MTN-020 (ASPIRE) Operational Guidance 4: Recording and Reporting Protocol Deviations

This operational guidance to MTN-020 sites is intended to define how Protocol Deviations (PDs) are recorded for the MTN-020 trial and to provide guidance related to reporting of these PDs to overseeing IRBs and Ethics Committees (ECs). Please note that t**his guidance is not intended to replace current IRB/EC reporting policies.**

Section 4 of the Guidance for Industry ICH Guideline E6 Good Clinical Practice: Consolidated Guidance (GCP) [http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073122.pdf] states that the investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and by the regulatory authority(ies) and which was given approval by the IRB/EC; the investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval from the IRB/EC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial; and that the investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.

Additionally, Section 3 of GCP states that the IRB/EC should establish procedures that include a requirement that the investigator promptly report to the IRB/EC:

- deviations from, or changes of, the protocol to eliminate immediate hazards to the trial subjects
- changes increasing the risk to subjects and/or affecting significantly the conduct of the trial
- all adverse drug reactions (ADRs) that are both serious and unexpected
- new information that may affect adversely the safety of the subjects or the conduct of the trial

For Protocol MTN-020, “A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase 3 Safety and Effectiveness Trial of a Vaginal Matrix Ring Containing Dapivirine for the Prevention of HIV-1 Infection in Women”, all PDs, both those that meet the criteria of affecting safety or study integrity as well as any other PD, are reported by research sites to the Microbicide Trials Network (MTN) statistical and data management center (SCHARP) in an ongoing manner via datafax using the MTN-020 PD case report form (CRF).

In addition to completing and faxing the MTN-020 PD CRF, it is recommended that sites report in an expedited manner to IRBs/ECs PDs that pose a potential safety risk to a participant(s) and those that could affect the integrity of the study according to the local IRBs/ECs’ standard operating procedures and guidelines.

It is also recommended that a complete list of all PDs occurring at the site, including PDs not meeting immediate reporting standards noted above, be submitted to the local IRBs/ECs in accordance with their reporting policies. If a local IRB/EC does not have a specific reporting policy, MTN recommends that this be done at the time of IRB renewal submission, annually or semi-annually per local requirements. These listings will be provided by MTN to the sites on request. Sites should request these PD listings from SCHARP at least two weeks prior to the planned date of submission to their local IRBs/ECs.

We encourage the site to forward this operational guidance to applicable regulatory bodies for each site so that they may be aware of the MTN Protocol Deviation Policy and the current internal MTN reporting requirements for MTN-020.

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