Strategies for maintaining high standards for Good Clinical Laboratory Practices

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South African Medical Research Council
BUILDING A HEALTHY NATION THROUGH RESEARCH

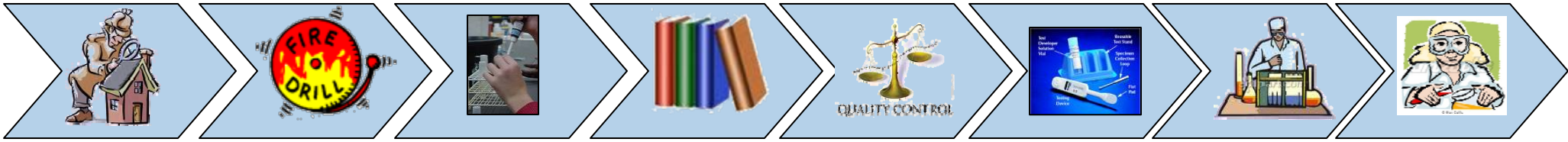
What is GCLP? Is your lab GCLP compliant?

- GCLP refers to Good Clinical Laboratory Practice-a culture and set- standards /systems which a laboratory needs to conform to.
- The GCLP concept possesses a unique quality, as it embraces both the research/pre-clinical and clinical aspects of Good Laboratory Practices (GLP).
- A constant application of GCLP is paramount in the success of any clinical trial. Study endpoints and participant safety data is largely laboratory in nature. Hence, if this laboratory data is called into question due to inconsistent practices, an entire trial effort could be deemed as a failure.
- DAIDS and GCLP:

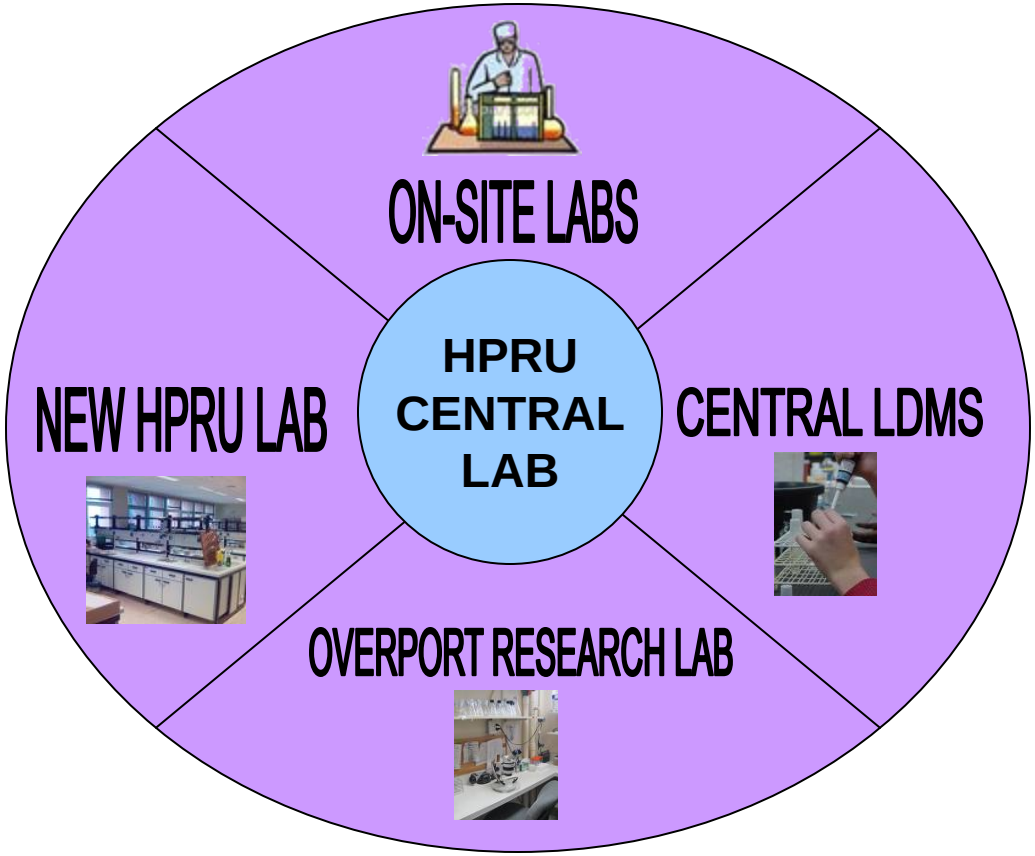
What are the components of GCLP?

