5: Data Accuracy

Definitions

Term	Definition
Acid-fast bacilli (AFB) smear	Microscopic examination of a specimen (e.g., sputum) or a processed sediment for detection of AFB. The most common method uses fluorescence staining. AFB-smear microscopy is not specific for *M. tuberculosis* complex. AFB-smear microscopy may also be performed to verify the presence of AFB in positive cultures prior to confirmatory species identification.
Calculated variable	CDC-developed variables, calculated from existing information, to simplify certain algorithms.
Case Verification Criteria (VERCRIT)	An RVCT calculated variable used for verifying a TB case.
Clinical specimen	Material taken directly from the patient (e.g., sputum, cerebral/spinal fluid, pleural fluid, or lung biopsy specimen).
Commercial surveillance software	A web-based surveillance system developed by a private company.
Completion of therapy (COT)	Therapy is completed within one year from start of treatment or as indicated by the patient's medical provider.
Data accuracy	The data submitted matches patient records maintained at the point of care. The recorded data in the surveillance system are consistent with what happens in a clinical encounter, whether or not it is clinically appropriate.

Term	Definition
Data validation	The process of verifying that the data provided originate from valid data. The process can be used to calculate the percent discordance between the TB patients' medical records and the surveillance system data.
Direct detection	Rapid detection (usually 2 days) of nucleic acid (i.e., RNA or DNA) sequences of interest in organisms present in a clinical specimen. Nucleic Acid Amplification (NAA) test is an example of direct detection.
Discordance	The data entered in the system are different from the data in the patient's medical records.
Electronic Report of Verified Case of Tuberculosis (eRVCT)	A web-based surveillance system for reporting TB cases developed by CDC's DTBE and available to all reporting jurisdictions. The system is based on the RVCT form.
Health Level 7 (HL7) code	A code developed to promote and facilitate use of international healthcare informatics interoperability standards. HL7 code provides a framework (and related standards) for the exchange, integration, sharing, and retrieval of electronic health information.
Isolate	A sample from a specimen that was identified as a certain organism such as *M. tuberculosis* complex from a culture. Culture media may be solid (e.g., Lowenstein-Jensen [LJ] or Middlebrook) or liquid (e.g., MGIT, VersaTrek, BacTAlert, 7H9 broth).
Miliary tuberculosis	Miliary TB is a serious type of disease. It is based on a histological or radiologic finding, rather than a site of disease. The diagnosis is supported by the appearance on radiograph as a great number of small, well-defined nodules that look like millet seeds scattered throughout the lungs, hence the name "miliary."
Mycobacterium tuberculosis	The bacterium that causes tuberculosis. It has a waxy cell wall and is slow growing. It is sometimes called the tubercle bacillus.
***Mycobacterium tuberculosis* complex (MTBC)**	In addition to *M. tuberculosis*, the complex includes seven other TB-causing mycobacteria: *M. bovis, M. africanum, M. microti, M. canetti, M. caprae, M. pinnipedii, and M. mungi.*
National Electronic Disease Surveillance System (NEDSS)	A web-based surveillance system with an infrastructure developed by CDC that uses specific Public Health Information Network (PHIN) and NEDSS messaging standards.
National TB Indicators Project (NTIP)	A monitoring system using standardized definitions, indicators, and calculations to track progress toward attaining national TB program objectives.

Term	Definition
National Tuberculosis Surveillance System (NTSS)	The only national repository of TB surveillance data in the United States. NTSS receives data on TB cases from reporting jurisdictions' web-based systems through a standardized data collection form, the Report of Verified Case of Tuberculosis (RVCT).
Nucleic Acid Amplification (NAA)	A technique that amplifies (copies) DNA or RNA segments, in order to directly identify microorganisms in sputum specimens.
Percent discordance	The calculation that divides the number of discordant records by the number of records reviewed.
Probe	A piece of single-stranded nucleic acid that hybridizes specifically to the complementary sequence of RNA or DNA in the sample. Probes are used to detect the presence of *M. tuberculosis* complex within a clinical specimen or culture.
Public Health Information Network (PHIN) code	A standardized code used by computer programmers to assign TB data to a specified RVCT variables. These variable codes are essential in transmitting data to CDC. Several data issues have been attributed to errors on data system programming involving PHIN codes. For example, if a code is incorrect, the data can disappear. If the data are all missing, check the PHIN Variable ID.
Report of Verified Case of Tuberculosis (RVCT)	The NTSS standardized data collection form. Data are collected by 60 reporting jurisdictions and submitted electronically to CDC. Data are used to monitor national TB trends, identify priority needs, and create the DTBE annual surveillance report, Reported Tuberculosis in the United States.
Secure Access Management Services (SAMS)	A federal information technology system that gives authorized personnel secure, external access to non-public CDC applications.
Skip pattern	Data response pattern that allows one to skip automatically when data entered for a field is not expected.
Tuberculosis Genotyping Information System (TB GIMS)	A secure web-based system designed to improve access, management, and application of genotyping data at the state and local level. As part of the NTSS, TB GIMS contains tools to detect and prioritize TB outbreaks.

Term	Definition
Tuberculosis Information Management System (TIMS)	TIMS was a Windows-based, client-server application that helped health departments and other facilities manage TB patients, conduct TB surveillance activities, and manage TB programs overall. TIMS replaced former DTBE software (SURVS-TB and TBDS) and provided for electronic transmission of TB surveillance data and program management reports. TIMS was replaced by web-based surveillance systems in 2009.

Quality Assurance Process for Data Accuracy

Primary Purpose

This section provides a quality assurance (QA) process to identify and correct inaccuracies in the surveillance data.

QA Process for Conducting Data Accuracy

Data accuracy is one of the most important QA components. Inaccurate data may result in improper follow-up of patients, inadequate resources (e.g., funding, staff, facilities, drugs, and supplies), inaccurate evaluation and policy development, misrepresentation of the public health burden of TB, and inability to measure TB program indicators based on surveillance data.

Reviewing medical records of TB patients and comparing them with the data recorded in the surveillance system is the best way to check for data accuracy or data consistency.

