

# Assessment of 21 Clinical Trial Sites in Africa to Measure their Readiness to conduct GCP/GLP-compliant Trials for new TB therapies

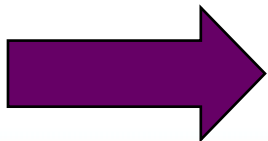
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Fourth EDCTP Forum,  
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GLOBAL ALLIANCE FOR  
TB DRUG DEVELOPMENT

## History of the TB Alliance

- Cape Town Declaration – Feb 2000
  - Hosts: Rockefeller Foundation & MRC S. Africa
  - Over 120 organizations (health, science, philanthropy and private industry)
- Results
  - Support goals of Stop TB Initiative
  - Create Scientific Blueprint
  - Develop Pharmacoeconomic Analysis



**Build a Global Alliance for TB Drug Development**

# The Global Alliance for TB Drug Development (The TB Alliance)

- International Public-Private Partnership (PPP)
- Independent, not-for-profit organization
- Based in New York, Brussels and Pretoria
- Entrepreneurial, virtual R&D approach
  - Out-source R&D to public or private partners, CROs, collaborators

# The TB Alliance

## *Mission*

- Discover and develop new, better and faster acting treatments for TB
- Ensure **A**ffordability, **A**ccess and **A**doption (AAA)
- Coordinate and catalyze TB drug development activities worldwide

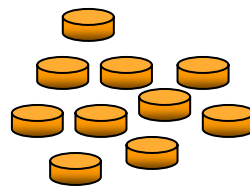
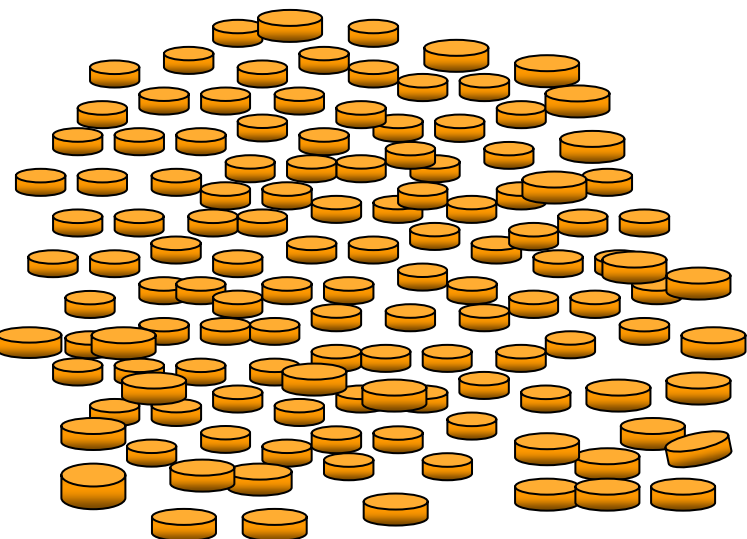
# VISION

*Shorten and Simplify*

*6 months*

*2 months*

*10 days*



**130 doses**

**10 doses**

# TB Drug Development Past and Present

- The current TB drugs were developed in the 1940's to 1960's when the process of developing new drugs and the regulatory environment differed significantly from today's
- The present decade has seen a reawakening of TB drug research and development
  - the largest number of early-stage projects and TB drugs under development in history
  - seven products in clinical development

## Global Clinical Trials Capacity

- Can global clinical trial capacity meet GCP/GLP registration standards Phase II and III trials to meet current and future needs?
- No objective assessment of the situation has been done
- Benefit sites directly, sponsors of clinical trials, and ability to generate resources to build global clinical trial capacity

# **Clinical Trial Sites**

## **Assessing & Building Infrastructure**

### **Objectives**

- Assess global site capacity for conduct of Phase II (including Early Bactericidal Activity studies) and Phase III GCP/GLP standard TB drug trials
- Develop user-friendly database of assessed clinical trial sites and associated laboratories, for utilization by a broad audience

# Clinical Trial Sites

## Assessing and Building Infrastructure

### Approach

- **Develop comprehensive site- & laboratory evaluation questionnaire**
  - **Primary clinical site**
  - **Pharmacy**
  - **Information systems, communication and data management**
  - **Laboratory: Mycobacterium & Safety; QC/QA**
  - **Regulatory and Ethics Committee (IRB or IEC) environment and procedures; Importation requirements**
  - **Satellite Site(s) – if applicable**
  - **TB & HIV Specific Information**
- **Conduct assessments – clinical and lab (*M.tb* and safety labs)**
- **Design, develop and deploy database**

