

# Case 1-

## Modification of an FDA-Approved IVD

- Lab is using an FDA-approved IVD (Assay A) for DST of INH, RMP, EMB, and PZA
- TB program has requested that lab routinely test “AB12.” This drug does not have an FDA-approved indication for TB therapy, so there is not an FDA-approved test for determining susceptibility to AB12.
- AB12 will be used to treat patients based on the lab results
- Lab does validation and begins performing test routinely

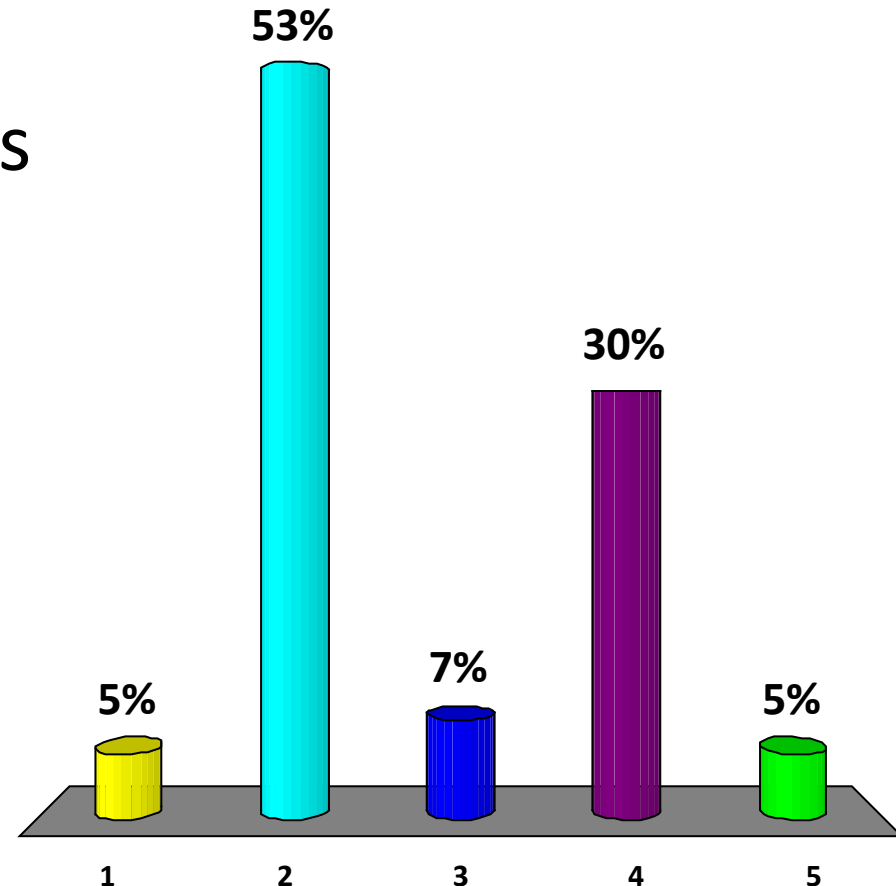
# Case 1 (#2)

- Validation:

- Literature review to determine concentration of drug to test
- Test MtbC isolates with known AB12 results:
  - CDC MPEP isolates
  - patient isolates tested against AB12 by another lab.
- NOTE: AB12-R isolates are rare

# What validation is sufficient?

1. 5 AB12-resistant and 5 AB12-susceptible isolates
2. 5 AB12-resistant and 15 AB-12 susceptible isolates
3. Either
4. Neither
5. I have no idea!

