



International Union
Against Tuberculosis
and Lung Disease

Promoting lung health in low- and middle- income countries

TREAT TB Update

Union Technical Consultants' Meeting
October 31, Lille



Technology, Research, Education, and
Technical Assistance for Tuberculosis



USAID
FROM THE AMERICAN PEOPLE

TREAT TB Update

- **Activity Update**
- **Challenges on STREAM Trial**
- **Financial Status**
- **Future Direction**

Challenges of STREAM



Current Focal Areas of TREAT TB

- Diagnostic Tools Initiative
- STREAM
- Country Support for Operational Research



Diagnostic Tools Initiative

PROVE IT

TREAT TB and its local partners are currently implementing an evaluation of Line Probe Assays called “Policy Relevant Outcomes from Validating Evidence on the Impact of Line Probe Assay” (PROVE IT) in Brazil, Russia, and South Africa.

The three evaluations began in 2011 and are expected to end in 2013.



Diagnostic Tools Initiative

Modelling

TREAT TB partners at the Liverpool School of Tropical Medicine, Harvard University, and the National University of Taiwan created an innovative modelling approach that combines the elements of operational and transmission models.

The modelling team is currently refining the model to assess diagnostic tools for drug-resistant TB and to evaluate Xpert MTB/RIF.



Diagnostic Tools Initiative

Systematic Reviews

TREAT TB and its partner, McGill University are currently conducting systematic reviews on two important issues in TB control:

- Systematic Review to Assess Quality and Methodologic Determinants of Economic Analyses in TB Research.
- Assessing the feasibility of implementing a new diagnostic test in resource limited settings.



Diagnostic Tools Initiative

Mapping Tool

TREAT TB created a webtool that provides a comprehensive overview of ongoing research activities assessing Xpert MTB/RIF worldwide.



The tool can be found on the TREAT TB website.

