MTN-020 (ASPIRE) Operational Guidance #10:
Reporting Protocol Deviations and Critical Events

The purpose of this guidance document is to summarize the responsibilities and reporting procedures for both protocol deviations and critical events. This guidance document applies to all ASPIRE site staff, the study management team, the DAIDS Office of Clinical Safety Oversight (OCSO), and PPD site monitors.

Protocol Deviations

Resources:
MTN Protocol Deviation Policy: http://www.mtnstopshiv.org/resources
ASPIRE SSP Section 3.2.3
ASPIRE Operational Guidance #4

All protocol deviations in ASPIRE should be reported by site staff via the Protocol Deviation CRF within 7 days of site awareness. It is expected that significant deviations, such as (but not limited to) those involving randomization, informed consent, product sharing, product dispensation errors, or the primary study endpoints, be reported to the ASPIRE management team or FHI 360 CRM as soon as the site becomes aware of the deviation.

ASPIRE protocol deviations are determined by the MTN Protocol Deviation policy, and events should only be determined to be deviations through the MTN. If sites are unsure about whether an event requires reporting as a protocol deviation, the ASPIRE management team and/or MTN regulatory should be consulted. Although study monitors cannot determine if a procedure or event constitutes a protocol deviation, they may identify potential protocol deviations when reviewing records at a site. When this happens, the study team should reference the MTN Protocol Deviation policy and consult with the management team and MTN Regulatory, as necessary, before reporting the deviation.

Protocol deviation summary line listings are available on Atlas (restricted use) and site-specific line listings of all deviations reported to date can be requested by site teams.

Critical Events

Resources:
DAIDS Critical Event Policy and Manual:
http://www.niaid.nih.gov/labsandresources/resources/daidsclinrsrch/Pages/Safety.aspx

Potential critical events may be identified by site staff, PPD monitors, or members of the ASPIRE management team, and should be reported immediately to the site OCSO PO. If a critical event is identified during a PPD monitoring visit, the monitor will notify the OCSO PO directly. Otherwise, this is the responsibility of the site staff. In some instances the event may also be classified by the MTN as a protocol deviation, therefore, it is requested that both the ASPIRE management team (or FHI 360 CRM) and OCSO PO, be made aware of the event simultaneously.

Regardless of how the event is identified, *it is the sole responsibility of the site OCSO PO* to confirm whether a critical event has occurred, as all CEs are determined by the DAIDS Critical Event policy. It is expected that the OCSO PO will guide the site per the DAIDS Critical Event policy, and determine whether or not the event meets the policy definition. The OCSO PO will email the site with this determination (clarifying whether it meets the definition of a critical event or not) and it is recommended that the site file this guidance with documentation of the event.

If a Critical Event also meets the MTN Policy definition of a Protocol Deviation, the site should complete and submit the Protocol Deviation CRF per the instructions in the ASPIRE SSP. For these cases (confirmed Critical Events that are also deemed Protocol Deviations), item 4 on the Protocol Deviation log CRF (PDL-1) should be marked "yes". If a previously reported protocol deviation is later deemed to be a Critical Event, update this item to indicate that the protocol deviation will be reported to DAIDS as a critical event.

Events that qualify as Critical Events per the DAIDS policy may result in the request for corrective action/preventive action (CAPA) to be documented, outside of what may already be documented on the Protocol Deviation CRF. The ASPIRE management team and OCSO PO will determine the way forward in collaboration, and streamline communication back to the site on any follow up required.

All Operational Guidance documents must be printed and filed with regulatory documentation.