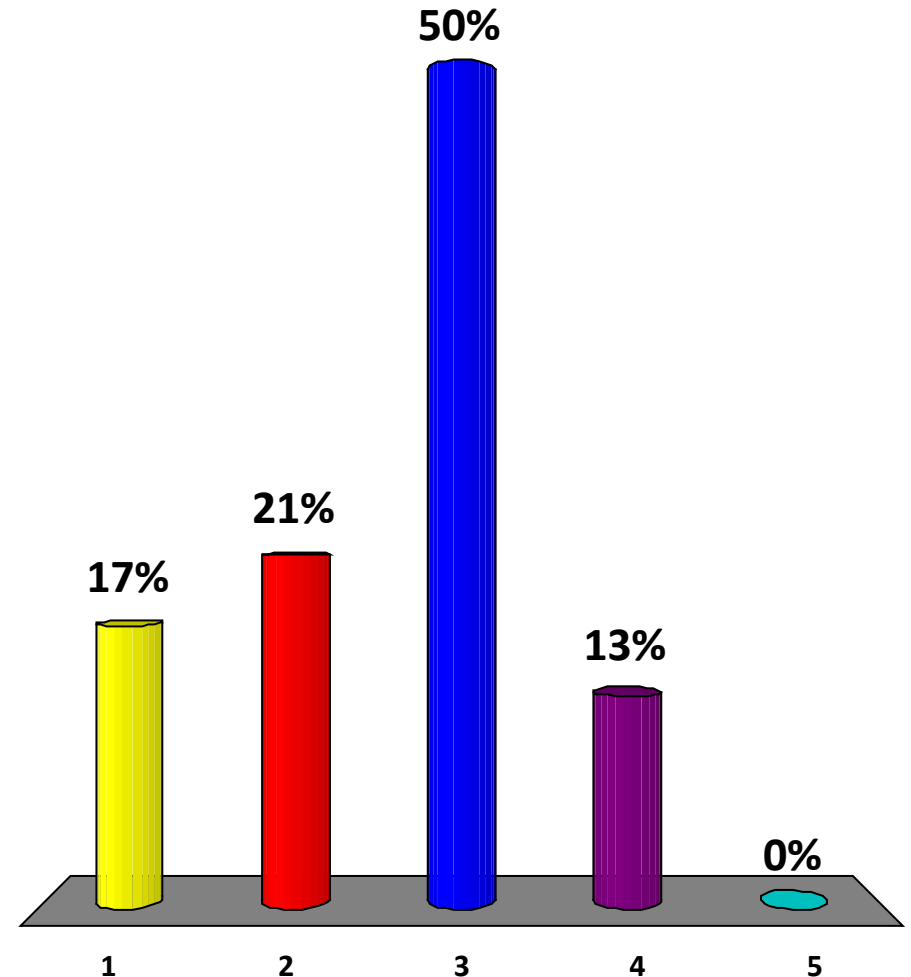


# Case 1 (#4)

- Reporting:
  - Lab reports AB12 results with results for INH, RMP, EMB, and PZA

# What disclaimer should be on the report regarding the AB12 test?

1. AB12 results based on in-house validation
2. AB12 test is not FDA-approved for Assay A
3. Both of the above comments
4. No comment is necessary
5. I have no idea!



# Case 1 (#6)

- Reporting:
  - FDA – should be a disclaimer
  - CMS – comment a good idea but only have standard language for an assay using an ASR
  - CAP-recommended comment:

“This test was developed and its performance characteristics determined by (laboratory name). It has not been cleared or approved by the U.S. Food and Drug Administration.”

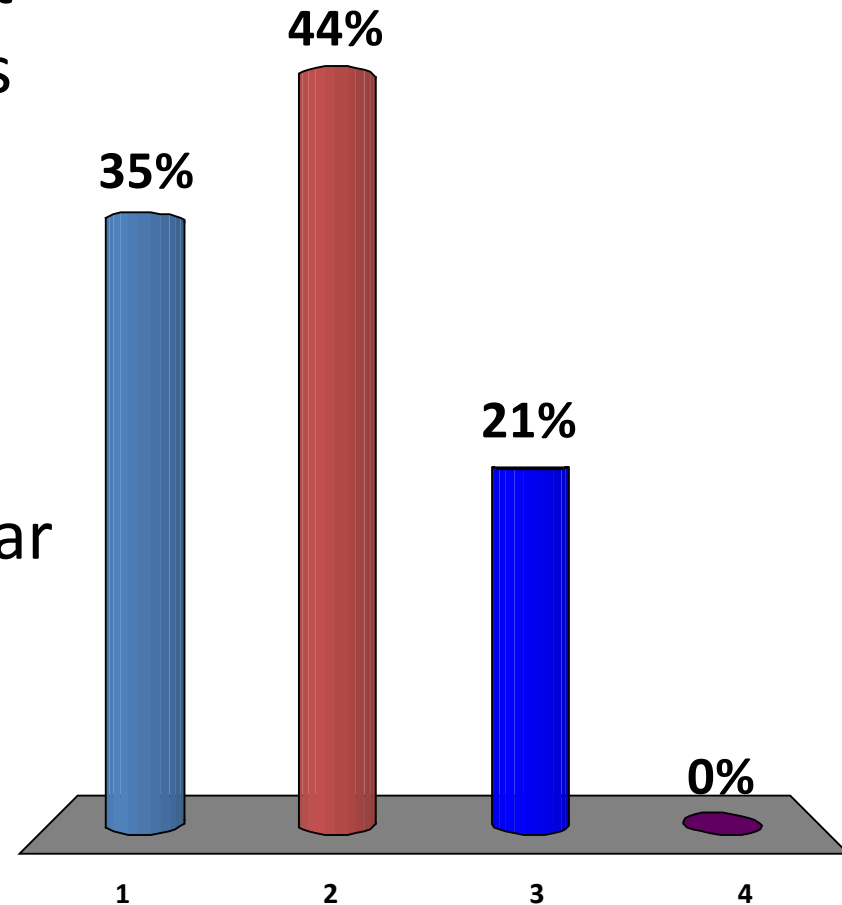
# Case 1 (#7)

