

# What is CDC doing to enhance domestic lab capacity?

Bonnie Plika ytis, M.S.

Deputy Chief, Mycobacteriology Laboratory Branch

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# Enhancing Domestic Laboratory Capacity

- ❑ Partnership development
- ❑ Clinical laboratory services
- ❑ Research

## Partnership Development

- ❑ U.S. Public Health Laboratories (USPHL)
- ❑ Association of Public Health Laboratories (APHL)
- ❑ National TB Controllers Association (NTCA)
- ❑ National Laboratory Training Network (NLTN)
- ❑ FDA & NIH
- ❑ Gates Foundation
- ❑ Colleagues in academia



## Partnership Development: MLB TB Laboratory Consultants

- ❑ Laboratory Consultants serve as a single point of contact for assigned areas
- ❑ Provide oversight and administration of laboratory component of TB cooperative agreements
- ❑ Facilitate coordination with state TB control programs
- ❑ Education and training

## Partnership Development: Education and Training

- ❑ Partner NLTN - Laboratory aspects of TB course –August 2010
- ❑ Partner USPHL - Quarterly interactive webinars for USPHLs
- ❑ Partner APHL & USPHL – 6<sup>th</sup> National TB Lab Conference
- ❑ Partner NTCA – Laboratory sessions at NTCA conference

# Partnership Development: FDA & NIH

- ❑ Workshop for advancement of TB diagnostics—June 2010
  - 2009 recommendation from Federal TB Taskforce
  - Hosted by FDA, CDC, NIH/NIAID
- ❑ Agenda: Advance TB diagnostics and biomarkers for
  - Point of care diagnostics
  - Biomarkers for durable cure
- ❑ Outcomes:
  - Identification of partners to develop “pipeline” for TB diagnostics: NIH/NIAID/DAIDS & DMID, ACTG, FIND, CDRC
  - Identification of partners to develop a “frozen trial initiative” for the development and evaluation of biomarkers for durable cure

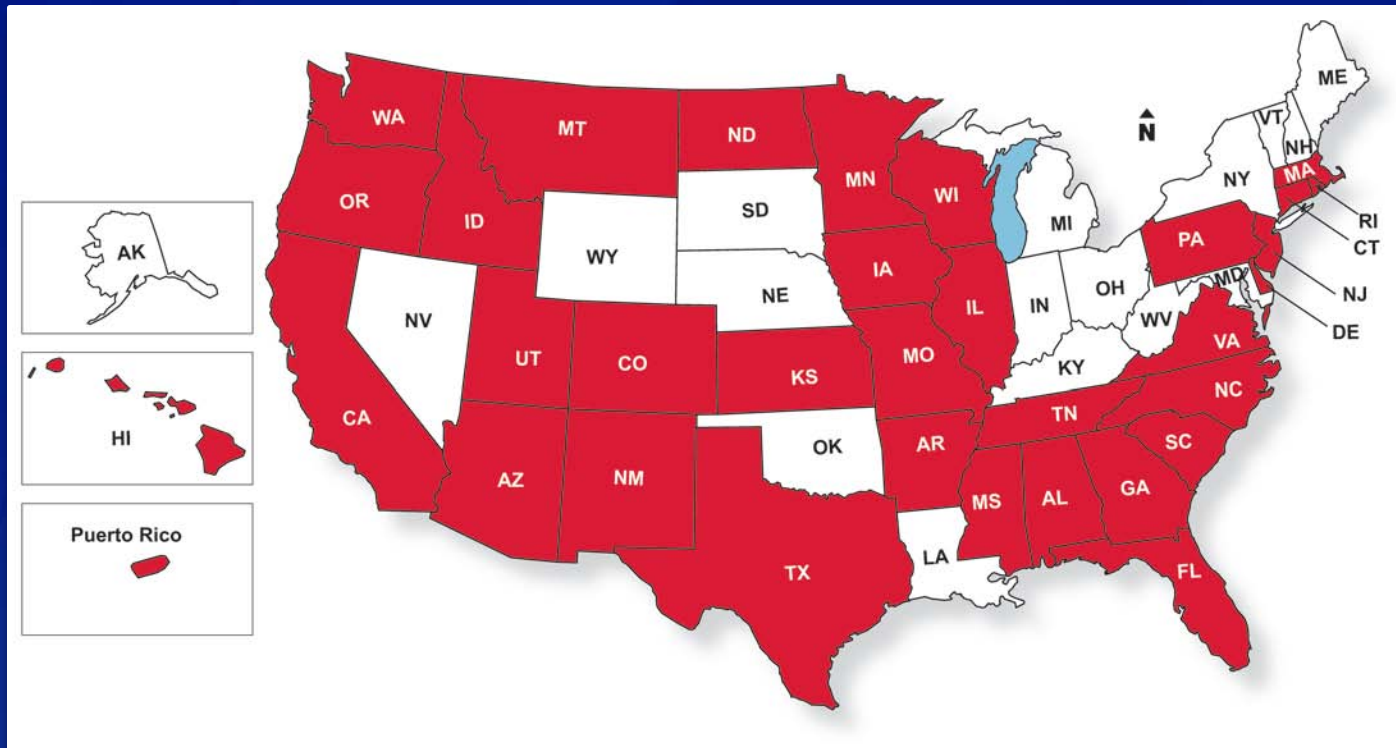
# Partnership Development: TB Drug Resistance Mutation Database

