

Update on drug resistance surveillance



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Outline

- History and Objectives of the Global Project
- Principles
- Issues in DRS
- New Guidelines
- Coverage and content report 4
- Future



History

- 1994 WHO/IUATLD Global project on drug resistance
- 1994 WHO/IUATLD Supranational Laboratory Network
- Surveillance Guidelines, 1997, 2003, 2007 interim
- Global reports 1997, 2000, 2004, 2007

Objectives

- Implement standardized methods to generate comparable data
- Estimate the magnitude of drug resistance globally
- Determine trends
- Evaluate TB programmes
- Data to inform policy decisions; MDR-TB management, Laboratory
- Regimen evaluation

Principles of Anti-Tuberculosis Drug Resistance Surveillance

1. Sample accurately represents population under study

- Representative group of new TB cases
- Representative group of previously treated TB cases
- Examples: surveillance, 100%, cluster, population proportionate cluster, sentinel

2. Quality assured laboratory results

- Supranational Laboratory Network:
26 laboratories, coordinating center, PT and QA

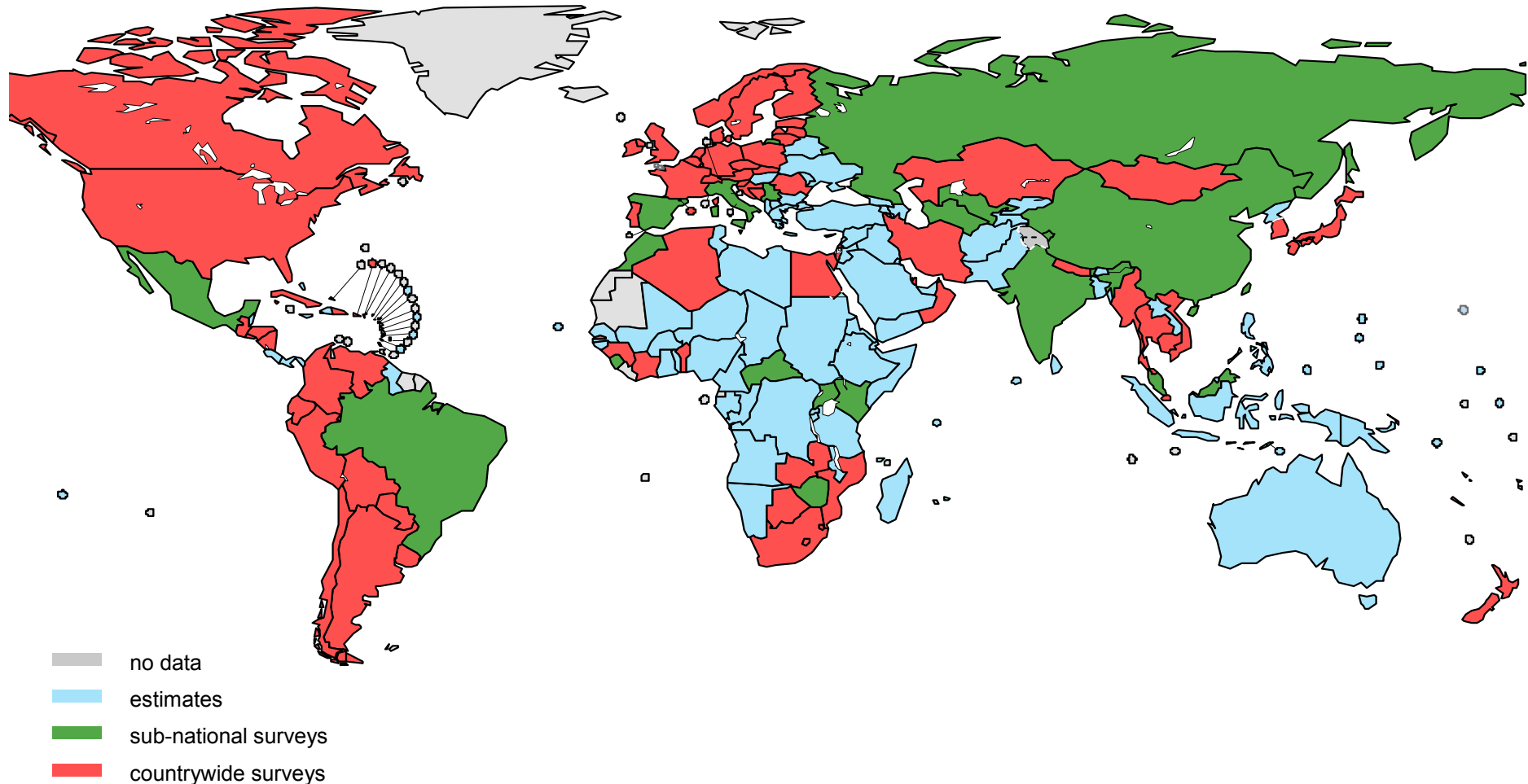
3. Differentiation between new and previously treated cases

