CLINICAL TRIALS – ADVERSE EVENT REPORTING (AEs, SAEs, AESIs, & UAES)

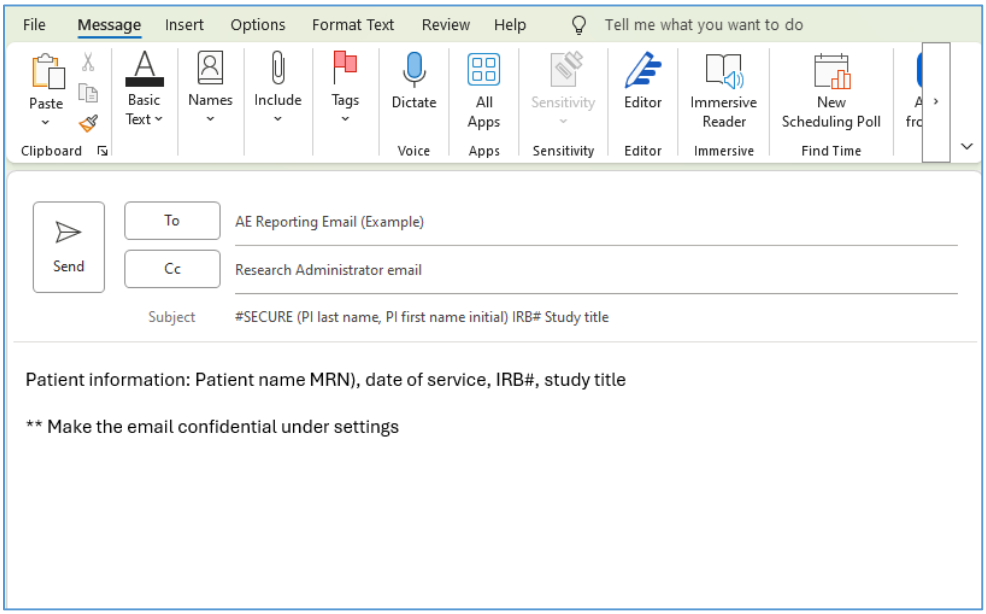
Revised August 22, 2025

OVERVIEW- ADVERSE EVENT REPORTING

- **Description:** Provides guidance regarding the procedures, processes, and responsibilities for identifying, assessing, recording, and reporting Adverse Events (AEs), Serious Adverse Events (SAEs), Adverse Events of Special Interests (AESIs). Reporting of adverse events is a critical part of the clinical research coordinator role. When and where to report adverse events, serious adverse events and/or adverse events of special interest will depend on whether the principal investigator (PI) or sponsor holds the Investigational New Drug (IND).
- **Timeline**: In general, any reportable events are due within 24 hours of the Adverse Event occurring, referring to the study protocol will give more of an insight to the study's specific AE notes.
    - **NOTE**: When an Adverse Event results in the passing of a patient, it must be submitted within 3 business days.
- **Definitions:**
    - Adverse Events and Unanticipated Events indicate a change in a subject's health status since baseline right before taking the study drug.
    - What is an **Adverse Event (AE)**?
        - An Adverse Event is considered any untoward medical occurrence associated with the use of a drug product in humans, whether or not it is considered related to the drug product. (21 CFR 312.32)
    - What is a **Serious Adverse Event (SAE)**?
        - An adverse event is considered "serious" if it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. (21 CFR 312.32)
    - What **are Unanticipated Adverse Events (UAE)**?
        - Unanticipated Adverse Events are any adverse events or suspected adverse events that is considered "unexpected" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigation plan or elsewhere in the current application, as amended. (21 CFR 312.32)
            - **NOTE**: These events are more common in phase I and II trials.
    - What is an **Adverse Event of Special Interest (AESI)**?
        - An Adverse Event of Special Interest is a pre-defined event in a clinical study or product development that a sponsor or investigator is specifically interested in monitoring and reporting. While this is not a commonly reported AE, it may be required depending on the sponsor.
            - An AESI is a pre-specified medically significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further special studies.
        - Adverse Events (AE) and Adverse Events of Special Interest (AESI) should be reported within 24-48 hours of the site learning about the event.

ACTION ITEMS

1. What is the Clinical Research Coordinator (CRC) role versus the Principal Investigator (PI) role in assessing and reporting any adverse events?
   a. Clinical Research Coordinators are responsible for immediately notifying the PI of the adverse event, collecting information, and submitting the information to the sponsor.
      - Additionally, the CRC should be familiar with the protocol requirements for reporting adverse events to the sponsor, ensuring that everything is documented properly and entered the necessary data capturing systems.
      - At UCLA, Clinical Research Coordinators are responsible for notifying:
        i. Regulatory Coordinator about adverse events that meet the requirement of being reportable to the IRB (AE Decision Tree)
        ii. Research Administrator when an SAE has been reported to ensure appropriate invoicing/billing follow through
        iii. Charge Reviewers can track the visit in CareConnect. They will need the patient's MRN and date of service to review which items in that visit should be charged to the study or insurance. This communication is vital in ensuring the correct billing occurs and that billing is within compliance.
           - (When sending emails containing patient sensitive information, be sure to place #SECURE in the subject line.)

