Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
Linked Policy: Clinical Research Operations & Compliance Policy	**Revised Date:** March 20, 2023

PURPOSE:

To establish the GW Medical Faculty Associates ("MFA") procedure outlines the responsibilities for research team members involved with reporting and providing updated information regarding reportable events associated with clinical research being conducted at MFA

SCOPE:

This SOP applies to all research team members responsible for reporting and providing updated information regarding AEs, SAEs, unanticipated adverse device effects and protocol deviations associated with clinical research being conducted at the MFA.

RESPONSIBILITY:

This SOP sets forth responsibilities for research team members involved with reporting and providing updated information regarding reportable events associated with clinical research being conducted at MFA. The Principal Investigator ("PI") retains this responsibility unless the PI has expressly delegated this duty to a research team member and the delegation is documented on a study specific *Delegation of Authority Log.*

PROCEDURES:

Reportable Events

A reportable event is an adverse event or incident that has the potential to be classified by the Institutional Review Board ("IRB") as an unanticipated problem posing risks to participants or others. An incident is determined to be reportable to the IRB when it is both:

1. **probably** or **definitely** related to participation in the research
2. unexpected in terms of nature, severity, or frequency

Identification and Assessment of Reportable Events

Assess the following to determine whether the event meets the definition of an AE, SAE and/or unanticipated Adverse Device Effect:

- Spontaneous reports by research subjects.
- Observations by clinical research staff.

Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
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- Reports to research staff by family or medical care providers.
- Possible events documented in the research subject's medical records, progress notes, etc; and Reports of a research subject's death within 4 weeks after stopping treatment or during the protocol-defined follow-up period, whichever is longer, whether considered treatment-related or not.

An AE is considered serious (SAE) if it:

- Results in death;
- Is life-threatening;
- Requires inpatient hospitalization or prolongs existing hospitalization;
- Results in persistent or significant disability/incapacity; or
- Is a congenital anomaly/birth defect.

An Adverse Device Effect is considered unanticipated if it:

- Has any serious adverse effect on health or safety or any life-threatening problem or death; and
- The effect/problem/death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application; or
- Any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Manage AE/SAE/Unanticipated Adverse Device Effect

1. Gather all available information pertaining to the event as follows:
   a. Examine subject to determine extent of disease or injury, when possible;
   b. Speak with subject and/or family members to obtain information regarding the event;
   c. If applicable, speak with staff member who received the phone call during which the event was first reported. This is to obtain any additional information that they are able to provide; and
   d. Request and make an effort to obtain all related medical and/or non-medical records and reports.
2. Manage the subject who experiences any adverse change (symptom, side effect) from their baseline or pretreatment condition, being sure that all appropriate measures are taken for subject safety and well-being.
3. If appropriate, institute the following to manage or resolve the adverse event:

Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
Linked Policy: Clinical Research Operations & Compliance Policy	**Revised Date:** March 20, 2023

a. Discontinue investigational product, comparator, or placebo;
b. Reduce or interrupt dosage of investigational product, comparator, or placebo (as per protocol);
c. Challenge research subject with investigational product, comparator, or placebo (as per protocol);
d. After consultation (if possible) with Sponsor, break the blind in order to meet the immediate medical care of a subject.

4. Record the details of the adverse event in the Source Document and complete the appropriate CRFs. This can be documented on the Adverse Event log in subject binder or Adverse Event log in the patients record in Epic (see appendix A below)
5. File all relevant documentation in the study regulatory binder and/or individual subject research file.
6. Follow subjects who experience AE/SAE/Unanticipated Adverse Device Effect until event is resolved, stabilized or subject is lost to follow-up.

Reporting AE/SAE/Unanticipated Adverse Device Effect Events:

1. Report AE/SAE/Unanticipated Adverse Device Effect event to Principle Investigator
   a. If the PI is not already involved in the adverse event reporting process, immediately inform the PI of the event. If the PI is not immediately available, proceed with the reporting process, as outlined below, and notify the PI as soon as possible/available.
   b. The PI determines the relationship of the event to study intervention.
   c. Involve the PI in the evaluating and reporting processes.
   d. PI must sign off on the paper log and AE/SAE/Unanticipated Adverse Device Effect entry in listed in Epic

2. Report to the Sponsor
   a. SAE Reporting to Sponsor: Report any SAE to the Sponsor within 24 hours of its occurrence or within 24 hours of learning of the event if no other timeline has been established by the protocol.
      i. SAE Sponsor Report should be completed per the sponsor's reporting instructions. At a minimum the information provided in the initial notification should include:
         - The protocol name and number;
         - Subject's identification data (initials and/or study number);
         - The nature of the SAE;

Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
Linked Policy: Clinical Research Operations & Compliance Policy	**Revised Date:** March 20, 2023

- The date and time the SAE occurred; and
- Investigator's evaluation of SAE and his opinion of the event relationship to study intervention.

ii. Provide Sponsor with all adverse event information available at the time of the initial report. Provide follow-up information according to Sponsor instructions, which may include copies of reports and/or Source Documentation related to the event, as the information becomes available.

b. Unanticipated Adverse Device Effect Reporting to Sponsor: Report unanticipated effects to the sponsor as soon as possible, but not later than 10 working days after the investigator first learns of the effect.