- Proficiency testing:

- Lab participates in a commercially available CMS approved mycobacteriology PT program and receives one isolate of MtbC 2 times/year for DST PT.
- PT program rarely, if ever, sends drug-resistant isolates for PT

# What is a sufficient number of PT challenges for MtbC DST?

1. The commercially available PT program described is sufficient for meeting CLIA requirements
2. The commercially available PT program should be supplemented with another program so that more isolates of MtbC are tested 2 times/year
3. Both of the above
4. I have no idea!



# Case 1 (#8)

- CLIA (493.913) specifies that PT program must provide at least one sample per testing event that includes mycobacterium tuberculosis that has a predetermined pattern of sensitivity or resistance to the common antimycobacterial agents.

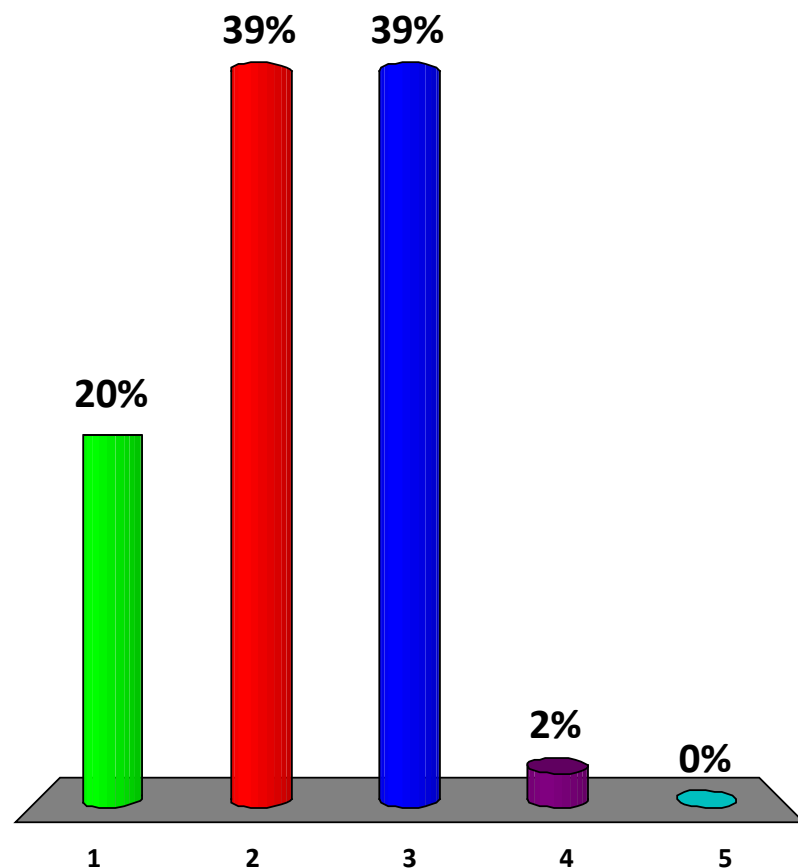
# Case 2

## Use of an RUO

- Lab is using a commercially available RUO test, “AutoAFB,” as a replacement for AFB microscopy
- The package insert and all other documentation from the company state “research use only; not for use in diagnostic procedures”
- Lab has validated this assay by literature review and testing 50 smear (+) and 100 smear (-) samples
- Lab reports results as “AFB (+) with quantitation” and “AFB(-)”