- ❑ Funded: Gates Foundation
- ❑ PI: Megan Murray, Brigham and Women's Hospital
- ❑ Goal: develop and populate a public database archiving sequences of drug resistance genes in *M. tuberculosis*
  - future diagnostic development
  - global TB surveillance
  - potentially the development of new TB treatments
- ❑ 26 genes from ~2000 well-characterized strains of *M. tuberculosis*
- ❑ MLB providing DNA from over 250 resistant strains

# Clinical Laboratory Services

- ❑ *M. tuberculosis* drug susceptibility testing (DST)
  - confirmation of resistance to first line drugs
  - testing of second line drugs
- ❑ Molecular Detection of Drug Resistance (MDDR): DNA sequencing of seven alleles to detect mutations associated with phenotypic drug resistance to INH, RIF, fluoroquinolones, amikacin, kanamycin and capreomycin
- ❑ MPEP (model proficiency evaluation program)
- ❑ New Initiative – Rapid detection of drug-resistant TB in persons at high risk (RDDR)

# Molecular Detection of Drug Resistance (MDDR)



■ States utilizing MDDR service

116 isolates from 33 states or territories

Poster # 1: Lentz, Sikes, Hartline, Diem, Metchock, & Driscoll

# Rapid Detection of Drug-Resistant TB in Persons at High Risk (RDDR)

## Three components:

- ❑ Rapid clinical diagnostic service for U.S.
- ❑ Evaluation of rapid clinical diagnostic service
- ❑ Point of care molecular testing in conjunction with US/Mexico binational TB control projects

# Rapid Detection of Drug-Resistant TB in Persons at High Risk (RDDR)

## □ High risk patients

- Previously treated for TB
- Contact with known drug resistant case
- Culture positive after 3 months of treatment
- Other criteria on case by case basis

## □ Service

- NAAT + sediments
- Molecular testing for rifampin and isoniazid resistance
- Targeted TAT 2 days
- If positive, initiate reflex protocol for culture then 1<sup>st</sup> and 2<sup>nd</sup> line DST

# Timeline for the Implementation of RDDR service

- ❑ Follow successful genotyping model: implement at CDC, then transfer to selected regional lab(s)
- ❑ Summer 2010
  - Development of protocols and algorithms
  - Engage with select USPHL to obtain specimen sediments
  - Train personnel
  - Develop assay
- ❑ Fall 2010
  - Validate assay
  - Develop standardized reporting language
- ❑ Early 2011: Implement service
- ❑ Fall 2010: Anticipate issuing a competitive FOA for selection of a PHL(s) to establish regional service in early 2012

# Research

- ❑ Operational: Collaborating with APHL to conduct comprehensive TB lab services survey in public and private sector
  
- ❑ Molecular Genetics
  - Molecular drug resistance survey
  - Investigation of unknown mechanisms of drug resistance
  - Functional genetics to determine if certain mutations confer resistance

## Molecular Genetics: Molecular drug resistance survey

- ❑ Summer 2009 - Completed sequencing and analysis of 7 loci (rpoB, inhA, katG, rrs, eis, tlyA, and gyrA) from 314 clinical isolates of *M. tuberculosis*
- ❑ This data was utilized to set analysis standards for the MDDR clinical service
- ❑ Currently – completing the sequence analysis of two additional loci (embB and pncA)

Poster # 8: Morlock, Hall, Sikes, Dalton, & Posey

## Investigation of unknown mechanisms of drug resistance

- ❑ Demonstrated that *embB306* mutations confer resistance to EMB (in process to include the *embB* loci in the MDDR clinical service)
- ❑ Identified new mechanism of KAN resistance: *eis* loci included in MDDR panel
- ❑ Work in progress to understand the level of cross resistance and the molecular mechanisms for resistance to fluoroquinolones

# Closing Remarks