- Organization and Personnel JE
- Facilities and Equipment
- Testing Facilities and Operations
- Verification of Performance Specifications
- Record and Reports
- Specimen Management and Tracking
- Laboratory Safety
- Laboratory Information Systems
- Laboratory Quality Management
- Laboratory Audits

QA CONTROL MEASURE AT EVERY COMPONENT & FOLLOW-UP & CLOSURE



MRC HPRU clinical trial sites and central laboratory
How is overall GCLP maintained?



SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

HPRU Laboratory Organogram

Building a healthy nation through research

HPRU DIRECTOR
GITA RAMJEE

Laboratory Manager
RASHIKA MAHARAJ

HPRU Laboratory Co-ordinator/QA/QC Officer
VACANT

Assistant HPRU Laboratory Co-ordinator/ Backup Med Tech:
NIRVANA RAMBARAN
HPTN 035, MDP III, Spartac, IPM 011, MTN 015, 001, 003 and New HPRU lab

HPTN 035
-Rashika Maharaj- Lab Co-ordinator
-Nonzwakazi Mnqonywa- Lab QC/QA Officer/Lab Co-ordinator
-Mandisa Skhosana- RKK Med Tech
-Ishana Naidoo - RKK Med Tech
Lindelwa Nkangane- Hlabisa Med Tech

MTN 001
-TBE- 3 Med Tech-Umk/Bhills

MDP III
-Krishnaveni Reddy- Site Lab Co-ordinator
-Nomfundo Maduna- Verulam
-Kubashni Woeber-Verulam
-Antonia Gwala- Isipingo
-Funeka Ntikinca-Tongaat

IPM 011
-Sandy Naidoo- Med Tech

MTN 015
-TBE 1 Med Tech & 1 Site lab Co-ordinator

Spartac
-Samantha Sukhdeo-Lab RA
T.Gounden-Lab RA

PEPFAR
-Motsei Ramokonupi-Lab RA

CENTRAL LDMS
-Sifiso Ndabezitha
-Emily Fakude

New HPRU Lab
-1 X Study Kits Officer-TBE
-1 X Probetec/Wblot/Molecular Med Tech-TBE
- 3 X Safety Testing benches-Med Techs-TBE
-1 X Specimen Receiving Lab RA-TBE
-1 X Data Lab RA-TBE
-3 X Central LDMS Officers- 1 TBE
-1x Lab RA-Resha Boodhram

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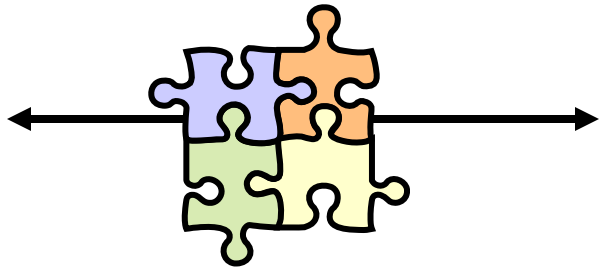
HPRU Central Lab And MTN On-site Laboratories in Durban

UMKOMAAS On-site Lab

B HILL On-site Lab

RK KHAN On-site Lab

OVERPORT On-site Lab



CENTRAL LAB

What does on-site lab do?

