Procedures, Challenges and Support Systems for Protocol-Related Testing at Study Sites

Allen Matubu PhD
UZ-CTRC
3-7 June 2023, Washington DC
Presentation Highlights

1. Role of Clinical Safety Lab in Clinical Trials, operational challenges & mitigatory measures
2. Synergistic relationship between lab and clinic teams is key to overall clinical trials success
3. A well structured & coordinated system is key to ensure robust execution of HIV prevention trials
Role of the Lab in Healthcare: *70/70 rule*

- 70% of medical patient records are made of laboratory data.
- 70% of medical decisions are based on laboratory results.
Role of Clinical Safety Lab in Clinical Trials

Pre study
- **Screen** – identify the correct participant
- **Enroll** – correct participant
- **Exclude** – unsuitable (screen: enrollment ratio)

During study
- **Study drug adverse effects** – start/stop decisions
- **Clinical efficacy** – study endpoint determination

Post study
- **Composite adverse events**
- **Drug/intervention clinical efficacy**
African Laboratories under HPTN LC Oversight

Botswana - 2
Zimbabwe - 6
South Africa - 7
Kenya - 2
Eswatini - 1
Malawi - 2
Uganda - 4
Total = 24
Clinic Laboratories
- HIV rapid testing
- Urine HCG
- Urinalysis
- Rapid Trichomonas vaginalis test

Centralized Laboratories
- HIV confirmatory testing
- Biochemical profiles
- Full blood count
- T cell profile
- 4th Gen HIV Ag/Ab
- HIV RNA
- Syphilis
- CTNG

Specialized Laboratories
- HIV resistance testing (for real-time clinical management)

NB: Testing at each laboratory is guided by a protocol analyte list reviewed by the LC and accepted by DCLOT.
Given the critical role that lab results play in decision making, it is critical to ensure lab results are:

- accurate
- precise
- reliable
Key considerations for QMS

Sample collection
Sample transport
Sample sorting
Sample processing
Reagent/sample storage

Review of results
Reporting of results
Automatic transfer of results
Validation of electronic results reporting systems
Disposal of samples

1. Restelli et al., 2017; 2. Carraro et al., 2007; 3. Plebani et al., 2006
### Quality Management Systems

<table>
<thead>
<tr>
<th>Staff training and competence</th>
<th>Environmental conditions</th>
<th>Equipment/method validation</th>
<th>Phlebotomy and specimen chain of custody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample acceptance &amp; rejection criteria</td>
<td>Daily quality control (QC) checks and preventative maintenance procedures</td>
<td>Daily QC trend analysis – Levy Jennings charts</td>
<td>Reagent lot to lot verification</td>
</tr>
<tr>
<td>Scheduled equipment service and maintenance</td>
<td>Test method Standard Operating Procedures (SOP)</td>
<td>External Quality Assurance</td>
<td>Reporting of results/recall/cancellation</td>
</tr>
</tbody>
</table>
Challenges & mitigatory measures

• Reagent supply chain challenges that hinder accurate inventory projections – share yearly requirements with suppliers and develop tools to accurately project future testing needs

• Equipment/method performance – troubleshoot, document probable causes and track

• Unsatisfactory EQA performance – investigate, troubleshoot, document and track
Strategies for optimizing laboratory reagent inventory

SOE/SSP provides guidelines on:
- Visit intervals
- Lab evaluations at each visit

LOA may provide updates on required lab tests

Internally generated schedules of anticipated visits per participant:
- Baseline = date of enrolment
- Subsequent visits “cascaded” based on SOE/SSP visit intervals

Visit cascades

Using Excel formulae, cross tabulate visit data and required lab evaluations to:
- Derive quarterly projected totals for each lab test (n)
- Determine number of kits to order (n/kit size).

Reagent requirements
Instruments being sunsetted sooner than anticipated – Requires conversations with companies, network partners, and DCLOT to determine:

• Realistic needs
• Anticipation of costs to include training, validations, maintenance, reagents
• Availability of service
• Similar back-up instrumentations
• Anticipation of unexpected costs including repeat parts of validations
Conclusions

• A synergistic relationship between lab and clinic teams is key to overall clinical trials success

• A well structured, resourced QMS is key to successful implementation of HIV prevention trials

• Innovative strategies to sustain adequate lab reagents are key to uninterrupted lab service
Thank you
Acknowledgments

- HPTN LC Leadership
- UZ-CTRC Leadership

Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID), Office of the Director (OD), National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under Award Numbers UM1AI068619-17 (HPTN Leadership and Operations Center), UM1AI068617-17 (HPTN Statistical and Data Management Center), and UM1AI068613-17 (HPTN Laboratory Center).

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.