False-Positive Investigation Toolkit

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Background

- **False-positive results:**
  - Can be difficult to identify, investigate, and resolve
  - Have serious implications for patient isolation, patient therapy, contact investigations, and unnecessary testing
  - Can be caused by pre-analytic, analytic, and post-analytic errors

- **Cross-contamination, mislabeling errors, specimen mix-ups, and use of non-sterile reagents can cause a false-positive**

- **An article published by Burman and Reves in 2000, reported the median rate of *Mycobacterium tuberculosis* false-positive cultures was 3.1% (interquartile range, 2.2%–10.5%)**
Background (2)

- “Recognition and Prevention of False-Positive Test Results in Mycobacteriology – A Laboratory Training Program,” video and booklet developed in 1997

- Designed to help mycobacteriology laboratorians recognize and prevent false-positive test results

- Program not updated since 1997 and similar publications or resource materials have been limited in recent years
False-Positive Investigation Toolkit

- **Goal:** Provide an updated set of resources to assist mycobacteriology laboratory personnel and tuberculosis (TB) control program staff in false-positive investigations

- **Objectives:**
  - Define false-positive results
  - Describe the importance of developing guidance, policies, and educational materials to be referenced by staff when necessary
  - Identify best practices to prevent false-positive results
  - Recognize possible scenarios for identifying potential false-positives
  - Describe the actions necessary to perform an investigation
  - Summarize how the laboratory and the TB Control Program should collaborate to conduct the investigation
  - Identify follow-up actions if a determination of false-positive result is made
False-Positive Investigation Toolkit (2)

- Intended target audience: laboratory staff, TB control programs, and other healthcare workers
- Toolkit to include: narrative document, job aids, posters, quick reference documents, and templates
- Online Case Module

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**Analytical**

- Review patient's past and current test results.
- Speak with TB program or healthcare provider to determine if patient symptoms are consistent with TB disease.
- Review specimen processing logs (the day of the suspected contamination and days prior to and after)

**Post-Analytical**

- Review test results to ensure the correct result was reported for the correct patient.
- Verify that the correct report was sent to the healthcare provider.
- Determine whether laboratory results and associated reporting language were received and interpreted correctly by the healthcare provider.
- Ensure that data entry or transcription errors did not occur when results were entered into the LIMS system.
- Review negative specimen processing control results to ensure growth was not observed.
- Ensure quality assurance procedures have been followed, e.g., secondary review.
- Cross-reference genotypes for specimens in question to any known positives processed the same day or to the H37 Rv/Ra control strain.

**Inquire with**

- Assess if pipettes/supplies used for specimen processing are also used with positive cultures and susceptibility testing.
- Review laboratory cleaning/decontamination records.
- Review BSC records to ensure BSC is operating properly.
- Review autoclave records to ensure autoclave is operating properly.
- Review non-conforming events (NCEs) for occurrences that may have caused a false-positive.
False-Positive Investigation Form

Patient Name: ____________________________  Accession Number: ____________________________

Date of Collection: ______________________  Specimen Source/Type: ____________________________

Laboratory Processing Information

Date of Processing: _______________________  Processing Technician: ____________________________

- Does the specimen container label match the specimen requisition form?  Yes  No
- Does the specimen requisition form information match LIMS information?  Yes  No
- Was the specimen(s) processed with another positive specimen?  Yes  No
- Is MTBC growing in only one culture?  Yes  No
  - Liquid?  Yes  No
  - Solid?  Yes  No
- Was a reprocessed MGIT processed in the same batch?  Yes  No
- Any unusual occurrences documented on day of processing (spills, leaking specimen container, etc.)?  Yes  No
- Any proficiency testing strains or quality control strains processed in same batch or previously in same BSC?  Yes  No

Laboratory Test Results

<table>
<thead>
<tr>
<th>Date Processed</th>
<th>MIR Sensitivity Result/Date</th>
<th>Liquid Culture Result/Date</th>
<th>Solid Culture Result/Date</th>
<th>MRAAT Result/Date</th>
<th>Species ID Result/Date</th>
<th>Genotype Result</th>
</tr>
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</tbody>
</table>

Submitter Information

Submitter: ____________________________  Submitter Point of Contact: ____________________________

Date Contacted: ______________________

- Was the specimen collected in the same location on the same date as another positive specimen?  Yes  No
- Was the specimen collected with the same instrument (e.g., bronchoscope)?  Yes  No
- Were specimen collection containers and specimen requisition forms labeled and filled out correctly?  Yes  No

TB Control/Clinical Information

Date Contacted: ______________________  Program/Healthcare Provider Contact: ____________________________

- Is the patient a suspected TB case?  Yes  No
- Is the patient a contact of a known positive case?  Yes  No
- Was the patient born outside of the United States?  Yes  No  Country: ____________________________

Patient Clinical Data:
- History of TB?  Yes  No
- Positive TST?  Yes  No
- Positive IGRA?  Yes  No
- Abnormal Chest X-ray?  Yes  No
- Clinical picture consistent with TB?  Yes  No
  - Symptoms include:
    - Current treatment for TB?  Yes  No
    - Prior treatment for TB?  Yes  No
    - Prior treatment for latent TB?  Yes  No
    - Genotyping results?  Yes  No  Result: ____________________________
    - Match to another case?  Yes  No  Notes: ____________________________
    - Match proficiency or quality control strain?