# What disclaimer regarding the RUO “AutoAFB” test should be included on the report?

1. Research use only ; results should not be used for diagnosis
2. AutoAFB is not FDA-approved; test validated in-house
3. Both of the above
4. No disclaimer is necessary
5. I have no idea!



## Case 2 (#3)

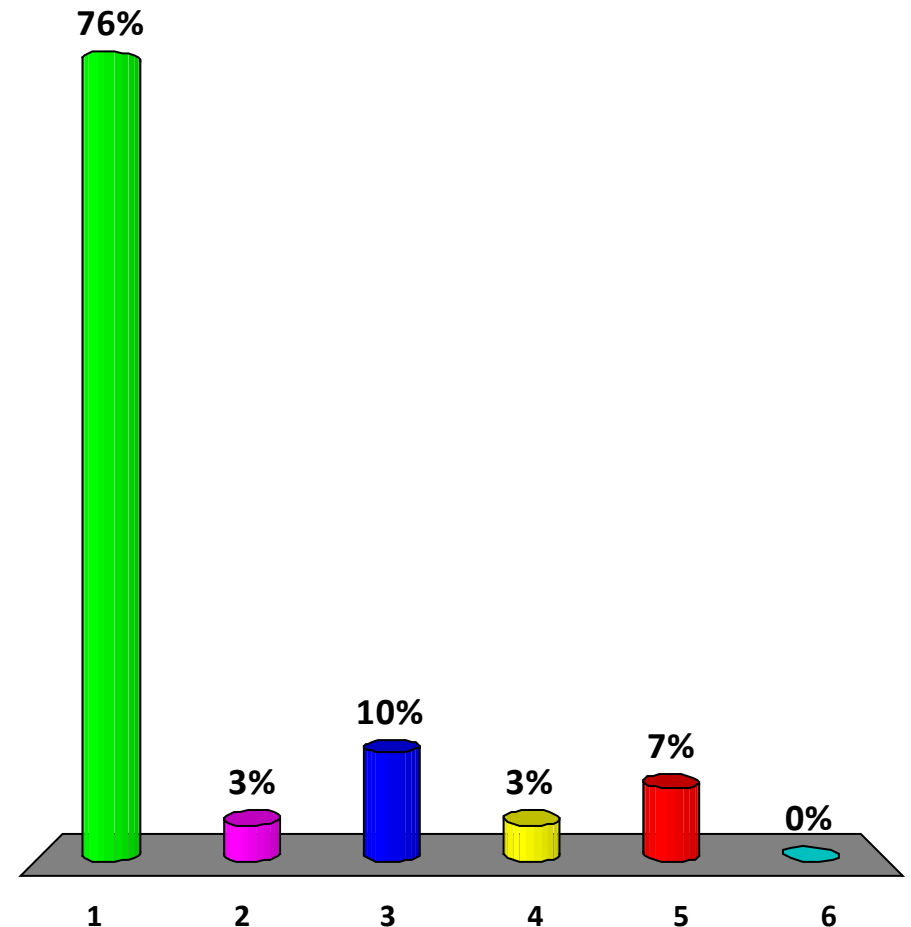
- FDA regulates manufacturers; CMS regulates laboratories.
- CLIA appendix C ; Interpretive guidelines 493.1291(c)(4):  
“Laboratories using manufacturer’s instruments, kits or test systems labeled for “IUO” or “RUO” must clearly state that the test results are not to be used for treatment or diagnostic purposes. If results of such tests are being reported without a disclaimer statement, or are being used by the provider for patient care, they are in the same category as in-house developed tests and the laboratory must establish performance specifications in accordance with 493.1253”

## Case 2 (#4)

- The “AutoAFB” has internal positive and negative controls. Each test has to have correct results for each of these controls or it is invalid.

