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

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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 decisions are based on laboratory results

70% of medical patient records are made of laboratory data

Role of Clinical Safety Lab in Clinical Trials

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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

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HPTN Laboratories Scope of Testing

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

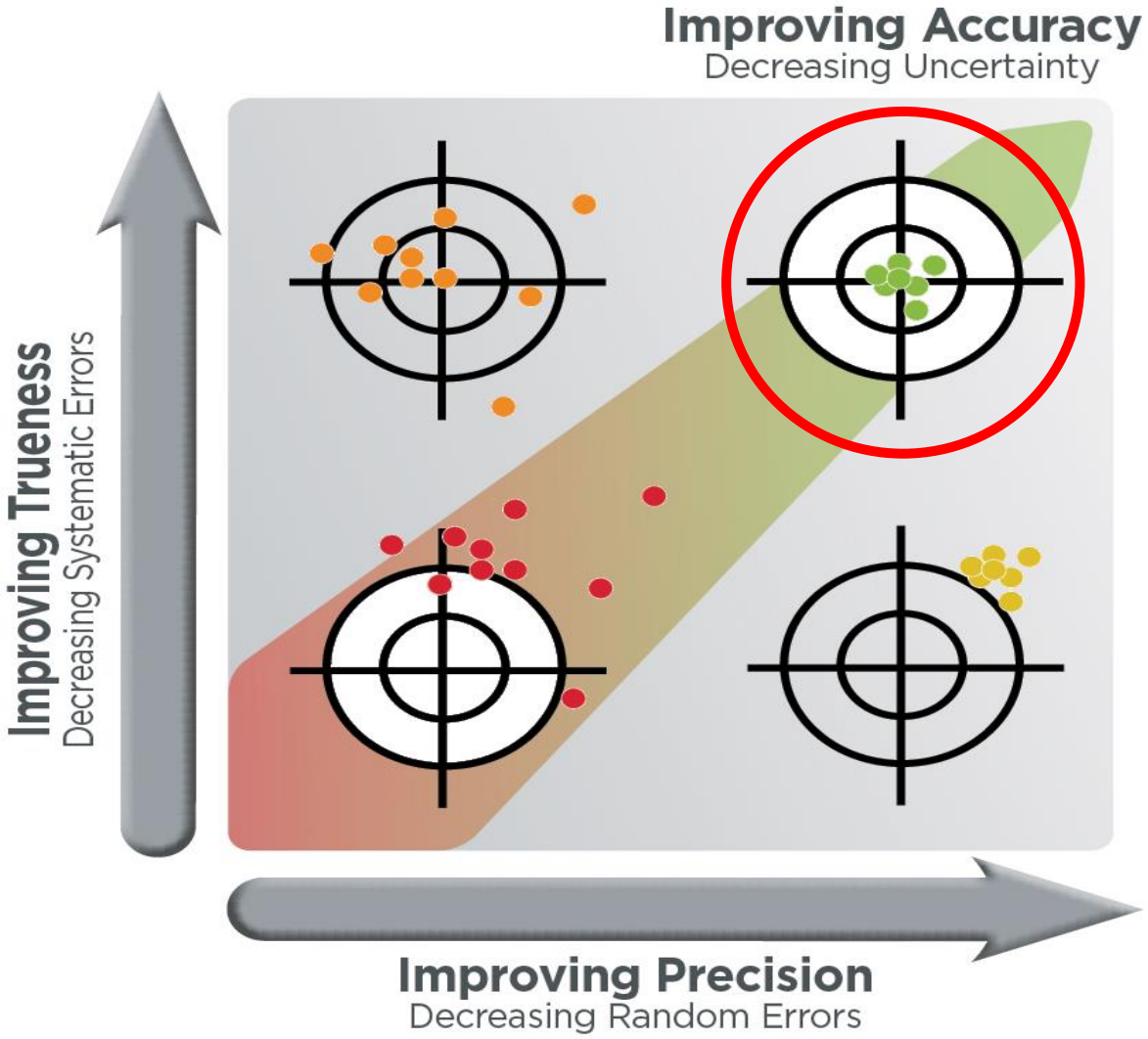
Specialized Laboratories

- 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.

