Interim recommendations for the surveillance of drug resistance in tuberculosis

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LIST OF ACRONYMS

DRS	Drug Resistance Survey/Surveillance
DST	Drug Susceptibility Testing
EQA	External Quality Assurance
FLD	First line drugs
IUATLD	International Union Against TB and Lung Disease (UNION)
LQAS	Lot Quality Assurance Sampling
MDR-TB	Multidrug-resistant tuberculosis
NRL	National Reference Laboratory
NTP	National Tuberculosis control Programme
QA	Quality Assurance
SLD	Second line drugs
SRL	Supranational Tuberculosis Reference Laboratory
TA	Technical Assistance
TB	Tuberculosis
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

INH	isoniazid
RMP	rifampicin
PZA	pyrazinamide
EMB	ethambutol
SM	streptomycin
FLQ	fluoroquinolone
PAS	para-aminosalycilic acid

SUMMARY

Revised drug resistance surveillance guidelines will become available later this year. In the interim, this document has been drafted to provide guidance on the areas that will be updated in the forthcoming guidelines. These interim recommendations build on guidelines that have already been published in 2003[1]. It is important to note that these recommendations are conceptual. For practical guidance please refer to the previous guidelines and/or a technical consultant that can provide assistance in designing the survey protocol and advising on specific logistics. There are three fundamental principles of the WHO/IUATLD Global project on drug resistance surveillance. These interim recommendations follow these principles:

1. Survey sample must represent the population under study.
2. TB patients must be differentiated by previous history of treatment.
3. Laboratory results must be quality controlled.
**4. Other areas of consideration (coordination, ethics, quality assurance, budget).

1. SURVEY METHODS

General

The overall goal of monitoring drug resistance in tuberculosis is to evaluate TB programme performance and provide information which can be used to guide public health action to reduce morbidity and mortality and to improve public health. Drug resistance is monitored either through continuous surveillance by provision of diagnostic culture and DST to all TB patients, or where infrastructure is not widely available, through periodic surveys. Sometimes a system employs a combination of the two[1].

Drug resistance surveys can also strengthen lab capacity, and transport and referral systems, as well as evaluate the correct classification of patients. Surveys can also provide a platform for other types of operational research. It is important that the NTP develop the survey objectives before starting and consider in advance the ways this information will be used. It is also important that expectations of survey data generated remain realistic recognizing that drug resistance surveys can determine prevalence of resistance within certain margins of error. In some cases these may preclude the ability to meaningfully determine trends. Information generated from drug resistance surveys must always be interpreted alongside other programmatic information.

Drug resistance surveys should only be undertaken when the laboratories conducting DST are safe and appropriately equipped with trained staff working with clear standard operating procedures and producing quality assured data. The data generated from surveys will be valid and useful where high quality lab data are matched by surveillance and clinical data produced by appropriately trained survey/surveillance staff with good communication between programme and laboratory staff. It is important to note that drug resistance surveys will heavily increase the workload of the reference laboratory, and should only be undertaken where capacity is sufficient.

[1] The term drug resistance surveillance in this document is defined as the ongoing and continuous assessment of drug resistance among all cases of tuberculosis. The term drug resistance survey refers to a cross-sectional survey that takes place at one point in time. Surveys are intended to be repeated at specified intervals with the aim of documenting changes in prevalence of resistance over time.

As treatment for drug resistant cases becomes more routinely available within the NTP, mechanisms for surveillance may be modified over time. It is extremely important that a National TB Programme documents the evolution of the surveillance system in order to appropriately evaluate drug resistance data over time, and interpret trends. It is also important to note that while nationwide surveys are desirable for programmatic reasons, surveys at smaller administrative levels are also acceptable provided they are designed correctly. The size and scope of the survey should be determined by ability of the NTP to ensure quality.

Each country should take a long term view of surveillance and should design a system that best fits the needs of the country, and is based on capacity that is sustainable and ideally will allow the evaluation of trends over time, which is the primary objective of surveillance. There are several models to choose from, all of which fit into the framework set out in these guidelines.

Survey models

-Some countries conduct continuous surveillance, or conduct culture and drug susceptibility testing (DST) on all suspected TB cases as a standard of routine diagnosis. This is the approach of most high income countries, and these routine diagnostic data constitute the basis for surveillance. For these countries such data usually forms the basis of the clinical management of drug resistant TB using tailored or individualized treatment regimens.
-Some countries conduct continuous surveillance (routine culture and DST) on risk populations (all retreatment cases, or specifically chronics, or failures of category 1 or category 2), supplemented with periodic surveys of drug resistance among new cases. As drug resistant treatment programmes scale up routine surveillance of