# How often should EXTERNAL (+) and (-) controls be included for this RUO?

1. Every run
2. Once per shift
3. When changing reagents
4. Depends
5. External controls are not needed
6. I have no idea!



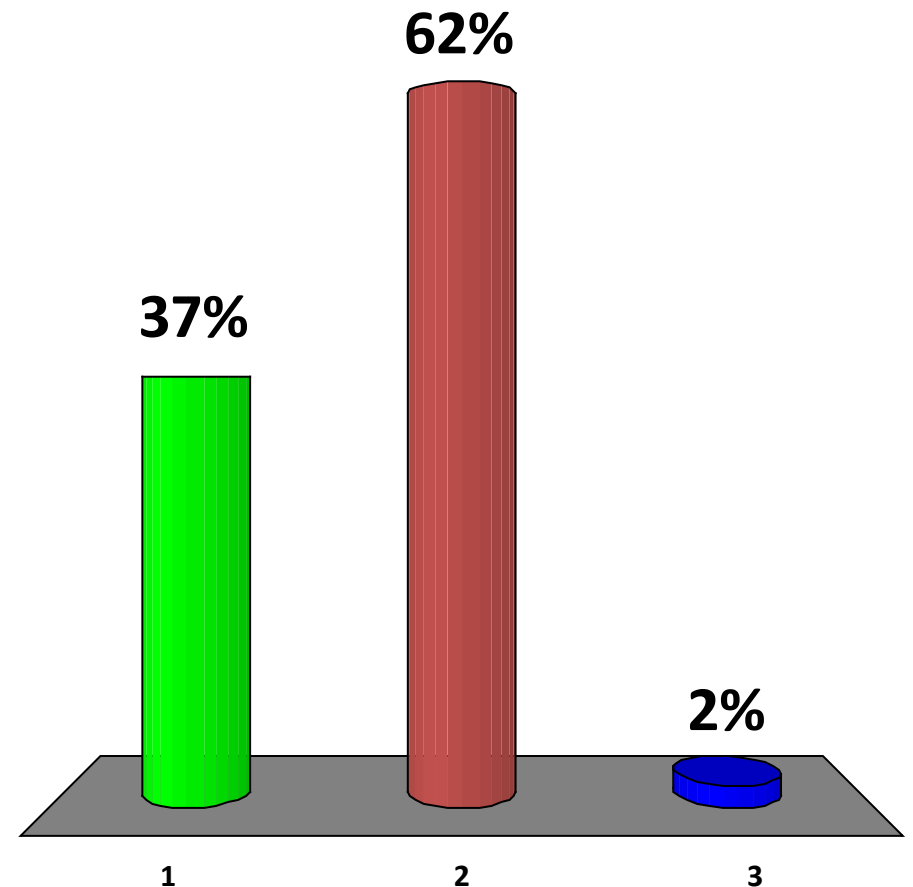
# Case 3

## Use of an LDT

- Lab is using an in-house developed (aka laboratory-developed test; LDT) real-time PCR assay to identify MtbC from clinical specimens.
- An ASR product (primer pair) is used in this assay.
- Lab reports results as “*M. tuberculosis* complex detected by real-time PCR assay”

