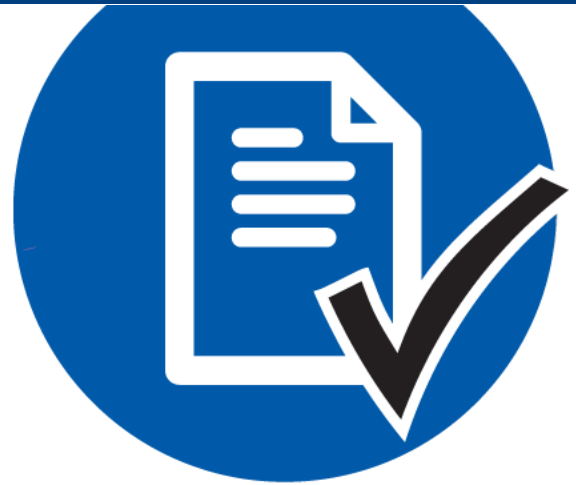


# Microbiology Checklist

CAP Accreditation Program



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# Microbiology Checklist



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## ON-LINE CHECKLIST AVAILABILITY AND RESOURCES

Participants of the CAP accreditation programs may download the checklists from the CAP website (cap.org) by logging into e-LAB Solutions Suite. They are available in different checklist types and formatting options, including:

- Master — contains ALL of the requirements and instructions available in PDF, Word/XML or Excel formats
- Custom — customized based on the laboratory's activity (test) menu; available in PDF, Word/XML or Excel formats
- Changes Only — contains only those requirements with significant changes since the previous checklist edition in a track changes format to show the differences; in PDF version only. Requirements that have been moved or merged appear in a table at the end of the file.

A repository of questions and answers and other resources is also available in e-LAB Solutions Suite under Accreditation Resources, Checklist Requirement Q & A.

## SUMMARY OF CHECKLIST EDITION CHANGES

### Microbiology Checklist

### 09/22/2021 Edition

The information below includes a listing of checklist requirements with significant changes in the current edition and previous edition of this checklist. The list is separated into three categories:

1. New
2. Revised:
  - Modifications that may require a change in policy, procedure, or process for continued compliance; or
  - A change to the Phase
3. Deleted/Moved/Merged:
  - Deleted
  - Moved — Relocation of a requirement into a different checklist (requirements that have been resequenced within the same checklist are not listed)
  - Merged — The combining of similar requirements

*NOTE: The requirements listed below are from the Master version of the checklist. The customized checklist version created for on-site inspections and self-evaluations may not list all of these requirements.*

#### NEW Checklist Requirements

<u>Requirement</u>	<u>Effective Date</u>
MIC.11385	09/22/2021
MIC.21855	09/22/2021
MIC.32150	06/04/2020
MIC.32170	06/04/2020
MIC.63340	09/22/2021
MIC.65620	06/04/2020

#### REVISED Checklist Requirements

<u>Requirement</u>	<u>Effective Date</u>
MIC.11023	09/22/2021
MIC.11035	09/22/2021
MIC.11380	09/22/2021
MIC.18968	09/22/2021

MIC.18985	09/22/2021
MIC.19035	09/22/2021
MIC.19840	09/22/2021
MIC.20530	09/22/2021
MIC.20540	09/22/2021
MIC.21240	09/22/2021
MIC.21815	06/04/2020
MIC.21835	06/04/2020
MIC.21950	09/22/2021
MIC.22273	09/22/2021
MIC.22630	06/04/2020
MIC.22635	09/22/2021
MIC.22640	09/22/2021
MIC.22870	06/04/2020
MIC.31100	09/22/2021
MIC.31120	09/22/2021
MIC.31380	09/22/2021
MIC.31680	09/22/2021
MIC.32140	06/04/2020
MIC.41200	09/22/2021
MIC.42110	09/22/2021
MIC.42120	09/22/2021
MIC.42130	09/22/2021
MIC.42350	06/04/2020
MIC.42550	09/22/2021
MIC.42600	09/22/2021
MIC.52195	06/04/2020
MIC.64770	09/22/2021
MIC.64960	06/04/2020
MIC.65200	09/22/2021
MIC.65220	09/22/2021
MIC.65590	09/22/2021

#### DELETED/MOVED/MERGED Checklist Requirements

<u>Requirement</u>	<u>Effective Date</u>
MIC.33050	09/21/2021
MIC.33300	09/21/2021
MIC.42620	09/21/2021
MIC.42680	09/21/2021
MIC.43250	09/21/2021
MIC.43300	09/21/2021
MIC.43350	09/21/2021
MIC.51210	06/03/2020
MIC.51220	06/03/2020
MIC.63050	09/21/2021
MIC.63100	09/21/2021
MIC.63150	09/21/2021
MIC.63200	09/21/2021
MIC.63220	09/21/2021
MIC.63250	09/21/2021
MIC.63322	09/21/2021
MIC.64760	09/21/2021
MIC.64956	09/21/2021
MIC.64968	09/21/2021
MIC.66200	09/21/2021

## INTRODUCTION

This checklist is used in conjunction with the All Common and Laboratory General Checklists to inspect a microbiology laboratory section or department.

Certain requirements are different for waived versus nonwaived tests. Refer to the checklist headings and explanatory text to determine applicability based on test complexity. The current list of tests waived under CLIA may be found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm>.



**Laboratories not subject to US regulations:** Checklist requirements apply to all laboratories unless a specific disclaimer of exclusion is stated in the checklist. When the phrase "FDA-cleared/approved test (or assay)" is used within the checklist, it also applies to tests approved by an internationally recognized regulatory authority (eg, CE-marking).

## GENERAL MICROBIOLOGY

Requirements in this section apply to ALL of the subsections in the microbiology laboratory (bacteriology, mycobacteriology, mycology, parasitology, molecular microbiology, and virology).

## PROFICIENCY TESTING

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>Are proficiency testing samples tested to the same level as clinical specimens?</li> </ul>
	<ul style="list-style-type: none"> <li>Select a representative clinical report of each culture type. Compare the extent of reporting for the relevant proficiency testing sample.</li> </ul>

#### MIC.00350 PT Extent of Testing

Phase II

**Organisms in proficiency testing specimens are identified to the same level as those from patient samples.**

*NOTE: If the laboratory's proficiency testing reports include incomplete identifications (eg, "Gram positive cocci" or "Mycobacterium species, not tuberculosis"), it must indicate that this matches the information produced by the laboratory's internal capabilities in patient reports. In other words, patient reports cannot be more specific than the identification level reporting in proficiency testing, unless the former contain more specific information provided by referral laboratories.*

#### MIC.00375 PT for Susceptibility Testing

Phase II





**If any susceptibility testing is performed on-site, the laboratory participates in a proficiency testing program for the related subspecialty (eg, bacteriology, mycology).**

