The CPTR Initiative: Mission and Objectives

Debra Hanna, Critical Path Institute
Accelerate the development of new, safe, and highly effective regimens for TB by enabling early testing of drug combinations.
The Challenge

- Need emphasis on combination study approaches rather than development of single agents
- Increasingly “fragile” TB drug development pipeline with the continued divestment of companies in the Anti-infective space
- Emerging need to accelerate the development of a clinically useful, WHO-qualified, regulatory approvable IVD assay for rapid TB-DST
CPTR Charter Has Expanded

Accelerate the development of a regulatory approvable in vitro diagnostic assay for rapid drug susceptibility testing of TB to facilitate drug development and rational use of new drug regimens.

In Partnership with NIAID
CPTR Organizational Structure

Biomarkers WG

Regulatory Science Consortium

Global Regulatory Pathways WG

Research Resources Group

Drug Development Coalition

In Partnership with NIAID
Rapid DST Consortium

Role in Enabling & Accelerating the Process:
• Support the development of iterative Target Product Profiles (TPP’s)
• Increase understanding of resistance trends to support rapid DST development
• Develop models that inform TPP’s and policies for use of DST
• Facilitate development of rapid DST assays that could be commercialized
• Reach scientific consensus by sharing expertise, information, data and database are key
CPTR Governance

CPTR Working Group

Coordinating Committee

LEGAL FRAMEWORK

- Regulatory Science Consortium
  - CRITICAL PATH INSTITUTE

Coordinating Committee

- Rapid DST Consortium
  - CRITICAL PATH INSTITUTE

Research Resources Group

- Bill & Melinda Gates Foundation
- Reagan-Udall Foundation
  - Food and Drug Administration

Drug Development Coalition

- TB Alliance
  - Global Alliance for Drug Development
Consortia “Principles”

• CPTR is a Global Consortium designed to meet the TB Global Health need

• Designed with the intent to align TB Drug Developers, Clinicians, Academicians, Government Agencies (etc.) with DST developers to ensure specifications for programs meet the needs of this community

• Purposeful alignment with CPTR Global Regulatory Pathways team consisting of:
  ✓ Regulatory experts from Industry
  ✓ WHO
  ✓ National Regulatory Agencies in countries of high burden
  ✓ FDA/EMEA
Confidentiality Basic Principles

• Each Member is obligated to maintain confidentiality of each other Member’s Confidential Information

• Member Confidential Information to be used solely for authorized Consortium purposes

• No requirement that a Member contribute any particular Confidential Information belonging to such Member

• HOWEVER it is each Member’s duty to share Confidential Information relevant to Consortium activities

• Ultimate goal of Consortium is broad public dissemination of Tools
Supporting Database Rationale

Expansion and evolution of CPTR Clinical trial database to support Rapid Diagnostic Consortium to enable:

The development of Rapid DST’s for existing and novel TB Drug Regimens

✓ Research and development
✓ Surveillance
✓ Resistance data to inform public health and clinical trials
✓ Biomarkers
✓ Clinical Use

Meet Health Authority Standards to support validation of approved tools and assays.

✓ Compliant with health authority requirements for IVD claims
<table>
<thead>
<tr>
<th>Work Group</th>
<th>Focus and Purpose</th>
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<tbody>
<tr>
<td>Enabling Science WG</td>
<td>Focus on the discovery and validation of the molecular basis for resistance and correlation of resistance with clinical outcome.</td>
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<tr>
<td>Assay Development WG</td>
<td>Facilitate developing Rapid TB DST assays to meet target product profiles &amp; coordinating with industry to develop commercial in vitro diagnostic assays for TB DST, meeting target product profiles.</td>
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<tr>
<td>Economic Assessment/Impact Modeling WG</td>
<td>Develop models that will inform decisions needed to develop target product profiles and to inform policy about use of DST with anticipated TB drug regimens.</td>
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DST TPPs Will Be Iterative

Existing

1st line regimens...
2nd line regimens...

Pipeline

Round 1 DST TPP for Industry (-PZA?)
November 2014 Round 2 TPP for Industry (+PZA?)
3/30/2015 Alere Case Detection Test

Future

Development/Clinical Trials/WHO Endorsement/Health Authority Approval

ReMOX launch? PaMZ PhIII clinical trial PaMZ launch? New regimen PhIII clinical trials

Stages:
- DST Consortium
- 10/31/2013 Round 1 DST TPP for Industry (-PZA?)
- 3/31/2013 Round 2 TPP for Industry (+PZA?)
- November 2014 Round 2 TPP for Industry (+PZA?)
- 3/30/2015 Alere Case Detection Test
- 6/30/2015 Alere Drug Resistance Test

Timeline:
- Oct 2013
- Jan 2014
- Apr 2014
- Jul 2014
- Oct 2014
- Jan 2015
- Apr 2015
- Jul 2015
- Oct 2015
- Jan 2016

July 4, 2013
January 2, 2016
Value of Data Sharing, Standards & Pooling

**Start Point**

- Nine member companies agreed to share data from 24 Alzheimer’s disease (AD) trials
- The data were not in a common format
- The data were remapped to the CDISC AD standard and pooled

**Result**

- A new clinical trial simulation tool was created and has been the first model endorsed by the FDA and EMA
- Researchers utilizing database to advance research

- Integrated database
- 24 studies, >6500 patients
- Database open to >200 qualified research teams in 35 countries
A Concept for Partnership Between CPTR & NDWG

Linking Global TB Sequence Researchers

- TB sequence community inputs
- Expert review to advance investigational biomarkers to validated status
- Can use separate or consolidated DBs
- FDA compliant CDISC architecture for regulatory submission DB

Approved members
- Academic labs
- Reference labs
- Commercial companies
- Others...

CPTR TB Drug Resistance DB

Investigational DB

- Sequence repository
- Anonymized sequence data
- Clinical annotation
- Phenotypic methods
- User friendly cloud interface

Analysis files generated

Approved biomarkers

CDISC architecture for regulatory submission DB

Expert Panel Review
Thank you