Clinical Trial Safety Reporting Form Completion Guidelines

Any event that meets the protocol definition of SAE, AESI, or other safety report (eg, DILI or UADE) due to any cause and regardless of relationship that occurs from the time the subject signs the informed consent form until subject's last scheduled trial visit for non-serious AESI or DILI and until an SAE is considered resolved and must be reported **within 24 hours of awareness**. This includes awareness of initial information as well as follow-up data received by the site.

The electronic data capture (EDC) system is the primary system for the collection of Safety Reports. As a back-up to the EDC system, please complete this safety reporting form and including the investigator signature, and send it to the email addresses below:

connectsafety.sm@thermofisher.com

pv@connectpharm.com

Note: The Sponsor has delegated Pharmacovigilance (PV) services (eg, safety reporting case processing) to PPD. PPD will return confirmation of receipt which should be archived with the report form. A PPD team member may contact you with any follow-up questions related to the event.

Section1: General Information/Report Type

Record the following:

- **Study Protocol Number** per the relevant study.
- **Report Version**: Mark 'Initial' when submitting safety information for the first time for the participant-event pair. Mark 'Follow-up' and enter the follow-up (FU) number, when submitting additional information pertaining to the safety report captured in the initial report submission. The FU Version will be numbered sequentially starting from 1.
- **Date of Report**: The date when this form is completed (DD/MMM/YYYY).
- **Date Investigator became aware:** Date the site was made aware of event (DD/MMM/YYYY).
- **Report Type**: Please check whether it is an SAE, AESI, and/or other safety report type (as defined in the protocol) with a descriptions for other report types (eg, DILI).

Section2: Participant Information

Record the following:

- **Date of Birth**: Date of the participant's birth (MMM/YYYY).
- **Age at time of event：Enter the subject's age at the time of event onset, including the units of age (e.g. years)**
- **Gender:** Enter the gender of the participant (ie. male or female)

- **Participant Number**: The participant number is a 6 digit number assigned number upon study enrollment (ie. 1-digit country code starting with 1 followed by a 2-digit site number and then a 3-digit subject number (eg, 101001)).
- **Height**: Enter the height of the participant and mark the units of measure (eg cm or in), if available.
- **Weight**: Enter the weight of the participant and mark the units of measure (eg, kg or lbs), if available.
- **Race**: Mark the appropriate race of the participant or select 'Other' and specify in the free text field and if race is not to be reported per local requirements, please indicate by stating 'not reported'.

Section 3: Investigational Product Administration

Record the following:

- **Investigational product**: this could include the study drug, study product (ie. syringe component), or the comparator product.
- **Date of first administration** of the investigational product (DD/MMM/YYYY)
- **Date of last administration prior to SAE Onset** (DD/MMM/YYYY)
- **Did site unblind treatment for the participant due to this event?** Yes/ No/ not applicable. This question is simply to ascertain if the participant was unblinded due to this event. DO NOT provide any additional information specific to the participants, if they are unblinded.

Section 4: Adverse Event Information

Record the following:

If there are no changes in the adverse event information since the previous report, then indicate by checking the box next to "no change from previous report".

- **Adverse Event term**: Only one event term should be provided per report form. Additional safety reports (eg, SAEs, AESIs, other) should be reported on separate safety report forms. Please see the protocol for definition of AE, SAE, AESI, DILI, and UADE) A concise medical diagnosis is preferred over signs/symptoms.
  - ✧ If signs/symptoms are initially provided, please revise the event term once a diagnosis is made.
  - ✧ If the subject was hospitalized because of the SAE, a diagnosis is often present on the hospital discharge summary. "Death" is not an appropriate event term; it is an outcome.
  - ✧ If the event is fatal, please provide the cause of death as the event term.
- **Whether it Occurs Before Administration of First Dose:** This box should be checked if the adverse event occurred at any time before the administration of the first dose of the

investigational product, even if both events happen on the same day. It is important to accurately capture the timing of the adverse event relative to the first dose administration.

- **Event Onset Date**: If the adverse event is serious (SAE), then the date when the event first met the SAE criteria should be captured (DD/MMM/YYYY). For other types, the date when the event first occurred should be provided (DD/MMM/YYYY).
- **Serious Criteria**: Select all serious criteria that apply. If the serious criteria of
  - **Resulted in Death**: Provide the following in each designated field when an event has a fatal outcome: Date of death, Indicate if an autopsy was performed by marking "Yes" or "No" as applicable, Provide an autopsy report if one is available as an attachment to the safety reporting form, If an autopsy report and/or cause of death cannot be provided, please state as such in the narrative field of section 8.
  - **Life-threatening**: An event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
  - **Hospitalization**: the event requires an inpatient hospitalization or prolongs an ongoing hospitalization.

    Date of admission: Enter the date the subject was admitted as an inpatient to the hospitalized or the date for when the hospitalization was prolonged due to the event (DD/MMM/YYYY).