# Do you need to put the method in the test answer?

1. Yes
2. No
3. Don't know

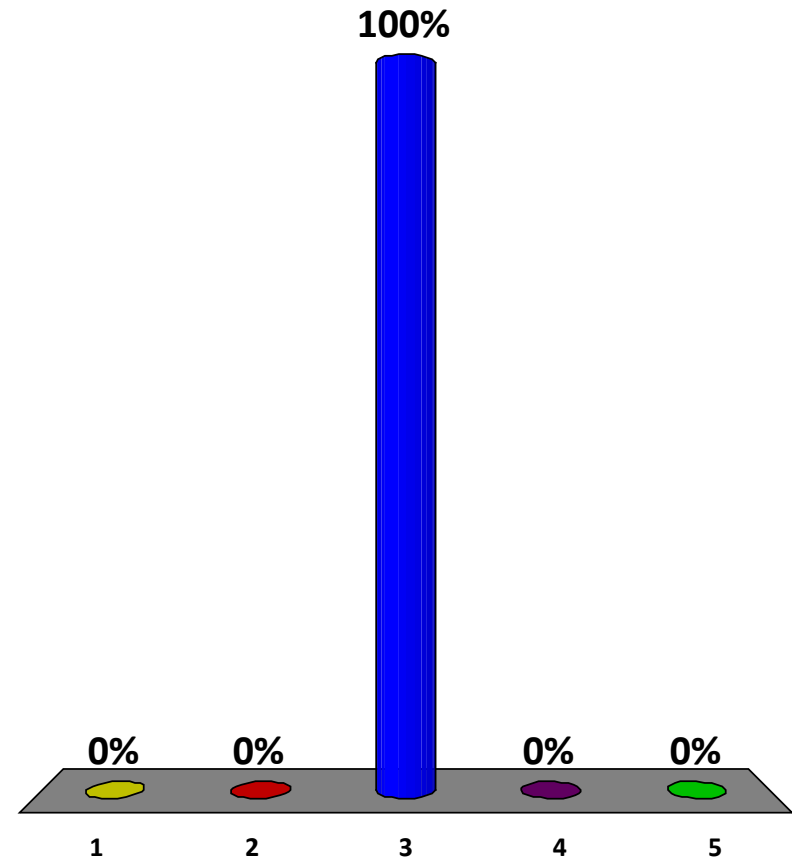


## Case 3 (#3)

- CLIA 493.1291 (c)(4) – the test report must indicate the test performed
- CLIA 493.1291 (e) – the laboratory must, upon request, make available to clients a list of test methods employed by the laboratory.....

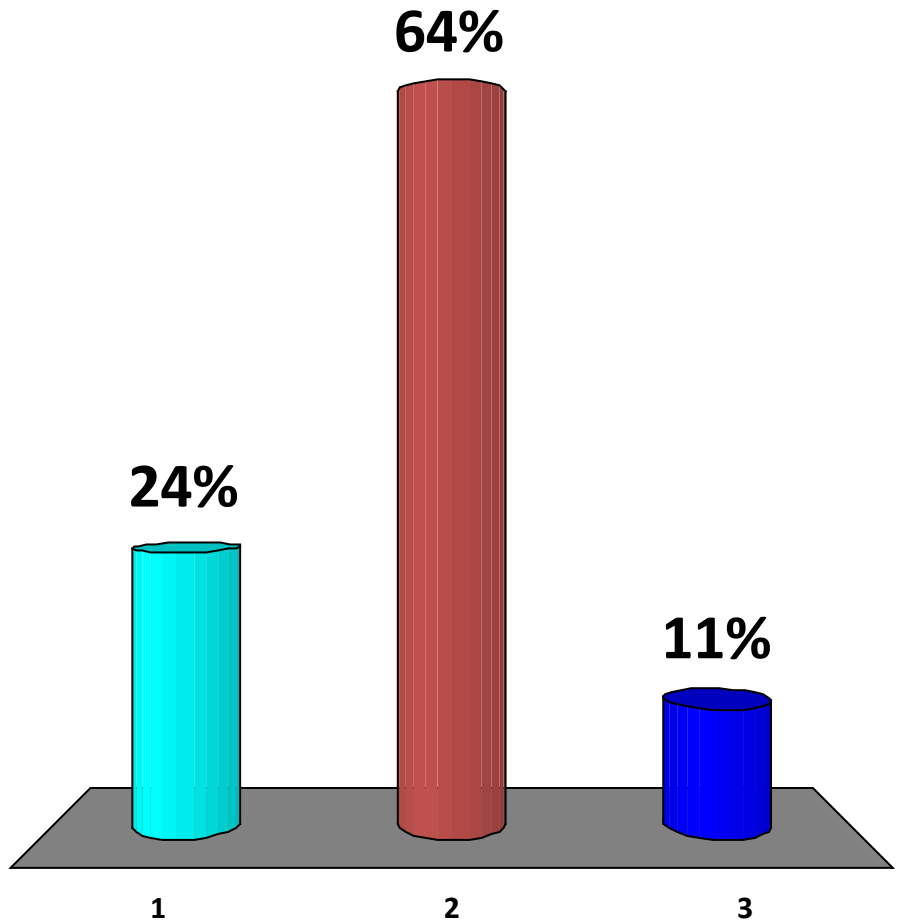
# What type of disclaimer regarding the method should be included with the result?