- treatment history
- clinical records

What does the global project do?

- Provides assistance (directly, through consultant) in survey design, protocol development
- Reviews protocols
- Assists in linking of SRL
- Provides monitoring of survey where necessary
- Assist in data analysis where needed
- Provides tools (guidelines, software)
- Collects and analyzes global data, and produces estimates.

Coverage of Anti-Tuberculosis Drug Resistance Surveillance



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Global Project on Anti-TB Drug Resistance Surveillance

1994-2004 109 settings surveyed in 90 countries

Global Estimate of MDR-TB

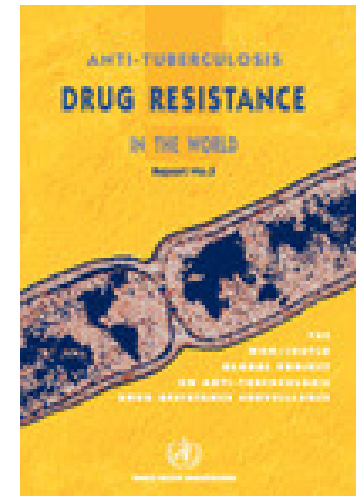
424,203

(95% CI, 376,019–620,061) incident cases in 2004

Estimated deaths 110,000

4.3%

(95% CI, 3.8%–6.1%) of all TB cases notified in 2004

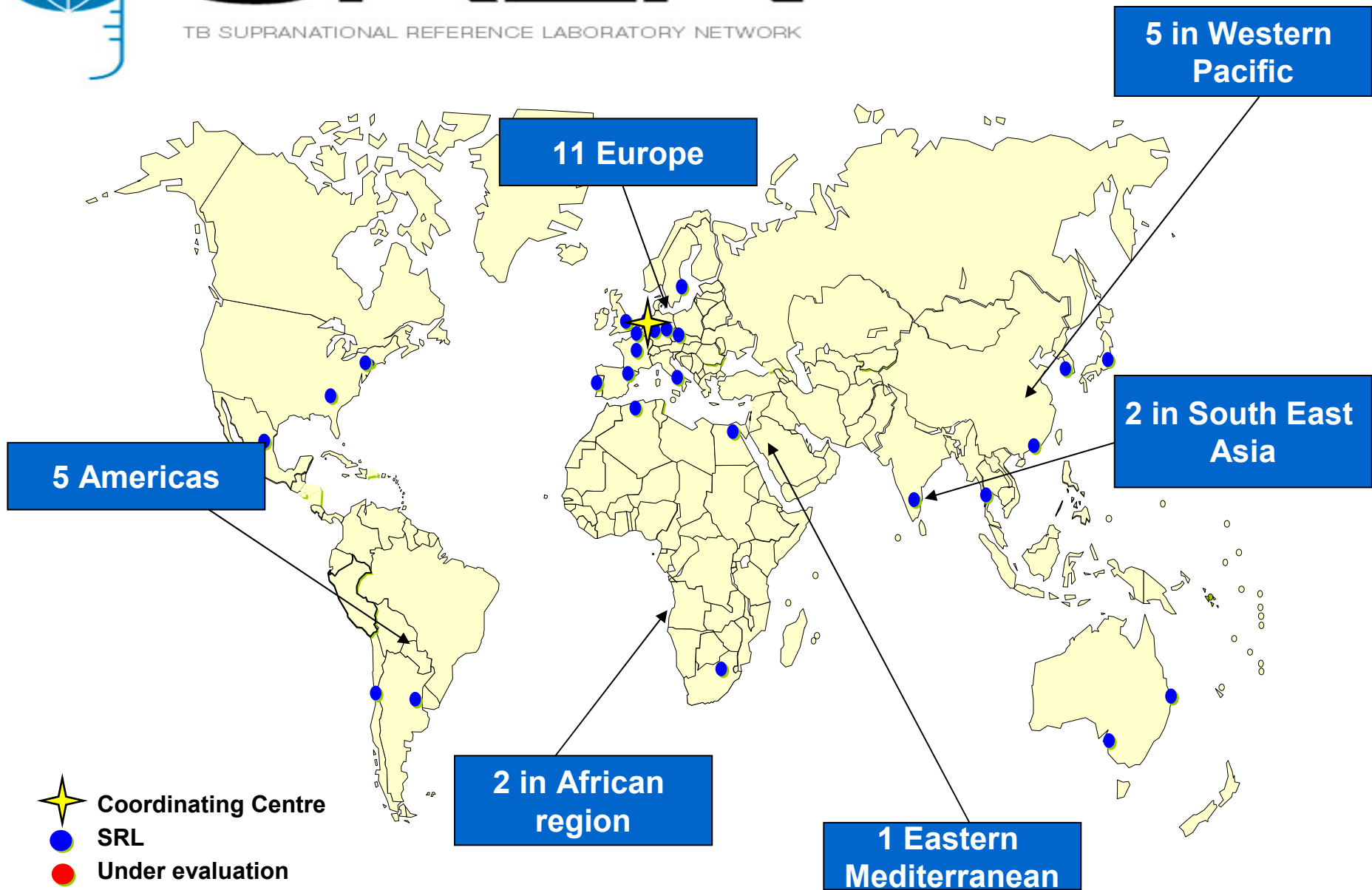


Zignol M et al (2006). Global Incidence of Multidrug-Resistant Tuberculosis, JID 2006:194 (15 August)