**Evidence of Compliance:**

- ✓ Records of proficiency testing performance

## QUALITY MANAGEMENT

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of QC policies and procedures</li> <li>• Sampling of QC records</li> <li>• Sampling of employee records of consistency of morphologic observation evaluation</li> <li>• Sampling of records for annual review of the susceptibility criteria used by the laboratory</li> </ul>
	<ul style="list-style-type: none"> <li>• Sampling of microbiology smear preparations (uniquely identified, proper smear thickness, free of precipitate, proper cell distribution, appropriate staining reactions, etc.)</li> </ul>
	<ul style="list-style-type: none"> <li>• How do you determine when QC is unacceptable and when corrective actions are needed?</li> <li>• How do you ensure consistency among personnel performing microscopic morphology?</li> <li>• How do you monitor for taxonomic changes that may affect the susceptibilities reported?</li> </ul>
	<ul style="list-style-type: none"> <li>• Review a sampling of QC data over the previous two-year period. Select several occurrences in which QC is out of range and follow records to determine if the steps taken follow the laboratory procedure for corrective action</li> <li>• Use QC data to identify tests that utilize internal quality control processes and confirm that the tests have an individualized quality control plan (IQCP) approved by the laboratory director, when required</li> </ul>

## QUALITY CONTROL - WAIVED TESTS

MIC.10060 QC - Waived Tests

Phase II

**The laboratory follows manufacturer's instructions for quality control, records and reviews results for acceptability prior to reporting patient results.**

*NOTE: Quality control must be performed according to manufacturer's instructions. Testing personnel or supervisory staff must review quality control data on days when controls are run prior to reporting patient results. The laboratory director or designee must review QC data at least monthly or more frequently if specified in the laboratory QC policy.*

*With respect to internal controls, acceptable control results must be recorded, at a minimum, once per day of patient testing for each device.\**

*\*Acceptable internal control results need not be recorded, if (and only if) an unacceptable instrument control automatically locks the instrument and prevents release of patient results.*



**Evidence of Compliance:**

- ✓ Written procedure consistent with manufacturer's instructions for each waived test **AND**
- ✓ Records showing confirmation of acceptable QC results

**MIC.10070 QC Corrective Action - Waived Tests Phase II**

**There are records of corrective action when quality control results exceed the acceptable range.**

## QUALITY CONTROL - NONWAIVED TESTS

**MIC.11015 QC Handling Phase II**

**Control specimens are tested in the same manner and by the same personnel as patient samples.**

*NOTE: QC specimens must be analyzed by personnel who routinely perform patient testing. This does not imply that each operator must perform QC daily, so long as each instrument and/or test system has QC performed at required frequencies, and all analysts participate in QC on a regular basis. To the extent possible, all steps of the testing process must be controlled.*

**Evidence of Compliance:**

- ✓ Records reflecting that QC is run by the same personnel performing patient testing

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7166 [42CFR493.1256(d)(8)].1256(f)]

**MIC.11016 Commercial Product - QC Phase II**

**When using a commercial product, QC is performed according to the manufacturer's instructions or CAP Checklist requirements, whichever is more stringent.**

**MIC.11017 QC Confirmation of Acceptability Phase II**

**Control results are reviewed for acceptability before reporting patient results.**

**Evidence of Compliance:**

- ✓ Written policy stating that controls are reviewed and acceptable prior to reporting patient results **AND**
- ✓ Records of control result approval

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24)1992(Feb 28):7166 [42CFR493.1256(f)]

**MIC.11018 QC Corrective Action Phase II**

**There are records of corrective action when control results exceed defined acceptability limits.**

*NOTE: Patient/client test results obtained in an analytically unacceptable test run or since the last acceptable test run must be re-evaluated to determine if there is a significant clinical difference in patient/client results. Re-evaluation may or may not include re-testing patient samples, depending on the circumstances.*

*Even if patient samples are no longer available, test results can be re-evaluated to search for evidence of an out-of-control condition that might have affected patient results.*

*The corrective action for tests that have an Individualized Quality Control Plan (IQCP) approved by the laboratory director must include an assessment of whether further evaluation of the risk assessment and quality control plan is needed based on the problems identified (eg, trending for repeat failures, etc.).*

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Oct 1):1046[42CFR493.1282(b)(2)]

### MIC.11020 Monthly QC Review

Phase II

**Quality control data are reviewed and assessed at least monthly by the laboratory director or designee.**

*NOTE: The review of quality control data must be recorded and include follow-up for outliers, trends, or omissions that were not previously addressed.*

*The QC data for tests performed less frequently than once per month should be reviewed when the tests are performed.*

*The review of quality control data for tests that have an IQCP approved by the laboratory director must include an assessment of whether further evaluation of the risk assessment and quality control plan is needed based on problems identified (eg, trending for repeat failures, etc.).*

#### Evidence of Compliance:

- ✓ Records of QC review including follow-up for outliers, trends or omissions

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### MIC.11023 Direct Antigen Test QC - Nonwaived Tests

Phase II

**For nonwaived direct antigen tests on patient specimens, positive and negative controls are tested and recorded at least daily, or more frequently if specified in the manufacturer's instructions, laboratory procedure, or CAP Checklist.**

*NOTE: This requirement pertains to nonwaived tests with a protein, enzyme, or toxin which acts as an antigen. Examples include, but are not limited to: Group A Streptococcus antigen, C. difficile toxin, fecal lactoferrin and immunochemical occult blood tests. For panels or batteries, controls must be employed for each antigen sought in patient specimens.*

*If an internal quality control process (eg, electronic/procedural/built-in) is used instead of an external control material to meet daily quality control requirements, the laboratory must have an individualized quality control plan (IQCP) approved by the laboratory director defining the control process, including the frequency and use of external and internal controls. At a minimum, external control materials must be analyzed with new lots and shipments of reagents or more frequently if indicated in the manufacturer's instructions. Please refer to the IQCP section of the All Common Checklist for the eligibility of tests for IQCP and requirements for implementation and ongoing monitoring of an IQCP.*

*For each test system that requires an antigen extraction phase, as defined by the manufacturer, the system must be checked with an appropriate positive control that will detect problems in the extraction process. If an IQCP is implemented for the test, the laboratory's quality control plan must define how the extraction phase will be monitored, as applicable, based on the risk assessment performed by the laboratory and the manufacturer's instructions.*

#### Evidence of Compliance:

- ✓ Written QC procedures **AND**
- ✓ Records of QC results including external and electronic/procedural/built-in control systems **AND**
- ✓ Manufacturer's product insert or manual

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1261(a)]
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. S & C: 16-20-CLIA: Policy Clarification on Acceptable Control Materials Used when Quality Control (QC) is Performed in Laboratories. April 8, 2016.

