Implementation of Good Clinical Laboratory Practices (GCLP) compliance in H3Africa Projects

Ernest Tambo
AWI-Gen, Overall Coordinator

AWI-Gen Project, 2012-2017
SBIMB,
University of the Witwatersrand,
South Africa
Genomic and environmental risk factors for cardiometabolic disease in Africans

AWI-Gen

Outline

• AWI-Gen Overview objectives and progress

• Key Elements in GCLP in AWI-Gen study across sites
  ➢ Organization and Personnel
  ➢ Facilities, equipment, materials and reagents
  ➢ Standard Operating Procedures (SOPs)
  ➢ Planning, conduct and reporting
  ➢ Quality Control, Assurance and Quality audits
  ➢ Retention of study documentation, archiving and prompt reports.
AWI-Gen

Wits-INDEPTH Partnership: Organization and Personnel

PI, Michele Ramsay
Oduro

Co-PI, Osman Sankoh

Catherine

Norris Shane

Halidou

Herman

Zodwa

Marianne

Tollman

UN Subregions of Africa
- Northern Africa
- Western Africa
- Central Africa
- Eastern Africa
- Southern Africa
AWI-Gen Collaborative Center overview

Wits Health Consortium

SBIMB
- Wits Bioinformatics
- School of Pathology
- School of Public Health
- DPHRU

AWI-Gen
Wits-INDEPTH Partnership

INDEPTH Board

INDEPTH Network
- Agincourt
- Dikgale
- Navrongo
- Nairobi
- Nanoro

High Impact Science – Tangible Benefits
Genomic, Genetic and Bioinformatics
Training and empowerment
Resource and Infrastructure development
Focus on disease and population health
Leading Healthier Lifestyle Changes
World Bank – Change in burden of disease (1990 to 2010)

WEST AFRICA

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<td>HIV/AIDS</td>
<td>483%</td>
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<td>Road Injury</td>
<td>112%</td>
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<td>Malaria</td>
<td>79%</td>
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<td>Cirrhosis</td>
<td>74%</td>
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<td>Sickle Cell</td>
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CENTRAL AFRICA

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<td>Malaria</td>
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<td>TB</td>
<td>57%</td>
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<td>Neonatal encephalopathy</td>
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<td>Meningitis</td>
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NORTH AFRICA AND MIDDLE EAST

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<td>Road injury</td>
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<td>Ischaemic heart disease</td>
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EAST AFRICA

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<td>Neonatal sepsis</td>
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<td>Neonatal encephalopathy</td>
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<td>Preterm birth complications</td>
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SOUTHERN AFRICA

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<tr>
<td>Interpersonal Violence</td>
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<tr>
<td>Diabetes</td>
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<td>Major depressive disorder</td>
<td>47%</td>
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<td>COPD</td>
<td>38%</td>
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<tr>
<td>Stroke</td>
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Change in obesity (1980 to 2008)

Stevens et al. Population Health Metrics 2012, 10:22
http://www.pophealthmetrics.com/content/10/1/22
AWI-Gen project aims

i. **Build sustainable infrastructure** (laboratories and biobank) and capabilities for genotyping and for genomic research on the African continent

ii. **Understand the genomic architecture of sub-Saharan populations from west, east and south Africa to guide genomic studies.**

iii. **Investigate the independent and synergistic genomic contributions to body fat distribution (BMI, hip/waist circumference, subcutaneous and visceral fat) in the populations considering the relevant environmental and social contexts.**

iv. **Investigate the effect of obesity and fat distribution on the risk for Cardiometabolic diseases in the cohort/longitudinal cohorts** (across six Centres in Africa (~12 000 individuals))
Overview of the progress

• **Phase 1 population structure studies**

  All samples and data from selected ethnic groups have been collected from all six AWI-Gen sites and will be part of H3 Africa Genomic samples for sequencing and Cardio-metabolchips.

• **Genomic studies**

  The pilot site Soweto, South Africa have enrolled so far 1,764 (1,000 women and 764 men) and plan to complete at early January 2015.