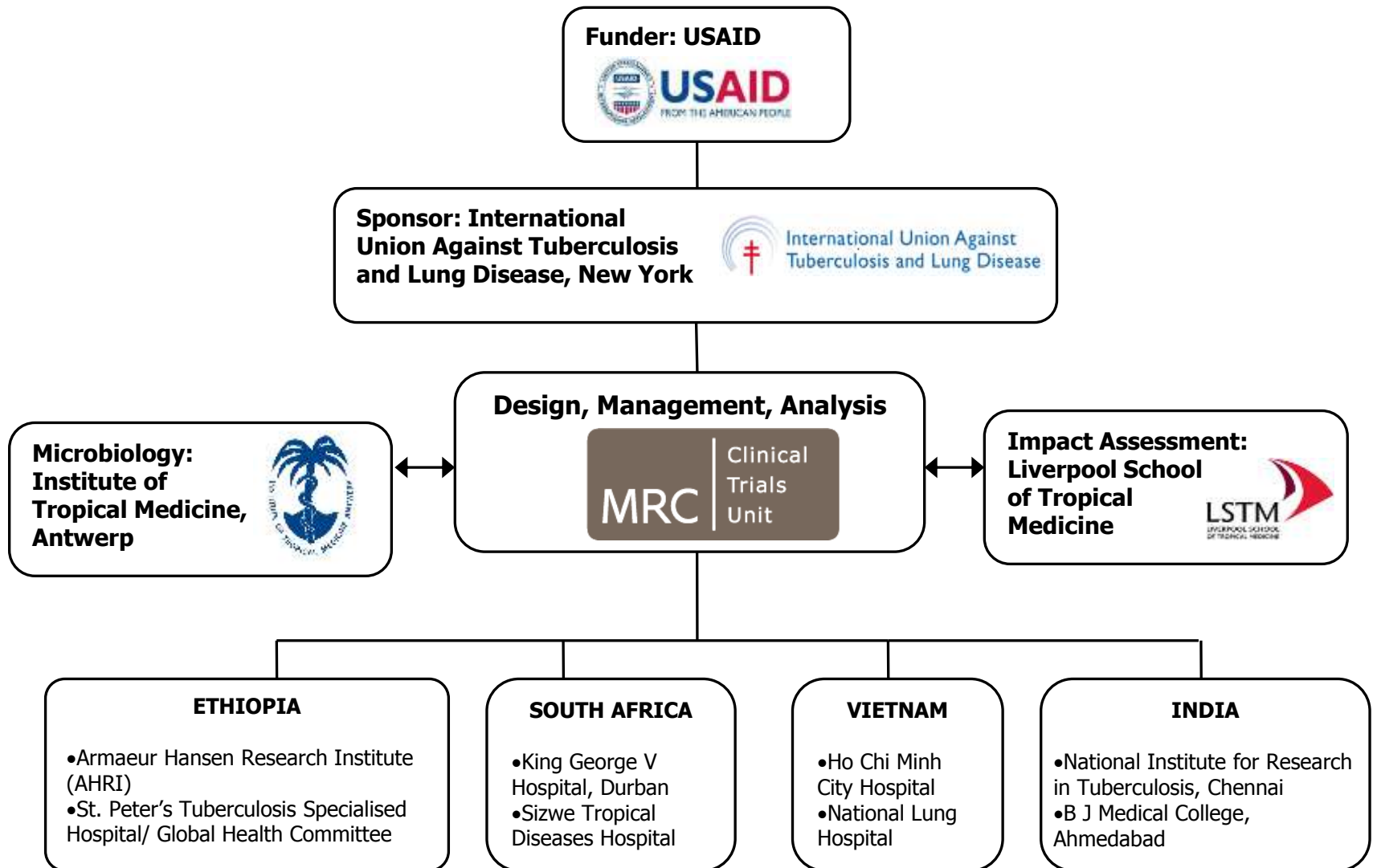


STREAM

- In partnership with the MRC-UK, TREAT TB will evaluate a standardized, 9-month regimen of anti-tuberculosis drugs for MDR-TB patients ('Bangladesh regimen') compared to the local WHO standardised regimen
- Recruitment to begin in January, 2012