**MIC.11025 Alternative Control Procedures****Phase II**

**If the laboratory performs test procedures for which control materials are not commercially available, there are written procedures for an alternative mechanism to detect immediate errors and monitor test system performance over time. The performance of alternative control procedures must be recorded.**

*NOTE: "Performance" includes elements of accuracy, precision, and clinical discriminating power. Examples of alternative procedures may include split sample testing with another method or with another laboratory, the testing of previously tested patient specimens in duplicate, testing of patient specimens in duplicate, or other defined processes approved by the laboratory director.*

**Evidence of Compliance:**

- ✓ Written procedures for alternative quality control **AND**
- ✓ Records of alternative control procedures

## REFERENCES

- 1) Elder BL, *et al*. Verification and Validation of Procedures in the Clinical Microbiology Laboratory. Cumitech 31, February 1997. ASM Press; Washington DC
- 2) Sharp S and Clark R. Verification and Validation of Procedures in the Clinical Microbiology Laboratory. Cumitech 31a. 2009. ASM Press; Washington, DC
- 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(h)].

**\*\*REVISED\*\* 09/22/2021****MIC.11035 Inspection of Media Shipments****Phase II**

**The laboratory has records showing that each shipment of purchased/acquired media is examined for breakage, contamination, appearance, and evidence of freezing or overheating. Unacceptable media is discarded, and problems identified during examination of media are recorded and reported to the manufacturer where indicated.**

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Quality Control for Commercially Prepared Microbiological Culture Media; Approved Standard*; 3rd ed. CLSI document M22-A3. Clinical and Laboratory Standards Institute, Wayne, PA, 2004.
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)(4)(iii)].

**GENERAL ISSUES - NONWAIVED TESTS****MIC.11060 Culture Result Reporting****Phase I**

**If the laboratory is reporting culture results other than simply "growth/no growth," the laboratory has the ability to perform Gram stains as part of its bacterial identification process.**

*NOTE: The performance of a Gram stain on colonies from a culture plate may be a necessary procedure for guiding culture workup and in confirming the identification of organisms, especially when atypical findings are noted during the workup.*

*Personnel performing Gram stains for this purpose are subject to competency assessment. Requirements for proficiency testing must be met through participation in the bacterial culture proficiency testing programs.*

**MIC.11075 Smear Preparation and Stain Quality****Phase I**

**The quality of smear preparation and staining is satisfactory for all microbiology stains (ie, proper smear thickness, free of precipitate, proper cell distribution, appropriate staining reactions, etc.).**

*NOTE: This can be evaluated by reviewing QC slides and random clinical slides.*

#### REFERENCES

- 1) Hata DJ, Thomson RB. Gram Stain Benchtop Reference Guide: An Illustrated Guide to Microorganisms and Pathology Encountered in Gram-Stained Smears. Northfield, IL: College of American Pathologists; 2017.

### MIC.11350 Morphologic Observation Evaluation

Phase II

**The laboratory evaluates consistency of morphologic observation among personnel performing Gram, trichrome and other organism stains at least annually.**

*NOTE: The laboratory must ensure the description of bacteria and other organisms is reported consistently amongst all personnel performing the microscopic analysis.*

*Suggested methods to accomplish this include:*

1. Circulation of a pre-graded set of organisms with defined staining characteristics.
2. Multi-headed microscopy
3. Use of photomicrographs with referee and participant identifications (eg, former CAP microbiology Surveys or other photomicrographs from teaching collections)
4. Use of digital images

*Acceptability criteria for agreement must be determined by the laboratory director or designee. The laboratory must maintain records of performance and record corrective actions taken for personnel demonstrating significant discrepancies from the group consensus.*

#### **Evidence of Compliance:**

- ✓ Written procedure defining the method(s) and criteria used for evaluation of consistency **AND**
- ✓ Records of evaluation

#### REFERENCES

- 1) Flournoy DJ. Interpreting the sputum gram stain report. *Lab Med.* 1998;29:763-768

### MIC.11375 Taxonomy Changes

Phase I

**The laboratory incorporates taxonomic changes that potentially affect the choice of appropriate antimicrobials to report and/or the interpretative breakpoints to use.**

*NOTE: The genus and/or species names of microorganisms may change as new methods are applied to their taxonomy. This can impact the antimicrobials that should be reported for that organism. It may also impact which breakpoints are used for reporting. For example, *Actinobacillus actinomycetemcomitans* was moved to the genus *Haemophilus* in 1985 and then to the new genus *Aggregatibacter* in 2006. The antimicrobials differ for *Haemophilus* species (CLSI M100, Table 2E) versus *Aggregatibacter* species (CLSI M45, Table 7). The laboratory should have a policy ensuring that clinically relevant taxonomic changes are reviewed at least annually by the laboratory in collaboration with prescribers, antimicrobial stewardship teams and infection control committees, as appropriate, and incorporated into reporting patient and proficiency testing results even when commercial identification systems have not been updated.*

*Bacterial taxonomic nomenclature is not valid until published in the International Journal of Systematic & Evolutionary Microbiology (IJSEM). For laboratories participating in the CAP's proficiency programs for microbiology, the Participant Summary Report Final Critique is a good source of information as the Microbiology Committee provides periodic updates in taxonomy through educational challenges.*

Additional information for specific specialties may be found through the mini-reviews published in the *Journal of Clinical Microbiology* (January 2019, Vol 57, No 2) or on-line using web sites, such as the following:

For bacteriology

- <http://www.bacterio.net/-classification.html>
- <http://www.dsmz.de/bacterial-diversity/prokaryotic-nomenclature-up-to-date.html>
- <http://enews.patricbrc.org/>

For mycology:

- <http://mycobank.org>
- <http://www.mycology.adelaide.edu.au>
- <http://www.fungaltaxonomy.org>

For parasitology:

- <http://www.cdc.gov/dpdx/>

#### Evidence of Compliance:

- ✓ Records showing that taxonomic changes were reviewed at least annually and incorporated by the laboratory in collaboration with prescribers, antimicrobial stewardship teams and infection control committees, as appropriate

#### REFERENCES

- 1) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline*; 3rd ed. CLSI document M45-ED3. Clinical and Laboratory Standards Institute, Wayne, PA, 2016.
- 2) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*; 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 3) Kraft CS, McAdam AJ, Carroll KC. A Rose by Any Other Name: Practical Updates on Microbial Nomenclature for Clinical Microbiology. *J Clin Microbiol.* 2017; 55(1):3-4.
- 4) Munson E, Carroll KC. What's in a Name? New Bacterial Species and Changes to Taxonomic Status from 2012 through 2015. *J Clin Microbiol.* 2017; 55(1):24-42. Erratum in: *J Clin Microbiol.* 2017; 55(5): 1595.
- 5) Simner PJ. Medical Parasitology Taxonomy Update: January 2012 to December 2015. *J Clin Microbiol.* 2017; 55(1):43-47.
- 6) Loeffelholz MJ, Fenwick BW. Taxonomic Changes and Additions for Human and Animal Viruses, 2012 to 2015. *J Clin Microbiol.* 2017; 55(1):48-52.
- 7) Warnock DW. Name Changes for Fungi of Medical Importance, 2012 to 2015. *J Clin Microbiol.* 2017; 55(1):53-59.
- 8) Mathison BA, Pritt BS. Medical Parasitology Taxonomy Update, 2016–2017. *J Clin Microbiol.* 2019; 57(2): e01067-18.
- 9) Munson E, Carroll KC. An Update on the Novel Genera and Species and Revised Taxonomic Status of Bacterial Organisms Described in 2016 and 2017. *J Clin Microbiol.* 2019(2); 57:e01181-18.
- 10) Warnock, DW. Name Changes for Fungi of Medical Importance, 2016–2017. *J Clin Microbiol.* 2019(2);57: e01183-18
- 11) Loeffelholz MJ, Fenwick BW. Taxonomic Changes for Human and Animal Viruses, 2016 to 2018. *J. Clin. Microbiol.* 2019(2); 57: e01457-18.