# Clinical Trial Sites

## Assessing & Building Infrastructure

### Activities

- 2 CROs hired
  - PPD for S. America
  - Quintiles for Asia, Africa, N. America and Europe
- 2 internationally-recognized *M. tb* lab experts hired to ensure quality of TB lab evaluations
  - Dr. Kathleen Eisenach, University of Arkansas for Medical Sciences, USA
  - Dr Frederick Sirgel, Medical Research Council, South Africa



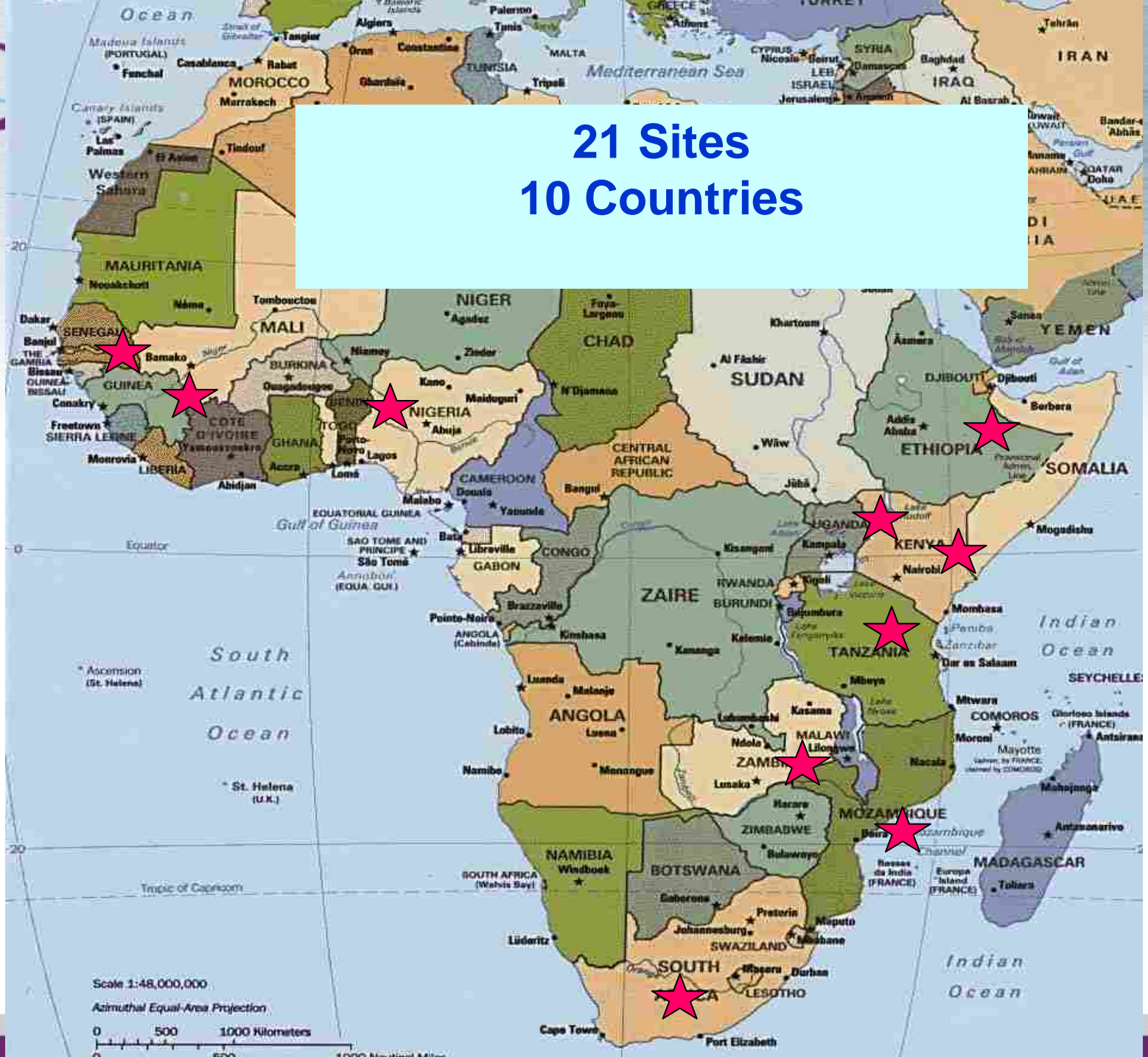
## Sites Assessed

**51 Sites**  
**25 Countries**  
**10 Languages**  
**5 Continents**  
**2 CROs**  
**1 Tool**

**Consistency and Integrity of  
Information Across Sites**



# 21 Sites 10 Countries



## Geographical Distribution of 21 Africa Sites and Laboratories Assessed

» Benin:	1
» Ethiopia:	1
» The Gambia:	1
» Guinea:	1
» Kenya:	1
» Mozambique:	1
» South Africa:	7
» Tanzania:	3
» Uganda:	3
» Zambia:	2