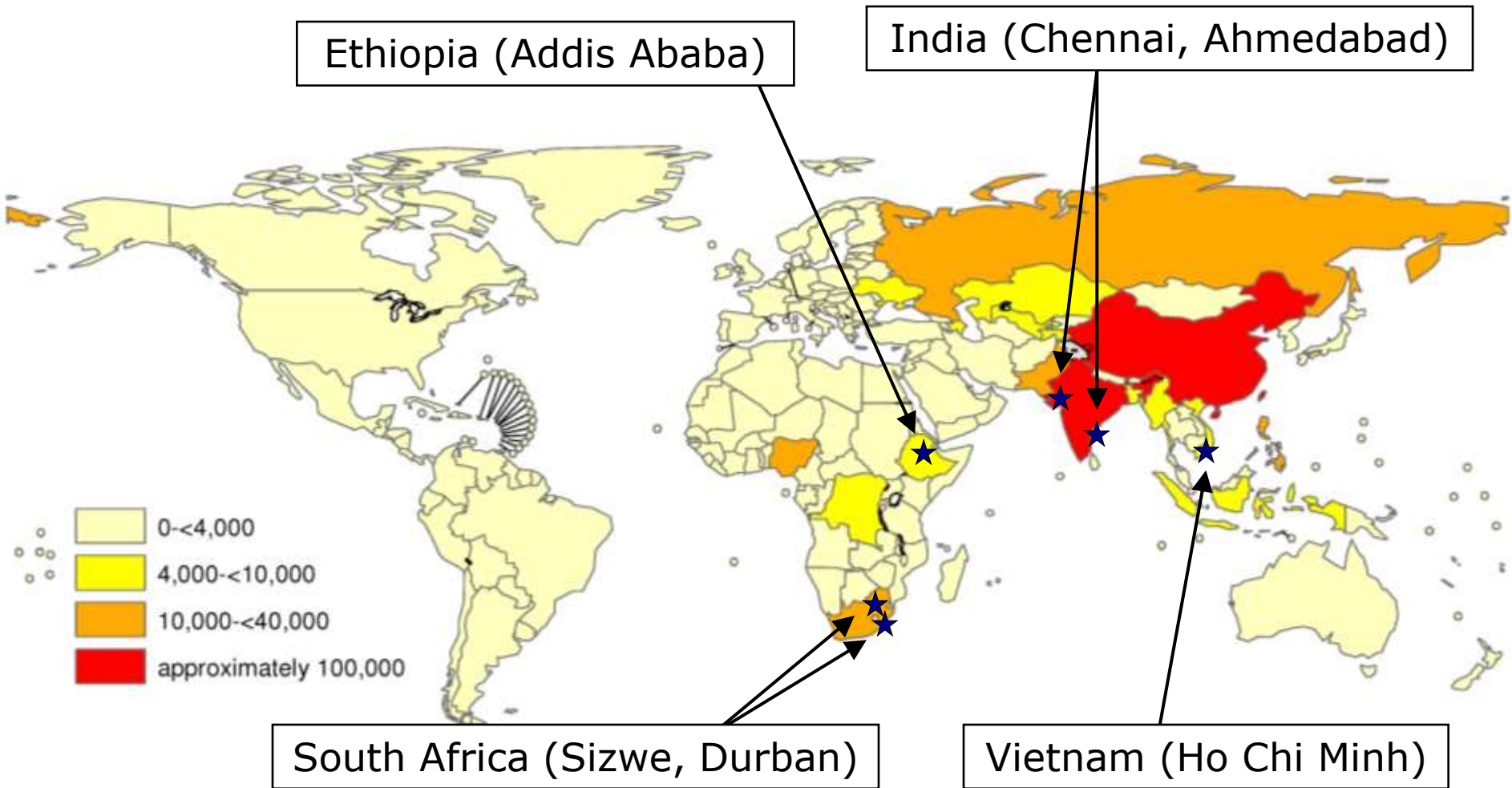


STREAM Partners



STREAM Sites

(Estimated absolute number of MDR-TB cases, 2009)



STREAM

- Within each country aim to recruit 100 patients (2:1 randomization of study regimen to control regimen)
- 387 patients in total required to demonstrate non-inferiority
- 80% power assuming 70% favourable outcomes in the control regimen and 75% in the study regimen and a 10% margin of non-inferiority (lower limit of 95% CI of difference)
- Will also conduct economic analyses at health system and patient levels



Challenges of STREAM

- Availability of Study Regimen
- Approvals and authorizations
- Finances
- Timelines



Availability of Study Regimen

- Principle of STREAM was to replicate the 'Bangladesh' regimen as closely as possible
- Unable to secure gatifloxacin with adequate GMP documentation to allow importation to study countries
- Necessitated move to alternative FQ for which experience with high dosing is limited



FQ Safety Issues

- Moxifloxacin causes QT prolongation
 - At standard dose approx 10-14msec
- QT prolongation related to plasma concentration
- Limited data on higher doses
 - No evidence of major problem



FQ Safety Issues

- STREAM precautions and monitoring:
 - Exclusion of patients with baseline QTc \geq 500ms
 - ECG monitoring: 2 hrs, 4 hrs, weeks 1-4, 12, 24, 36
 - 24 hour ECG for patients with QTc \geq 450msec
 - Discontinue moxifloxacin if QTc \geq 500msec
(Unless another cause identified)
 - IDMC review of ECG data



Approvals and Authorizations

- Multiple approvals and authorizations required at country level which differ by country and can be dynamic in nature and number
- Approvals include ethics approvals at multiple levels and Ministry of Health review/approval
- Authorization to import medicines and other study equipment requires completion of approval process(es)



Trial Finances

- Revised study budget much less than originally anticipated
- Anticipated shortfall remains in funds needed to complete trial
- USAID funding cycle and regulations create additional implementation challenges
 - annual funding cycle
 - staff support restrictions