• **Nairobi, Burkina Faso, Ghana, Agincourt and Dikgale** have all secured their Ethical Clearance and plan to start in November 2014.
Soweto Roll out sheet
2013-2014

Total enrolled in AWI-Gen Soweto Pilot site
Women= 1000
Men = 764

Number of Participants

2013
2014

Months
Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep
Why H3Africa GCLP compliance?

- Best practices and quality assurance issues have become of paramount importance in all clinical studies and trials.

- The implementation of GCLP in clinical study and laboratories is essential for quality data and data sharing.

- What is quality data and How do we define quality in clinical research?
GCLP requirements relating to Standard Operating Procedures (SOPs)

- **Key Compliance Indicators**
  - Trained and qualified personnel/retraining
  - Field/Lab SOPs validation, Design and planning
  - Risk management, Preventive and Corrective measures
  - Stepwise QC/QA process
  - Calibration frequency daily/weekly
  - Accuracy daily
  - Precision daily
  - Document control and continuous performance+
  - Validation and Verification
  - Reproducibility
  - Data management, safety and security
  - Suitability and stock of reagents
  - Errors (systemic errors and Random errors & ambiguity)

- QUALITY DATA required achieving below 5% coefficient of variation (CV)
  - Questionnaire
  - Samples collection and processing
  - Equipment and SOPs
  - Anthropometric measurements
  - Ultrasound measurements
  - Each will need to scan 15 volunteers twice on each of the above (SCAT, VAT & CiMT)
AWI-Gen DATA

- **Demographic Data Collection** using a barcoded AWI-Gen informed consent and questionnaire (Age, Gender, family health history, Diet, Physical activity and substance use/abuse)

- **Phenotypic Data Collection** (Standing height, Weight, Waist and Hip Circumference and cIMT/VAT/SCAT)

- **Sample Collection** (1) Fasting Blood or Saliva, (2) spot Urine

- **REDCap** data Online tool and Quality control

- **Genetic and Genomic Markers of cardiometabolic risk** using Genomic Wide Association Studies or Exome sequencing.

- **Cardiometabochips in assessing risk factors and obesity related diseases**

- **Data and Samples Management & Biobanking**
Key Elements: Facility

- DEMONSTRABLY FIT-FOR-PURPOSE (QUALITY SAMPLE/DATA)
- Trained and qualified staff
- Size and Space
  - suitable size, structure and location
  - space to avoid sample mix-up or contamination
    - separation of activities
    - Restricted access?
  - storage areas
    - temperature controlled, monitored, limits set, alarmed, back up
- Risk management both in Labs, field and logistics
- good housekeeping
Equipment and Standard Operating Procedures

Facilities, Equipment & Reagents

• Equipment
  ➢ Mastering and acceptance testing prior to use
  ➢ Appropriately maintained & calibrated
    ➢ With records to demonstrate this
    ➢ Trend analysis of calibration checks?
    ➢ Validated computer systems in use
    ➢ May need to keep records of usage

➢ Reagents
  ➢ Suitable labelled and stored

Standard Operating Procedures

• Approved by WITs-INDEPTH management
• Controlled historical file maintained.

• To cover areas such as:
  ➢ Format, control and review of SOPs
  ➢ Sample handling-receipt, chain of custody, storage, repeat analysis, etc
  ➢ Methods or control of methods
  ➢ Equipment use and maintenance
  ➢ Record keeping

• QA/QC & Audit procedures
• Documentation, reporting and archiving

• Data safety and security (secure storage & unauthorised access)
AWI-Gen comprehensive program ensuring compliance to GCLP

**Quality Audits**

- Quality Assurance and Quality control
- The quality sample and data audit system
- Audits of safety labs and GCLP compliance
- Biweekly Study coordinator or Monthly internal meetings & audits by site staff

**Challenges**

- Critical non-compliance
- Major non-compliance
- Minor non-compliance
- Inspection and evaluation of field(s) and laboratories performance
AWI-Gen Community Engagement

AWI-Gen community Mobilizers
Adapt to the local context and realities

Digkale, SA

Nairobi, Kenya
AWI-Gen site staff training and QC

AWI-Gen field Training sessions

Oct 2014

Digkale, SA
AWI-Gen Cooperative Learning & Quality checks
## AWI-Gen Staff performance Assessment (Intra/Inter-variability)

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AWI-Gen RedCaP and LIMS systems

- Real time RedCaP data capturing
- Real time RedCaP data independent QC (aspect specific)
- Real time RedCaP data curation
- Real time RedCaP data sharing & policies
- Online Real time RedCaP & LMIS analysis & data

Data security
Samples security
Anonymous and confidentiality
Quality in clinical research may be defined as...