For practical purposes, data accuracy and data consistency are used interchangeably in this manual.

If reviewing medical records is not possible, the following questions can be used to review the accuracy of their TB data.

1. Is the field completed in a way that makes logical sense? For example, an 80-year-old should not have a birthdate of January 1, 2000.
2. Does the response match what the laboratory reports and other readily available medical records (e.g., x-ray reports) indicate?
3. Are the local or district health departments following what is outlined in the TB Cooperative Agreements (CoAg) with the reporting jurisdiction or CDC?

In the CoAg, the QA process for conducting data accuracy includes evaluating accuracy and validity of Report of Verified Case of Tuberculosis (RVCT) data by reviewing patient's medical records **at least annually**. Also, assessing the knowledge, skills, and abilities of staff and providing training if needed is important in ensuring data accuracy.

Chapter 9: Quality Assurance Cross-cutting Systems and Process provides additional tools and systems (i.e., the National Tuberculosis Indicators Project [NTIP]; Tuberculosis Genotyping System [TB GIMS]; and Cohort Review that can be used for improving data accuracy.

Table 5.1 includes a table format for the surveillance section of CoAg requirements for ensuring data accuracy and possible data sources.

Table 5.1
Data Accuracy Quality Assurance Process
CoAg Requirements

Note: The requirements are based on Fiscal Year 2014 CoAg and may need to be updated when the CoAg is updated. The CoAg is reformatted into the following table with an addition of possible data sources and activities.

Data Accuracy Requirements

CoAg Requirements	Description	Possible Data Sources and Activities
Evaluate accuracy or validity of RVCT data.	**At least annually** • Evaluate the accuracy or validity of RVCT data by comparing RVCT data and the jurisdiction's TB registry data to original data sources.	Review and evaluate accuracy of • RVCT data collection forms • Patients' medical records • TB database.
Assess knowledge, skills, and abilities of staff and provide training if needed.	**Assess the knowledge, skills, and abilities of** all existing personnel and new hires whose duties involve the collection and reporting of registry and RVCT data.	Determine staff competencies • Review personnel files. • Conduct staff interviews. • Observe and evaluate staff skills.
	Provide training and evaluation • Focus training on accurate and timely completion of the revised RVCT. • Train all existing staff on the revised RVCT data collection; new staff should be trained **within 2 months of hire date.**	Train staff as needed.

Example: National Tuberculosis Surveillance System (NTSS)

Primary Purpose

The primary purpose of this section is to present tools for evaluating TB data and validation checks to ensure accurate data.

Background

Previously one data software system, the Tuberculosis Information Management System (TIMS), was used to report all cases to CDC from all reporting areas. Reporting areas with their own reporting systems were required to submit their data in a TIMS-compatible format through the TIMS Surveillance Import Utility (TSIU). In 2009, the RVCT data collection form was revised to collect additional information. Modifications to how other data were previously reported also occurred.

Some of the changes to data collection include:

- Anatomic codes for diagnostic tests are now available for tests with negative and positive results.
- Miliary disease is reported from the chest x-ray or chest CT scan instead of from site of disease.
- U.S.-born patient records are required to show country of birth.

For more information, see the Report of Verified Case of Tuberculosis Fact Sheet at http://www.cdc.gov/tb/publications/factsheets/statistics/rvct.htm.

Currently there are four types of systems used to collect and send data to CDC from the states. CDC receives these data through the TB Case Notification message.

1. **The National Electronic Disease Surveillance System (NEDSS)-Base System**, an electronic disease surveillance system sponsored by CDC
2. **The eRVCT**, a CDC-developed electronic Report of Verified Case of Tuberculosis (RVCT) application
3. **Commercial systems**, developed by various vendors and tailored to a state's individual needs
4. **State-developed systems,** which may serve purposes other than just surveillance

Upgrades and Enhancements for Data Collection

Nucleic Acid Amplification Test Result

Nucleic acid amplification (NAA) test results are accepted as a means to verify cases. However, some systems initially did not make provisions for this option, which created an inability to verify cases when the algorithm was incomplete. PHIN codes for diagnostic test results at the state have sometimes been incompatible with CDC code. This can result in data that exist in state systems but cannot be transferred to CDC. Therefore, some cases cannot be confirmed by laboratory results.

Transition from TIMS

Migration from TIMS software has added to a state's flexibility in developing a system to meet their specific surveillance and case management needs. However, data can now be interpreted in many different ways. HL7 messaging and PHIN vocabulary are informatics tools and are not intuitive to many data analysts.

Public Health Information Network (PHIN) Code Mapping

Mapping translates the PHIN numerical data codes into understandable terms. As data collection transitioned to the new systems, CDC examined the PHIN code mapping to ensure accuracy. In addition, data flow and skip-pattern rules were evaluated for consistency. An extensive set of checks was developed. The two CDC-developed systems (NEDSS Base System and the eRVCT) have undergone extensive testing and include built-in validation procedures. Commercial- and state-developed systems have varying levels of validation.

In order to analyze data consistently at CDC, certain rules guide the interpretation of the data. When data are entered for a field without the proper response in a preceding field, the subsequent data are ignored. For example,

- Initial drug susceptibility test results for individual drugs are ignored if the record does **not** show that the patient had a positive culture result and that initial susceptibility testing was done.
- Type of correctional or long-term care facility is ignored if patient is **not** a resident of a correctional or long-term care facility, respectively.
- Collection dates and results reporting dates for diagnostic tests are ignored when diagnostic tests are shown as "**Not Done**."

Variables Modified from TIMS

Some variables have been modified from TIMS. Examples of several of these are described in Table 5.2.