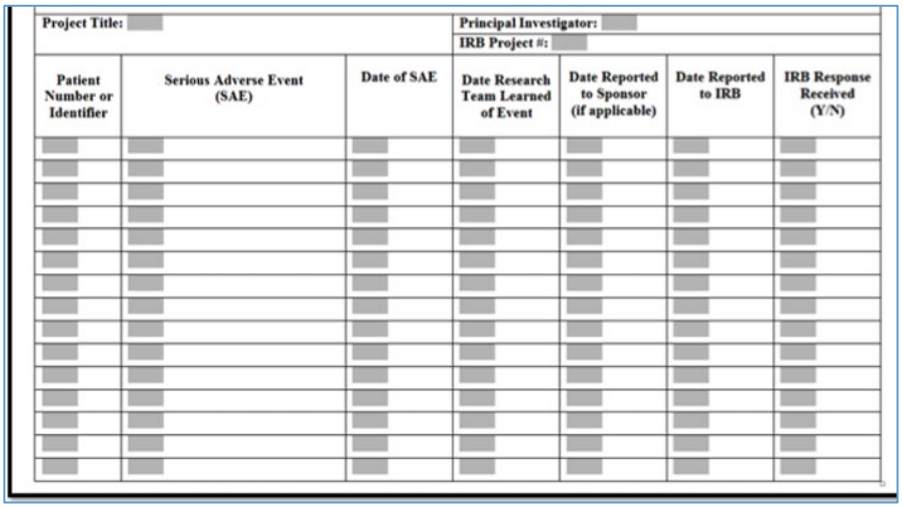


   b. Principal Investigators assume responsibility to ensure adverse events are reported to the sponsor and IRB. This includes assessing the relatedness, severity, expectedness, and seriousness of the adverse event.
      - In certain cases, CRCs may be responsible for reporting on behalf of the PI.
   c. Regulatory coordinators are responsible for submitting the adverse event to Bruin IRB/Central IRB.

2. How are AE/SAE/AESI/UAEs documented?
   a. It is important to follow the clinical trial protocol as to how these adverse events should be documented and reported.
   b. General guidance for documenting requires the following information when reporting adverse events:

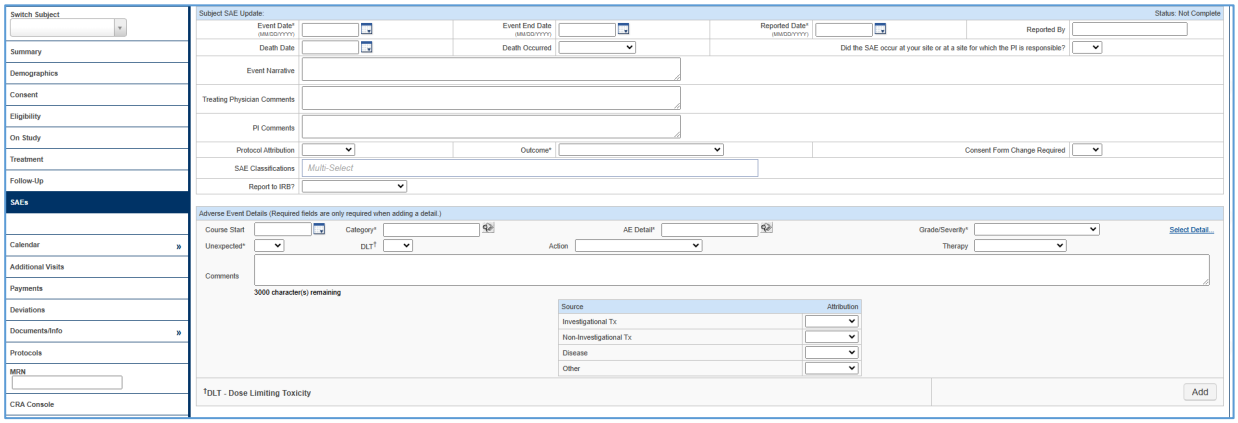
i. Description of the Event: what occurred? What is the medical term for the event?
   i. This information can be found in the medical record (doctor or nurses notes, lab results, etc.), verbally communicated by the patient or family member, directly observed, or reported in participant diaries/journals.
ii. Date of Occurrence & Date of Resolution: when did the patient notice the onset of symptoms? When did the symptoms subside?
iii. Severity: mild, moderate, severe, etc. (Refer to CTCAE guidelines)
iv. Relatedness/Causality: Is there a reasonable possibility that the event is related to the study drug or study device?
v. Expectedness: Has this event been observed or documented previously?
vi. Seriousness: did the event result in death, life-threatening, prolonged hospitalization, etc.?

It is important to keep a log of each participant's reported adverse events.



Project Title: Principal Investigator: IRB Project #:

Patient Number or Identifier	Serious Adverse Event (SAE)	Date of SAE	Date Research Team Learned of Event	Date Reported to Sponsor (if applicable)	Date Reported to IRB	IRB Response Received (Y/N)



c. At UCLA, documentation of AEs can also be entered into OnCore (PC Console > *Select Protocol* > Subject Console > *Select Subject* > SAEs)
   i. For SAEs and AESIs, the sponsor may require additional documentation via SAE or AESI forms that need to be completed within 24 hours and either emailed or faxed over to the sponsor/medical monitor. **(See protocol for more information)**

3. When should an AE be submitted to IRB vs. when an SAE should be submitted to IRB?
    a. While CRCs are responsible for collecting all data regarding an adverse event, the Regulatory Coordinators are the ones required to submit the incidents to **BruinIRB**. (Find the AE log here)

CONTACT/RESOURCES

- UCLA DOM CTP: DOMCTP@mednet.ucla.edu
- Link for information on PI AE Submissions Post Approval Reporting | UCLA Office of the Human Research Protection Program
- CTSI Guidance on Reporting Adverse Events
- CTSI Adverse Event Definitions
- FDA – Serious Adverse Event
- IRB AE Reporting Decision Tree
- (PAR Log) PAR_Summary_Log.doc