Quality Management Systems (QMS)

- 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

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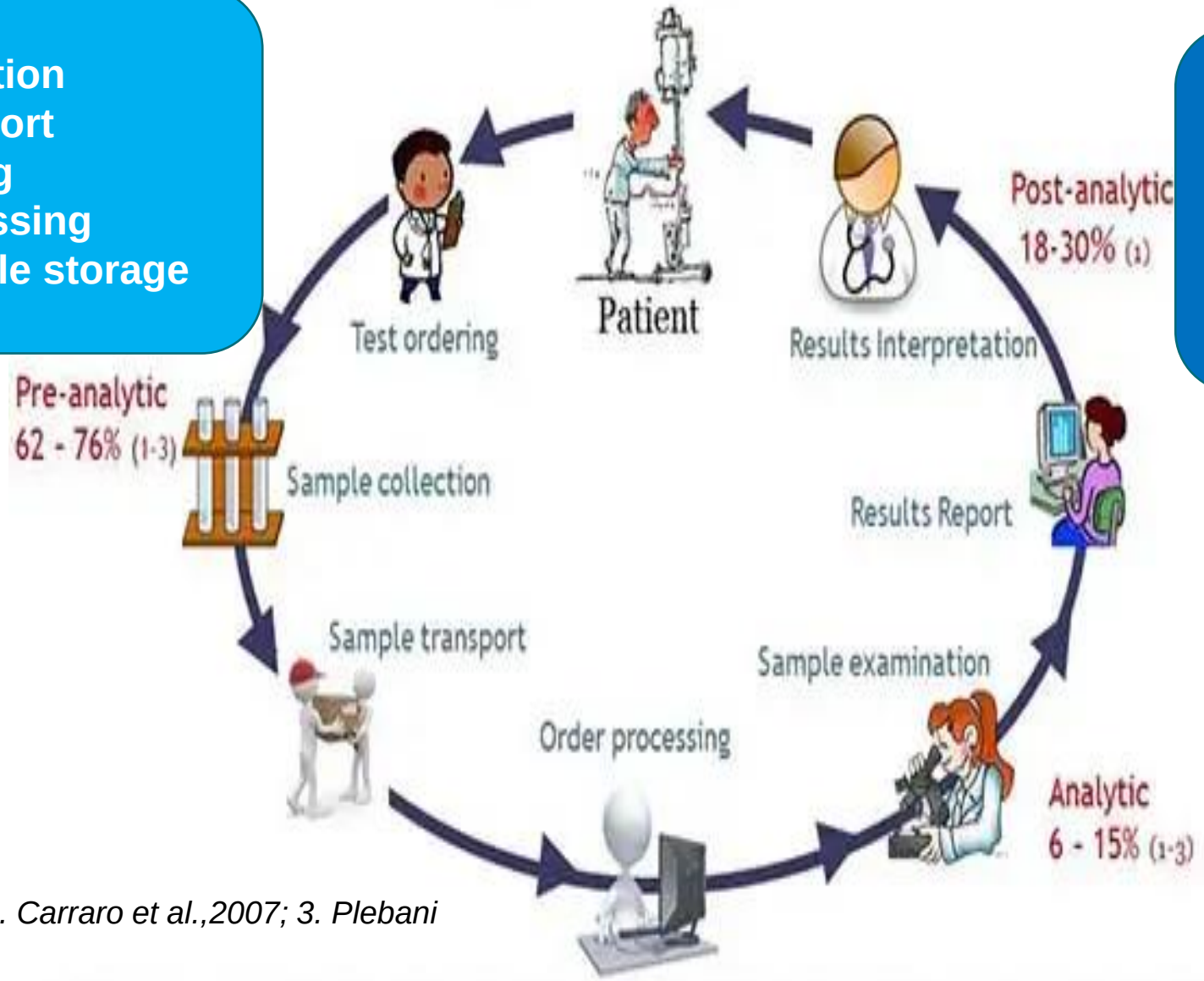
Sample collection
Sample transport
Sample sorting
Sample processing
Reagent/sample storage



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

Training
Competence
Environmental conditions
Equipment – validation, service, calibration
Procedures
Quality control (IQC & EQA)