Table 5.2
Selected Modified TIMS Variables

RVCT #	Item	Modified Variables
3	**Case Numbers**	The new state case number is 15 digits in length and consists of the year reported, reporting area and nine-digit locally assigned ID number.
21	**Nucleic Acid Amplification Test Result**	The results of a positive nucleic acid amplification test are accepted in the hierarchy of verifying a TB case. The new hierarchy is: 1. Positive culture 2. Positive NAA test 3. Positive smear (in the absence of a positive or negative culture) 4. Clinical case 5. Provider diagnosis
22 A	**Initial Chest Radiograph**	The responses for the initial radiograph status question have not changed. The cavitation question no longer evaluates whether it is consistent with TB; just whether there is evidence of a cavity. The TB stability question has been eliminated. A question on evidence of miliary disease has been added.
30	**Primary Occupation Within Past Year**	The multiple occupation choice is eliminated. Only the primary occupation during the past 12 months is requested. In addition, two new choices are available, "Retired" and "Not Seeking Employment."

Special Variables for Analysis

CDC identified certain concepts that are better defined through the development of algorithms. This allows consistent interpretation of the concept. The following descriptions explain how CDC identifies cases that complete therapy within 1 year among those eligible, and also how case with multidrug-resistant (MDR) and extensively drug-resistant (XDR) disease among those patients with sufficient initial susceptibility test results are identified.

Completion of Therapy in One Year

Most patients, if fully sensitive to their anti-TB drugs, can complete therapy within 6-9 months. Certain conditions extend therapy to 12 months and beyond. Table 5.3 indicates the criteria that enable a patient to be eligible to complete therapy within 1 year.

Table 5.3
Eligibility to Complete Therapy within One Year

Eligibility Criteria
Patients must • Be alive at diagnosis, • Be on one or more anti-TB drugs, • NOT die during therapy, • NOT be rifampin resistant, • NOT be a pediatric TB case with evidence of miliary disease or a positive blood culture, and • NOT have meningeal disease.

The 2015 national objective goal for completion of therapy (COT) is 93% within 1 year among those patients who are eligible. This is a major indicator of program performance. Table 5.4 indicates when the calculation for completion of therapy is performed.

Table 5.4
Calculation for Completion of Therapy

When Calculation is Performed
• The patient is alive at diagnosis, • On one or more anti-TB drugs, and • Did not move out of the United States during treatment.

To determine if a patient has completed therapy within 1 year, the reason therapy stopped must be "Completed." CDC determines whether both start and stop therapy dates are full dates. If neither date has a missing day, both dates are used as provided and completion of therapy should occur within one year (366 days). If **not**, CDC allows for a missing day value (i.e., 12/??/2011) for either start or stop date or both but the calculation is more conservative (Table 5.5).

Table 5.5
Calculation for Duration of Therapy
Missing Day Value for Start or Stop Date

CDC Requirements	Missing Day	Comments
COT in less than or equal to 351 days	If either a start or stop date is missing a "day" value (e.g., 12/??/2011)	The missing "day" value is replaced with the 15th of the month.
COT in less than or equal to 336 days	If both start and stop dates have a missing "day" value (e.g., 12/??/2011)	The missing "day" value is replaced with the 15th of the month.

The COT percentage is determined by those patients who complete therapy within 1 year among those eligible to complete.

MDR and XDR TB

With concern focused on identifying cases of MDR and XDR TB, CDC has created algorithms that provide quick detection to indicate the likelihood of these cases. Presently the algorithms examine only initial susceptibility test results. To frame the patient group that can be examined for MDR, there is a subset based on the patient having a positive culture result and initial susceptibility testing to at least isoniazid and rifampin. Patients resistant to at least isoniazid and rifampin are classified as MDR TB patients.

To frame the patient group that can be examined for XDR, there is a subset based on the patient having a positive culture, initial susceptibility testing to at least isoniazid and rifampin and at least one second-line injectable (i.e., amikacin, kanamycin or capreomycin) and at least one fluoroquinolone (e.g., ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin, or other fluoroquinolone). Patients initially resistant to at least isoniazid and rifampin, at least one second-line injectable, and at least one fluoroquinolone are classified as XDR TB patients.

Exercises 5.1-5.5: Data Accuracy Examples

5.1	**Charles died during therapy. His death date is recorded as 11/25/2012. What should you put in RVCT item 15, Status at TB diagnosis?**
	Answer (provide an explanation):

5.2	**Can a patient have a "Date sputum smear was collected" without a "Date sputum smear result was reported"?**
	Answer (provide an explanation):

5.3	**Kirk's sputum culture result report date was 06/11/2012 and his sputum culture collection date was 06/27/2012. How long did it take for Kirk's sputum culture result to be reported?**
	Answer (provide an explanation):

5.4	**Maya's chest x-ray was Abnormal. Should there be a response to Evidence of a cavity or Evidence of miliary TB?**
	Answer (provide an explanation):

5.5	**Dwayne's record shows that he was not under the custody of Immigration and Customs Enforcement (ICE). What RVCT item is needed to be responded to first in order to provide this information?**
	Answer:

Data Accuracy Checklist

Table 5.6 describes some of the data issues that are in conflict with RVCT instructions, and pinpoints data items for review.

Table 5.6
Data Accuracy Checklist

Data Issue	Description/Comment
Calculated variables	CDC-developed variables, calculated from existing information, to simplify certain algorithms. These algorithms are used to help frame the subset of records that are eligible for the calculations (e.g., eligible to complete therapy within 1 year).
Text fields	Text fields, in many cases, do not have a defined structure and can contain all types of information. Unusual and confusing responses in these fields are ignored in favor of the PHIN code that defines the response more accurately.
Data response patterns	Data response patterns, or skip patterns, ensure that no data are entered for a field where a response is not expected or by allowing one to skip questions that are not relevant.
Date fields	Evaluate date fields to ensure that no future dates or swapped dates appear in your files (e.g., a stop therapy date prior to a start therapy date OR a results reporting date precedes a collection date).
Suspicious or unlikely results	Check suspicious results in certain fields (such as infants in a federal prison or elderly in juvenile detention facilities). These can indicate that data warrant a closer look.
Impact of data collection changes	Check the impact of data collection changes as you provide trends of certain information to include data from TIMS and your new system. Be sure that data are being collected in the same way.
NTIP mismatches	Use NTIP reports to compare information from CDC with data in your system to identify discrepancies and instances where CDC data do **not** appear to be as up to date as your data.