3. Reporting to IRB of SAEs Associated with MFA Enrolled Subjects
   a. Notify the appropriate IRB of any SAEs meeting reporting requirements as soon as possible, and within the time frame required by the IRB.

Chart Details of Event in Source Document and CRF

1. Promptly record the event in the appropriate Source Document, corresponding CRF, electronic record in Epic and other additional forms as required by the Sponsor.
2. Continue to gather pertinent information on the event from the subject and other institutions where subject was treated.
3. If additional assessments are indicated, capture assessments in Source Document and CRF and/or SAE report forms;
4. Report additional assessments to the Sponsor and the IRB, if required.
5. Chart final outcome of event in Source Document and CRF and/or SAE report forms.

Investigation New Drug (IND) Safety Reports

- Promptly review IND safety reports received from Sponsors and assess significance as it applies to MFA enrolled subjects.
- Promptly submit IND safety reports to the appropriate IRB per that IRB's Promptly Reportable Events Policy or when required by sponsor.
- File IND safety reports in the study specific regulatory binder.
- Implement any action requested by Sponsor.

Sponsor-Investigator who hold an IND are required to report to the FDA:

Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
Linked Policy: Clinical Research Operations & Compliance Policy	**Revised Date:** March 20, 2023

IND Application sponsors are required to notify the FDA in written safety report of:

- Any adverse experience associated with the use of the drug that is both serious and unexpected or
- Any findings from test in laboratory animals that suggest a significant risk for human subjects including reports of mutagenicity, teratogenicity and carcinogenicity.

Protocol Deviations

Protocol deviations must be documented and reported. Protocol deviations may result in a significant added risk to study subject and may occur when:

- A subject/investigator has failed to adhere to protocol requirements impacting on enrollment eligibility, safety, endpoint outcomes, test article handling/accountability; and/or
- There is non-adherence to SOP, GCPs, etc.

1. Protocol Deviation Documentation:
   Document deviations in subject Source Documents as follows:
   a. Reason for deviation; and
   b. All attempts to prevent or correct them.
   c. Document deviations on sponsor study-specific deviation form, if required.
2. Reporting Protocol Deviations to the appropriate IRB (GWIRB or WIRB):
   Report protocol deviations to the IRB in accordance with the IRB Promptly Reportable Events Policy of that IRB.

Reporting timelines:

- Unexpected serious suspected adverse reactions and observations from animal studies suggesting significant risk to human subjects must be reported to FDA as soon as possible but no later than within 15 calendar days following the sponsor's initial receipt of the information.
- Unexpected fatal or life-threatening suspected adverse reactions represent especially important safety information and must be reported to FDA as soon as possible but no later than 7 calendar days following the sponsor's initial receipt of the information.
- Any relevant additional information obtained by the sponsor that pertains to a previously submitted IND safety report must be submitted as a Follow-up IND Safety Report. Such report should be submitted without delay, as soon as the information is available but no later than 15 calendar days after the sponsor receives the information.

Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
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Definitions:

Adverse Device Effect - Any serious adverse effect on health or safety, 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 application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Adverse Events – Any untoward medical occurrence associated with the use of a drug or device in humans, whether or not if it is considered drug or device related. Adverse events may be mild, moderate, or severe, and may be caused by something other than the drug or therapy being given. The Principal Investigator is the only one who can assign the severity grade of an Adverse Event.
Serious Adverse Events – Any untoward medical occurrence that results in death, is life-threatening, which refers to an event in which the patient was at risk of death at the time of the event; requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Attachments

Sample Protocol Deviation Log
Sample AE Log
Sample Serious AE Log

REFERENCES:

21 CFR 312.53 Selecting investigators and monitors.
21 CFR 312.60 General responsibilities of investigators.
21 CFR 312.61 Control of the investigational drug
21 CFR 312.62 Investigator recordkeeping and record retention.
21 CFR 312.64 Investigator reports.
21 CFR 312.66 Assurance of IRB review.
21 CFR 312.68 Inspection of investigator's records and reports.
21 CFR 312.69 Handling of controlled substances.

