Principles of anti-TB drug resistance surveillance

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Outline

- History of the Global Drug Resistance project
- Supranational Laboratory Network
- Principles and protocol
- Overview of surveillance mechanisms
- Issues in testing and surveillance

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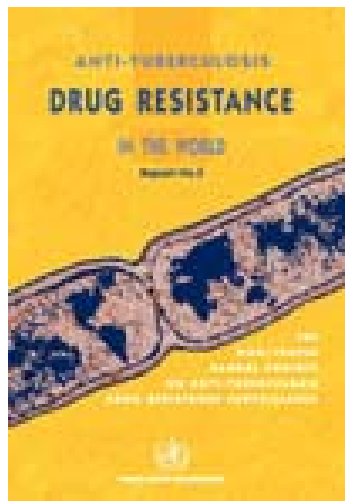
History of the Global Project

1994	Task Force
1994	Supranational Laboratory Network
1997	Surveillance guidelines (Revision 2003 and 2007)
1997	1st Global report 35 settings
2000	2nd Global report 58 settings
2004	3rd Global report 77 settings
2007	4th Global report
2006	Data from 56 new settings expected, cumulative total 125 settings. Data representing >50% of new smear positive cases globally



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Objectives of surveillance

- Estimate the magnitude of drug resistance globally
- Determine trends
- Evaluate the progress of TB programmes
- Strengthen laboratory networks
- Data to inform policy decisions; MDR-TB management, laboratory
- Regimen evaluation

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The Supranational Laboratory Network

- 1994 Ottawa, Canada 14 Laboratories
- 1999 Antwerp, Belgium 26 laboratories
- 13 rounds of proficiency testing, **150** reference laboratories have received panels

Africa: 2

Americas: 5

Middle East: 1

Europe: 11

South Asia: 1 and 1 candidate

Western Pacific: 5

- 4 annual network meetings
- Link/subgroup/regional networks
- Two ongoing SLD studies
- Other studies planned

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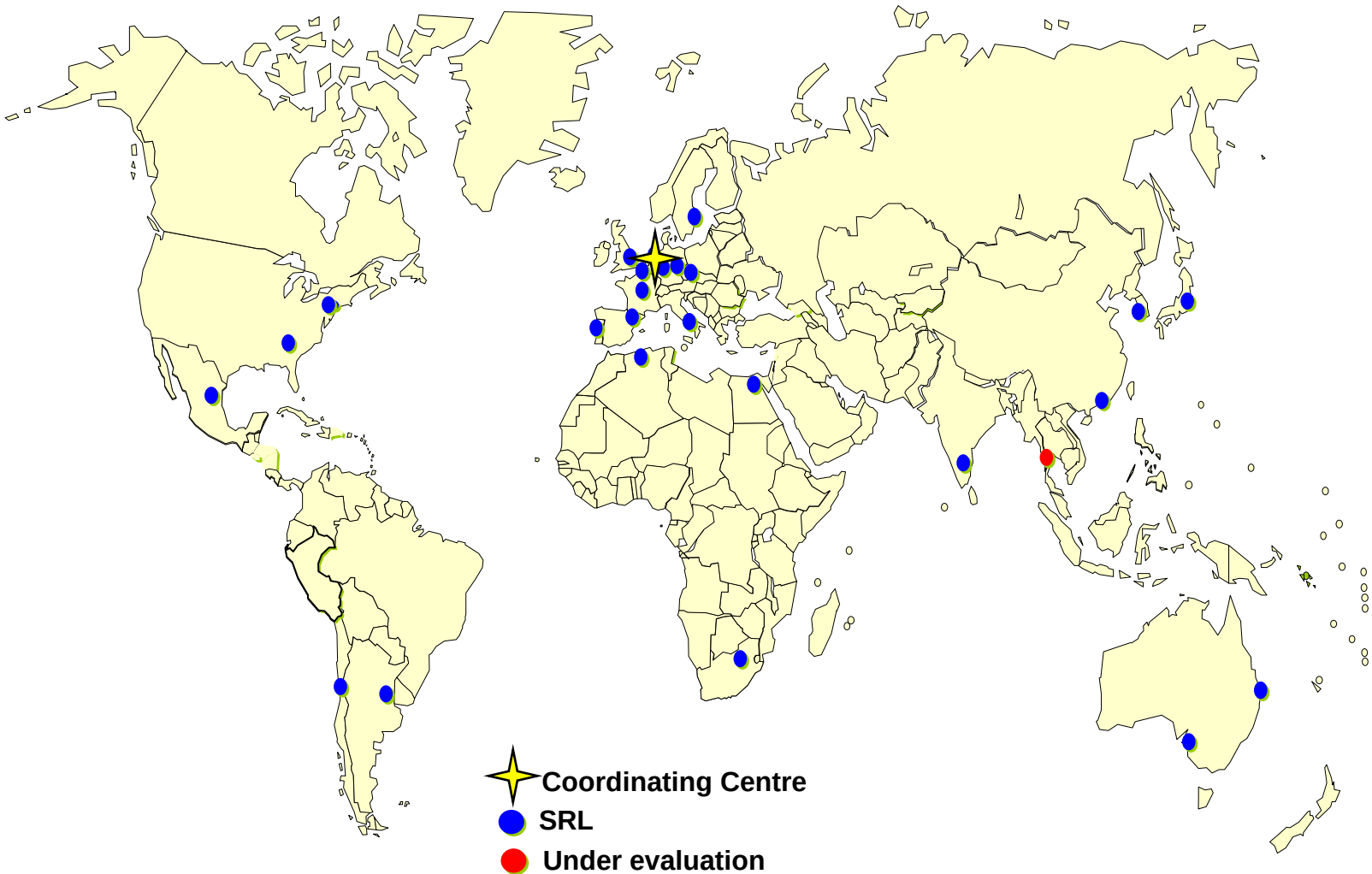
The Supranational Laboratory Network 2006 (links with >120 countries)



