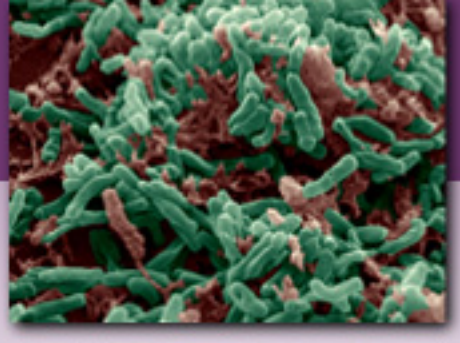

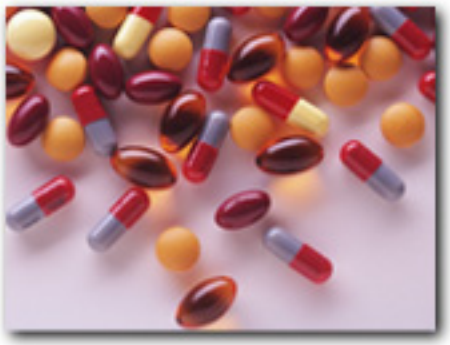

Assessment of 21 Clinical Trial Sites in Africa to Measure their Readiness to conduct GCP/GLP-compliant Trials for new TB therapies

Christo van Niekerk, MD, FCPaed, MFPM

Fourth EDCTP Forum,
Ouagadougou, Burkina Faso
22-24 October 2007

GLOBAL ALLIANCE FOR
TB DRUG DEVELOPMENT

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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

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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

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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

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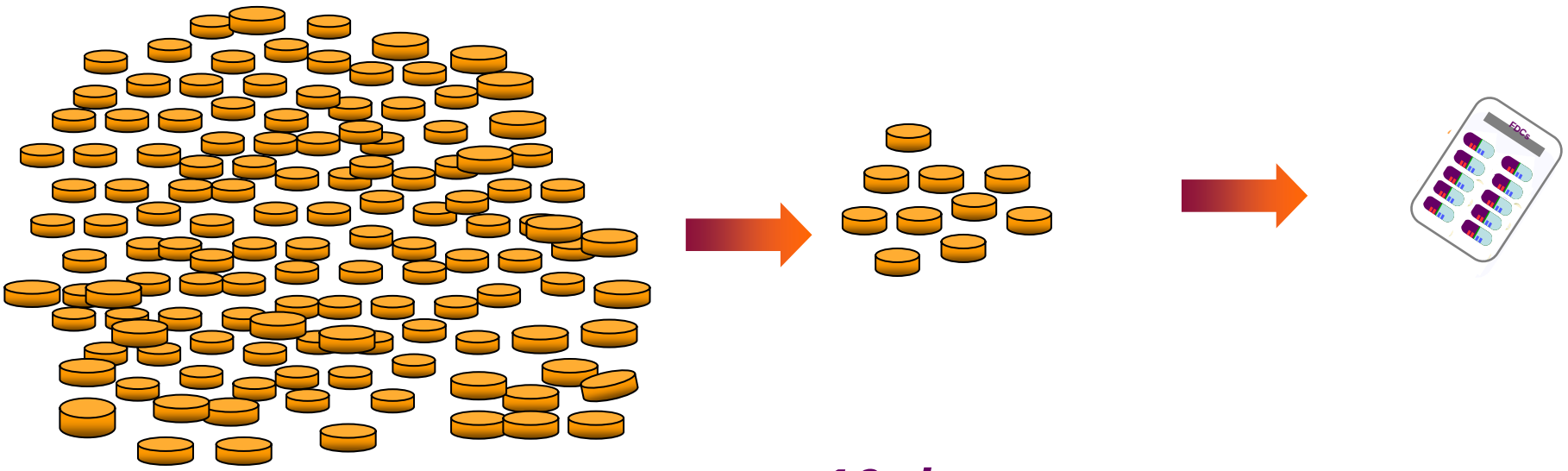
VISION

Shorten and Simplify

6 months *2 months* *10 days*



130 doses ***10 doses***

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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

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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

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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

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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

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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

