PUBLIC HEALTH DIVISION
Oregon State Public Health Laboratory
Tina Kotek, Governor

Oregon Health Authority

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August 1, 2024

Dear Colleagues,

Becton, Dickinson and Company (BD) recently released a recall notice affecting the MGIT™ pyrazinamide (PZA) Kit used by OSPHL for drug susceptibility testing. These kits are recalled because they "may intermittently produce falsely resistant results" for PZA on Mycobacterium tuberculosis (MTB) isolates.

What the recall means for OSPHL results already released:
At this time, a limited number of previous OSPHL test results are affected by the recall. Affected patient results have been revised to "Indeterminate" with a result comment describing the recall situation.

What the recall means for OSPHL testing:
The Oregon State Public Health Laboratory (OSPHL) is currently unable to perform PZA susceptibility testing using this method, as are many other laboratories nationwide including CDC's TB Reference Laboratory.

Until testing can be resumed, PZA results will be released as "Test Not Performed" with a comment describing the recall situation.

For patient circumstances when PZA might be essential for building a multidrug treatment regimen or in other situations where PZA results are critical, please contact the OHA TB Program at 503-358-8516 or heidi.behm@oha.oregon.gov.

What is the next step?
OSPHL is exploring other options for PZA susceptibility testing. In addition, CDC's Division of TB Elimination (DTBE) Laboratory Branch is working with the Association of Public Health Laboratories (APHL) to determine which laboratories may be able to assist with testing. OSPHL will provide updates to you when more information is available.

We recognize that Oregon's MTB healthcare community has previously expressed concern about PZA susceptibility testing. This recall verifies that those of you caring for patients with MTB know your work and patients well. Thank you for your candor and working with the OSPHL staff. OSPHL investigated the concern within our scope of awareness and control at the time, but individual laboratory staff do not have access to the same level of information as manufacturers.

A letter from the CDC Division of Tuberculosis Elimination to Public Health Laboratories is attached to this message for reference and additional information.

Thank you for the dedication you put into caring for patients with MTB each day. Please do not hesitate to contact us with questions or concerns:

- Laboratory Technical: 503-693-4100
    - Marisa Frieder, General Microbiology Section Manager – marisa.d.frieder@oha.oregon.gov
    - Mackenzie Clary, Tuberculosis Testing Lead – mackenzie.clary@oha.oregon.gov
- Clinical consultation regarding treatment regimen:
    - OHA TB Program – 503-358-8516 or heidi.behm@oha.oregon.gov

Sincerely,

Akiko Saito, MPH, MPA
OSPHL Business Director

Attachment: Letter to Public Health Laboratories from the CDC Division of Tuberculosis Elimination

Attachment: Letter to Public Health Laboratories from the CDC Division of Tuberculosis Elimination

Dear Colleagues,

Intermittent quality control failures and increased rates of false PZA-resistance have been reported for several months from laboratories across the United States. Becton, Dickinson and Company (BD), the manufacturer of the BD BACTEC™ MGIT™ 960 pyrazinamide (PZA) kit, wrote to customers on July 18, 2024, reporting specific lots of the PZA test kit should not be used and should be discarded immediately. BD indicated the root cause of the false resistance has been found and action is being taken to prevent recurrence. At this time, it is unknown when new product may be released.

Given this communication and instruction to discard testing kits, some laboratories may be unable to perform phenotypic PZA susceptibility testing. **CDC's TB Reference Laboratory is impacted, and effective immediately, we will be suspending phenotypic PZA susceptibility testing.**

Until new phenotypic PZA susceptibility testing kits are available, the following information is provided for consideration.

1. PZA monoresistance for non-multidrug-resistant (MDR) *Mycobacterium tuberculosis* complex (MTBC) is rare except for *M. bovis,* which is intrinsically resistant to PZA because of a specific nonsynonymous mutation (Asp57His) in the *pncA* gene. When feasible, *M. bovis* should be identified to differentiate from other members of the MTBC. This may require referral to another laboratory for identification.

2. Sequencing of *pncA* is an acceptable approach for determining PZA susceptibility as most PZA resistance is associated with mutations in *pncA*.
    a. Wild-type *pncA* (i.e., no mutations detected) correlates well with susceptibility to PZA.
    b. The understanding of PZA-resistance associated mutations has advanced and the positive predictive value is high for many *pncA* promoter and nonsynonymous mutations. The WHO Catalogue of mutations in Mycobacterium tuberculosis complex and their association with drug resistance, 2nd ed. is an available resource for interpretation.
    c. The correlation of some *pncA* mutations with PZA resistance is unknown. In these cases, healthcare providers should be advised to seek expert consultation through the jurisdictional TB program or CDC's TB Centers of Excellence for Training, Education, and Medical Consultation (COE).

3. Capacity for *pncA* sequencing is limited to a few U.S. laboratories. Resources for additional test volume may be constrained, especially considering that many laboratories might need to suspend phenotypic PZA susceptibility testing. Therefore, TB programs may need to prioritize which isolates will be referred for *pncA* sequencing. These might include isolates that are rifampin-resistant or multidrug-resistant (MDR) or isolates from patients whose treatment response is of concern. PZA resistance is more common in MDR isolates.

4. For situations when PZA might be essential for building a multidrug treatment regimen, but PZA susceptibility cannot be ascertained, COE consultation in conjunction with the TB program is strongly recommended.

Submitters may reach out to CDC's TB Reference Laboratory to determine if capacity is available to assist with *pncA* sequencing. CDC's Division of TB Elimination (DTBE) Laboratory Branch is working with the Association of Public Health Laboratories (APHL) to determine which laboratories may be able to assist with testing. Partners may reach out to the assigned CDC TB Laboratory Consultant, or to Sarah Buss at APHL for additional assistance.

We will provide updates as they become available.

Best,
Angela

Angela M. Starks, PhD | Chief | Laboratory Branch | Division of Tuberculosis Elimination | Centers for Disease Control and Prevention