VA Northeast Ohio Healthcare System
Medical Research Service
Standard Operating Policy and Procedure (SOP)

Effective Date: June 2, 2022

SOP Title: Sponsor - Unanticipated Adverse Device Effect Reporting (UADE)

SOP Number: Human Researchers – HSP-027

SOP Version: .02

1. Purpose

To define procedures and responsibilities which are to be followed by the Sponsor and/or its designee regarding unanticipated adverse device effects.

2. Policy

Following these stated procedures and responsibilities is a requirement of research staff and Sponsor-designees conducting clinical studies involving human subjects under the authority of the Sponsor, VA Northeast Ohio Healthcare System.

3. Definition.

Sponsor and/or its designee must notify the reviewing IRB of any unanticipated adverse device effects occurring during an investigation as soon as possible but no later than 5 working days after the investigator and/or designated research staff member first learns of the effect (812.150(1)). The Office of the ACOS (Associate Chief of Staff) for Research will also be provided a copy of the report.

The Sponsor VA Northeast Ohio Healthcare System and/or its designee (the party responsible for conducting an evaluation of an unanticipated device effect, usually investigator(s) and/or the research nurses in conjunction with a regulatory affairs staff member) shall report the evaluation to FDA within 10 working days after the Sponsor first receives notice of the effect. On multi-site studies all reviewing IRB's and participating Investigators, will also be notified of the effect, if applicable. Thereafter, the Sponsor and/or its designee shall submit such additional reports concerning the effect as FDA requests (812.150(7)(b)(1)).

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 (in this case) device that relates to the rights, safety, or welfare of subjects.

A Sponsor and/or its designee shall immediately conduct an evaluation of any unanticipated adverse device effect. Should the Sponsor and/or its designee determine that an unanticipated adverse device effect presents an unreasonable risk to research subjects, the Sponsor may terminate all investigations or parts of investigations presenting that risk as soon as possible, but not later than 5 working days after making this determination and not later than 15 working days after the Sponsor first receives notice (812.46(b)).

ICH GCP Consolidated Guideline Part 4.11 Safety Reporting
As an aid in determining how and when to report the event, the categories below help define the severity, if the adverse event is associated with the protocol, and the outcome of the adverse event.

Associated with the device/protocol - there is a reasonable possibility that they have been caused by the device/protocol.

Disability - a substantial disruption of a person's ability to conduct normal life functions.

Life-threatening adverse experience - any adverse experience that places the patient or subject at immediate risk of death from the reaction as it occurred.

Serious adverse event - any adverse experience that results in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity or a congenital anomaly/birth defect.

Unanticipated adverse event - any adverse experience, the specificity or severity of which is not consistent with the current investigational plan or the risk information described in the general investigational plan or consent form.

4. Responsibility

Per this Sponsor SOP, the principal investigator, the regulatory affairs staff, and any research nurse(s), is/are responsible for determining that an unanticipated adverse device effect has occurred and for reporting it to the Sponsor, if applicable, as soon as possible, but not later than 10 working days after learning of the event. The Sponsor and/or its designee will assure that the principal investigator evaluates the effect, makes a reasonable risk determination, signs and dates appropriate checklists/reports summarizing the effect and the patient’s well-being, and reporting the results of the evaluation to the FDA, to all Investigators

and all reviewing IRBs, and under guidance from the named regulatory affairs staff member or research nurses.

5. Procedure

VA Northeast Ohio Healthcare System and/or its designee(s) are responsible for training all investigators on their responsibilities outlined under this SOP. As appropriate, the Sponsor will do likewise for new investigators as they are added to an existing site.
The Sponsor and/or its designee(s) requires Investigators to include in their reports the following:

- PI name / address / contact information (including telephone, fax and email).
- Subject ID (study specific) and birth date.
- Date of subject enrollment.
- Date of event/effect.
- Date of report.
- Relevant medical history.
- Description of event / effect and attach any supporting documentation. (Note: copies of medical records must have all subject identifiers redacted – except for initials, and have the study specific ID written on each attached page or item.
- Description of any concomitant / subsequent treatment or procedure and course of hospitalization (when known).
- Relevant clinical findings, tests performed and relevant laboratory data (if any is available).
- Outcome of the event / effect including disposition of the subject (i.e. death, discharged to long-term facility, discharged home, remains hospitalized at this time, etc.).
- Investigator's statement of seriousness
- Investigator's assessment of causation (definitely related, probably related, possibly related, not related).
- Date of report to the reviewing IRB (permitted to substitute copy of IRB report / notification).