The following Data Accuracy Tools include checklists and a data dictionary that are helpful when detecting the accuracy of TB surveillance data:

- 1a–Quality Assurance Data Accuracy Checklist
- 1b–Data Accuracy Checklist CDC SAS Code
- 1c–CDC TB Surveillance RVCT Data Dictionary

For more information and examples, see Chapter 10: Toolkit for Quality Assurance, Data Accuracy Tools.

Exercise 5.6: Detect Probable Data Errors in the RVCT Items 11 and 12

The following four cases include data from RVCT **Race** (item 11) and **Country of Birth** (item 12). Detect probable data errors for each case.

Case #	RVCT Race (item 11)					RVCT Country of Birth (item 12)		
						U.S.-born		Country of Birth
	American Indian or Alaska Native	Asian	Black or African American	Native Hawaiian or other Pacific Islander	White	Yes	No	
1.			X				X	United States
2.					X	X		
3.	X					X		India
4.				X			X	Philippines

What are the possible data errors? Write your answers in the space provided.

Case #	Your Answer
1.	
2.	
3.	
4.	

Exercise 5.7: Detect Possible Data Errors in the RVCT Items 18, 20, 39, and 40

The following three cases include data from RVCT **Sputum Culture** (item 18), **Culture of Tissue and Other Body Fluids** (item 20), **Initial Drug Susceptibility Testing** (item 39), and **Initial Drug Susceptibility Results** (item 40). Detect the possible data errors for each case.

Key for Possible Responses

Key for RVCT Items 18 and 20	Key for RVCT Item 39	Key for RVCT Item 40
P=Positive N=Negative ND=Not Done UK=Unknown	No=Not Performed Yes=Performed UK=Unknown	R=Resistant S=Susceptible ND=Not Done UK=Unknown

Case #	Item 18 Sputum Culture				Item 20 Culture of Tissue and Other Body Fluids				Item 39 Initial Drug Susceptibility Testing			Item 40 Initial Drug Susceptibility Results															
												Isoniazid				Rifampin				Pyrazinamide				Ethambutol			
	P	N	ND	UK	P	N	ND	UK	No	Yes	UK	R	S	ND	UK	R	S	ND	UK	R	S	ND	UK	R	S	ND	UK
1.	X							X	X				X				X				X				X		
2.		X					X			X		X					X				X				X		
3.			X		X					X			X				X								X		

What are the possible data errors? Write your answers in the space provided.

Case #	Your Answer
1.	
2.	
3.	

Example: Accuracy in Laboratory Data

Primary Purpose

This section provides an overview of laboratory definitions, functions, and processes that affect laboratory data.

Laboratory Testing

Laboratory test results provide data critical for the treatment and management of the patient. Laboratory test results are also used as criteria to determine whether a patient's disease meets the public health case definition of TB.

Challenges to accurate interpretation and reporting of laboratory data can be caused by a variety of factors such as

- Variables for results from new tests being collected in the RVCT (e.g., NAA),
- Unfamiliarity with laboratory technical terms, processes, or test results, and
- Differences among laboratories in policies, scheduling processes, and procedures for sharing data. They may also use different terminology, forms, reports, and communication procedures.

One of the most important solutions for clarifying laboratory reports is good partnerships and communication with laboratories providing data. They can provide explanations about the type of laboratory, how to interpret test results, how to determine specimen type, how to find dates, and other issues that might arise when reviewing laboratory reports.

This section provides an overview of potential TB laboratory issues that may be confusing to non-laboratory staff. Areas of discussion include clarifying types of laboratories, types of tests, technical terminology, processes, and schedules. NAA test is emphasized because this variable is a new item on the RVCT.

Types of TB Laboratories

The laboratory type is collected in the RVCT item 18, **Sputum Culture**, and item 20, **Culture of Tissue and Other Body Fluids**, as either public, commercial, or other. Table 5.7 provides a description of the three laboratory types included on the RVCT form.

Table 5.7
Types of TB Laboratories

Type of Laboratory	Description (per RVCT definition)
Public health laboratory	Any laboratory associated with a local or a state health department
Commercial laboratory	Any laboratory that charges a fee for each specimen processed or test performed
Other	Any other laboratory that is not considered a public health laboratory or a commercial laboratory. For example, hospital laboratories (e.g., National Jewish Health hospital laboratory) or laboratories associated with federal public health agencies (e.g., CDC, Veterans Administration, Indian Health Service, Tribal Health Department, or Bureau of Prisons).

Types of TB Tests

A variety of different laboratory tests are useful for providing information necessary to diagnose TB infection or disease. Table 5.8 compares the features of four common tests that are used in the laboratory.

Table 5.8
Comparison of Laboratory Tests for *Mycobacterium tuberculosis* Complex (MTBC)

