary by the investigator.

b. SAEs Involving Non-GWU Subjects. SAEs at other sites (i.e., involving non-GWU enrolled subjects) that are both unexpected and definitely or probably study related must be reported to the GWU IRB on a monthly basis following notification of the event from the sponsor (or other entity or organization). Such SAEs shall be reported via the IND Safety Report Notification Form, accompanied by the SAE Table if deemed necessary. Both of these forms are available at http://www.gwumc.edu/research/forms.htm. Please keep in mind that SAEs involving non-GWU subjects may require ICF/protocol modifications; therefore a proposed modified ICF/protocol should accompany the IND Safety Report Notification Form, when applicable. If a PI is involved with a study in which the sponsor requires all
SAEs to be reported to the GWU IRB, i.e., regardless of whether the SAEs were study-related or expected, the PI should report such SAEs via the IND Safety Report Notification Form, accompanied by the SAE Table.

c. **Deaths of GWU and non-GWU Subjects.** All deaths of subjects, whether enrolled into a study with a GWU ICF or another institution’s ICF, need to be reported to the GWU IRB as soon as possible, but no later than 48 hours after the PI becomes aware of the death, regardless of whether the death was study-related or resulted from other causes (e.g., automobile accident). Such deaths must be reported on a SAE Notification Form for GWU Subjects or IND Safety Report Notification Form, as appropriate.

d. **Data Safety Monitoring Board (DSMB) Reports of Multi-Center.** For those studies utilizing a DSMB, the DSMB plays an essential role in protecting the safety of subjects by, among other things, periodically reviewing the developing outcome and safety data and memorializing such outcome and safety data findings in a periodic report. The GWU IRB tracks SAE information obtained from other multi-center studies via these DSMB reports. A PI involved with a study utilizing a DSMB shall draft a cover memorandum to attach to the DSMB report. Such a DSMB report must be submitted to the GWU IRB immediately upon receipt of the DSMB report. Please note, however, that such DSMB reporting does not replace the PI’s responsibility regarding reporting SAEs involving GWU enrolled subjects.

2. **Unexpected Adverse Device Effects Involving GWU Subjects**

All unexpected adverse device effects involving GWU subjects, regardless of study-relatedness, shall be reported to the GWU IRB as soon as possible, but no later than 10 working days after the investigator becomes aware of the effect. 21 CFR 812.150(a)(1). Such effects shall be reported via the SAE Notification Form for GWU Subjects.

3. **Unexpected Adverse Events Involving GWU Subjects**

All unexpected adverse events (AEs) involving GWU subjects (i.e., subjects enrolled into a study with a GWU ICF) must be reported to the GWU IRB on a monthly basis following awareness of the unexpected AE. In order to report such an event, the PI must complete a SAE Notification Form for GWU Subjects.

As a general matter, expected adverse events involving GWU subjects need not be reported to the GWU IRB as they are already described in the protocol, investigator brochure, and ICF.

4. **Failure to Obtain Informed Consent/Research Subject Authorization from GWU Subjects**

If an investigator uses a study intervention without first obtaining informed consent/research subject authorization from a GWU subject, the investigator must report such use to the GWU IRB within 5 working days after the use took place. Such reports shall be made via a memorandum explaining the circumstances that led to the un-consented use, the consequences
of the un-consented use, and any proposed corrective action plan to be initiated as a result of
the un-consented use.

5. **Complications & Complaints**

ICFs that are approved by the GWU IRB contain statements informing the subject of how to
voice a question, concern, or complaint about reporting serious adverse events/research related
injuries, study procedures, the informed consent process, and any other rights as a research
subject. The contact person listed for voicing questions, concerns, or complaints regarding
study related complaints is the PI and/or research coordinator. With the exception of SAEs, the
above-referenced complaints received by the PI and/or research coordinator must be reported
to the GWU IRB at the time of the study’s next continuing review via the Continuing Review
Data Collection & Project Termination Form.

The contact person listed for voicing questions, concerns, or complaints related to the informed
consent process or rights as a research subject is the GWU Assistant Vice President for Health
Research, Compliance and Technology Transfer (OHRCTT). Each question, concern, or
complaint received by OHRCTT is investigated. The outcome of the inquiry is shared with the
GWU IRB. The GWU IRB will investigate questions, concerns, and/or complaints, in
conjunction with OHRCTT Compliance staff, and will advise other GWU offices, as
appropriate.

6. **Protocol Deviations**

a. **Deviations from the investigational plan to protect the life or physical well being of a
subject in an emergency.**

   Such deviations must be reported to the GWU IRB as soon as possible, but in no event later
   than 5 working days after the emergency occurred. The PI shall report such a deviation via
   a memorandum explaining the circumstances that led to the deviation, the consequences of
   the deviation, and any proposed corrective action plan to be initiated as a result of the
deviation. 21CFR 812.150(a)(4).

b. **Deviations from the investigational plan that increase risks to subjects.**

   The GWU IRB recognizes that deviations from the IRB approved investigational plan that
increase risks to subjects may sometimes occur. When such a deviation occurs, the PI is
responsible for reporting the deviation to the GWU IRB within 10 working days of
becoming aware that the deviation occurred, explaining the circumstances that led to the
deviation, the consequences of the deviation, and any proposed corrective action plan to be
initiated as a result of the deviation.

