Inspections in the Network Structure and Responsible Parties

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Division of AIDS (DAIDS) Role as the funder of MTN 020

- Through grants, DAIDS provides resources and funds to support the performance of human research to ensure participants are protected
  - MTN-020 study receives U.S. federal funding
  - MTN network sites conducting MTN 020 are funded by DAIDS
  - MTN CORE and FHI360 are Operations Centers for the MTN network which is funded by DAIDS
- For MTN-020 there is an agreement between the Regulatory Sponsor, IPM and the funder, DAIDS, regarding regulatory and operational requirements
  - Regulatory activities, such as safety reporting, protocol registration, and monitoring, are managed by DAIDS through DAIDS systems
  - DAIDS provides regulatory documentation to IPM for submission to the FDA, MCC, EMA

DAIDS Role in Supporting the IPM IND for MTN 020

- CRS submits safety reports to DAIDS Safety Office. DAIDS Safety Office processes and provides safety data to IPM for submission
- CRS submits regulatory documents (i.e., Form FDA 1572, IRB/EC approvals, site ICs, etc.) to DAIDS Protocol Registration Office (PRO). DAIDS PRO processes and provides regulatory documents to IPM for submission
- CRSs are monitored by the DAIDS monitors. Monitoring reports are provided to IPM

Who is Responsible for MTN 020 at the Site?

- The Investigator of Record (IoR) at the Clinical Research Site (CRS) is responsible for the conduct of the study at that site

Who Signs the FDA Form 1572 and Why

- The IoR at the CRS signs the Form FDA 1572, Statement of Investigator, demonstrating he/she is qualified for the role and documenting that the site is an appropriate location for the study to be conducted
- The IoR may or may not be the CRS Leader. If the CRS Leader signs the Form FDA 1572 for a specific study, then he/she is the IoR for that study in addition to the Leader role at the site
- The signed Form FDA 1572 is ***an agreement*** between the FDA and the site person (IoR) responsible for the study and safety of its participants
- This agreement informs the IoR of his/her obligations and responsibilities related to pertinent FDA regulations

Role of Investigator of Record on the Form FDA 1572

- To protect the rights, safety, and welfare of study participants
- The Form FDA 1572 is used in the US and internationally for studies conducted under a U.S. FDA Investigational New Drug Application (IND)

Form FDA 1572

- Completed, signed, and dated by the IoR at each site participating in a study under IND
- Form FDA 1572 must be reviewed and approved by DAIDS prior to implementation of the protocol at a site
- For MTN 020, these forms are forwarded by DAIDS to IPM, the IND sponsor. For DAIDS INDs, they are sent to company collaborators

Form FDA 1572

- Any major change to the information requires an updated Form FDA 1572 be signed, dated and sent to the sponsor (sites should keep all copies in the regulatory file)
- The sponsor sends a copy of the form to the FDA
- **This is an important document to guide an inspection**
  - Identifies the responsible investigator for overall conduct of the trial at the site
  - Identifies other investigators at the site who are involved in the trial
  - Maintains up-to-date information on trial conduct over time
  - Provides names and locations of laboratories, pharmacies and ethics committees to the sponsor and FDA

Commitment of the IoR per the Form FDA 1572

- By signing the 1572, the IoR affirms that he/she agrees to the following commitments:
  - Adherence to the protocol
  - Personal supervision of the trial at the site
  - Agreement to inform subjects of the trial via the informed consent process
  - Agreement to report adverse experiences to the sponsor
  - Statement that the IoR has read the Investigator's Brochure and understands the risks and benefits of the investigational product
  - Ensures that all sub-investigators are informed about their obligations related to the conduct of the trial

Commitment of the IoR per the Form FDA 1572

- By signing the 1572, the IoR affirms that he/she agrees to the following commitments:
  - Records will be maintained per the regulations and made available for inspections
  - IRB/EC compliance with 21 CFR 56 for human subject protection and informed consent
  - Compliance with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312
  - Ensure that appropriate staff are adequately trained

IoR on the Form FDA 1572

- It is the IoR that is the responsible party for all conduct of a study at a specific site, not the CRS leader
- A willfully false statement on the 1572 is a criminal offense
- An investigator may be subject to a disqualification proceeding for a deliberate, false statement made on the 1572

IoR Success at the Site Leads to a Successful Study

- IoRs who understand the agreement represented in the 1572 pave the way for success at the site for the study
- IoRs who ignore the agreement or do not take it seriously may jeopardize both the study and his/her own career
- Citations related to 1572 problems are low-hanging fruit for inspectors. For example:
  - Sub-investigators not involved in the trial or involved but not adequately trained;
  - Laboratories that are no longer used during the course of a trial;
  - Co-investigators on one 1572: the term is not defined in FDA regulations, so each much sign a 1572;
  - IoRs who have not read the 1572 and do not understand its importance and legal standing

Conclusion

- The Division of AIDS, through Protocol Registration Training and Network meetings is committed to IoRs who understand the reason for the FDA Form 1572 and who know their personal responsibilities in the conduct of research regulated by the U.S. FDA