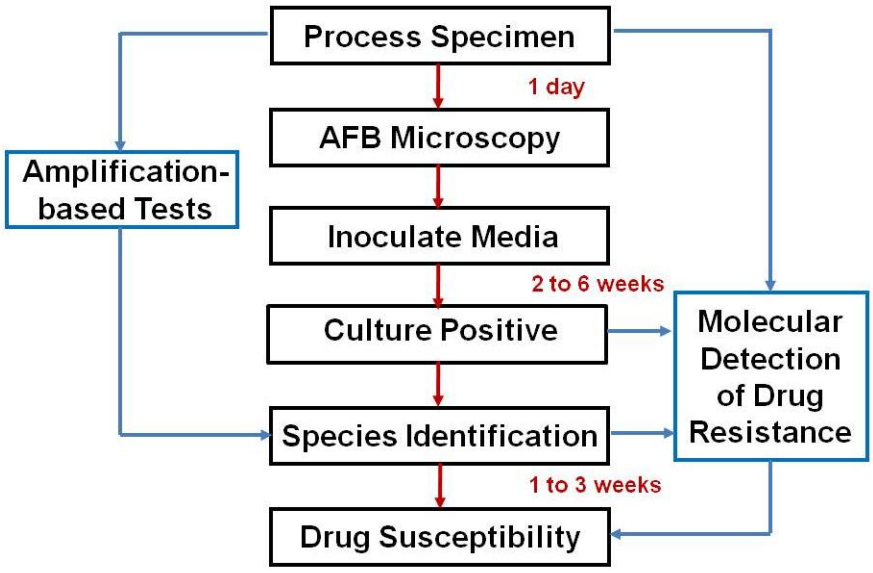
Feature	Type of Test			
	Acid-fast Bacillus (AFB) Smear Microscopy	**Direct Detection (e.g., NAA)**	**AFB-culture and Identification**	**First-line Drug Susceptibility Test (DST)**
Purpose	• Look for AFB on slide under microscope.	• Detection of specific nucleic acid sequence of MTBC in clinical specimen	• Growth in liquid or on solid media and identification of organism from positive culture as MTBC, contaminant, or other mycobacteria	• Determine the susceptibility of initial isolate of MTBC to first-line drugs.
Significance of a positive report	• AFB detected in clinical specimen (i.e., smear positive) • Not specific for MTBC • Smear grade (e.g., 1+, 2+, 3+) can indicate relative level of bacterial burden and potential infectiousness.	• MTBC was detected in clinical specimen.	• **Confirms a diagnosis of TB disease**	• A report indicating resistance to first-line drugs (rifampin, isoniazid, ethambutol, and pyrazinamide) may prompt additional testing for confirmation and evaluation of susceptibility to second-line drugs.
Significance of a negative report	• Does not rule out TB disease (culture may be positive). • Patient is probably not infectious.	• A single negative result should **not** be used to definitively exclude TB • Negative results must be interpreted in context of clinical situation and smear result.	• No live tubercle bacilli found in specimen. • Does **not** rule out TB disease (live tubercle bacilli may be in other specimens and/or body sites).	
RVCT Item	• **Sputum Smear** (item 17)	• **Nucleic Acid Amplification Test Result** (item 21)	• **Sputum Culture** (item 18)	• **Initial Drug Susceptibility Testing** (item 39) • **Final Drug Susceptibility Testing** (item 48)

Recommended Turn-Around Times for Laboratory Test Results

The turn-around time (TAT) for test results depends on laboratory testing algorithms (i.e., batching and staffing, hours of operation, testing performed in-house or referred). Each laboratory sets its own schedule and timeframes. However, current recommendations for TAT are as follows (Figure 5.1):

- AFB-smear microscopy
  - Reported within 1 day of specimen receipt in laboratory
- Direct detection (e.g, NAA test)
  - Reported within 2 days of specimen receipt in laboratory
- Identification of *Mycobacterium tuberculosis* complex (MTBC) in culture
  - Reported within 21 days of specimen receipt in laboratory
    - **Remember:** Cultures are routinely held for 6–8 weeks before reporting as negative.
    - Specimens with low bacterial loads (e.g., smear negative, 1+ smear) generally take longer to grow than specimens with high bacterial loads (e.g., 3+, 4+ smear).
    - Follow-up specimens from patients on therapy may take longer to grow than initial diagnostic specimens.
- First-line drug susceptibility testing (DST)
  - Reported within 28 days of specimen receipt in laboratory
    - This TAT is if all the "pieces fit together" perfectly.
    - Many laboratories performing culture must refer to another laboratory for DST.

Figure 5.1
Laboratory Testing Algorithm



For more information on the other laboratory tests that are listed in the RVCT, please refer to the Report of Verified Case of Tuberculosis Self-Study Modules.
http://www.cdc.gov/tb/programs/rvct/default.htm

Use of Molecular Diagnostics in the TB Laboratory Workflow

Molecular diagnostics are critical because they allow for rapid detection of MTBC in a clinical specimen and, depending on the testing platform, can provide additional information about potential resistance to anti-TB drugs while results are pending from growth-based conventional methods (Table 5.9).

Table 5.9
Molecular Diagnostics in the TB Laboratory

Purpose of Molecular Diagnostics	Diagnostic Questions
1. Direct detection in clinical specimen	• Is it MTBC, or not MTBC? • If MTBC, are mutations associated with drug resistance present?
2. Confirmatory identification of AFB in culture	• Is it MTBC or not MTBC? • If not MTBC, is it a common non-tuberculous mycobacterium (NTM)
3. Detection of resistance-associated mutations in MTBC isolate	• Are mutations commonly associated with rifampin and isoniazid resistance present (i.e., rapidly detecting MDR TB)? • Are mutations associated with second-line drug resistance present?

Direct Detection: Nucleic Acid Amplification (NAA) Testing

NAA testing attempts to exponentially amplify specific sequences of nucleic acid in MTBC to detect the presence of these bacteria in a clinical specimen. Table 5.10 compares positive and negative results for detecting MTBC using NAA tests. These amplified sequences (amplicons) are then usually detected through the use of a labeled DNA probe or analyzed by DNA sequence analysis. The two most common types of NAA tests are polymerase chain reaction (PCR) and transcription mediated amplification (TMA).

Table 5.10
Detection of MTBC Using NAA Tests

Positive Result	Negative Result

• Demonstrates the presence of MTBC
• Does not distinguish live and dead bacilli
	• Does not necessarily mean the absence of MTBC
	  ○ Inhibition of amplification
	  ○ Target below the limit of detection

Table 5.11 provides a list of NAA tests that a laboratory might use for direct detection and the current FDA approval status of these tests. In addition, a list of laboratory-developed tests is included. Some of the tests listed below are also capable of providing information about genetic mutations associated with drug resistance. For the purposes of the RVCT, areas should only report drug susceptibility test results from growth-based methods (i.e., positive culture) and not the results from rapid molecular tests (e.g., DNA sequencing, HAIN, GeneXpert®, pyrosequencing) performed for identifying genetic mutations associated with resistance (e.g., *rpoB* mutations associated with rifampin resistance).

For more information see Chapter 10: Toolkit for Quality Assurance, Accuracy Tool 5–Nucleic Acid Amplification Tests which compares features of various NAA tests.

