TDR activities in support of new TB diagnostics

Jane Cunningham
Medical Officer
Tuberculosis Diagnostic Initiative (TBDI) launched by the WHO Global TB Control Program

Tuberculosis added to TDR's portfolio and TBDI transferred to TDR

Grants from the Bill and Melinda Gates Foundation, USAID, Rockefeller

FIND launched

FIND/TDR Joint Workplan
Shifting Philosophy

- TBDI

  - stimulate and facilitate industry to adapt available technologies for new diagnostics rather than the direct funding of competitive product development

  - Conclusion ..... this is not enough

  - Evolution of FIND
"Bright Ideas Grants Programme" — conduit to screen new technologies and attract new tool developers to the field

2001-2003

- Novel concepts for detecting MTB
- Novel or improved methods for smear microscopy
- 28 investigators funded, including 5 industry groups
Approved Projects - $1,884,623

- Tool Development
- Discovery Research
- Evaluation
- Smear microscopy
- Withdrawn
Product Development

Generating evidence base to inform the design of tools with the greatest impact.

Stimulating R&D in diagnostics for TB

TB Diagnostics Market Analysis
Quantifying the TB Diagnostic Process

4 country field study measuring delays in diagnosis, and the economic impact of the diagnostic process.

1600 newly diagnosed TB patients
1000 Respiratory symptomatics
Mathematical modelling

To predict the impact of new diagnostic tools with varying operational and performance characteristics.

Sake de Vlas & Nico Nagelkerke developed a model

**Main components of the model**
- TB biology, including extra-pulmonary TB and HIV
- The TB diagnostic process
- Organization of health care system
- Health-seeking behavior
Laboratory Based Evaluation

- New tools vs. existing tools
- Well characterized reference materials are a necessity
- TB Specimen and Strain Banks
TB Specimen Bank

- Serum, urine, saliva, sputum from TB patients and negative controls
- Patients = 1116 (605 TB+; 441 TB-; 343 HIV +; 772 HIV-)
- Aliquots 8 925
- Projected No. aliquots = 26 500
- Updated website info
TB Specimen Bank Collection Sites

Original collection sites, started 1999

- Respiratory Hospital, Winnipeg, Canada
- Catalan Health Inst., Barcelona, Spain
- MRC, Banjul, The Gambia
- Hospital Universitario Prof. Edgar Santos, Salvador, Brazil
- Uganda/CWRU Research Collaboration, Kampala, Uganda
- MRC, Durban South Africa

New collection sites, starting end 2004

- MRC, Durban South Africa
- ICDDR,B, Dhaka, Bangladesh
- KEMRI, Nairobi, Kenya
- Corporación para Investigaciones Biológicas, Medellín, Colombia
- Instituto de Medicina Tropical “Alexander von Humboldt”, Lima, Peru
- Pham Ngoc Thach Hospital, Ho Chi Minh City, Viet Nam
Requests are considered by a TB Specimen Bank Review Committee
TB Strain Bank

- Promote the development of novel technologies for drug susceptibility testing (DST) appropriate for use in disease endemic countries;
- Facilitate the laboratory evaluation of new (and existing) DST methods and;
- Provide reference materials to support quality control and proficiency testing programs in endemic countries

Institute of Tropical Medicine in Antwerp

8 laboratories contributing 239 strains

Operational by Summer 2005
TDR Strain Bank Contributing Laboratories

Massachusetts State TB Laboratory, Boston, USA 16 strains

Inst. Of Tropical Medicine, Antwerp, Belgium 120 strains

Universidad Autónoma, Barcelona, Spain 22 strains

Instituto Adolfo Lutz, São Paulo, Brazil 12 strains

Kuratorium Tuberkulose in der Welt e.V., Gauting, Germany 26 strains

MRC, Pretoria, South Africa 12 strains

Korean Inst. Of Tuberculosis, Seoul, Republic of Korea 21 strains
TB Serologic Test Evaluation

- Inventory of commercially available serological assays - > 50
- Limit evaluation to rapid test formats (24 companies invited)
- 17 companies have agreed
- 200 HIV+; 200 HIV– serum samples from the TB Specimen Bank (+56 samples for reliability testing)
- Scheduled to begin January 2005
Participating Companies

1. ABP Diagnostics
2. Advanced Diagnostics
3. American Bionostica
4. Ameritek
5. Chembio
6. CTK Biotech
7. Hema Diagnostic
8. Millenium Biotechnology
9. Minerva Biotech
10. Mossman Associates
11. Pacific Biotech
12. Premier Medical Corporation
13. Princeton BioMeditech
14. Span Diagnostics
15. Standard Diagnostics
16. Syntron Bioresearch
17. Veda Lab

Focus Sure Check TB
Tuberculosis Rapid Test
Rapid Test for TB
dBest One Step TB Test
TB Stat-Pak II
TB Antibody onsiteRapid Screening Test Kit
Rapid 1-2-3 TB Test
Immuno-Sure TB Plus
V Scan
MycoDot
Bioline TB
First Response Rapid TB
BioSign M. tuberculosis
TB Spot ver. 2.0
SD Rapid TB
QuikPac IV OneStep TB
TB Rapid Test
Clinical Trials Support

- Phase III Trial Comparing Four Alternative Methods for Drug Susceptibility Testing of MTB. tuberculosis with Gold Standard in SS+ pulmonary Tuberculosis in Lima, Peru
  - Indirect and direct LJ drug susceptibility testing to rifampin and isoniazid, FASTPlaque RIF-Response test, INNO LiPA Rif TB test, and indirect MTT drug susceptibility testing.

- GLP/GCP training

- Diagnostics Expert Evaluation Panel (DEEP)
Diagnostics Expert Evaluation Panel (DEEP)

Goal:
To provide best practice guidelines for the evaluation of new diagnostic tests.

Scope:
To help those designing evaluations at all levels (from test manufacturers to end users)
To guide critical review of published and unpublished evaluations, with a view to selecting or approving tests that have been evaluated and shown to meet appropriate performance targets
To facilitate the setting of appropriate standards for test evaluation
Demonstration Projects

- Guidelines for appropriate use
- Facilitate procurement
- Operational research

Near future:

DOTS-plus MGIT demo projects

Improved smear microscopy methods.