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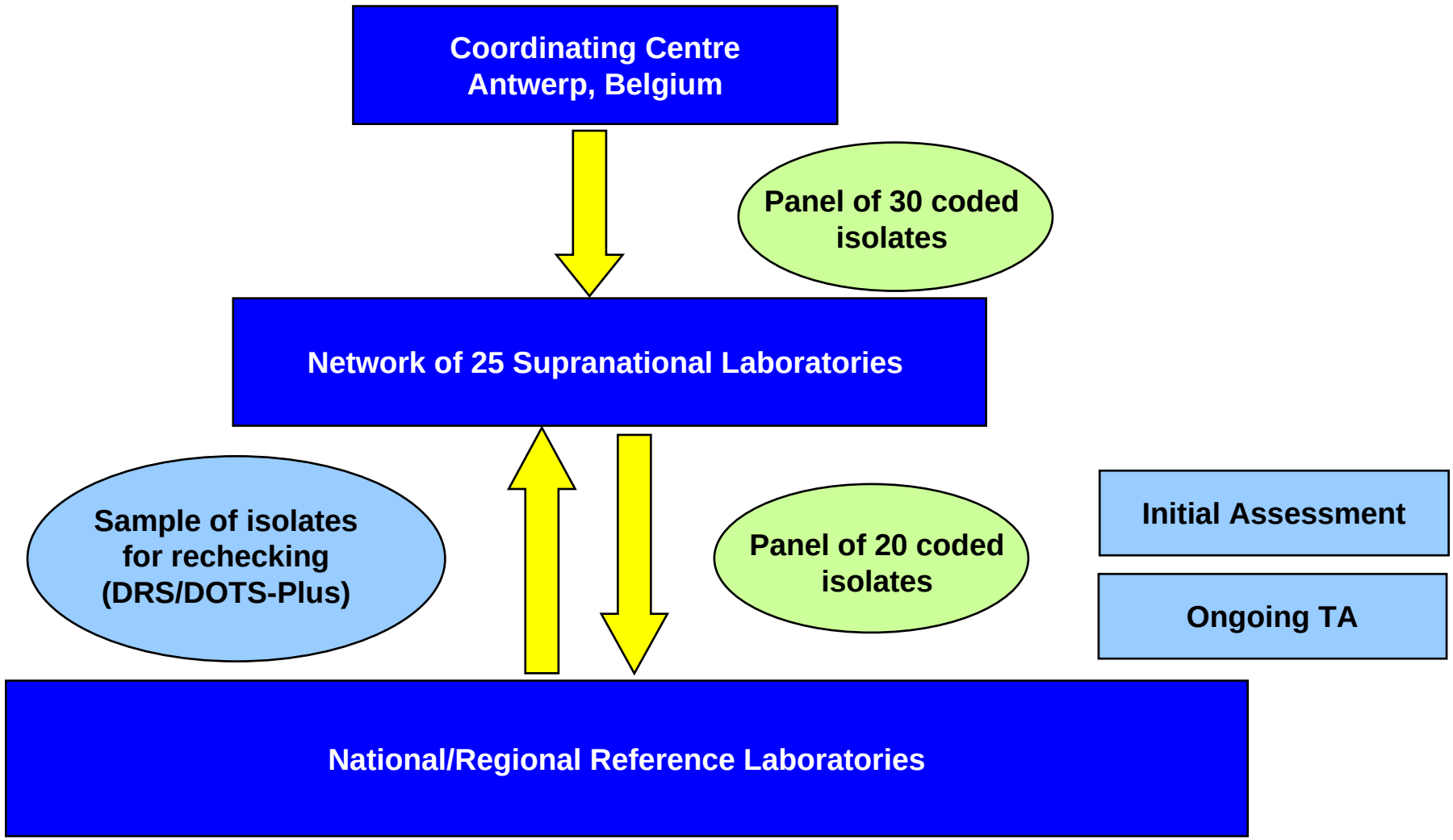
SRLN system of external quality assurance



