8. CHANGE IN PARTICIPANT STATUS

8.1 Off Study Agent

Some protocols document a difference in procedure for when a participant is temporarily off the study drug/agent. The criteria are similar to those for being 'off study.' There are two events that define an "Off Study Agent" event. The first is that a study participant may discontinue use of a study agent but continue to be followed in a study. In this case, the participant's status is identified as "Off Study Agent," and the participant continues to be followed as specified by the protocol. The second event is that a participant who completes the protocol interventions and any protocol-specified follow-up period or evaluations may also be considered as "Off Study Agent." This applies to specific protocols written to include this distinction. Reasons that participants may stop a study agent include:

- Any AEs or SAEs as reported on the completed AE/SAE Form;
- Noncompliant participant (includes refused study agent and/or assessments);
- Concomitant medication contraindicated by protocol;
- Medical contraindication (e.g., pregnancy);
- The discretion of the investigator; or
- Other (which should be described in the source document and noted on the case report form).

When a participant has permanently discontinued the study agent, the final study visit and clinical/laboratory evaluations must be obtained as specified in the protocol (when applicable). All study agents or supplies need to be returned to the site staff.

8.1.1 Required Follow-up for Off Study Agent Status

The study forms required at the time of permanent discontinuation of a study agent are specified in the "Off Study Agent" section in the protocol. The procedures and/or clinical evaluations completed for "Off Study Agent" are specified in the protocol and should be consistent with the end points described in the objectives and statistical analysis sections of the protocol.

8.1.2 Off Study

Participants who are considered to be "Off Study" are those who are permanently discontinued from the study agent or who do not wish to participate in the study any longer. This includes those participants who have completed all study visits and the protocol-specified evaluations. The following are some reasons a participant can go off study:

- Completed (completed protocol intervention and any protocol-specified follow-up period or evaluations);
- Any AEs or SAEs as reported on the completed AE/SAE Form;
- Noncompliant participant (includes refused study agent, assessments);
- Concomitant medication contraindicated by protocol;
- Medical contraindication (e.g., pregnancy);
- The discretion of the investigator;
- Lost to follow-up;
- Withdrew consent;
- Death (complete Death CRF); or
- Other (which should be described in the source document and noted on the case report form).

NOTE: Any participant who is withdrawn for AEs must be followed until resolution of the event or until the PI considers it unnecessary to continue follow-up. Documentation of this reason to discontinue follow-up must be noted and maintained in the participant's study chart. Relevant information should be abstracted into the "Continuing AE" section of the Off Study Form.

8.2 Death

All known deaths of participants enrolled in DCP-funded clinical studies are to be reported as an SAE regardless of the relatedness or attribution to the study agent. The SAE report is forwarded to the DCP Medical Monitor for review. The SAE procedures in Chapter 6 of this Manual include instructions on completing an SAE form and details about submission timeframes. In general, the following information should be submitted on the SAE form at the time the death is reported:

- Name and phone number of the reporter;
- Participant's study identification number;
- Date of death;
- Primary cause of death (if known);
- Name of study agent(s);
- Date study agent(s) last given;
- Assessment of whether death was related to study agent; and
- Brief history leading to death. (Submit autopsy report if available.)

Deaths are to be reported using the protocol-specific death form usually located with the protocol-specific CRFs. A Death CRF is to be completed for each protocol in which the participant was enrolled. The purpose of this form is to gather information regarding the participant's death and when it occurred during the study. If the exact date and time of the death are unknown despite attempts to obtain this information, an estimate based on known facts is allowed.