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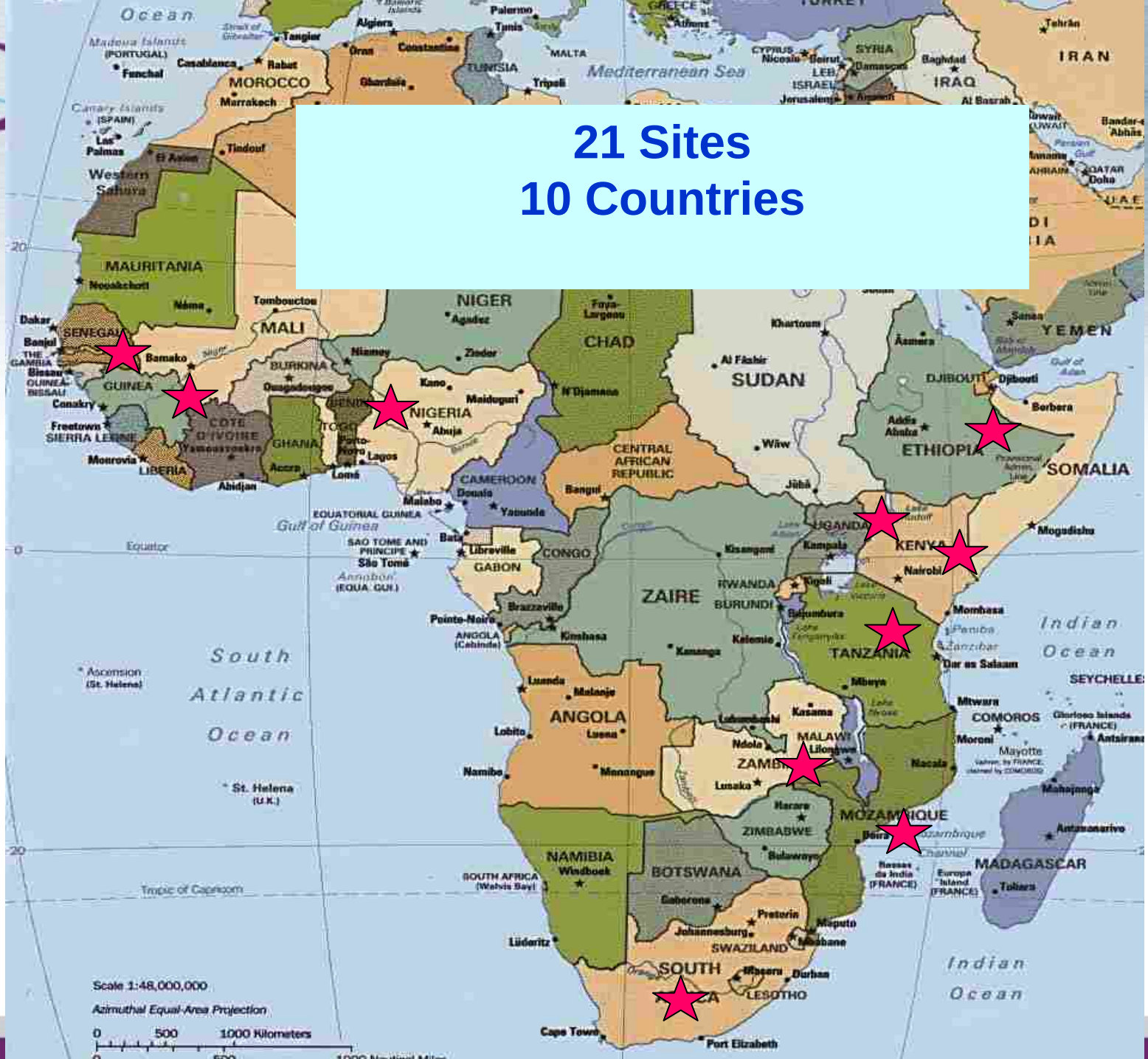
Sites Assessed

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

Consistency and Integrity of Information Across Sites


21 Sites
10 Countries
Mediterranean Sea
MOROCCO
MAURITANIA
SENEGAL
MALI
NIGER
CHAD
SUDAN
NIGERIA
GUINEA
BURKINA
GHANA
COTE D'IVOIRE
LIBERIA
SIERRA LEONE
CAMEROON
CENTRAL AFRICAN REPUBLIC
ETHIOPIA
SOMALIA
KENYA
UGANDA
ZAIRE
RWANDA
BURUNDI
TANZANIA
CONGO
GABON
ANGOLA
ZAMBIA
MALAWI
MOZAMBIQUE
ZIMBABWE
NAMIBIA
BOTSWANA
SOUTH AFRICA
SWAZILAND
LESOTHO
MADAGASCAR
COMOROS
SEYCHELLES
YEMEN
IRAN
IRAQ
SYRIA
Equator
South Atlantic Ocean
Indian Ocean
Tropic of Capricorn
Scale 1:48,000,000
Azimuthal Equal-Area Projection
0 500 1000 Kilometers

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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

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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

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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
Southern Africa - 10	4	6	0	0
East Africa - 8	8	0	0	0
West Africa - 3		2	1	0
TOTAL - 21	12	8	1	0

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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
Southern Africa - 7	1	3	3	0
East Africa - 7	3	1	2	1
West Africa - 3	0	0	2	1
TOTAL – 17*	4	4	7	2

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

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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
Southern Africa - 10	0	6	4	0
East Africa - 8	4	1	2	1
West Africa - 3	0	0	2	1
TOTAL - 21	4	7	8	2

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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
Total - 17	2	4	2

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

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

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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
Total – 17	12	11

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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

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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.

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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.