1. Restelli et al.,2017; 2. Carraro et al.,2007; 3. Plebani et al.,2006

Quality Management Systems

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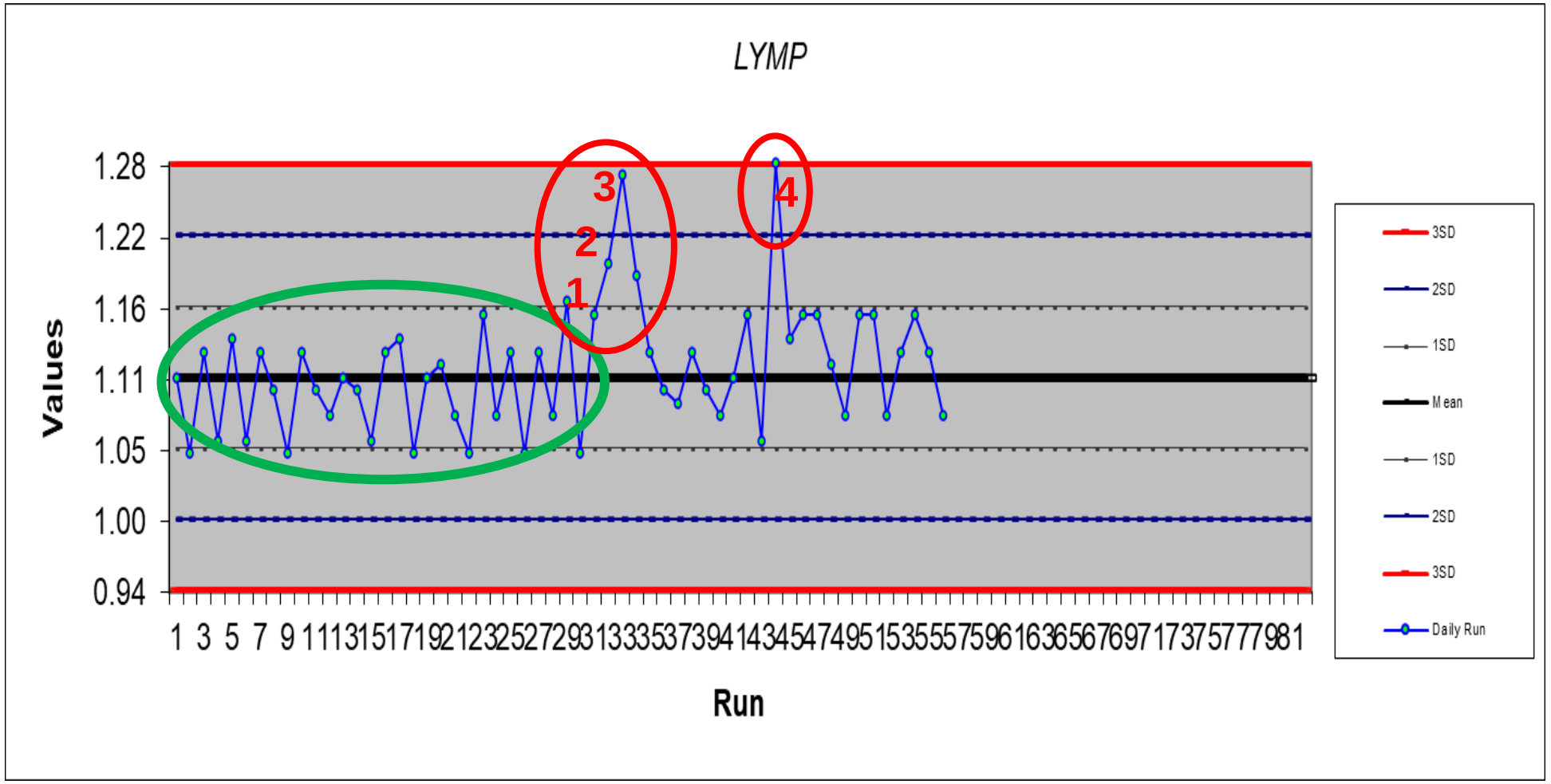
Staff training and competence	Environmental conditions	Equipment/method validation	Phlebotomy and specimen chain of custody
Sample acceptance & rejection criteria	Daily quality control (QC) checks and preventative maintenance procedures	Daily QC trend analysis – Levy Jennings charts	Reagent lot to lot verification
Scheduled equipment service and maintenance	Test method Standard Operating Procedures (SOP	External Quality Assurance	Reporting of results/recall/ cancelation

LJ Charts Application



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

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

LOA may provide updates on required lab tests

SOE/SSP, LOA

Visit cascades

Internally generated schedules of anticipated visits per participant:

- **Baseline = date of enrolment**
- **Subsequent visits "cascaded" based on SOE/SSP visit intervals**

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

Instrument Challenges

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

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