**\*\*REVISED\*\* 09/22/2021**

**MIC.11380 Antimicrobial Susceptibility Test Interpretation Criteria**

**Phase II**

**For antimicrobial susceptibility testing systems, there are written criteria for determining and interpreting minimal inhibitory concentration (MIC) or zone diameter sizes as susceptible, intermediate, resistant, non-susceptible, or susceptible dose-dependent. These criteria are reviewed annually.**

*NOTE: This checklist item applies to all antibacterial, antifungal, and antimycobacterial agents tested in the laboratory. The same criteria applied to clinical test results must be used for proficiency testing results.*

*Since 2010 the interpretive criteria (otherwise known as breakpoints) applied to antimicrobial susceptibility tests have been continuously updated in response to new and emerging antimicrobial resistance mechanisms and clinical data. The microbiology laboratory must ensure that the breakpoints being used meet current standards of care for recent updates and dosing recommendations. This may be done in consultation with medical and pharmacy leadership.*

*The laboratory may use interpretive criteria from standards development organizations such as Clinical and Laboratory Standards Institute (CLSI) or EUCAST, the FDA, or in rare instances, validated institution-specific criteria.*



The source of the breakpoints applied to interpret AST results must be documented for both manual and automated antimicrobial susceptibility testing methods, including the reference with the year it was published (eg, CLSI M100-S31, 2021). For automated susceptibility testing systems, laboratories may contact the manufacturer to understand the breakpoints applied by the automated expert rules programmed into the system for the test panels in use, if not already known.

Criteria must be reviewed by the laboratory and with the antimicrobial stewardship program in the institution (if applicable) annually. The records of the review must be available.

#### Evidence of Compliance:

- ✓ Listing of antimicrobial susceptibility test interpretive criteria applied to test results and the specific source document for these **AND**
- ✓ Patient reports with reporting of antimicrobial agents following written protocol **AND**
- ✓ Records of annual breakpoint review **AND**
- ✓ Proficiency testing susceptibility results following written policy

#### REFERENCES

- 1) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 2) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*; 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 3) Clinical and Laboratory Standards Institute (CLSI). *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 4) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria*. 9th ed. CLSI standard M11. Clinical and Laboratory Standards Institute, Wayne, PA, 2018.
- 5) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1263(b)(1)].
- 6) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts*. 4th ed. CLSI standard M27. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.
- 7) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi*. 3rd ed. CLSI standard M38. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.
- 8) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts*. 3rd ed. CLSI guideline M44. Clinical and Laboratory Standards Institute, Wayne, PA, 2018.

**\*\*NEW\*\* 09/22/2021**

**MIC.11385**

**Current Antimicrobial Susceptibility Test Interpretation Breakpoints**

**Phase I**

**Effective January 1, 2024, the laboratory uses current breakpoints for interpretation of antimicrobial minimum inhibitory concentration (MIC) and disk diffusion test results, and implements new breakpoints within three years of the date of official publication by the FDA or other standards development organization (SDO) used by the laboratory.**

*NOTE 1: SDOs that develop breakpoints include the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST).*

*For laboratories subject to US regulations, a breakpoint is considered obsolete three years after publication of an update by the FDA, though the laboratory may use currently accepted breakpoints from other SDOs with validation to support use. Whether using breakpoints from the FDA or other SDOs, laboratories must adopt the change within three years of the official publication date of the updated breakpoint.*

*NOTE 2: Not all FDA-cleared susceptibility test systems apply current FDA-recognized breakpoints. Laboratories must determine if the breakpoints applied by their system are current and if they are not, validate changes to breakpoints as needed prior to use in patient result interpretation. Laboratories may also validate susceptibility test systems for use with alternative breakpoints (eg, those from SDOs).*

*NOTE 3: In rare instances, hospital-based laboratories may choose to use alternative breakpoints (eg, institution-derived breakpoints not recognized by SDOs or the FDA) that address unique patient and/or antimicrobial stewardship needs. In this case, the laboratory must have written documentation (eg, minutes from a pharmacy and therapeutic committee meeting, a letter of approval signed by stakeholders) for the following:*

- Scientific and medical reasoning and institutional review/approval of institution-specific breakpoints

- *Review and agreement to use alternative breakpoints by stakeholders (eg, chief medical officer, pharmacy, infectious diseases, and/or antimicrobial stewardship partners).*

**Evidence of Compliance:**

- ✓ Written policy for updating breakpoints used for antimicrobial susceptibility test interpretations **AND**
- ✓ Records of validation reports for breakpoints that differ from those included in the FDA-clearance of an instrument **AND**
- ✓ Records of the interpretive criteria used for antimicrobial susceptibility testing **AND**
- ✓ Source document (including year of publication) from which the interpretive criteria were derived **AND**
- ✓ Patient or LIS reports with interpretations matching the source document

**REFERENCES**

- 1) Antibacterial Susceptibility Test Interpretive Criteria. US Food and Drug Administration. Accessed February 3, 2021. <https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria>.
- 2) Clinical and Laboratory Standards Institute. *Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems, 1st ed.* CLSI Document M52-Ed1. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.

**MIC.11395 Referral of Isolates for Susceptibility Testing****Phase I**

**If the laboratory is unable to perform susceptibility testing on-site, there is a mechanism to refer clinically significant isolates for which susceptibility testing is deemed necessary (eg, isolates obtained from blood or other sterile sites).**




**Evidence of Compliance:**

- ✓ Written policy defining situations where isolates must be referred for susceptibility testing **AND**
- ✓ Records of referral of isolates for susceptibility testing

**SPECIMEN COLLECTION AND HANDLING**

*Culture specimens are often collected by nurses or others outside the laboratory. An important aspect of quality control is the provision of adequate instructions to ensure proper collection and handling of specimens before they are received by the laboratory.*

**Inspector Instructions:**

	<ul style="list-style-type: none"> <li>• Sampling of specimen collection and handling policies and procedures</li> <li>• Sampling of requisitions for completeness</li> </ul>
	<ul style="list-style-type: none"> <li>• Sampling of microbiology specimens (transport media, timely delivery, labeling)</li> </ul>
	<ul style="list-style-type: none"> <li>• What is your course of action when you receive unacceptable microbiology specimens?</li> </ul>