The Sponsor will permit investigators to report initial data and supply additional items as they obtain records. Subsequent reports must be made as soon as possible but no later than 10 working days after the investigator learns of the effect or obtains follow-up information.

The Sponsor, VA Northeast Ohio Healthcare System and/or its designee, or the research staff member who initially receives a report of an unanticipated adverse device effect, will generate a contact report (telephone, email, or handwritten) for any unanticipated adverse device effect report received and distribute copies to any/all appropriate investigators and VA Northeast Ohio Healthcare System staff members. This list will be study- and Center/Department-specific but will likely include regulatory affairs staff, research nurses, investigators (PIs, co-

investigators, responsible investigators) at the lead site and at any affiliate sites on multi-site trials. This will be done within 10 days of initially reporting an unanticipated adverse device effect to the IRB.

The Sponsor, VA Northeast Ohio Healthcare System and/or its designee(s), which may include regulatory affairs or research nursing staff, will log in the reported effect into the subject's CRF, the regulatory files in support of creating a complete and compliant audit trail, and the investigators' password-protected databases or spreadsheets when one is used. The Sponsor, VA Northeast Ohio Healthcare System and/or its designee(s) which may include regulatory affairs or research nursing staff, will initiate a draft of the required report to FDA using whatever information is available at the time of learning of the effect. The Sponsor will obtain follow-up information for further reporting to FDA and authoritative IRB's as it is required and able to do so. Follow-up will be performed to the extent the research staff is able to do so or until the effect is resolved (which will also be reported). Patients lost to follow-up will be noted in the investigator's file.

VA Northeast Ohio Healthcare System and/or its designee, possibly alongside the principal investigator, the regulatory affairs staff, and any research nurse(s), will conduct an evaluation of the UADE immediately upon receipt of the initial report. The Sponsor, VA Northeast Ohio Healthcare System and/or its designee holds responsibility for writing a safety report detailing the event and reporting the results of the evaluation to FDA, all reviewing IRBs and all investigators (investigational sites if applicable) within 10 working days after the Sponsor first learns of the effect.

If the sponsor VA Northeast Ohio Healthcare System and/or its designee determines that unanticipated adverse effect resulting in a device study represents an unreasonable risk to subjects, all studies or parts of studies presenting that risk with the device(s) will be terminated as soon as possible for SR and NSR trials. Termination will occur no later than 5 working days after such a determination is made and not later than 15 days after the Sponsor first receives notice of the UADE. Individual patient safety will ultimately determine how this rule will be applied and any exception will be noted in the patient's CRF and reported to reviewing IRBs and the FDA at annual review. Termination will be communicated by phone, fax and in writing (receipt requested) to all investigators (investigative sites, if applicable), all reviewing IRBs and FDA. All phone logs, fax, associated fax or electronic confirmations and receipt requested notifications will be maintained in the study files. The monitor or Sponsor designee shall ensure all devices associated with such termination are packaged for return to the Sponsor (or manufacturer) within 5 days of the notice.

The Sponsor's designated personnel are responsible for assuring that reviewing IRBs have been informed in writing of the reported effect. A copy of the written notification and any acknowledgment / correspondence to and from IRBs relating to the report will be obtained and filed in the investigator and/or study files. The

Sponsor and/or its designee will be provided with these reports for documentation and inclusion in subsequent monitoring visits records.

The sponsor will ensure that all records associated with the unanticipated adverse device effect will be dated and maintained in the study regulatory files maintained on behalf of the principal investigator and Sponsor.

6. Reference

CFR - Code of Federal Regulations Title 21 (fda.gov)

IDE Reports | FDA

7. Rescission.

Sponsor – Unanticipated Device Effect Reporting HSP-027 dated January 1, 2011 was rescinded. Review date for this policy is June 1, 2025

8. Follow up Responsibility.

Investigator(s)/co-investigator(s) and, when delegated by the investigator(s) with permission of the Sponsor, also clinical research staff. Designated individuals who monitor sites and those named as responsible for performing data management and regulatory affairs by the Sponsor, VA Northeast Ohio Healthcare System.