SRLN

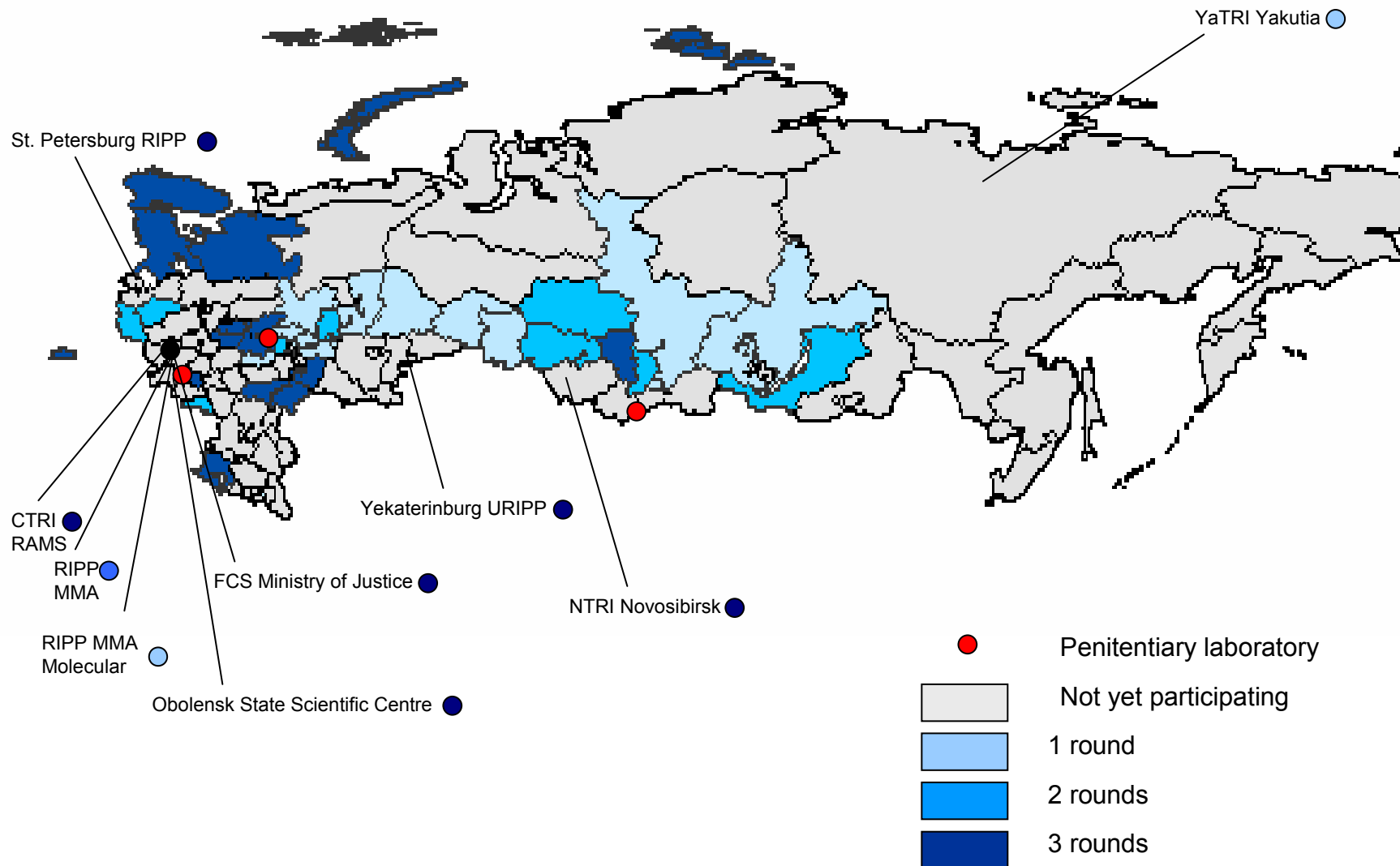
TB SUPRANATIONAL REFERENCE LABORATORY NETWORK



The supranational reference laboratory network - 2007

- 26 Laboratories
- >100 proficiency panels a year
- > 50 countries rechecking, SLD DST for 15
- > 25 laboratories receiving on site training
- Introducing SLD into proficiency testing panels
- All regions plan to expand SRLN
- Regional and sub-regional Global Fund proposals
- SLCS working towards better coordination/integration of SRLN, consultants, other lab networks

Laboratories participating in proficiency testing for DST of first line drugs in the Russian Federation



Issues in Anti-TB Drug resistance Surveillance and testing

- Generally under financed (average 20-50k)
- Capacity limits repeated surveys, thus poor trend determination in countries conducting surveys.
- Wide CI's around surveys, trend determination problematic (3-5 year intervals)
- Absence or slow integration of HIV testing and SLD DST, molecular techniques
- Few settings have assessed sm- population
- Surveillance systems changing over time, shifting to diagnostic reporting in some settings
- Laboratory capacity, safety and performance largest obstacle

Issues in Anti-TB Drug resistance Surveillance

- No assessment of private sector or chronic pool.
- Representative sample sizes of retreatment cases difficult to achieve and difficult to compare between countries
- Better differentiation of sub-categories of retreatment
- Classification of patients prone to errors requires validation in all settings
- Weaknesses in rechecking in some settings because of shipment and customs issues.
- Absence of IRB or ethical review board
- No capacity to determine true acquired resistance

Successes of the Global project

- Comparable drug resistance data from 100+ countries
- Robust data on new cases
- Designed an international EQA system for DST
- Has identified high prevalence *emergency settings
- Strengthened lab networks
- Strengthened transport networks
- Good platform for OR (transport, classification, outcome)
- Useful preparatory exercise for MDR-TB treatment programmes