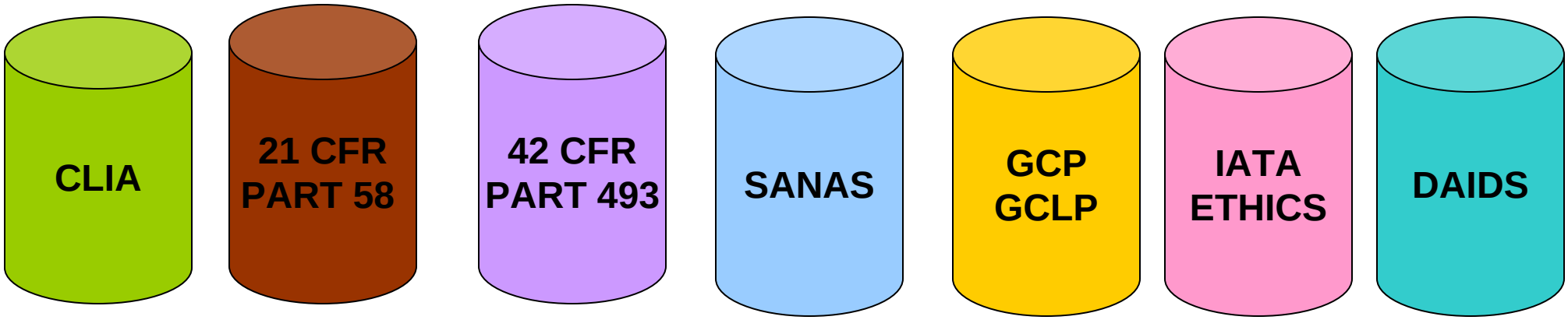
Complete management and co-ordination
Daily Laboratory Testing, tracking, shipping and storage
Perform Weekly Quality Assurance Programme specific to MTN
Ensure systematic Laboratory Documentation and Administration
Daily interaction with Outsourced Laboratories and Courier Service
Comply to Laboratory Safety
Ensure monthly Stock Control
Ensure calibration of Lab Equipment
Monitor with TAT and QC errors with Outsourced laboratory and new HPRU lab
On-site QC daily basis on testing, IQA, documentation , storage being shipped and study kits
Bimontly reports to gauge challenges
Corrective action reports to Core within 5 days of being monitored

What does Central lab do?

Oversight of Laboratory Personnel AND On-site Peripheral Laboratories set-up for MTN
Set-up of entire laboratory component of MTN studies centrally-lab only
Set-up of Laboratory Testing and Validations
Comprehensive Laboratory Quality Assurance Programme for MTN on-site labs
Audits/Monitoring of on-site laboratories conformance to DAIDS, PNL , CFR part 21, GCLP and SANAS
Competency and Proficiency assessment for MTN on-site labs
Development of Laboratory Documentation and Administration -total of 100 SOPs, 33 logs
LOP development, cheat sheets, QC programme cheat sheets
Laboratory Trainings and Capacity Development
Laboratory Safety, QC of Stock Control and Lab Equipment
All budgets-Lab component
Timeline docs for MTN-submission to MTN PNL
Back-up services and Review of all MTN lab docs submissions
100% off-site QC of all testing logs, sops, documentation, regulatory, IQA logs etc.
Monthly audits and monitoring-conformance to DAIDS requirements
Trainings for DAIDS studies
FINAL APPROVALS OF ALL LAB DOCS PRIOR TO SUBMISSIONS TO MTN
SET-UP OF NEW HPRU LAB AND RESEARCH LAB AT OVERPORT

HOW DO WE CONFORM TO GCLP ?

- QA/QC for all lab-related aspects that form part of GCLP components.
- A template audit/monitoring lab QA/QC report is generated detailing all issues or non-compliance
- Corrective action is due 5 days from report date.
- Corrective action is verified at next visit.



Organization and Personnel
21 CFR part 58

Qualifications	Trainings	Competency/Proficiency
Diploma or Degree in relevant category as per local professional council	On-line ethics +GCP	Entry competency on study-use of LT1/2/3/4 forms for Med Techs/Lab RA/LDMS/Lab QA/QC RA
Proof of Registration with professional council in specialist category	Lab Safety training	Annual competency assessment and documented on lab procedures for protocol Certification of competency
Scope of work as per registration with professional council	IATA-renewal every 2 years [also MCC and DOH requirement in 2008]	Proficiency-registered with National or International QA programme to assess proficiency for peer review Certification of Proficiency for IQA and EQA
Signed Med Tech Oath and declaration of confidentiality	GCLP-1 key lab staff member responsible for overall lab QA	Rapid Test IQA and CAP Wet Mount-Bi-annual proficiency Wet mount-Kodachromes proficiency assessment Certification of proficiency by CAP and HPRU [wet mount]