Table 5.11
NAA Tests for Direct Detection of MTBC

FDA-approved (For use with respiratory specimens)	Non–FDA-approved (Research use only or not available in the United States)	Laboratory-Developed Tests (LDT)
• Amplified MTD® (*Mycobacterium tuberculosis* Direct) Test: Gen-Probe, Inc. • Cepheid GeneXpert® MTB/RIF	• Hain Lifescience Genotype® MTBDRplus and MTBDRsl • Innogenetics INNO-LiPA Rif.TB • COBAS® TaqMan® MTB Test • Akonni TruArray® MDR-TB • AutoGenomics Infinity® MDR-TB	• DNA sequencing • Loop-mediated isothermal amplification (LAMP) • Real-time PCR assays including molecular beacons

Potential for Confusion: AccuProbe® (Gen-Probe, Inc.)

AccuProbe® (Gen-Probe, Inc.) culture identification tests are DNA probes used by many laboratories to identify specific mycobacteria **after growth is detected in the culture.**

- Use of AccuProbe does **not** require NAA and should not be confused as an NAA test.
    - Natural "amplification" of the nucleic acid target takes place in culture as the bacteria multiply.
    - Typically, more bacteria are present in a culture than in a clinical specimen and therefore many copies of the target detected by AccuProbe are present. Therefore, NAA is not required.

Laboratories may report results from AccuProbe as "probe positive for MTBC." However, laboratories may also report results from an NAA test for direct detection as "probe positive for MTBC." In addition, GenProbe also manufactures the Amplified MTD test used for detecting *M. tuberculosis* directly in a clinical specimen. Herein lies the potential for confusion when examining a laboratory report.

When trying to discern the correct result for variables on the RVCT, it is important to examine the laboratory report for temporal sequence and context. If a laboratory report indicated GenProbe for the name of the test, the chronological sequence and time from specimen receipt must be carefully examined as these will be the best indicators for determining if the results are for NAA testing or culture identification.

- Accuprobe is performed **after** a culture is positive.
- NAA tests for direct detection (e.g., GenProbe AMTD) are performed from a clinical specimen.

Test Result Examples

The four examples below provide information from public health laboratory reports. Each example is from a different laboratory and illustrates how laboratories provide different information in various ways. Explanations about the reports are also included.

Example 1
Public Health Laboratory Report
(Found elsewhere on report: Sputum collected 4/14/2012 [Thursday]
and received in lab 4/14/2012)

Test	Date	Result
Culture	5/17/2012	*Mycobacterium tuberculosis* complex
Culture	5/17/2012	Method for ID: Gen Probe
Culture	5/17/2012	See previous positive culture
MTBC DNA PCR	4/18/2012	Positive for *Mycobacterium tuberculosis* complex DNA
ME – Microscopic Exam	4/16/2012	Many
ME – Microscopic Exam	4/16/2012	Acid fast bacilli seen
ME – Microscopic Exam	4/16/2012	Concentrated smear

Explanation: The information on this report is in reverse chronologic order (i.e., the most recent information is at the top). Please note that three separate lines are needed to describe the AFB-smear results on 4/16/2012 due to character limitations in each field. The information for the corresponding RVCT variables is

- **RVCT item 17 or 18, Date Collected Sputum** collection date 4/14/2012
- **RVCT item 17, Sputum Smear,** positive date 4/16/2012
- **RVCT item 21, NAA Test Result** (Direct detection) positive date 4/18/2012 (this laboratory calls their NAA test "MTBC DNA PCR")
- **RVCT item 18, Sputum Culture** positive date 5/17/2012 (the organisms growing in the culture were identified as *M. tuberculosis* by a DNA probe test) ("Method for ID: Gen Probe"). Although it is reported simply as GenProbe, in this example, the identification from culture was made by using GenProbe Accuprobe test. As mentioned previously, the chronological order and context are critical for determining the corresponding RVCT variable. Multiple lines are needed to describe the culture result, most likely because of field character limitations.

Example 2
Public Health Laboratory Report
(Found elsewhere on report: Sputum collected 5/31/2012 [Tuesday])

Test	Date	Result
AFB Smear (Conc., Fluorochrome)	6/2/2012	No acid fast bacilli seen
Amplified Mycobacterium Tuberculosis Direct Test (MTD)	6/2/2012	Positive for *M. tuberculosis* complex rRNA
AFB culture	6/20/2012	AFB detected (ZN smear positive)
Organism ID	6/22/2012	Probe positive for *Mycobacterium tuberculosis* complex

Explanation: The information on this report is in chronologic order. The information for the corresponding RVCT variables is

- **RVCT item 17, Sputum Smear Date Collected** – 5/31/2012
- **RVCT item 17, Sputum Smear** – Smear negative result ("No acid fast bacilli seen") date 6/2/2012
- **RVCT item 21, NAA Test Result** (direct detection) – NAA test positive result date 6/2/2012 (this laboratory performs the Amplified MTD test as their NAA test)
- **RVCT item 18, Sputum Culture** – Culture positive result date 6/22/2012 (the culture became positive on 6/20 but the organisms growing in the culture were not definitively identified as *M. tuberculosis* until 6/22; the organisms growing in the culture were identified as *M. tuberculosis* by a DNA probe test)

Example 3
Public Health Laboratory Report
(Found elsewhere on report: Sputum collected 6/30/2011 [Thursday])

Test	Date	Result
AFB Smear	7/1/2011	Acid fast bacilli present 10-90/F (fluorochrome stain)
AMTD Test	7/5/2011	Positive
Culture	7/7/2011	*Mycobacterium tuberculosis* complex detected by DNA probe

Explanation: The information on this report is in chronologic order. The information for the corresponding RVCT variables is

- **RVCT item 17, Sputum Smear Date Collected** – 6/30/2011
- **RVCT item 17, Sputum Smear** – Smear positive result date 7/1/2011
- **RVCT item 21, NAA Test Result** (direct detection) – NAA test positive result date 7/5/2011 (this laboratory performs the AMTD test as their NAA test)
- **RVCT item 18, Sputum Culture** – Culture positive result date 7/7/2011 (the organisms growing in the culture were identified as *M. tuberculosis* by a DNA probe test)

Example 4
Public Health Laboratory Report
(Found elsewhere on report: Sputum collected 5/31/2012 [Tuesday])