**MIC.13175 Viral Culture Specimens****Phase I**

**Specimens for viral culture are collected appropriately and transported to the laboratory without delay.**

*NOTE: The laboratory must provide procedures for the appropriate collection, transport and storage of all specimen types tested in the laboratory. Specimens should be delivered to the laboratory promptly, ideally within 2-4 hours of sample collection and preferably within 1 day of collection. This may not be possible for laboratories that refer samples to offsite referral laboratories for viral testing. In these instances, samples must be stored and shipped under conditions that would preserve the integrity of the sample. Unless otherwise indicated, specimens should be refrigerated or frozen depending on the duration of storage prior to testing.*

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline*. CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.
- 2) Ginocchio, CC. Quality Assurance in Clinical Virology. In: Spector S, Hodinka RL, Young SA, editors. *Clinical Virology Manual*. Fourth Edition. Washington: ASM Press; 2009.p. 3-17

**MIC.13200 Requisitions Phase I**

**Requests for analysis include source of specimen, test or tests requested and, when appropriate, type of infection and/or organism expected.**

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7162 [42CFR493.1241(c)]

**MIC.13250 Specimen Collection/Handling Phase II**

**There are written instructions for microbiology specimen collection and handling that include all of the following.**

1. **Method for proper collection of culture specimens from different sources**
2. **Proper labeling of culture specimens**
3. **Use of appropriate transport media when necessary**
4. **Policies for safe handling of specimens (tightly sealed containers, no external spillage)**
5. **Need for prompt delivery of specimens to ensure minimum delay and processing (eg, CSF, wound cultures, anaerobes)**
6. **Method for preservation of specimens if processing is delayed (eg, refrigeration of urines)**

*NOTE: Manufacturer's recommendations must be followed when there is a delay in delivery or processing of specimens for automated instruments (eg, blood culture instruments).*

**REFERENCES**

- 1) Jorgensen JH (ed), et al. *Manual of Clinical Microbiology*. 11th ed. Washington, DC: ASM Press; 2015.

**MIC.13275 Specimens for Molecular Amplification Phase II**

**The laboratory has written procedures for the handling of specimens that will be tested using molecular amplification methods.**

*NOTE: Special precautions must be taken to avoid sample cross-contamination that may not affect culture-based methods but may lead to false positive results when tested using molecular amplification methods. For example, proper methods to prevent cross-contamination must be used when samples are processed in the same biohazard hood in which virus cultures are manipulated post-inoculation. Please refer to the Molecular Microbiology section of this checklist.*

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Collection, Transport, Preparations, and Storage of Specimens for Molecular Methods*. 2nd ed. CLSI guideline MM13. Clinical and Laboratory Standards Institute, Wayne, PA; 2020.



## REPORTING OF RESULTS

### Inspector Instructions:



- Sampling of patient preliminary reports

#### MIC.15000 Preliminary Reports Phase I

**When indicated, preliminary reports are promptly generated.**

**Evidence of Compliance:**

- ✓ Written policies defining when preliminary results are issued

#### MIC.15020 Azoospermic Specimen Result Reporting Phase I

**For azoospermic and post-vasectomy seminal fluid specimens, the laboratory clearly communicates the findings of the assay and either employs a concentrating technique on seminal fluid or includes a comment in the patient report indicating that a concentrating technique was not performed.**

*NOTE: Without a concentration technique, the presence of both motile and non-motile sperm may not be detected. The method for detection of motile and non-motile sperm and the laboratory findings must be clearly communicated on the patient report so that the clinician can interpret the results in context to the method performed. The decision on the method used and extent of testing to be performed should be made in consultation with the medical staff served.*

*The American Urological Association (AUA) Vasectomy Guideline recommends a careful evaluation of an uncentrifuged specimen, and does not recommend centrifugation of the specimen for further assessment. The AUA Guideline also recommends reporting both the presence and absence of sperm and presence or absence of sperm motility on the patient report. If no sperm are seen in the uncentrifuged specimen, the guideline recommends reporting that the presence of sperm is below the limit of detection.*

**Evidence of Compliance:**

- ✓ Patient report with concentration findings or appropriate comment indicating that concentration was not performed


**REFERENCES**

- 1) Evaluation of the Azoospermic Male. *Fertil Steril.* 2008; 90 (S74-7)
- 2) Diagnostic Evaluation of the Infertile Male: A Committee Opinion. *Fertil Steril.* 2012; 98:294-301
- 3) American Urological Association (AUA) Guideline. American Urological Association Education and Research, Inc. 2012; amended 2015. [https://www.auanet.org/guidelines/vasectomy-\(2012-amended-2015\)](https://www.auanet.org/guidelines/vasectomy-(2012-amended-2015))
- 4) Vasectomy Update 2010. *Can Urol Assoc J.* 2010 October; 4(5):306-309

## INSTRUMENTS AND EQUIPMENT

*The checklist requirements in this section should be used in conjunction with the requirements in the All Common Checklist relating to instruments and equipment.*

**Inspector Instructions:**

 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Incubators (adequate space, maintained)</li> </ul>
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**MIC.16550 Adequate Incubators****Phase I**

**There are sufficient, clean, and well-maintained incubators available at specified temperature ranges.**

## MATRIX-ASSISTED LASER DESORPTION IONIZATION TIME-OF-FLIGHT (MALDI-TOF) MASS SPECTROMETRY

*This section applies to laboratories using MALDI-TOF systems to perform organism identification. Refer to the Test Method Validation section in the All Common Checklist for validation requirements pertinent to laboratory-developed tests.*

**Inspector Instructions:**

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of mass spectrometer policies and procedures</li> <li>• Identification criteria compliance</li> <li>• Sampling of calibration and control records</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• How does your laboratory verify assay performance each day of use?</li> </ul>

**MIC.16575 Instrument Operation****Phase II**

**There are written procedures for the operation and calibration of the mass spectrometer.**

**MIC.16595 Mass Spectrometer Calibration****Phase II**

**A calibration control is performed during each run each day of patient testing, or with each change in target plate, or according to manufacturer's recommendations.**

*NOTE: Acceptable tolerance limits for calibration parameters must be defined.*

**Evidence of Compliance:**

- ✓ Written policy defining calibration requirements

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Methods for the Identification of Cultured Microorganisms Using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry*; 1st ed. CLSI document M58-Ed1. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.

**MIC.16605 Mass Spectrometer Controls****Phase II****Appropriate control organisms are tested on each day of patient testing.**

*NOTE: Consideration should be given to analyzing appropriate control organisms on a schedule determined by the manufacturer and relevant regulatory guidelines. Appropriate controls would include at least one representative organism for each class of organism tested (eg, a bacterium, a yeast, a filamentous fungi, an aerobic actinomycete, and a mycobacteria. For FDA-cleared/ approved platforms, the organisms or calibrator(s) required by the manufacturer must be used.*

*For laboratory developed tests, choice and use of control organisms is at the Laboratory Director's discretion. Control organisms must be subjected to the same testing conditions throughout the testing procedure as patient specimens and an extraction control should be included if any of the organisms being tested are run with extraction.*

*In formats of testing where a target plate is reused, a blank control needs to be run, varying the target location, after each cleansing to control for proper cleaning and decontamination of the entire testing surface (demonstrating a lack of peaks prior to testing). QC failures must be recorded and reviewed periodically to detect problems that may indicate problems with testing.*

**Evidence of Compliance:**

- ✓ Written policy defining QC requirements **AND**
- ✓ QC records at defined frequency

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Methods for the Identification of Cultured Microorganisms Using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry*; 1st ed. CLSI document M58-Ed1. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.