Interim guidelines

- Flexible approaches to provide more programmatically relevant data
 - Routine culture/DST to all cases gold standard
 - Periodic surveys among new cases, routine culture/DST to retreatment
- Larger samples for new and retreatment
- Retreatment by subcategory (relapse, RAD, RAF, retreatment other)
- Stronger QA of patient classification, and data management
- Consideration of ethical issues (treatment, testing)
- Inclusion of HIV where possible (primarily for patient benefit)
- SLD DST on all R resistant isolates at a minimum (at SRL in most places)
- Stronger section on transport
- Supplement surveys with
 - surveys of risk populations
 - longer term epidemiological studies (explore sentinel surveys)
 - use of molecular methods (under pilot)
 - platform for OR
- Better financing of survey protocols and work done at SRLs
- Analysis done in conjunction with notification and other programmatic data (better retreatment data)

Two models

Continuous surveillance (routine diagnosis)

- Conduct periodic surveys to verify routine data collection.
- Focus on QA of lab, and standardized classification and interpretation
- Ultimately goal is to monitor drug resistance through routine diagnostic DST data
- In EUR routine MDR-TB data reported to WHO already correlate well with survey data

Survey data

- 100% retreatment, periodic surveys among new
- Sentinel, or open cluster
- Molecular

4th report coverage

	4th settings	Not previously reported	1994-2007
AFR	5 settings (5 countries)	Ethiopia, Madagascar*, Rwanda, Senegal, Tanzania*	31 settings (23 countries)
AMR	11 settings (11 countries)	Costa Rica, Guatemala (final), Paraguay	21 settings (21 countries)
EMR	7 settings (7 countries)	Syria, Lebanon, Jordan	9 settings (9 countries)
EUR	41 settings (37 countries)	Georgia, Armenia, Azerbaijan (Baku), Spain (Aragon), Ukraine (Donetsk), Russian Federation Archangelsk, Uzbekistan (Tashkent)	45 settings (39 countries)
SEAR	9 settings (6 countries)	India (Gujarat state), India (3 districts) Indonesia (Miimeka province), Myanmar, Sri Lanka	14 settings (6 countries)
WPR	19 (16 countries)	China (Beijing, Shanghai, Inner Mongolia, Heilongjiang, Macao SAR), Philippines, Fiji, Vanuatu, Guam, Northern Marianas, and Solomon islands.	27 settings (18 countries)
Total	92 settings (86 countries)	37 settings (29 countries)	147 (116 countries)

Expected in the 4th report

<i>Trends (3+ data points)</i>	All countries with routine culture DST (Nepal, Thailand, Russian oblasts, Cuba, Poland, Korea, Uruguay)	52 settings (49 countries with 3 or more data points)
<i>HIV</i>	Argentina, Cuba, Honduras, Barcelona, Archangelsk RF, Tomsk RF, Donetsk, Ukraine, Uruguay, Costa Rica.	9 settings
<i>SLD DST</i>	Rwanda, Argentina, US, Canada, Latvia, Armenia, Georgia, Azerbaijan, 2 Russian oblasts, China Macao SAR, Hong Kong SAR, Japan, Australia, Singapore, Ukraine Donetsk (partial), (Gujarat, India, Thailand) (dataset from EuroTB 10 countries)	~17 (+10 EuroTB) Not in time: Ethiopia, Senegal, Madagascar, Morocco, Yemen, Nepal, Sri Lanka, Tanzania, Philippines, Tashkent, Uzbekistan
<i>Retreatment by sub-category</i>	Senegal, Honduras, Cuba, Syria, 1 oblast Russia, Georgia, Nepal, Macao SAR, Morocco, Gujarat, India (?)	~10 settings
<i>Prison sector</i>	Azerbaijan, Armenia, Georgia, Cuba	4 settings

Future

- Meeting in 2008 to review current methods
- Development of a variety of protocols
- Pilot new methods
- Scale up of and access to culture/DST and/or molecular methods
- Increased incorporation of HIV testing and SLD DST, and OR built in
- Better link to treatment programmes

Acknowledgements

- Participating National TB programmes
- Participating laboratories
- EuroTB
- Supranational Reference Laboratories
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