Procedure Name: Reporting Events Procedure	**Number:** SOP 9 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
Linked Policy: Clinical Research Operations & Compliance Policy	**Revised Date:** March 20, 2023

21 CFR 812.7 Prohibition of promotion and other practices.
21 CFR 812.40 General responsibilities of sponsors.
21 CFR 812.42 FDA and IRB approval.
21 CFR 812.43 Selecting investigators and monitors.
21 CFR 812.46 Monitoring investigations.
21 CFR 812.100 General responsibilities of investigators.
21 CFR 812.110 Specific responsibilities of investigators.
21 CFR 812.140 Records.
21 CFR 812.145 Inspections.
21 CFR 812.150 Reports.
ICH E6 (R2) Integrated Addendum to International Council for Harmonization
(ICH) E6 (R1): Guideline for Good Clinical Practice E6 (R2)
GWU, OHR Investigator Guidance Documents and IRB policies/SOPs
Oct 2015 MFA Investigational Drug Service Policies and Procedures
WIRB Investigator Handbook A Guide for Researchers (pdf)
June 2017 GWU Clinical Research SOPs
SOP 03: Regulatory Binder and Study File Maintenance
SOP 06: Source Documentation
SOP 12: Subject Recruitment

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DEVIATION LOG

Protocol ID: _____ IRB Number: _____ PI: _____ Sponsor: _____

Subject ID	Date of Deviation	Date Identified	Deviation Description	Deviation Code [a]	Report to IRB? Yes/No (circle) **If Yes to 1 OR 2 OR 3 COMPLETE AND file Report Form to IRB w/in 5 days of awareness of event	Corrective Action Plan	PI Initial	PI Date
					Yes, date:_____ No			
					Yes, date:_____ No			
					Yes, date:_____ No			
					Yes, date:_____ No			
					Yes, date:_____ No			
					Yes, date:_____ No			

[a]**Deviation Codes: A** - Consent Procedures **B** - Inclusion/Exclusion Criteria **C** - Con Med/Therapy **D** - Lab Assessments/Procedures **E** - Study Procedures **F** -SAE Reporting/Unanticipated Problem **G**- Randomization **H** -Visit Schedule/Interval **I** -Efficacy Ratings **J**-Procedures/Study Drug Dosing **K**-Other- specify

IRB Reporting Requirements: **If Yes to 1 OR 2 OR 3 COMPLETE PROTOCOL DEVIATION REPORT AND Report Form to IRB

1. Intended to eliminate apparent immediate hazard to a research participant (such as changing the dose of a medication due to possible toxicity), **or**
2. Harmful, caused possible harm to participants or others, or places them at increased risk of harm includes physical, psychological, economic, or social harm, such as a breach of confidentiality), **or**
3. Possible serious or continued noncompliance (such as a deviation that has happened previously and is now being repeated).

(At close out of study) **PI Signature**: _____ Date: _____

Office of Clinical Research

ADVERSE EVENT LOG

Protocol ID: ____________________ IRB Number: __________________ PI: _______________________

Site/#: ____________________

Subject ID	Adverse Event Type Description	Onset Date (mm/dd/yy)	End Date (mm/dd/yy)	AE Intensity	Relationship to Study Drug	Expected	Action Taken with study drug	ConMed/CM# (if applicable)	SAE	Treatment	Outcome	Investigator Review
			☐ Ongoing	1 2 3 4 5	1 2 3 4	☐ Yes ☐ No	1 2 3 4		☐ Yes ☐ No (if Yes, report SAE)	1 2 3 4	1 2 3 4 5 6	Date: Signature:
			☐ Ongoing	1 2 3 4 5	1 2 3 4	☐ Yes ☐ No	1 2 3 4		☐ Yes ☐ No (if Yes, report SAE)	1 2 3 4	1 2 3 4 5 6	Date: Signature:
			☐ Ongoing	1 2 3 4 5	1 2 3 4	☐ Yes ☐ No	1 2 3 4		☐ Yes ☐ No (if Yes, report SAE)	1 2 3 4	1 2 3 4 5 6	Date: Signature:

AE Intensity
1= Mild
2= Moderate
3= Severe
4= Life threatening
5= Death

Relationship to Study Drug
1= Not Related
2= Unlikely Related
3= Possibly Related
4= Probably Related
5= Definitely Related

Action Taken
1= None
2= Dose Not Changed
3= Drug Interrupted
4= Drug Withdrawn

Treatment for Event
1= None
2= Medicine Taken
3= Non-drug Therapy
4= Other Medication Dose Modified

Outcome
1= Resolved
2= Resolved w/ Sequelae
3= Ongoing
4= Death
5= Ongoing at Death
6= Unknown

PI Signature at conclusion of study participation:

PI Signature:		Date:	

Office of Clinical Research

SERIOUS ADVERSE EVENT LOG

Study: _____ IRB #: _____ PI: _____ Sponsor: _____

#	Subject ID	SAE	Onset Date	Date Site First Aware of SAE	Date SAE reported to Sponsor/CRO	SAE Report	IRB Submission Date	Comments
						☐ Initial ☐ Follow-up		
						☐ Initial ☐ Follow-up		
						☐ Initial ☐ Follow-up		
						☐ Initial ☐ Follow-up		
						☐ Initial ☐ Follow-up		
						☐ Initial ☐ Follow-up		

PI Signature: _____ Date: _____