**MIC.16615 Mass Spectrometer Reagent Grade****Phase II****Reagents and solvents are of appropriate grade.**

*NOTE: Only the manufacturer's specified grade of solvents are used for this procedure.*

**Evidence of Compliance:**

- ✓ Reagent logs

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Methods for the Identification of Cultured Microorganisms Using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry*; 1st ed. CLSI document M58-Ed1. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.

**MIC.16625 Mass Spectrometer Consumables****Phase II****Consumables appropriate to the instrument and assay are required.**

*NOTE: For FDA-approved platforms, consumables utilized are specified by the manufacturer. Deviation from the manufacturer's recommendation must be validated.*

**Evidence of Compliance:**

- ✓ Consumable logs **AND**
- ✓ Validation of alternative consumables not specified by the manufacturer




**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Methods for the Identification of Cultured Microorganisms Using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry*; 1st ed. CLSI document M58-Ed1. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.

## LABORATORY SAFETY

Items in this section apply to ALL areas of the microbiology laboratory.

### Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of safety policies and procedures</li> <li>• Sampling of bench top decontamination logs</li> <li>• Records of biological safety cabinet certification</li> <li>• Infectious waste disposal policy</li> </ul>
 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Patient specimens (sealed, leak proof containers)</li> <li>• Storage of ether</li> <li>• Use of appropriate personal protective equipment (eg, N-95 mask, respirator, gown, gloves) and biological safety cabinet based on biosafety level and occupational risk as defined in laboratory policies and procedures</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• How would you recognize a potential agent of bioterrorism? What action would you take if you encountered a suspect organism?</li> <li>• How does your laboratory dispose of specimens and contaminated media?</li> </ul>

**\*\*REVISED\*\* 09/22/2021**

**MIC.18968 Agents of Bioterrorism**

**Phase II**

**The microbiology laboratory follows written policies and procedures for the recognition and safe handling of isolates that may be used as agents of bioterrorism.**

*NOTE: Microorganisms likely to be utilized as biological weapons include Bacillus anthracis (anthrax), Brucella species (brucellosis), Clostridium botulinum (botulism), Francisella tularensis (tularemia), Yersinia pestis (plague) and variola major (smallpox).*

*As part of an institution-wide plan to prepare and respond to a bioterrorism event, the microbiology laboratory must have policies and procedures for the recognition of isolates that may be used as agents of bioterrorism.*

*Safe handling includes such activities as handling organisms under a certified biological safety cabinet, and not subjecting the isolates to identification utilizing automated instruments.*

#### REFERENCES

- 1) Snyder JW. Role of the hospital-based microbiology laboratory in preparation and response to a bioterrorism event. *J Clin Microbiol.* January, 2003
- 2) Gilchrist MJR. Laboratory Safety, Management, and Diagnosis of Biological Agents Associated with Bioterrorism
- 3) Robinson-Dunn B. The microbiology laboratory's role in response to bioterrorism. *Arch Pathol Lab Med.* March 2002; 126
- 4) Morse SA. Bioterrorism: Laboratory Security. *Lab Med.* June 2001
- 5) Sewell, DL. Laboratory safety practices associated with potential agents of biocrime or bioterrorism. *J. Clin. Microbiology.* July 2003;41(7):2801-2809
- 6) American Society for Microbiology Laboratory Response Network (LRN). Sentinel Level Clinical Laboratory Protocols. <https://asm.org/Articles/Policy/Laboratory-Response-Network-LRN-Sentinel-Level-C>. Accessed April 26, 2021.
- 7) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 6th ed. June 2020.

**MIC.18976 Bioterrorism Response Plan**

**Phase I**

**The laboratory is recognized in the institution's bioterrorism response plan and the role of the laboratory is outlined in the plan.**

**Evidence of Compliance:**

- ✓ Organizational bioterrorism plan describing the role of the laboratory

## REFERENCES

- 1) Snyder JW. Role of the hospital-based microbiology laboratory in preparation and response to a bioterrorism event. *J Clin Microbiol.* January 2003
- 2) Gilchrist MJR. Laboratory Safety, Management, and Diagram of Biological Agents Associated with Bioterrorism
- 3) Robinson-Dunn B. The microbiology laboratory's role in response to bioterrorism. *Arch Pathol Lab Med.* March 2002; 126
- 4) Morse SA. Bioterrorism: Laboratory Security. *Lab Med.* June 2001

**\*\*REVISED\*\* 09/22/2021****MIC.18985 Spill Handling****Phase II**

**The laboratory follows written policies and procedures for handling spills of infectious materials.**

## REFERENCES

- 1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 6th ed. June 2020.

**MIC.19010 Bench Top Decontamination****Phase II**

**There are records of daily decontamination of bench tops.**

**\*\*REVISED\*\* 09/22/2021****MIC.19035 Safe Specimen Processing****Phase II**

**There are written policies and procedures for the safe handling and processing of specimens, including those suspected to contain highly infectious pathogens.**

*NOTE: Suggested topics to be considered in the policies and procedures for the safe handling and processing of specimens include the need for tight sealing of containers, avoiding spills of hazardous materials, requirements for wearing gloves, the need for respirator protection, availability and use of vaccinations, and the hazards of sniffing plates.*

*For samples suspected of containing highly infectious pathogens, laboratories must review national, federal, state (or provincial), and local guidelines for the handling of samples from patients suspected to have high risk pathogens, such as Francisella tularensis, avian influenza, Ebola, MERS coronavirus, SARS coronavirus, SARS-CoV-2 coronavirus, or any infectious agent that has a high potential to cause a disease to individuals and the community.*

## REFERENCES

- 1) Jamison R, et al. Laboratory Safety in Clinical Microbiology, Cumitech 29, July 1996, ASM Press; Washington DC
- 2) Fleming DO, Hunt DL. Biological Safety, Principles and Practices, 3rd ed. ASM Press; Washington DC

**MIC.19060 Biosafety Levels - Occupational Risk****Phase II**

**Policies and procedures have been developed to minimize the occupational risk of exposure to infectious agents handled in the microbiology laboratory, in accordance with current recommendations regarding the biosafety levels for working with different organisms.**

*NOTE: The laboratory director is responsible for the maintenance of precautions in the laboratory to minimize the risk of personnel infection. Precautions must be appropriate for the types of organisms tested and the nature of the studies performed.*

*Each level consists of combinations of equipment, processes and techniques, and laboratory design that are appropriate for the type of laboratory and infectious agent handled.*

## REFERENCES

- 1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 6th ed. June 2020.