    Date of discharge: Enter the date the subject was discharged from the hospital (DD/MMM/YYYY).
  - **Other Serious (medically important event)**: select when an event may not have resulted in death, considered life-threatening, or require hospitalization, but may be considered serious when based upon medical judgement, they may have been jeopardize the participant and may require medical or surgical intervention to prevent one of the other seriousness criterion)
  - **Persistent/significant disability/incapacity**: if selected, please describe disability or incapacity in section 8.
  - **Congenital anomaly/ birth defect:** if selected, please describe in section 8.
- **Date of end of event**: the end date of the SAE is the date when the serious adverse event/reaction reached a final outcome. This data element captures the date the event is reported as resolved/recovered or resolved/recovered with sequelae. If the event is not resolved at the end of the study, the stop date should be left blank and 'Ongoing' should be selected. If the subject died due to the AE, enter a stop date (i.e. date of death); however, leave the stop date for other ongoing AEs blank and mark them as ongoing, as they were ongoing at the time of death.

- **Outcome**: Select the outcome that best applies to the date of end of event.
  - ✧ Fatal: The participant died due to this event
  - ✧ Recovered/Resolved: The participant has fully recovered from the event or returned to a stable condition or baseline.
  - ✧ Not Recovered/Not Resolved/ongoing: The subject has not recovered from this event
  - ✧ Recovered/Resolved with sequelae: The subject is experiencing the after effects of a condition or injury (sequelae). Describe the sequelae in Section 8.
  - ✧ Unknown: Select "Unknown" if there is insufficient information to determine the final outcome of the event.
- **Severity** (CTCAE): Mark one box associated with the highest severity grade associated with the event, as defined in the protocol.
  - ✧ Following a decrease in severity (ie patient condition improves), please DO NOT change severity on the form in follow-up reports.
  - ✧ Following an increase in severity (ie patient condition worsens), please DO change the severity reported on the form in follow-up reports.
- **Relation to Investigational product**: Mark one of the following:
  - ✧ Unlikely related: there is not a reasonable possibility that the administration of the study drug caused the event, there is no temporal relationship between the study drug and event onset, and/or no alternate etiology has been established.
  - ✧ Possibly related: The event is known to occur with the study drug, there is a reasonable possibility that the study drug caused the event, or there is a temporal relationship between the study drug and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study drug and the AE.

  The causality assessment is one of the criteria used when determining regulatory reporting requirements. The investigator may change his or her opinion in light of follow-up information and amend the eCRF or safety report form, as applicable.
- **Alternate etiology**, if any: Check all that apply to identify and specify all alternate etiologies that may have contributed to the adverse event, if any. Provide specific details in the designated spaces.
- **Treatment for event**: Select “No” for no treatment or “Yes” and list treatment for event. Select unknown if it is unknown whether the participant received treatment for the event.
- **Action Taken with Investigational product**: Mark the box corresponding to the appropriate action taken with investigational product as a result of the event. For events occurring prior to first dose of investigational product or after completion of study dosing regimen, a value of ‘Not Applicable’ should be selected.

Section 5: Relevant medical history

Record medical history relevant to the event being reported. If there are no changes in the information since the previous report, then indicate by checking the box next to “no change from previous report”. Include the relevant disease term, Start date, Ongoing (Yes or No) and/ or End date. If the patient has no relevant medical history, select “none”. If data is pending at the time of the report, select “Unknown”.

Section 6: Relevant Concomitant Medications

Record concomitant medications taken within 30 days prior to the onset of the reported event(s) and those used for more than 30 days, suspected to be related to the reported adverse events taken by the participant. Medications should include prescription and over the counter products (including herbal products and vitamins). Include: Product trade and/or generic name, indication for use, dose, dose unit, dosage form, frequency, route, start date and end date (if applicable). If there are no changes in the since the previous report, then indicate by checking the box next to “no change from previous report”. If the participant has no relevant concomitant medication, select “none”. If data is pending at the time of the report, select “Unknown”. Treatment medications should not be included under concomitant medications and rather be described in the narrative (Section 8 of the form).

Section 7: Relevant diagnostic test results

Provide any relevant diagnostic test results that pertain to the case. Be sure to include name of test, test date and results, unit and the upper limit of normal and lower limit of normal. If the participant has no relevant diagnostic test results, select “none”. If there are no changes in the information since the previous report, then indicate by checking the box next to “no change from previous report”.

Section 8: Narrative

Provide a description of the clinical course detail along with event relevant treatment in chronological order. Including pertinent diagnostic tests, interventions, and rationale for assessment of the relationship to study drug.

Section 9: Investigator/Reporter Information

Provide the complete address of the study site, Principal Investigator or Sub-Investigator’s, and Reporter (Person Filing the report) phone and email address. and signature. The Investigator must sign and date the completed form to attest that they have reviewed the Safety Report and agree with its content.