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Principles of anti-TB 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

2. **Quality assured laboratory results**
   - Supranational Laboratory Network:
     - 25 laboratories, coordinating center, PT and QA

3. **Differentiation between new and previously treated cases**
   - treatment history
   - clinical records

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Protocol

- Introduction and background
  - epidemiological situation, lab network, previous data
- Objectives
  - clear and concise
- Methods
  - survey design and sampling strategy
- Intake period and logistics
  - inclusion criteria, sputum collection, forms, transportation
- Laboratory methods
  - proportion, absolute concentration, radiometric
- Quality assurance
  - internal, external
- Data management
  - data collection, double entry, analysis
- Human resources needed
  - principal investigator, team
- Financial resources
  - 40,000-150,000 US$, very detailed

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Types of surveillance and trend data 109 settings 1994-2002

TYPE OF SURVEILLANCE	SETTINGS	1 data point	2 data points	3 or more data points
Continuous surveillance	44	4(9.0%)	14 (32.0%)	26 (59.0%)
survey	61	50 (82.0%)	7 (11.0%)	4 (7.0%)
sentinel	4	2 (50.0%)	0	2 (50.0%)
TOTAL	109	55 (50.0%)	21 (19.0%)	32 (29.0%)

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Trend data

- **Global Trends:** Early to say Global map incomplete, few trend data from low resource settings make global assumptions regarding direction of trends difficult.

- **Increases:** Tomsk oblast, Lithuania, Poland, Botswana

- **Decreases:** US, Hong Kong, Cuba, Thailand, Latvia, Slovakia, Netherlands

- **Issues:**
- Few data points make interpretation with certainty difficult
- Often first data points wobbly
- Changing surveillance systems over time
- Must look at patients as well as prevalence, within the context of the overall programme

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ISSUES in anti-TB drug resistance surveillance and testing

- Methodological
- Representative sample sizes of retreatment cases difficult to achieve and difficult to compare between countries
- Classification of patients prone to errors
- Surveillance systems changing over time, shifting to diagnostic reporting in some settings
- Testing to expand to different populations depending on region

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ISSUES in anti-TB drug resistance surveillance and testing

- **Logistics**
- **Periodic surveys require human and financial resources**
- **Logistics for shipment of specimens in and out of country often complicated**

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ISSUES in anti-TB drug resistance surveillance and testing

Laboratory

SAFETY of Culture and DST

QUALITY of Culture and DST

AVAILABILITY of Culture and DST

NO standardized methods for 2nd line DST, DST for some drugs unreliable

Transport of strains expensive, legal/ethical implications

SRLN bears much of the cost, and TA often limited to PT and initial assessments

No capacity to determine TRUE acquired resistance

New technologies must be combined with functional and safe conventional methods-Slow integration of new technologies- pilots with MGIT, starting to pilot genetic methods

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ISSUES in anti-TB drug resistance surveillance and testing

- **Ethical**
- **Routine surveillance part of programme remit; however appropriate treatment in public sector often unavailable**
- **Most countries do not require patient consent and results are not blinded, in context of routine surveillance**
- **Further ethical considerations will need to be addressed if rapid methods for identification/isolation expand and treatment remains unavailable**
- **Additional ethical considerations if combined with HIV surveillance**

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