7. **Investigational Device Recalls or Destructions Regardless of Significant/Non-significant
Risk Categorization**

   Such recalls or destructions shall be reported to the GWU IRB within 30 working days of the
recall or destruction. Such reporting applies to all studies. The report should be submitted
via a memorandum including an explanation regarding the circumstances necessitating such a recall/destruction.

B. **Serious or Continuing Noncompliance with Applicable Regulations or GWU IRB Approval Requirements or Determinations.**

This category includes reporting of any violations of GWU IRB approval stipulations, and/or OHRP/FDA requirements, including violations noted in audit findings conducted by non-GWU entities, e.g., sponsors, monitors, etc. A serious or continuous noncompliance example include failure to report certain events. Reports of this nature must be reported to the GWU IRB immediately upon becoming aware of such noncompliance. The violations must be reported via a memorandum including a summary of the noncompliance, the consequences of the noncompliance, and any proposed corrective action plan to be initiated as a result of the noncompliance.

C. **Suspension or Termination of Human Subject Research**

1. **GWU IRB Initiated Suspensions or Terminations**

The GWU Medical IRB may suspend or terminate previously approved research when such research is not being conducted in accordance with regulatory or GWU IRB requirements or when such research is associated with serious harm to human subjects. Such GWU IRB suspensions/terminations will be reported promptly to the principal investigator. The report will be in writing and will provide a detailed explanation of the reasons for the suspension or termination action. All protocols that are suspended or terminated by the GWU IRB are required to be reported to OHRP and, if applicable, FDA.

2. **Principal Investigator/Sponsor/Other IRB Initiated Suspensions or Terminations**

A PI, sponsor, or an IRB of another institutions associated with a multi-center study in which GWU is involved may suspend or terminate research for any number of reasons. Suspensions or terminations that are initiated by the PI or sponsor must be reported promptly to the GWU IRB via a completed GWU Continuing Review Data Collection and Project Termination Form. Suspensions or terminations that are initiated by another IRB associated with multi-center studies in which GWU is involved must be reported promptly to the GWU IRB via a memorandum explaining the circumstances leading to the suspension or termination. Promptly is defined as follows:

   a. As soon as possible, but within 48 hours of receipt of the suspension/termination notice if the suspension/termination is based on a change in the risk/benefit ratio of study participation (e.g., numerous SAEs, failure of the intervention, etc.)

   b. Within 10 days of receipt of the suspension/termination notice if the suspension/termination is for any other reasons (e.g., loss of funding, inability to meet accrual rates, etc.).

IV. **SCOPE OF REPORTING EVENTS POLICY**
The reporting responsibilities outlined above may be reported to the IRB at any time, e.g., while the study is ongoing or after it has been completed at GWU, with the exception of adverse events and serious adverse events. The reporting responsibility for such adverse events/serious adverse events is limited, that is it extends from the date of GWU IRB approval of a study to the date when all research related activities have been completed at GWU. Thus, a PI is not required to report adverse events/serious adverse events to the IRB subsequent to the completion of all research related activities at GWU, i.e., following study close out/termination, unless otherwise specifically required by a entity/institution involved in the study, e.g., IRB, sponsor, DSMB, federal agency, etc.

V. FAILURE TO ABIDE BY THIS REPORTABLE EVENTS POLICY

Following University policy(s), the GWU IRB may take action against/sanction any PI that become aware of a reportable event associated with his/her study, but fails to report such an event to the GWU IRB in accordance with this policy. Such GWU IRB actions/sanctions will vary depending on the severity of the violation. For instance, a minor violation of this policy may result in a GWU IRB educational outreach initiative with a particular research team. Alternatively, a major violation of this policy may result in a PI losing his/her research privileges. In all instances, the GWU IRB actions/sanctions will be in accordance with provisions of the Faculty Code or the Manual of Personnel Policies for the Use of Supervisory Staff, and OHRP policies and regulations.
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<td>SAEs Involving Non-GWU Subjects</td>
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<td>Suspensions or Terminations Initiated by PI/Sponsor/IRBs of Other Institutions</td>
<td>Suspensions or terminations initiated by PI, sponsor, or IRBs of other institutions associated with multicenter studies in which GWU is involved</td>
<td>ASAP, but NLT 48 hrs after PI becomes aware of suspension or termination if based on change in risk benefit ratio; W/in 10 working days if for other reason</td>
<td>For PI or Sponsor Initiated – CR Data Collection &amp; Project Termination Form; For Other IRB Initiated - Memo explaining the circumstances leading to the suspension or termination</td>
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