## Per Site Summaries

For each clinical site and each laboratory:

- Estimated time required to ready site for participation in a registration-standard, Phase III TB drug trial or an EBA trial –specified:
  - **< 6 Months**
  - **6 -12 Months**
  - **1 - 2 Years**
  - **> 2 Years**
- Capacity-building recommendations

# CLINICAL SITES: Time Required to Ready Site for Participation in a Phase III TB Drug Registration Trial

	< 6 Months	6 - 12 Months	1 - 2 Years	> 2 Years
<b>Southern Africa - 10</b>	<b>4</b>	<b>6</b>	<b>0</b>	<b>0</b>
<b>East Africa - 8</b>	<b>8</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>West Africa - 3</b>		<b>2</b>	<b>1</b>	<b>0</b>
<b>TOTAL - 21</b>	<b>12</b>	<b>8</b>	<b>1</b>	<b>0</b>

## LABORATORIES:

# Time Required to Ready Laboratory for Participation in a Phase III TB Drug Registration Trial

	< 6 Months	6 - 12 Months	1 - 2 Years	> 2 Years
<b>Southern Africa - 7</b>	<b>1</b>	<b>3</b>	<b>3</b>	<b>0</b>
<b>East Africa - 7</b>	<b>3</b>	<b>1</b>	<b>2</b>	<b>1</b>
<b>West Africa - 3</b>	<b>0</b>	<b>0</b>	<b>2</b>	<b>1</b>
<b>TOTAL – 17*</b>	<b>4</b>	<b>4</b>	<b>7</b>	<b>2</b>

\* 3 sites in South Africa use the same lab and 2 sites in Uganda use the same lab

# Time Required to Ready Site and Laboratory for Participation in a Phase III TB Drug Registration Trial

	< 6 Months	6 - 12 Months	1 - 2 Years	> 2 Years
<b>Southern Africa - 10</b>	<b>0</b>	<b>6</b>	<b>4</b>	<b>0</b>
<b>East Africa - 8</b>	<b>4</b>	<b>1</b>	<b>2</b>	<b>1</b>
<b>West Africa - 3</b>	<b>0</b>	<b>0</b>	<b>2</b>	<b>1</b>
<b>TOTAL - 21</b>	<b>4</b>	<b>7</b>	<b>8</b>	<b>2</b>

## Laboratories accredited and/or a quality assurance system and/or a quality manual in place

Laboratories	Accreditation	Quality Assurance System	Quality Manual
Southern Africa - 7	1	3	2
East Africa - 7	1	1	0
West Africa - 3	0	0	0
<b>Total - 17</b>	<b>2</b>	<b>4</b>	<b>2</b>

**Laboratories with SOPs in place,  
comprehensive, implemented and regularly  
reviewed**

<b>Laboratories</b>	<b>SOPs Available</b>	<b>SOPs Comprehensive</b>	<b>SOPs Implemented</b>	<b>SOPs Regularly Reviewed</b>
<b>Southern Africa - 7</b>	<b>7</b>	<b>3</b>	<b>6</b>	<b>2</b>
<b>East Africa - 7</b>	<b>7</b>	<b>1</b>	<b>3</b>	<b>2</b>
<b>West Africa - 3</b>	<b>2</b>	<b>0</b>	<b>1</b>	<b>2</b>
<b>Africa - 17</b>	<b>16</b>	<b>4</b>	<b>10</b>	<b>5</b>

# Laboratories capable of performing drug-sensitivity testing and TB strain typing

Laboratories	Drug-sensitivity Testing	TB Strain Typing
Southern Africa - 7	6	6
East Africa – 7	3	3
West Africa – 3	3	2
<b>Total – 17</b>	<b>12</b>	<b>11</b>

## User-friendly Database

- All data stored in a single database
- System consists of two main areas
  - Site / Laboratory Information
  - Supporting Documents and Policies
- Open to broad audience of relevant stakeholders (drug sponsors, trial, sites)

[www.tballiance.org](http://www.tballiance.org)

## Summary

- Overall, clinical sites in a more advanced state of readiness than laboratories.
- Many of the laboratories were not certified or accredited and did not have a quality control system nor quality control manuals in place .
- Although SOPs were in place, in many instances, they did not cover all the laboratory areas and are not reviewed annually.

## **Conclusion**

**Need to develop adequate clinical trial site and laboratory capacity in many of the high burden countries to meet the global registration of new, improved treatment regimens in appropriately diverse populations.**