Findings/Conclusions

- Likelihood that result(s) is a false-positive  High  Moderate  Low  None
- Describe finding(s) that could of resulted in false-positive result or cross contamination

Date of Investigation: ______________________  Microbiologist: ____________________________

Date of Resolution: ______________________

- Resolved by:
  - Notified Submitter on ______________________
  - Notified TB Program/Healthcare Provider on ______________________
  - Updated/Corrected Test Results on ______________________
  - Reviewed/Updated Standard Operating Procedures on ______________________
Do’s and Don’ts to Prevent Cross-Contamination

**DO**
- Use individual or daily aliquots of processing reagents and discard any leftover
- Keep specimen tubes tightly closed and clean outside prior to mixing or handling
- Wait 5 minutes after mixing before uncapping a tube and open gently to avoid aerosol generation
- Pour decontamination reagents slowly down side of tube to prevent splashing
- Process specimens of known positive patients last within batch
- Use a splash-proof discard container to avoid production of aerosols

**DON’T**
- Use common beakers or flasks of reagents when processing specimens
- Touch lip of tube with container during addition of reagents
- Keep more than one tube open at the same time
- Place tubes too close to each other in the rack
- Use positive controls
- Process laboratory proficiency or quality control strains in same batch as patient specimens
- Disturb or impede airflow in the biological safety cabinet (BSC)
- Work in a BSC if uncertain about airflow
Online Case Module

- In collaboration with APHL, an interactive-online training module has been developed consisting of five case studies.

- Designed for laboratorians at all levels of experience.

- Includes pre-analytical, analytical, and post-analytical examples, to guide participants through conducting potential false-positive investigations.

- Knowledge checks included through interactive elements.
Mycobacteriology False-Positive Case Studies

Guided, interactive TB laboratory case scenarios (5) will lead you through investigating potential false-positive results.

Primary audience: Mycobacteriology lab supervisors and technologists

Also helpful to: Quality-assurance staff members, TB Control Programs, healthcare providers, case managers, and epidemiologists
<table>
<thead>
<tr>
<th>Date Processed</th>
<th>Accession Number</th>
<th>Patient Information</th>
<th>Specimen Type</th>
<th>AFB Smear Result</th>
<th>AFB Culture Result- MGIT (date positive)</th>
<th>AFB Culture Result- 7H11 (date positive)</th>
<th>Organism Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 16</td>
<td>CC18-0012</td>
<td>AB</td>
<td>Sputum</td>
<td>3+</td>
<td>+ (2/6)</td>
<td>+ (2/12)</td>
<td>MTBC</td>
</tr>
<tr>
<td>February 9</td>
<td>CC18-0039</td>
<td>AB</td>
<td>Sputum</td>
<td>4+</td>
<td>+ (2/28)</td>
<td>+ (3/5)</td>
<td>MTBC</td>
</tr>
<tr>
<td>March 5</td>
<td>CC18-0074</td>
<td>AB</td>
<td>Sputum</td>
<td>3+</td>
<td>+ (3/25)</td>
<td>+ (4/1)</td>
<td>MTBC</td>
</tr>
<tr>
<td>April 6</td>
<td>CC18-0102</td>
<td>AB</td>
<td>Sputum</td>
<td>1+</td>
<td>+ (4/26)</td>
<td>+ (5/2)</td>
<td>MTBC</td>
</tr>
<tr>
<td>May 6</td>
<td>CC18-0132</td>
<td>AB</td>
<td>Sputum</td>
<td>Negative</td>
<td>No Growth</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
<tr>
<td>June 12</td>
<td>CC18-0175</td>
<td>AB</td>
<td>Sputum</td>
<td>Negative</td>
<td>No Growth</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
<tr>
<td>July 2</td>
<td>CC18-0215</td>
<td>AB</td>
<td>Sputum</td>
<td>4+</td>
<td>Pending</td>
<td>Pending</td>
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</tr>
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</table>

You notice that there are two negative AFB smears and AFB cultures in a row and then a positive AFB smear result. What should you do next?

- Give this information to PA Patel so she can determine what is going on with her patient.
- Perform an additional review of the specimen processing logs and patient records.
- Call PA Patel back and inform her that this appears to be a new case of TB or a relapse of prior TB infection.
Lessons Learned—Case Study 2

Takeaways from this case study include:

• Review patient laboratory results and monitor laboratory data to reveal any sudden increase of cultures positive for *Mycobacterium tuberculosis*. This may help to identify potential false-positive cases and initiate timely investigations.

• Process specimens from previous culture positive TB patients at the end of the batch to prevent contamination of subsequent specimens.

• Avoid processing large batches of specimens at the same time as this may lead to an increased risk of cross-contamination.
Summary

- Laboratory personnel, TB control program staff, and other healthcare workers will now have updated resources available to help prevent, identify, and investigate potential false-positive results.

- Toolkit allows laboratories to develop internal false-positive investigation procedures to help identify the most likely cause of erroneous test results.

- Online case studies module allows participants to actively use techniques described in the toolkit to investigate a potential false-positive result.
Availability

- False-positive investigation toolkit and online training module will be available in 2019
  - Toolkit is currently under review
  - Online Module will be available soon on the APHL website
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- **U.S. TB Control Programs**
Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.