Test	Date	Result
AFB Smear	6/2/2012	Acid fast bacilli seen: numerous
### Amplified *Mycobacterium tuberculosis* Direct Test	6/2/2012	Positive
### HAIN Test GenoType MTBDRplus	6/8/2012	• No rpoB point mutation detected • No katG point mutation detected • inhA point mutation detected
### AFB culture		Pending
### Organism ID by PRA	6/14/2012	*Mycobacterium tuberculosis* complex

Explanation: The information on this report is in chronologic order. The information for the corresponding RVCT variables is

- **RVCT item 17, Sputum Smear Date Collected** – 5/31/2012
- **RVCT item 17, Sputum Smear** – Smear positive result date 6/2/2011
- **RVCT item 21, NAA Test Result** (direct detection) – NAA test positive result date 6/2/2012 (this laboratory performs the AMTD test as their NAA test)
- **RVCT item 18, Sputum Culture** – Culture positive result date 6/14/2012 (the organisms growing in the culture were identified as *M. tuberculosis* by a polymerase chain reaction restriction analysis [PRA] test)

Example: Data Validation Pilot Project

Primary Purpose

This section provides an example of how to validate the data in a TB surveillance system. This example compares data from both the patient TB patients' medical record and the National Tuberculosis Surveillance System (NTSS).

Introduction

The overall plan was to review surveillance procedures and validate surveillance data.

Goals for the data validation project were to:

- Determine RVCT data accuracy.
- Examine surveillance activities and procedures at local areas.
- Determine the feasibility of implementing a nationwide data validation protocol.

Method

In order to review surveillance procedures, principal surveillance staff members were interviewed and related documents were reviewed. Specific interests included flow of data and patient information from initial notification to close out, data collection procedures, and staff assignments.

Surveillance data were examined by calculating the percent discordance between the medical record reviewer's results and the NTSS record. To obtain this, an abstraction of medical records was performed at a local TB clinic. An RVCT was completed from the medical/clinical record in order to compare the abstracted RVCT data to CDC's NTSS data.

A pilot test was performed April-August 2006. Three sites, chosen for convenience and cooperation, were as follows:

- Chicago
- Washington, D.C.
- Miami

A random sample of cases was reviewed at one site. At two other sites the medical records were chosen as a convenience sample. A blind abstraction procedure was followed; only the RVCT identifiers were known (i.e., state case number, soundex, sex, and date of birth). For each patient record reviewed, the pairs of NTSS data and medical record abstraction data were compared.

Percent discordance was calculated by dividing the number of records that were discordant by the number of records reviewed at each site. Results were multiplied by 100 to achieve percent discordance. Conflicting data or missing data in either NTSS or the medical record for Yes/No variables qualified as a discordant pair. Categorical data qualified as discordant if data were missing from one record while present in the other record, or if not missing, the response did not match. Date data qualified as discordant if the dates were off significantly or missing in one record.

Results

The exercise found highly variable responses in data validation. Table 5.12 provides common problems and suggested solutions.

Table 5.12
Common Problems and Suggested Solutions

Common Problems	Suggested Solutions
• Lack of data checking • Not correcting errors • Incomplete understanding of Report of Verified Case of Tuberculosis (RVCT) variable definitions	• Designate staff for data input into TIMS. • Conduct independent review of each patient's RVCT. • Train local clinical staff on RVCT definitions and procedures.

A total of 94 medical records and 88 RVCT variables were reviewed at the three sites and revealed a highly variable response.

- **Initial Drug Regimen** at one site reported <15% discordant but >54% at another site.
- **Month-Year Reported** had a range of 22% to 78% discordant.
- **Directly Observed Therapy (DOT)** ranged from 12% to 68% discordant.
- Many variables that were >50% discordant were **Time or Date Sensitive** or related to **DOT**.
- Variables that were <15% discordant included **Sex, Date of Birth, Country of Origin, Vital Status at Diagnosis, Resident of a Long-Term Facility, Resident of a Correctional Facility, and Major Site of Disease.**

Problems discovered in the validation procedure included

- Inability to determine who verifies cases,
- Lack of data checking in state surveillance system before sending to NTSS,
- Lack of data correcting after cohort review (or other systematic review), and
- An incomplete comprehension of RVCT variable definitions by the local staff.

Discussion and Conclusion

Suggestions to improve surveillance reporting included:

- Train local staff on RVCT definitions.
- Identify sources of data.
- Indicate where to go for questions.
- Designate staff for each function.
- Review RVCT data conducted by a clinical person.
- Create a flow diagram of initial patient notification until close out.

Future data validation efforts should include

- Determining which variables to abstract as well as implementing random sampling and blind abstraction,
- Using original sources for data where possible, and
- Receiving ample input from local staff.

Revolving these sites over a 3- to 5-year period will help ensure better validation efforts without overburdening state and local staff.

Example: System Quality Assurance Reports

Primary Purpose

This section describes the various reports available through the National TB Surveillance System (NTSS) Reports Application.

Secure Access Management Services (SAMS)

SAMS is a federal information technology system that gives authorized personnel secure, external access to non-public CDC applications. There are three data systems that can be accessed through the SAMS portal:

- TB Genotyping Information Management System (TB GIMS)
- National TB Surveillance System (NTSS)
- National TB Indicators Project (NTIP)

NTSS Reports Application

NTSS is a secure application that allows jurisdictions access to QA reports. These reports:

- Allow flexibility to access reports specific to the jurisdiction.
- Provide security in viewing the data reports.
- Provide a stable accessibility to all state and local users.

The various reports can help jurisdictions conduct QA for accuracy in the RVCT data.

Table 5.13 includes a description for each of the reports.