**MIC.19160 Biosafety Levels - Engineering Work Practice Controls Phase II**

**Engineering and work practice controls appropriate to the Biosafety level of the laboratory are defined and implemented.**

*NOTE: Each increasing BSL number (1 to 4) implies increased occupational risk from exposure to an agent or performance of a process, and therefore is associated with more stringent control and containment practices.*

**REFERENCES**

- 1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 6th ed. June 2020.
- 2) Richmond J. BSL-4 Laboratories. Anthology of Biosafety V: American Biological Safety Association, Mundelein, IL January 2002
- 3) Richmond J. Biosafety Level 3. Anthology of Biosafety VII: American Biological Safety Association, Mundelein, IL December 2003

**\*\*REVISED\*\* 09/22/2021**

**MIC.19840 Biological Safety Cabinet Phase II**

**A biological safety cabinet (BSC) or hood is used for handling specimens or organisms considered highly contagious by airborne routes and meets minimum requirements for its use.**

*NOTE: For mycobacterial, mycologic, and virology work:*

- Exhaust air from a class I or class II BSC must be filtered through high efficiency particulate air (HEPA) filters.
- Air from Class I and IIB cabinets is hard-ducted to the outside.
- Air from Class IIA cabinets may be recirculated within the laboratory if the cabinet is tested and certified at least annually. It may also be exhausted through a dedicated stack that protects against backflow of air from adverse weather conditions or through the building exhaust air system in a manner (eg, thimble connection) that avoids any interference with the air balance of the biological safety cabinet or building exhaust system.

**Evidence of Compliance:**

- ✓ Written policy defining the types of safety cabinets, filtration systems and exhaust systems used **AND**
- ✓ Records of HEPA filters used for filtration of all BSC classes **AND**
- ✓ Records of exhaust mechanism **OR** recirculation, if appropriate

**REFERENCES**

- 1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 6th ed. June 2020.

**MIC.20520 Biological Safety Cabinet Phase II**

**The biological safety cabinet (BSC) is certified at least annually to ensure that filters are functioning properly and that airflow rates meet specifications.**

**Evidence of Compliance:**

- ✓ Maintenance schedule of BSC function checks **AND**
- ✓ Records of testing and certification

**REFERENCES**

- 1) NSF/ANSI Standard 49-2012 Biosafety Cabinetry: Design, Construction, Performance and Field Certification. Ann Arbor, MI: NSF; 2012.
- 2) Kruse RH, Puckett WH, Richardson JH. Biological safety cabinetry. *Clin Microbiol Rev.* 1991;4(2):207-241.
- 3) Kimman TG, Smit E, Klein MR. Evidence-based biosafety: a review of the principles and effectiveness of microbiological containment measures. *Clin Microbiol Rev.* 2008;21(3):403-425. doi: 10.1128/CMR.00014-08.

**\*\*REVISED\*\* 09/22/2021**

**MIC.20530 Infectious Waste Disposal Phase II**

**Microbiology specimen residuals and contaminated media are disinfected, sterilized, and disposed of in a manner to minimize infectious hazards to personnel after completion of testing.**

*NOTE: Sterilization or decontamination within the microbiology section before disposal is preferred. If such material is transported before treatment, it must be placed into a leak-resistant rigid container, and appropriately labeled.*

**Evidence of Compliance:**

- ✓ Written policy for the handling and disposal of microbiology waste

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Laboratory Waste Management; Approved Guideline—Third Edition*. CLSI document GP05-A3 (ISBN 1-56238-744-8). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 2011.

**\*\*REVISED\*\* 09/22/2021**

**MIC.20540 Ether Safety - Parasitology**

**Phase II**





**If a procedure uses ether, the diethyl ether is stored on open shelves in a well-ventilated room using the smallest can feasible (as shipped by manufacturer).**

*NOTE: The use of concentration techniques other than those requiring the use of ether is recommended.*

## BACTERIOLOGY

### MEDIA

#### Inspector Instructions:

<p><b>READ</b></p> 	<ul style="list-style-type: none"> <li>• Sampling of media QC policies and procedures</li> <li>• Sampling of media supplier records of QC</li> <li>• Sampling of records for QC performed by the laboratory</li> </ul>
<p><b>OBSERVE</b></p> 	<ul style="list-style-type: none"> <li>• Sampling of media (expiration date, condition, contamination)</li> </ul>
<p><b>ASK</b></p> 	<ul style="list-style-type: none"> <li>• What is your QC procedure when receiving a new lot of media?</li> </ul>
<p><b>DISCOVER</b></p> 	<ul style="list-style-type: none"> <li>• Follow a shipment of new media from receipt, examination and QC (if applicable). Determine if practice follows laboratory policy.</li> </ul>



**\*\*REVISED\*\* 09/22/2021****MIC.21240 Media QC - Purchased/Acquired****Phase II**

**An appropriate sample from each lot and shipment of each purchased/acquired medium is checked before or concurrent with initial use for each of the following:**

- 1. Sterility**
- 2. Ability to support the growth of organisms intended to be isolated on the media by means of stock cultures or by parallel testing with previous lots and shipments**
- 3. Biochemical reactivity, where appropriate**

*NOTE: The laboratory must have records showing that all media are sterile, able to support growth, and are appropriately reactive biochemically.*

*An individualized quality control plan (IQCP), including all required elements of IQCP, may be implemented by the laboratory to allow for the acceptance of the quality control performed by the media supplier for media listed as "exempt" in the CLSI Standard M22-A3, Quality Control for Commercially Prepared Microbiological Culture Media. The media supplier's records must be retained and show that the QC performed meets the CLSI standard and checklist requirements. Please refer to the IQCP section of the All Common Checklist for the requirements for implementation and ongoing monitoring of an IQCP. End user quality control must be performed on the following, regardless of the exempt status:*

- *Campylobacter agar;*
- *Chocolate agar;*
- *Media for the selective isolation of pathogenic Neisseria;*
- *Other media not listed on Table 2 of M22-A3 (eg, dermatophyte test medium);*
- *Media used for the isolation of parasites, viruses, Mycoplasmas, Chlamydia;*
- *Mueller-Hinton media used for antimicrobial susceptibility tests; or*
- *Media commercially prepared and packaged as a unit or system consisting of two or more different substrates, primarily used for microbial identification.*

*Laboratories receiving media from media suppliers must have records showing that the quality control activities performed by the media supplier meet the CLSI Standard M22-A3, or are otherwise equivalent. Problems with media deterioration or loss of reactivity in properly-stored media prior to the expiration date must be reported to the manufacturer, with records retained by the laboratory as part of corrective action.*

*Laboratories using exempt media that have not implemented an IQCP or are using media that do not qualify for an IQCP must continue to test each lot and shipment of media and retain records of such testing.*

*Laboratories that supply uninoculated media to referring laboratories are responsible for the quality control of the media. The laboratory must provide records or certification of media quality control with each shipment. If the laboratory uses an IQCP for media, a copy of the applicable approved IQCP or IQCP summary statement must be available to the referring laboratory upon request. Records of media quality control or the manufacturer's certificates of quality for each shipment must be available to the recipient.*

**Evidence of Compliance:**

- ✓ Written procedure for QC on new lot numbers or shipments of purchased/acquired medium **AND**
- ✓ Individualized quality control plan for the media approved by the laboratory director, as applicable **AND**
- ✓ Records of media quality control **AND**
- ✓ Records of reports of media problems/defects to manufacturers or referral laboratories supplying media

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Quality Control for Commercially Prepared Microbiological Culture Media; Approved Standard*; 3rd ed. CLSI document M22-A3. Clinical and Laboratory Standards Institute, Wayne, PA, 2004.