Facilities and Equipment

- Class II Safety Cabinet for rapid testing and level 2/3 agents
- Adequate ventilation to maintain RT-15-25 degrees celcius
- Adequate lighting and bench space
- Clean and dirty area demarcated
- Back-up generator and UPS for essential lab equipment
- Facilitate workflow generated for protocol-lab component
- Safety equipment and first aid box-accountability of stock a ce
- Updated lab organogram-lab staff reporting and accountability
- Annual calibration of lab equipment
- Colourful cheat sheets enable better adherence to the SSP manual and serve as reminders.

ARE YOU CHECKING UP ON THIS AS PART OF YOUR QA PROCESS?

Lab Documentation Records and Reports:

- Standardized template across studies -Standard Operating Procedures (SOPs)
- A Document Control Plan must exist to facilitate the review for accuracy and relevance of all SOPs.
- Annual review of lab sops are essential-reminder must be sent out annually, latest reviewed version must be on file, **all FINAL approval goes thru the HPRU Central lab group after the PL/PM have reviewed.**
- Track version change and sops distribution and receipt
- Ensure if staff have resigned or leaving-that they have read off and signed off prior.

Rapid Testing and IQA & EQA at on-Site Labs

- Are you conforming to prescribed SSP Manual and lab specific requirements?
- Development of IQA programmes specific to MTN studies requirements.
- Adherence to IQA and EQA programmes set up for study-Non-adherence results in poor performance
- Verification of rapid test controls compatibility with set tests for MTN study
- Follow-up on discordant HIV rates across kits used
- Set-up of outsourced lab for specialist testing, minute all items, action items and double check set-up for MTN study for SI units, DAIDS toxicity table, specific analytes for MTN studies, shipping and logistical requirements, service agreement, TAT penalty clause, courier services-cost of samples responsibility and payment, lab manuals, approval of request forms, technical protocol set-up, storage , regulatory, activation requirements

Laboratory Regulatory Documents

NORMAL LAB REG

- Proof of laboratory accreditation/certification
- Updated annual Laboratory Director CV
- EQA or proficiency certification of safety testing

HPRU LAB REG

- A spreadsheet - all the tests that will be done for the trial,
- Normal ranges, Master list of all the laboratory's SOPs
- Permits to ship internationally-annually renewed with DOH for gram, plasma, serum, GUD swabs etc.
- Copy of approved signed request forms, list of outsourced lab tests and in house testing
- Copy of laboratory manual signed if using outsourced lab, technical protocol –signed on file
- Protocol signed by PI on file
- LN2F in house, for outsourced labs---Lab Notes to file enhance the QC process and enables tracking of any changes to lab procedures and systems within the study
- Memos for laboratory
- In-house validation for rapid testing on file e.g. HIV rapids
- **WHEN IN DOUBT ALWAYS CONTACT PNL-ESTELLE, TED AND LORNA**

Essential Monthly Submissions

- Timeline for documentation submission for on-site lab staff ensures timeous submission to CL for the whole year.
- Follow-up and Timeline docs for DAIDS submission to international reference labs include:
  - Report Cards
  - CAP entry on-line by selected staff for rapid testing for on-site labs
  - Monthly inventory for all MTN sites
  - Conf call monthly and site feedback and challenges
  - Weekly QC of 100% of protocol specific storage
  - 100% LDMS reconciliation with CRFS for samples entered onto LDMS
  - Lab Staff working on study and any changes
  - LN2F submission when ever an event occurs
  - Protocol events submission for lab events e.g. incorrect timing of test

Study-specific Specimen Management Plan

- Each study must have a specimen management plan
- Shipments of specimens -International Air Transport Association (IATA) shipping regulations with certified lab staff and drivers [couriers used]
- Proof of training in IATA shipping regulations (certification) , Trained LDMS technician, Latest version upgrade of LDMS. access to system by LDMS staff
- Weekly export of samples, Weekly QC of 100% protocol specified samples
- **QA control check at each point to ensure adherence**