Table 5.13
NTSS Reports Application

Reports		Description
General Reports	**TB Case List Report**	This report provides a snapshot of the information the reporting jurisdiction entered for a specific case. This is useful when comparing data between the jurisdiction and CDC.
	Case Verification Report	This report lists discrepancies between the case verification a jurisdiction sends to CDC for a counted case, and the CDC calculation from the data that was entered on the case. This is useful when comparing count information.
	Content Validation Report	This report lists RVCT validation errors by error code. This report is useful in determining if variables have the correct mapping.
Invalid, Missing, and Unknown (MUNK) Report		The MUNK report lists all verified and counted cases with an invalid, missing, and or unknown data item. This report is useful when ensuring all RVCT variables are completed.
Counted Case Reports		This report lists the total number of counted cases for a particular year. This report is useful when comparing case counts with CDC.
Missing and Deleted Reports		The Missing report lists cases determined to be verified and counted by the reporting jurisdiction that are missing the report date or count date. Therefore they do not have enough information to be counted at CDC. The report is useful when reconciling counts. The deleted report lists all cases previously sent to CDC that have now been deleted by your jurisdiction.

Case Verification Criteria (VERCRIT)

To count a TB case, CDC uses a case verification criteria to calculate a calculated RVCT variable, "Vercrit," using the data that are entered on a case. See Chapter 10: Toolkit for Quality Assurance, QA Plan Tool–4, Case Verification Criteria (Vercrit) Calculation.

Exercise 5.8: Reconciling Case Count

The fictitious state of San Price needs to reconcile the annual count for 2011 that is shown in the NTSS TB Case List Report below.

- The state says they have 10 verified counted cases in 2011.
- CDC only shows that there are 4 verified counted cases.

Use the TB Case List Report below for 2011 to identify case(s) that CDC is **not** counting, and describe why in space provided on the next page.

TB Case List Report, 2011

Case #	County	Report Date	Count Date	Count Status Description	CDC Vercrit Code	CDC Vercrit Description
1.	A	20110107	20110107		4	Verified by Provider Diagnosis
2.	A	20110218	20110218	Count as a TB Case	1A	Positive NAA
3.	D	20110320		Verified Case-Counted by another US area	1	Positive Culture
4.	B	20110323	20110323	Count as a TB Case	5	Suspect
5.	E	20110326	20110326	Count as a TB Case	1A	Positive NAA
6.	C	20110710	20110710		0	Not a verified Case
7.	B	20110106	20110106		1A	Positive NAA
8.	G	20110410	20110410	Count as a TB Case	1A	Positive NAA
9.	C	20110114	20110114		3	Clinical Case Definition
10.	D	20110416	20110416	Count as a TB Case	3	Clinical Case Definition

1. Identify the following:

- Cases CDC has counted.
- Cases CDC has not counted.
- Describe why CDC has not counted the cases.

2. Write your answers in the space provided.

Case #	CDC Counted Case. (check)	CDC Has Not Counted. (check)	Describe Why it Is Not Counted by CDC.
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			

Additional Information

TB Applications Support
Email – NTSS@CDC.gov
Phone number – 678-460-7828

Data Accuracy Tools

The Data Accuracy Tools are listed below (Table 5.14). Tools 1a, 1b, and 1c are especially helpful for checking the accuracy of RVCT items. Examples of the tools are located in Chapter 10: Toolkit for Quality Assurance. To view or download the tools, please visit: http://www.cdc.gov/tb/programs/rvct/default.htm.

Table 5.14
Data Accuracy Tools

Tool #	Tool Name	Description and How to Use	Format	Source Contact
Accuracy–1a	**Data Accuracy Checklist for RVCT**	Checklist for reviewing RVCT data for accuracy.	Word 9 pages	CDC/DTBE
Accuracy–1b	**Data Accuracy Checklist CDC SAS Code**	SAS code corresponding to the Data Accuracy Checklist – Accuracy Tool - 1a; based on CDC RVCT variable names.	Word 7 pages	CDC/DTBE
Accuracy–1c	**CDC TB Surveillance RVCT Data Dictionary**	Data dictionary for interpreting the CDC RVCT variable names used in Data Accuracy Checklist CDC SAS Code – Accuracy Tool - 1b.	Excel 16 pages	CDC/DTBE
Accuracy–2	**Options for Prioritizing Medical Chart Reviews When Resources Are Limited**	Various options to help prioritize medical chart reviews when resources are limited.	Word 1 page	CDC/DTBE
Accuracy–3	**RVCT Surveillance Data Base Audit Form for Timeliness and Accuracy**	Checklist for checking the accuracy of RVCT.	Word 1 page	CDC (adapted from New Hampshire)

Tool #	Tool Name	Description and How to Use	Format	Source Contact
Accuracy–4	**Accuracy Checklist for Sputum Culture Conversion**	Table used to indicate number of days for culture conversion by jurisdiction. This applies to cases that are sputum culture-positive only. There are built-in features/tools that calculate the dates that are 30 and 60 days from treatment start (once the Date Therapy Started is entered). There is also a built-in calculation for the number of days to sputum culture conversion. This helps identify those patients who did not meet the NTIP objective of converting their sputum culture within 60 days of treatment initiation.	Excel 1 page	Tennessee TB Elimination Program
Accuracy–5	**Nucleic Acid Amplification (NAA) Tests**	Comparison of NAA tests.	Excel 1 page	CDC/DTBE
Accuracy–6	**Culture-Based (Phenotypic) Laboratory Tests for Drug Susceptibility Testing**	Comparison of culture-based (phenotypic) laboratory tests for drug susceptibility testing.	Excel 1 page	CDC/DTBE
Accuracy–7	**Molecular-Based Laboratory Tests for Detecting Mutations Associated with Drug Resistance**	Comparison of molecular-based laboratory tests for detecting mutations associated with drug resistance.	Excel 1 page	CDC/DTBE
Accuracy–8	**2009 RVCT Form with PHIN Variable IDs**	2009 RVCT Form with Public Health Information Network (PHIN) Variable IDs, by RVCT item number, to use as a reference for reporting codes.	PDF 6 pages	CDC/DTBE
Accuracy–9	**Comparison of Concordant and Discordant RVCT Items - Summary**	A list of RVCT variable items suggested for surveillance review.	Word 2 pages	CDC/DTBE
Accuracy–10	**Health Level 7 CDC Race and Ethnicity Code Set**	A comprehensive list of race and ethnic groups including tribes for HL7 coding.	PDF 38 pages	CDC