- **Reliability and credibility of information**
  providing an answer to a scientific question
- **Compliance** of the study process with defined requirements
AWI-Gen Show cards tools

- CE/IC show card for participants
- CE/IC take home card
- Obesity show card
- Cardio disease show card
- GPAQ show card
- Alcohol show card
- Diet show card

- AWI-Gen training manual
- AWI-Gen reporting system

(AWI-Gen Study Coordinator forum & AWI-Gen data manager meeting)
AWI-Gen research participants requirements

All AWI-Gen Sites have secured Ethical Clearance

Ethical standards: Declaration of Helsinki

Law & regulations/local legislation

Good practice standards: ICH GCP, ICH, GLP

AWI-Gen sites community engagement have been done
AWI-Gen Quality Management System, definition based on ISO 9000

- A set of interacting elements established to direct and control an organisation with regards to quality
- QMS is a tool to establish and continuously & consistently achieve quality objectives based on project’ requirements.
- In clinical research these objectives are:
  - Compliance with ethical, regulatory and GXP standards
  - Credibility and reliability of clinical data
AWI-Gen standard components of Quality Management System

Quality Assurance

Quality Control

AWI-Gen Protocol

Collection & Analysis of data

Training, CV

Project report

Standardized Procedures
AWI-Gen Quality Control

- Activities & techniques applied to ensure that data/samples consistently fulfil requirements
  
  systematic checks on project compliance, credibility of data process & reliability

  - Performed at every step of AWI-Gen project
  - Applied to each stage of data/samples handling.
Quality Control

Sponsor approval & sign off

monitoring of investigational sites

proof-reading, validation, generation of queries

identification of non-PPT cases

Protocol

Collection of data

Pooling of data in the database

Analysis

Project report

IEC approval

analysis of outlier data variability & trends approval & sign-off
AWI-Gen Quality Control Process

Every AWI-Gen staff

Centre designated RedCap data manager

Centre designated staff responsible for aspects of QA/QC (IC, Q, Anthro, Ultrasound, redcap...)

Centre AWI-Gen Project Manager and PI

Overall AWI-Gen Project Manager and PI/CoPI on all aspects of QA/QC (IC, Q, Anthro, Ultrasound, redcap...)
Quality Assurance audits

- Project specific audits
- Systems audits

System: A selected process plus all related activities, resources, organisation, documents (including SOPs & records), facilities and equipment

e.g.: Pharmacovigilance, Data Management
QA specific audits plans

Audit of the study protocol

Audit of sites

Audit of database

Audit of report

Protocol

Collection of data

Pooling of data in the database

Analysis

Report

Audit of CRF, IB

Audit of graphs, tables & stats
QA systems audits

Audits of computerised data collection systems (validation audits)

Audit of monitoring system

Audit of management & distribution system

Audit of document management & archiving

Collection & Handling of data

Audits of central lab & other service providers

Audit of sponsor’s pharmacovigilance system
Benefit of AWI-Gen QMS

It supports continuous quality improvement

Implement recommendations
QA audits
QC activities

development of trial protocol & instructions training,
AWI-Gen process in line with SOPs
Conclusions

The overall AWI-Gen study relies on

- COMPLIANCE with requirements and credibility & reliability of Quality data

AWI-Gen Quality Management System rely on its set of tools and show cards to ensure, maintain and improve participant understanding and quality data samples and collection

- Improved quality systems, results, greater efficiency and teamwork are the key benefits.
Thanks!!!