1. Testing performed by in-house developed assays
2. Testing performed by assay that is not FDA approved
3. This test was developed and its performance characteristics determined by Laboratory A. It has not been cleared or approved by the U.S. Food and drug Administration.
4. No disclaimer is necessary
5. I have no idea!



# Do you need to state that an ASR is used in the assay?

1. Yes
2. No
3. Don't know



# Case 3 (#6)

ASR Rule:

This test was developed and its performance characteristics determined by Laboratory A. It has not been cleared or approved by the U.S. Food and Drug Administration.

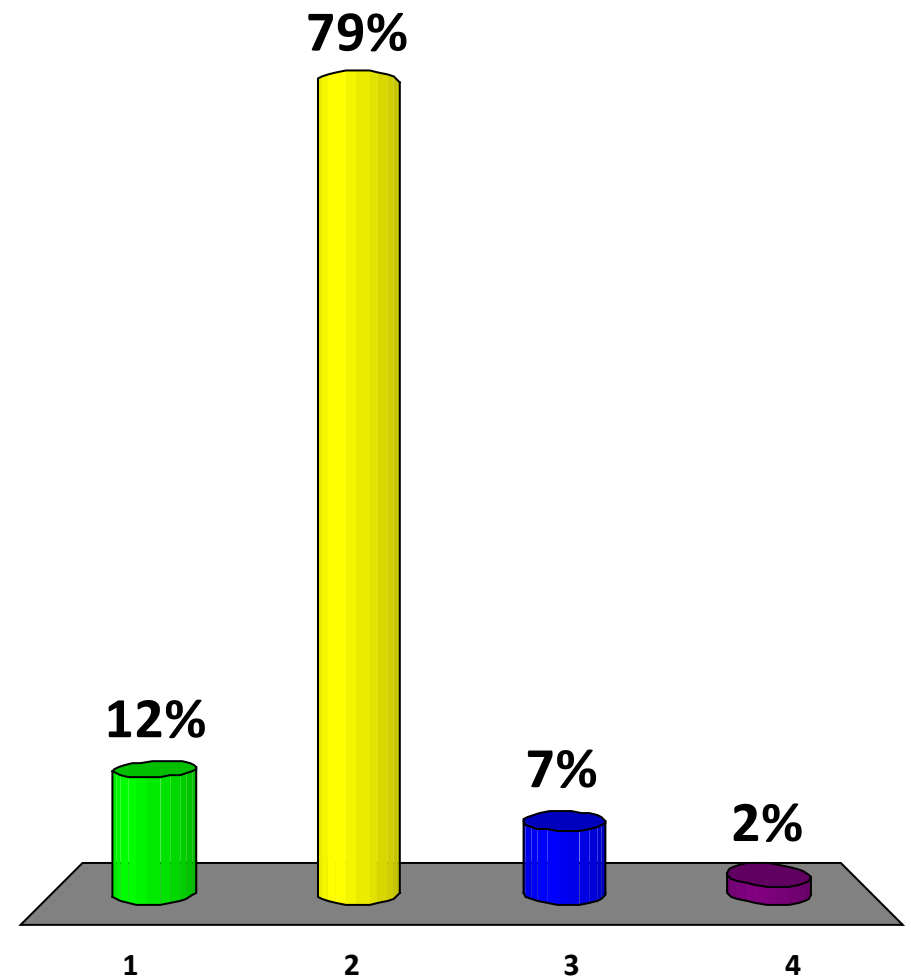
CLIA Appendix C – interpretive guidelines  
493.1291(c)(4)

## Case 3 (#7)

- The lab has validated this LDT with frozen remnants of clinical specimens previously tested in their lab

# Is the use of frozen specimens in the validation acceptable?

1. Yes, use of only frozen specimens is acceptable
2. Yes, but fresh specimens should also be included
3. No, validation should only be performed prospectively with fresh specimens
4. I have no idea!



# How often should (+) and (-) controls be included for this LDT?

1. Every run
2. Once per shift
3. When changing reagents
4. Depends
5. I have no idea!