Laboratory-specific Auditing

- **Internal 100% audit by Central lab on monthly basis per site**
- DAIDS and/or its contractors will conduct laboratory-specific audit visits to determine laboratory readiness.
- PPD will assess blind samples
- International Reference lab will annually assess the on-site labs and outsourced laboratory to ensure conformance to DAIDS and FHI requirements
- FHI will also QC on-site rapid testing.
- Prior to any audits or monitoring, 100% weekly QC must be done for all protocol specified samples, 10% QC of random samples-vertical audit and LDMS documentation, LDMS JD-100% daily QC of samples being entered onto LDMS.
- Follow-up of Corrective Action on LDMS CRF recon with SCHARP
- PPD also checks lab regulatory-this is normally QC on monthly basis as part of monthly QC of on-site labs.

So What is a Lab Violation at MRC HPRU?

- Non-collection of samples as indicated in the protocol
- Non-completion of test at that time point
- Non-conformance to the lab SOPs, IQA and EQA programmes
- Non-qualified/specialized staff performing testing contrary to local council standards
- Constant pick-up on monitoring report after first re-train
- Performance assessed and rostered for annual performance bonus

GCLP Lessons Learnt

- GCLP effectiveness-the lab management must set the example.
- QA checks and control measures at every point of the pre-analytical to the post-analytical phase
- BUT follow-up of all aspects must be done to ensure compliance or the practice will fail.
- Lab Staff who are competent and follow-up.
- Refresher trainings once a month during meetings for all lab staff on DAIDS, CFR part 21, GCLP, GCP, ethics, SANAS and MTN PNL requirements, safety or new procedures on protocol.
- Lab staff awareness and timeline docs so submissions

THANK YOU

QA/QC MONITORING
ON SITE LABORATORY ASSESSMENT STANDARD OPERATING PROCEDURE

SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

Unit Laboratory Co-ordinator_____
Date of Assessment_____
Study/Site of Assessment _____

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OBJECTIVES OF LABORATORY VISIT BY INTERNAL CO-ORDINATOR

1. The On-Site Laboratory:
To check the laboratory workflow, the equipment, the space and ventilation are satisfactory to ensure reliable, reproducible and valid results and the adherence to the Good Laboratory Practice guidelines.

2. Safety in the Laboratory:
To check if the laboratory is a safe environment to work in and all the equipments have been installed properly and safely. To ensure personal protective equipment [PPE] is available and used according to the guidelines of universal precautions.

3. Calibrations and Servicing Of Laboratory Equipment:
To check that the on site equipment are in good working condition, have been calibrated and serviced in order to ensure validity of results.

4. Laboratory Files and Logs:
To perform QA/QC on random files and laboratory logs and to check if relevant information is logged in and if logs are up-to-date and filed in a systematic and methodical way.

5. Source Documents (SD) and Case Record File (CRF):
To perform QA/QC on laboratory source documents and CRF's in random participant files and check for correct result entry, transcription of results from logs, correct signatures and dates ensuring adherence of Good Laboratory Practice guidelines.

6. Lab Results From Outsourced laboratories:
To perform QA/QC on randomly select files and look at the Outsourced laboratory reports and check for Outsourced laboratory headers, Trial name, PID No., visit code, specimen type, specimen collection dates, results interpretation and faxed version of results if the original is not available.

7. Previous Corrective Action Report
To check that the preceding corrective action as per QA/QC monitoring report has been completed and actioned as indicated by the site laboratory.

Mark with a tick where applicable!

1. **GENERAL INFORMATION**

1.1 Laboratory Technologist Name: _____

1.2 Have there been any recent changes in personnel? Yes _____ No_____

1.3 Have there been any recent changes in the facilities or the equipment? (Major repairs, new equipment, etc)?

_____

_____

_____

1.4 When was the lab lasted monitored and by whom?

Internal Monitoring: _____

External Monitoring: