

Design and Implementation of Data Exchange Formats for Molecular Detection of Drug-Resistant Tuberculosis

Wilfred Bonney, PhD^{1,2}, Sandy F. Price, PMP¹, Roque Miramontes, MPH¹

¹Data Management, Statistics and Evaluation Branch, Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Office of Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA; ²Public Health Informatics Fellowship Program, Division of Scientific Education and Professional Development, Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention, Atlanta, GA, USA

Abstract

Drug-resistant tuberculosis (TB) remains a public health threat to the United States and worldwide control of TB. Rapid and reliable drug susceptibility testing (DST) is essential for aiding clinicians in selecting an optimal treatment regimen for TB patients and to prevent ongoing transmission. Growth-based DST results for culture-confirmed cases are routinely reported to the U.S. Centers for Disease Control and Prevention through the National TB Surveillance System (NTSS). However, the NTSS currently lacks the capacity and functionality to accept laboratory results from advanced molecular methods that detect mutations associated with drug resistance. The objective of this study is to design and implement novel comprehensive data exchange formats that utilize the Health Level Seven (HL7) version 2.5.1 messaging hierarchy to capture, store, and monitor molecular DST data, thereby, improving the quality of data, specifications and exchange formats within the NTSS as well as ensuring full reporting of drug-resistant TB.

Introduction

Drug-resistant tuberculosis (TB) is a communicable disease that remains a public health threat to the United States and worldwide control of TB^{1,2}. Rapid and reliable drug susceptibility testing (DST) is essential for aiding clinicians in selecting an optimal treatment regimen for TB patients and to prevent ongoing transmission. DST is crucial for detecting primary or emerging resistance and for monitoring the incidence of drug-resistant TB cases.

Molecular DST methods provide a rapid and robust diagnosis of drug-resistant TB case detection with credible sensitivity and specificity³. For some drugs, molecular DST methods are able to detect genetic mutations associated with lower levels of phenotypic resistance that may be missed by certain growth-based DST methods^{2,4}. The ability to identify these genetic mutations, therefore, may be clinically “useful in optimizing treatment by switching the more potent drug regimens: an advantage over conventional DST that reports only the results from the critical concentration tested”² (p. 3).

Growth-based DST results are routinely collected with the Report of Verified Case of Tuberculosis (RCVT) form and reported to the U.S. Centers for Disease Control and Prevention (CDC) through the National TB Surveillance System (NTSS)^{5,6}. However, the NTSS currently lacks the capacity and functionality to accept electronic laboratory test results from the advanced rapid and robust molecular methods^{3,7-10} that detect genetic mutations associated with drug resistance. This limitation prohibits the comprehensive capture of data for drug-resistant cases and impedes accurate reporting¹¹. The objective of this study is to design and implement novel comprehensive data exchange formats that utilize the Health Level Seven (HL7) version 2.5.1 messaging hierarchy to capture, store, and monitor molecular DST data, thereby, improving the quality of data, specifications and exchange formats within the NTSS as well as ensuring full reporting of drug-resistant TB through the revised RVCT to be implemented in 2020.

Methods

The design setting utilized a congruence or similarity of standardization protocols that involved many published implementation guides by HL7 International and the use of reference terminology standards.

Use of Published Implementation Guides

Designing the Division of Tuberculosis Elimination (DTBE) message hierarchy utilized two published reference documents. These included *HL7 Version 2.5.1 Implementation Guide: Electronic Laboratory Reporting to Public Health, Release 1 (US Realm)* and *HL7 Version 2.5.1 Implementation Guide: Electronic Laboratory Reporting to Public Health, Release 2 (US Realm)*^{12,13}. Both guides contain necessary specifications and constraints for reporting

laboratory test results to appropriate federal, state, local and territorial health agencies. In particular, these two guides address messaging content and formats related to the transmission of reportable laboratory result messages or ELR using HL7 v2.5.1 ORU^R01 Unsolicited Observation Message standard^{12, 13}.

In order to support data representation of molecular DST, additional implementation guides, published by the HL7 Clinical Genomics Work Group, were used and adopted for the purpose of this study. The implementation guides are *HL7 Version 2 Implementation Guide: Clinical Genomics; Fully LOINC-Qualified Genetic Variation Model, Release 2 (U.S. Realm)*, and *HL7 Version 2 Implementation Guide: Clinical Genomics Coded Reporting – “Lite”, Release 1 (1st DSTU Ballot) – US Realm, Standard for Trial Use, July 2016*^{14, 15}. These implementation guides are modeled after established laboratory reporting standards and detail how to structure genetic test results into electronic health records (EHRs) utilizing HL7 v2.5.1 messaging standard specifications^{14, 15}. For example, the *HL7 Version 2 Implementation Guide: Clinical Genomics; Fully LOINC-Qualified Genetic Variation Model, Release 2 (U.S. Realm)* specifically “covers the reporting of genetic test results for sequencing and genotyping based tests where identified DNA variants are located within a gene”¹⁴ (p. 2). In the context of molecular DST data representation, the interest is on identified DNA variants located within the TB genome.

Use of Standard Vocabulary and Value Sets

The study also used a set of recommended standard vocabulary and value sets including but not limited to Logical Observation Identifiers Names and Codes (LOINC) and Systematized Nomenclature of Medicine - Clinical Terms (SNOMED CT). Whereas the LOINC codes and associated long common names were used for identifying resulted laboratory tests, the SNOMED CT concept identifiers and associated preferred terms were used for reporting specimen types and microbiology related test results. Use of these recommended standard vocabulary and value sets not only simplifies the complexity of the message components of the molecular genetic data, but also enhances the quality of segments and components of the TB case notification messages generated by the variety of molecular DST platforms¹⁴.

Identifying drug resistance-associated genetic mutations in isolates of *Mycobacterium tuberculosis* complex (MTBC) required the use of a reference terminology known as RxNorm for antituberculosis drug names. The RxNorm system, initially developed by the U.S. National Library of Medicine in November 2004, is a single, multipurpose standard terminology for representing medications or clinical drug components¹⁶. More specifically, RxNorm is a standardized nomenclature for clinical drugs that enables storage, retrieval, analysis, and interoperability of clinical data¹⁶⁻¹⁹.

Results

The Role of Electronic Laboratory Reporting (ELR) in Public Health Surveillance

Electronic Laboratory Reporting (ELR) plays an integral role in improved communicable disease surveillance by representing and transmitting exchangeable nationally notifiable laboratory data to public health agencies. Participating in ELR allows incoming laboratory data to be translated, processed, and routed to appropriate public health recipients (e.g., Local Health Departments and State Programs) for rapid and immediate public health action²⁰. ELR is, therefore, critical for an effective public health response to nationally notifiable diseases and potential bioterrorism agents^{21, 22}.

Wurtz and Cameron²¹ defined ELR as the “direct, automated messaging of reportable disease laboratory information from clinical laboratory information management systems (LIMS) directly to the appropriate public health jurisdiction’s communicable disease reporting system” (p. 1639). Specifically, ELR relies solely on the electronic exchange of laboratory data with participating public health agencies. ELR has also been demonstrated to improve the completeness and timeliness of communicable disease surveillance and reduce manual data entry errors^{21, 23-25}.

The Health Information Technology for Economic and Clinical Health (HITECH) Act authorized the Centers for Medicare and Medicaid Services (CMS) to incentivize the nationwide implementation and adoption of ELR for communicable disease surveillance through a program commonly known as *Meaningful Use* (MU)^{23, 25, 26}. The stages 2 and 3 of the MU criteria provide incentive payments to eligible professionals, eligible hospitals, and critical access hospitals who adopt and successfully demonstrate electronic submission of laboratory data for reportable disease cases to public health departments²⁵. These MU requirements, coupled with incentive payments, have directed many federal and state public health agencies and standards development organizations (SDOs) to create standard specifications for secure systems for electronic data transmission to not only support the MU requirements, but also improve the quality of the electronic exchange of laboratory data with external public health agencies^{22, 23, 26}. As a case in point, CDC has accelerated the use and adoption of ELR by advancing standards for messaging, vocabulary, and data formats; and by conducting an extensive outreach campaign to state and local public health departments^{22, 25, 27}. Moreover, HL7

International, which is an ANSI-accredited SDO, has developed and published many implementation guides for ELR involving the use of HL7 v2 messaging standard.

Designing the DTBE ORU^R01 Message Hierarchy

Laboratory information is usually reported through the HL7 Observation Report – Unsolicited (ORU) trigger event R01 (represented as ORU^R01) message to public health agencies. The ELR message is a constrained ORU^R01 message for transmitting reportable laboratory results and observations from the testing source to public health agencies^{12, 13}. The ORU^R01 message is the only acceptable message format or standard to follow for creating ELR messages for MU in order to support electronic data exchange of laboratory results of reportable diseases^{20, 28, 29}.

The ORU^R01 message structure or hierarchy for the HL7 v2.3.1 ELR standard, released in 2005, utilized Message Header (MSH), Patient Identification (PID), Next of Kin (NK1), Common Order (ORC), Observation Request (OBR), Observation Result (OBX), and Notes and Comments (NTE) segments. The release of HL7 v2.5.1 ELR standard in 2010, however, expanded the optionality to include segments such as Software (SFT) and laboratory specimens (SPM). This expansion not only addressed requests from state public health departments and clinical laboratories, but also resolved a conflict with the eXtensible Markup Language (XML) implementations of the HL7 standard¹². The Venn diagram (Figure 1) depicts the key differences in supported segments between the HL7 v2.3.1 ELR message and the HL7 v2.5.1 ELR message. Segments displayed without brackets are required (e.g., PID). Segments enclosed in square [] brackets are optional (e.g., [ORC]). Segments enclosed in curly {} brackets are required and may repeat (e.g., {OBR}). Segments enclosed in both square [] and curly {} brackets are optional, but if included these segments may repeat (e.g., [{SPM}])^{12, 20}.

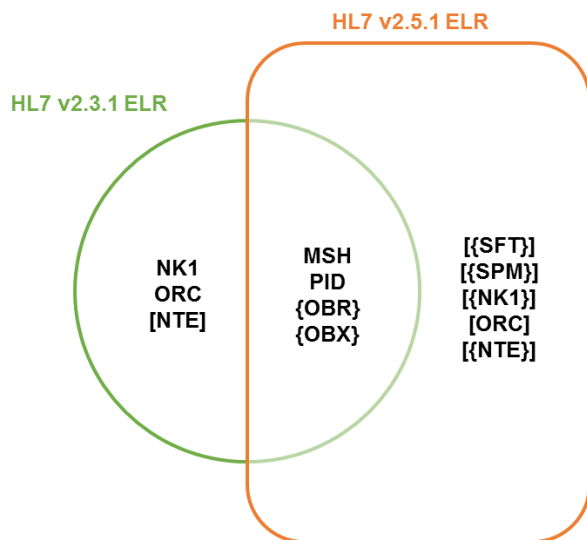


Figure 1. Supported segments between the HL7 v2.3.1 ELR message and the HL7 v2.5.1 ELR message.

Using the HL7 v2.5.1 ELR message specifications as the foundation, the DTBE ORU^R01 message hierarchy (Figure 2) was developed to support comprehensive data representation, capture, storage and monitoring of all proposed RCVT 2020 data elements that include molecular DST data. Whereas the Additional Demographic (PD1) segment contains demographic information that is likely to change about the patient, the Patient Visit (PV1) segment is used to communicate information about the patient’s visit to institutions and healthcare facilities³⁰.

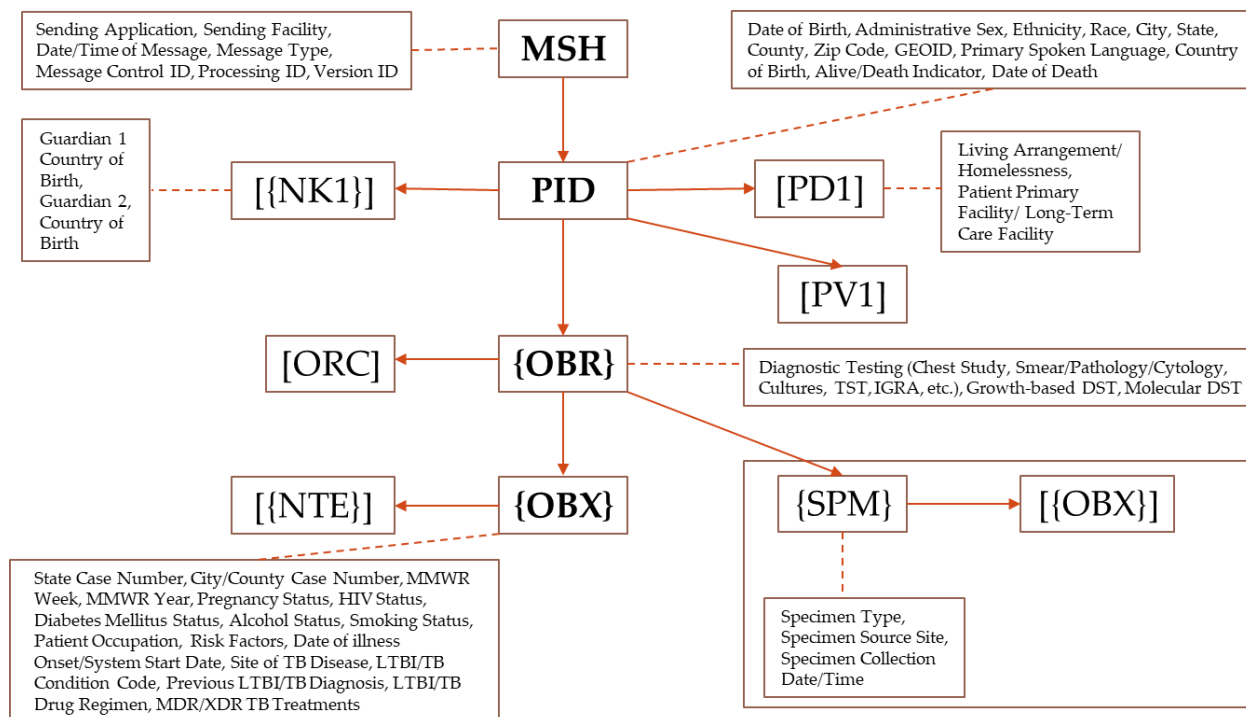


Figure 2. DTBE ORU^R01 Message Hierarchy with key RVCT 2020 Data Elements.

Identification of Molecular DST Data Elements

Molecular DST methods are gaining popularity in TB diagnostics because they offer robust and rapid detection of genetic mutations associated with resistance to antituberculosis drugs^{1, 31-35}. Another contributing factor to their popularity is the rapidly changing laboratory methodology for TB diagnostics and sensitivity testing.

Lin and Desmond³ categorized molecular DST into two types: *Probe-based* and *Sequence-based* methods. Whereas *Probe-based* methods report the presence or absence of mutations in the gene, *Sequence-based* methods report the identity of specific mutations in the gene^{1, 3}. Examples of sequence-based methods include pyrosequencing, Sanger sequencing, next generation sequencing and whole genome sequencing. Probe-based or non-sequencing methods include Cepheid GeneXpert® MTB/RIF, Hain MTBDRplus and MTBDRsl, and INNO-LiPA RIF³. It is recommended that detected genetic mutations from non-sequencing methods (e.g., Cepheid GeneXpert®) is confirmed with sequence-based methods^{3, 36}. The CDC's Molecular Detection of Drug Resistance (MDDR) service utilizes the combination of Sanger sequencing and pyrosequencing^{1, 3, 10, 31}. For the purposes of this study, the focus or interest was primarily on two key questions: 1) *How should we capture and store Rifampin resistant results from Cepheid GeneXpert® MTB/RIF?* and 2) *How should we capture and store specific genetic mutations detected using sequence-based assays (e.g., CDC's MDDR Service)?*

Data Representation of Rifampin Resistant Results from Cepheid GeneXpert® MTB/RIF

The Cepheid GeneXpert® MTB/RIF has U.S. Food and Drug Administration (FDA) market authorization for use with raw sputum or sputum sediments³⁷. The Cepheid GeneXpert® MTB/RIF assay utilizes a self-contained, disposable cartridge to provide rapid and robust detection of mutations associated with RIF resistance^{3, 38}. Essentially, the Cepheid GeneXpert® MTB/RIF test is a cartridge-based fully automated nucleic acid amplification test (NAAT) for simultaneous detection of MTBC and mutations associated with rifampin resistance^{1, 39}.

Hence, in the context of the Cepheid GeneXpert® data representation, there are two resulted laboratory reports to be considered: (a) identification of MTBC via NAAT method; and (b) detection of mutation in the Rifampin resistance (rpoB) gene. At its simplest, the majority of coded results for GeneXpert® will fall into three categories: MTBC identification with NAA probe detection (i.e., 38379-4^Mycobacterium tuberculosis complex DNA [Presence] in Unspecified specimen by NAA with probe detection^LN), MTBC detected (i.e., 260373001^Detected^SCT) or not

detected (i.e., 260415000^Not detected^SCT) as well as whether a mutation in the Rifampin resistance (rpoB) gene has been detected or not been detected. Table 1 depicts the key molecular DST data elements and their associated vocabulary and minimum data representations in HL7 v2.5.1 ELR. The convenience and automation of the Cepheid GeneXpert® assay has the potential to provide rapid access to patient laboratory results³⁸.

Table 1. Key Cepheid GeneXpert® molecular DST data elements and their associated minimum data representations in HL7 v2.5.1 ELR.

Key GeneXpert® Molecular DST Data Element	Standard Vocabulary and Value Sets	Minimum Data Representation in HL7 v2.5.1 ELR*
Test Type 1 (e.g., NAA method) Test Result 1 (e.g., MTBC detected)	LOINC Code: 38379-4 LOINC Long Common Name: Mycobacterium tuberculosis complex DNA [Presence] in Unspecified specimen by NAA with probe detection SNOMED CT Concept ID: 260373001 SNOMED CT Preferred Term: Detected	OBX 1 CWE 38379-4^Mycobacterium tuberculosis complex DNA [Presence] in Unspecified specimen by NAA with probe detection^LN 1 260373001^Detected^SCT A^Abnormal^HL70078^^^2.5.1 F 20180220144700 20180221130016 <cr>
Test Type 2 (e.g., Rifampin resistance (rpoB) gene method) Test Result 2 (e.g., Rifampin resistance (rpoB) gene detected)	LOINC Code: 89372-7 LOINC Long Common Name: Mycobacterium tuberculosis complex rpoB gene rifampin resistance mutation [Presence] by Molecular genetics method SNOMED CT Concept ID: 260373001 SNOMED CT Preferred Term: Detected	OBX 2 CWE 89372-7^Mycobacterium tuberculosis complex rpoB gene rifampin resistance mutation [Presence] by Molecular genetics method^LN 260373001^Detected^SCT F 20180218175900 20180221133259 <cr>
Specimen Type (e.g., Sputum) Specimen Collected DateTime (e.g., 20180218175900)	SNOMED CT Concept ID : 119334006 SNOMED CT Preferred Term: Sputum specimen	SPM 1 119334006^Sputum specimen^SCT 20180218175900 20180221105743 <cr>

* See Illustration A for full representation of supported segments.

Data Representation of Specific Genetic Mutations Detected from CDC's MDDR Service

Since September 2009, the Mycobacteriology Laboratory Branch of the DTBE at CDC has offered Clinical Laboratory Improvement Amendments (CLIA)-compliant molecular diagnostics reference service known as Molecular Detection of Drug Resistance (MDDR)^{31, 37}. The CDC's MDDR service uses conventional DNA sequencing (Sanger sequencing) for the identification of genetic mutations associated with multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB^{33, 37, 40}. In June 2012, however, the service was expanded by incorporating pyrosequencing into the testing algorithm to more efficiently perform the service and serve as an initial screen for MDR TB^{31, 32, 40}. If mutations are detected by pyrosequencing, then the full panel of Sanger sequencing assay is performed.

The CDC's MDDR service examines DNA from isolates or NAAT positive sediments at specific targets to determine if mutations known to be associated with resistance are present. Growth-based DST is performed concurrently^{33, 37}. The data representation of molecular DST from the CDC's MDDR service, therefore, focuses on capturing and storing data elements relating to antituberculosis drug names, TB gene names, amino acid changes, indels, nucleic acid changes, specimen types, test types, and results indicating if genetic mutation is present or not at each relevant target

(Table 2). Even though this study used the CDC’s MDDR service as an example, the minimum data representation in HL7 v2.5.1 ELR would be the same for any clinical or public health laboratories performing sequencing-based assays.

Table 2. Key CDC’s MDDR Service molecular DST data elements and their associated minimum data representations in HL7 v2.5.1 ELR.

Key CDC’s MDDR Service Molecular DST Data Element	Standard Vocabulary and Value Sets	Minimum Data Representation in HL7 v2.5.1 ELR*
Drug Name (e.g., Isoniazid)	LOINC Code: 51963-7 LOINC Long Common Name: Medication assessed [ID] RxNorm RxCUI: 6038 RxNorm Concept Name: isoniazid	OBX nn CWE 51963-7^Medication assessed [ID]^LN 1 6038^isoniazid^RxNorm
Gene Name (e.g., katG)	LOINC Code: 48018-6 LOINC Long Common Name: Gene studied [ID] NCBI-gene ID: 885638 NCBI-gene Symbol: katG	OBX nn CWE 48018-6^Gene studied [ID]^LN 2a 885638^katG^geneCodeNCBI
Amino acid change (e.g., Ser315Thr)	LOINC Code: 48005-3 LOINC Long Common Name: Amino acid change	OBX nn CWE 48005-3^Amino acid change^LN 2a Ser315Thr^^HGVS
Indel (e.g., Substitution)	LOINC Code: 48019-4 LOINC Long Common Name: DNA change [Type] LOINC Code: LA6690-7 LOINC Long Common Name: Substitution	OBX nn CWE 48019-4^DNA change [Type]^LN 2a LA6690-7^Substitution^LN
Nucleic Acid Change (e.g., AGC>ACC)	LOINC Code: 47998-0 LOINC Long Common Name: DNA sequence variation display name [Text] Narrative	OBX nn ST 47998-0^DNA sequence variation display name [Text] Narrative^LN 2a AGC>ACC
Result (e.g., Mutation present)	LOINC Code: 69548-6 LOINC Long Common Name: Genetic variant assessment SNOMED CT Concept ID: 52101004 SNOMED CT Preferred Term: Present	OBX nn CWE 69548-6^Genetic variant assessment^LN 2a 52101004^Present^SCT
Test Type (e.g., Sequencing)	LOINC Code: 81304-8 LOINC Long Common Name: Variant analysis method [Type] SNOMED CT Concept ID: 117040002 SNOMED CT Preferred Term: Nucleic acid sequencing	OBX nn CWE 81304-8^Variant analysis method [Type]^LN 2a 117040002^Nucleic acid sequencing^SCT
Specimen Type (e.g., Sputum) Specimen Collected DateTime (e.g., 20180218175900)	SNOMED CT Concept ID: 119334006 SNOMED CT Preferred Term: Sputum specimen	SPM 1 119334006^Sputum specimen^SCT 20180218175900 20180221105743

* See Illustration B for full representation of supported segments.

Discussion

Molecular DST data are challenging and difficult to standardize for ELR. The majority of complicated genetic and molecular DST results are currently reported by clinical and public health laboratories in pure narrative text formats (e.g., Word or PDF format) with no computer accessible coding and processing of the results^{15, 24}. The overarching goal of this study is to make it easier to structure molecular DST results with standardized vocabulary, thereby, enabling the delivery of structured data that could be used in clinical decision support systems and medical record queries to facilitate evidence-based medicine and translational research. Early implementation and adoption of the developed data exchange formats in this study could be relatively simple for clinical and public health laboratories that already use HL7 v2.5.1 ELR¹⁵.

The data exchange formats, therefore, would (a) optimize early detection and reporting of drug-resistant TB cases; (b) provide a national standardized protocol for public health and clinical laboratories to use reference terminologies such as LOINC, SNOMED CT, and RxNorm to report molecular DST data to state public health departments that would use the same to report to CDC; (c) provide a high-quality data-driven decision-making process for TB public health administrators; (d) generate high-quality datasets to enhance reporting or analyses of TB surveillance data and drug resistance; and (e) ensure that critical or important clinical information is not hidden in the notes and comments segment of the HL7 v2.5.1 ELR.

The study supports structural and semantic interoperability as it not only uses HL7 v2.5.1 ELR message as the preferred data format for the molecular DST data, but also uses LOINC, RxNorm, and SNOMED CT as the preferred terminologies, respectively, for laboratory tests, antituberculosis drugs, and specimen types. The study also provides a comprehensive informatics platform to continuously, systematically, and seamlessly collect and monitor molecular DST data to support epidemiological studies of drug-resistant TB cases for public health surveillance. Appropriate use of the developed data exchange formats will support accurate, timely, coherent and consistent data representations for public health laboratories that identify reportable or nationally notifiable conditions to support comprehensive public health surveillance.

Beyond the flexibility of implementing the data exchange formats, it is important to understand that molecular DST methods have several caveats and limitations that differ depending on the drug^{3, 37}. One of the key limitations is that molecular DST is not available for all antituberculosis drugs. Not all mutations confer resistance and not all mutations associated with resistance are known. More importantly, there exist some discordance between molecular and growth-based DST results^{3, 32, 33, 37}. Also, sensitivity and specificity for molecular DST are less than 100%³. These limitations inherently affect the reliability of the data exchange formats and might subsequently affect the results of epidemiological studies.

Conclusion

The implementation of the data exchange formats is still progressing at DTBE. There is also a plan to pilot molecular genetic data exchange in the NTSS using California Department of Public Health and New York State Department of Health as external partners. In conclusion, this study demonstrates that it is possible to apply standardized protocols to enhance data specifications and exchange formats within the NTSS, thereby streamlining the seamless exchange of drug-resistant TB incident cases in an integrated public health environment supporting TB surveillance, informatics, and translational studies. Moreover, the methodology applied in this study could be replicated across other disease surveillance systems that seek to exchange molecular genetic data and maximize data quality of information exchanges.

Disclaimer

The views expressed are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC) or the United States Government. References in this manuscript to any specific commercial products, process, service, manufacturer, or company does not constitute its endorsement or recommendation by the U.S. Government or CDC.

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Illustration A: Sample Supported Segments for Cepheid GeneXpert®

OBR|1||89371-9^MTB complex DNA and rpoB RIF resistance mutation panel [Presence] - Isolate or Specimen^LN||20180218175900|||||||||20180220144700||F|<cr>
OBX|1|CWE|38379-4^Mycobacterium tuberculosis complex DNA [Presence] in Unspecified specimen by NAA with probe detection^LN|1|260373001^Detected^SCT||A^Abnormal^HL70078^^^2.5.1| ||F||20180220144700||||20180221130016||||<cr>
OBX|2|CWE|89372-7^Mycobacterium tuberculosis complex rpoB gene rifampin resistance mutation [Presence] by Molecular genetics method^LN||260373001^Detected^SCT||||F| ||20180218175900||||20180221133259||||<cr>
SPM|1||119334006^Sputum specimen^SCT|||||||||20180218175900|20180221105743|<cr>

Illustration B: Sample Supported Segments for CDC's MDDR Service

OBR|1||81247-9^Master HL7 genetic variant reporting panel^LN||20160729|||||||||20160805||F|
OBX|1|CWE|51963-7^Medication assessed [ID]^LN|1.a|9384^Rifampin^RxNorm|
OBX|2|CWE|51963-7^Medication assessed [ID]^LN|1.b|6038^isoniazid^RxNorm|
OBX|3|CNE|48018-6^Gene(s) assessed^LN|1.a|888164^rpoB^geneCodeNCBI|
OBX|4|CNE|48018-6^Gene(s) assessed^LN|1.b|885638^katG^geneCodeNCBI|
OBX|5|CWE|48018-6^Gene studied [ID]^LN|2a|888164^rpoB^geneCodeNCBI|
OBX|6|CWE|48005-3^Amino acid change^LN|2a|Ser531Leu^^HGVS|
OBX|7|CWE|48019-4^DNA change [Type]^LN|2a|LA6690-7^Substitution^LN|
OBX|8|ST|47998-0^DNA sequence variation display name [Text] Narrative^LN|2a|TCG>TTG|
OBX|9|CWE|69548-6^Genetic variant assessment^LN|2a|52101004^Present^SCT|
OBX|10|CWE|81304-8^Variant analysis method [Type]^LN|2a|117040002^Nucleic acid sequencing^SCT|
OBX|11|CWE|48018-6^Gene studied [ID]^LN|2b|885638^katG^geneCodeNCBI|
OBX|12|CWE|48005-3^Amino acid change^LN|2b|Ser315Thr^^HGVS|
OBX|13|CWE|48019-4^DNA change [Type]^LN|2b|LA6690-7^Substitution^LN|
OBX|14|ST|47998-0^DNA sequence variation display name [Text] Narrative^LN|2b|AGC>ACC|
OBX|15|CWE|69548-6^Genetic variant assessment^LN|2b|52101004^Present^SCT|
OBX|16|CWE|81304-8^Variant analysis method [Type]^LN|2b|117040002^Nucleic acid sequencing^SCT|
SPM|1|3000654137||258589002^Lymph node sample^SCT|||||||||20160729|

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