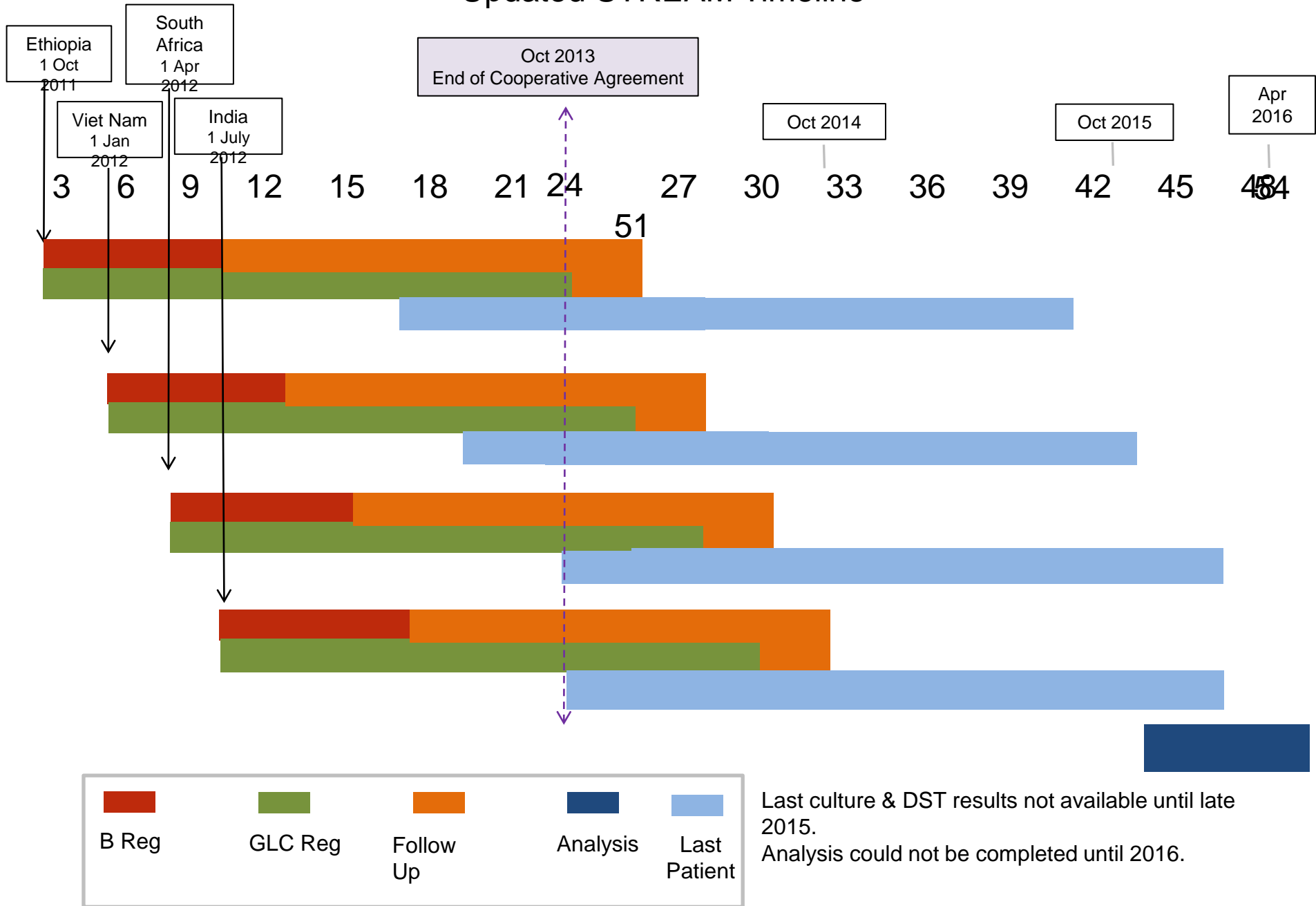


Trial Timeline

- Timeline of STREAM extends well beyond end of Cooperative Agreement (September 30, 2013)



Updated STREAM Timeline



Country Support

- TREAT TB is currently working with the Desmond Tutu TB Centre in South Africa to implement the Operational Research Assistance Project (ORAP)
- TREAT TB will work closely with the Union South East Asia Office to implement a new Mission supported project on several aspects of research in India, including support of the STREAM trial



Financial Status

- CORE budget for year four (October 1, 2011 to September 30, 2012) of USD 5.3 million (flat from previous year)
- Mission support for year four (South Africa and India) totaling USD 2.3 million
- Carry forward of USD 2.1 million from years 1-3 for a total planned expenditure of USD 9.7 million in year four



Future Direction

- Successful completion and dissemination of current research portfolio
- Increase awareness and uptake of innovative approaches utilized in TREAT TB e.g. impact assessment and policy transfer analysis
- Remain responsive to dynamic research needs and gaps contingent on available funds
- Work with USAID and other partners to mobilize necessary resources to complete current research efforts





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