Critical Path to TB Drug Regimens
Accomplishments & Future Direction
Accelerate the development of new, safe, and highly effective regimens for TB by enabling early testing of drug combinations.

AND........

Accelerate the development of a clinically useful, regulatory approvable, WHO-qualified in vitro diagnostic assay for rapid drug susceptibility testing of TB to facilitate drug development and rational use of new drug regimens.
CPT Working Group Structure

**Regulatory Science Consortium**
- Data Standards & Integration WG
- Biomarkers & Clinical Endpoints WG
- Preclinical & Clinical Sciences WG
- Modeling and Simulation
- Health Authorities Submission WG

**Rapid DST Consortium**
- Enabling Sciences WG
- Assay Development WG
- Economic Assessment & Impact Modeling WG
- Surveillance WG

**Research Resources Group**
- Clinical Trials Infrastructure WG
- Global Regulatory Pathways WG
- Stakeholder & Community Engagement WG
- Access & Appropriate Use WG
Future State TB Regimen Development

*Increase Confidence & Decrease Risk*

PRECLINICAL
- In Vitro Models

PHASE I-IIa
- Safety PKPD
- Dose-Ranging PK 14-Day EBA

PHASE IIb
- Dosing POC-human

PHASE III
- Randomized Controlled Trial Efficacy

CONFIRMATORY PROOF OF COMBINATION EFFICACY

Critical Path Drug Development Decisions

- PBPK Modeling
  - Evaluation of \textit{in vivo} PKPD models by PCS-WG

- Quantitative Assessment of Liquid Culture Biomarker
- PopPKPD Modeling
- Population PKPD

BIG GAP

Penultimate Clinical Trial Simulation Tool

Drug-Disease-Trial Model
- Systems Pharmacology/ Mechanism Based Models
## Our Successes: TB Trial Data Sets In-House

<table>
<thead>
<tr>
<th>STUDY NAME</th>
<th>CONTRIBUTOR</th>
<th>STUDY DRUG</th>
<th># OF SUBJECTS</th>
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Critical Path Institute (C-Path) Online Data Repository (CODR): Critical Path to TB Drug Regimens (CPTTR) Database of CDC studies
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Data Contribution Agreement Signed
**CPTR Successes: Regulatory Science Consortium**

*Regulatory Science Consortium*

*Research Resources Group*

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**Methods Improvement to enable TB Drug Development:**

- EMA Qualification Opinion rendered for the HFS-TB for TB Drug Development; co-publication strategy with FDA
- Statistical Analysis Plan for Liquid Culture BM discussed with FDA via Pre-IND & work launched
- 9 Clinical Trial Data sets in-hand and mapped to TB Standard
- 6 modeling and simulation projects launched with SIMCYP PBPK model completed (TB infected lung/South African Population)
CPTR Successes: Rapid DST Consortium

Facilitate the development of Rapid DST’s for TB:

- First iterative TB DST Target Profile presented by FIND/NDWG to WHO and endorsed
- Legal and CDA agreements executed to enable data and information sharing
- Data platform collaboration between C-Path/CPTR and FIND/NDWG to support DST development in final planning phase

In partnership with NIAID
Improving Global Regulatory Pathways, Collaboration & Access:

- Engaged regulators from high burden TB and high burden MDR-TB countries on the risk benefit assessments that were made by FDA and EMA on recent approval decisions for new TB drugs.
- Created dialogue with diverse stakeholders across different regions and research sites on strategies to evaluate and measure the impact of community engagement on TB drug research.
- Established a community of practice to connect individuals working in community engagement across different regions and research sites.
- Mycobacteriology lab manual currently being applied by investigators.
Thank You CPTR Members and Partners

Regulatory Science Consortium Members

Government/Regulatory participants

Industry members

Non-profit research members

RDST Consortium Members

Members (Member Agreement)

Non-Voting Participants (CDA)

Organizations

Individuals

Invited & Pending

BioMerieux

Hain Lifescience

Otsuka