- 2) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)]

**MIC.21300 Media QC - Laboratory Prepared****Phase II**

**For microbiology media prepared by the laboratory, there are records showing that an appropriate sample of each medium is checked before or concurrent with initial use for each of the following:**

1. **Sterility**
2. **Ability to support the growth of organisms intended to be isolated on the media by means of stock cultures or by parallel testing with previous batches**
3. **Biochemical reactivity (where appropriate)**

**Evidence of Compliance:**

- ✓ Written procedure for testing media prepared by the laboratory
- ✓ Records of media quality control

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)].

**MIC.21420 Media Visual Examination****Phase II**

**All media are in visibly satisfactory condition (with expiration date, plates smooth, adequately hydrated, uncontaminated, appropriate color and thickness, tubed media not dried or loose from sides).**

**MIC.21460 Quality Control Organisms****Phase II**

**Appropriate quality control organisms are used to check stains, reagents and susceptibility test methods.**

## NOTE:

1. *Quality control organisms may be ATCC strains or well characterized laboratory strains unless specified by the manufacturer*
2. *Quality control organisms are maintained in a manner to preserve their bioreactivity, phenotypic characteristics and integrity*

## REFERENCES

- 1) Jones RN, *et al*. Method preferences and test accuracy of antimicrobial susceptibility testing. Updates from the College of American Pathologists microbiology surveys program (2000). *Arch Pathol Lab Med*. 2001;125:1285-1289

**STAINS****Inspector Instructions:**

- Sampling of staining policies and procedures
- Sampling of stain QC records/logs

**MIC.21530 Direct Gram Stain Procedures****Phase I**

**There are written policies for use of Gram stain results to provide a preliminary identification of organisms, evaluate specimen quality when appropriate, and to guide work-up of cultures.**

*NOTE: The laboratory should have policies for the interpretation of the Gram stain, including the quantification, stain reaction, and morphotypes of organisms and cells (eg, neutrophils or squamous epithelial cells). The policy should address correlation of direct Gram stain results with final culture results. Laboratories may use the correlation of Gram stain results with the final culture results as a component of the quality management system.*

*This does not mean that interpretation of the Gram stain morphology suggesting a specific organism identification (eg, gram positive diplococci morphologically suggestive of pneumococcus) is required.*

**Evidence of Compliance:**

- ✓ Written policy for Gram stain

**MIC.21540 Gram Stain QC**

**Phase II**

**Quality control of Gram stain reagents is performed for intended reactivity and recorded for each new batch or lot, and shipment of stains and at least weekly against known gram-positive and gram-negative quality control organisms.**

*NOTE: Personnel who perform Gram stains infrequently must run a gram-positive and gram-negative control each day of testing.*

**Evidence of Compliance:**

- ✓ Written procedure for Gram stain QC

**REFERENCES**

- 1) August, Hindler, Huber, Sewell. Quality control and quality assurance practices. In: Clinical microbiology, Cumitech 3A. Washington, DC: American Society for Microbiology, 1990
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1261(a)(2)]

**MIC.21560 Non-Immunofluorescent Stain QC**

**Phase II**

**Quality control of all non-immunofluorescent, non-immunologic-based stains (other than Gram stains) is performed and recorded with a positive and negative quality control organism for intended reactivity each day of use, and for each new batch, lot number and shipment.**

*NOTE: Refer to MIC.51160 for requirement pertaining to parasitology permanent stains.*

**Evidence of Compliance:**

- ✓ Written procedure for QC of non-immunofluorescent stains

**MIC.21570 Fluorescent Stain QC**

**Phase II**

**Quality control of fluorescent stains is performed for positive and negative reactivity each time of use.**

**Evidence of Compliance:**



- ✓ Written procedure QC of fluorescent stain

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7146 [42CFR493.1256(e)(3); 493.1273(a)]

## REAGENTS

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of reagent QC policies and procedures</li> <li>• Sampling of reagent QC records</li> <li>• CO<sub>2</sub> monitoring procedure and CO<sub>2</sub> recording log</li> <li>• Anaerobic incubation condition monitoring records</li> <li>• Campylobacter incubation condition records</li> </ul>
	<ul style="list-style-type: none"> <li>• What is your QC policy when receiving a new lot of identification system materials?</li> </ul>

#### MIC.21624 Reagent QC

Phase II

**Positive and negative controls are tested and results recorded for each new batch, lot number, and shipment of reagents, disks/strips and stains.**

*NOTE: Reagents subject to this requirement include (but are not limited to) catalase, coagulase (including latex methods), oxidase and indole reagents; bacitracin, optochin, streptococcal grouping reagents, ONPG, X, V, and XV disks/strips. This does not include tests for antimicrobial susceptibility.*

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): 3708 [42CFR493.1256 (e) (1) and (2)]

#### MIC.21626 Identification System QC

Phase II

**Appropriate positive and negative control organisms are tested and results recorded for each new lot and shipment of reagents used in bacterial identification systems.**

*NOTE: An individualized quality control plan (IQCP) may be implemented by the laboratory to allow for the use of streamlined QC for commercial microbial identification systems (MIS). Refer to the IQCP section of the All Common Checklist for the requirements. The laboratory may use QC organisms in addition to those required for the streamlined QC. In order to qualify for streamlined QC, the user must fulfill initial and ongoing requirements as defined by the manufacturer and CLSI Guideline M50-A, Quality Control for Commercial Microbial Identification Systems, including the retention of test system verification and historical QC review as long as the streamlined QC is used, but in no case for less than two years.*

*For user-developed identification systems, commercial systems for which a streamlined QC process has not been developed, or any commercial system whose use is altered in any way from the manufacturer's instructions, all biochemical tests in each new lot number and shipment must be evaluated with known positive and negative control organisms.*

*Any test (eg, oxidase test) required for interpretation of MIS results that is not part of the MIS cannot be included in MIS streamlined QC procedures. QC requirements for such tests, including the use of positive and negative controls for each new batch, lot number and shipment are given in MIC.21624 (Reagent QC).*

**Evidence of Compliance:**

- ✓ Written procedure for QC on new lot numbers or shipments of reagents for each MIS **AND**
- ✓ Individualized quality control plan for the MIS approved by the laboratory director, as applicable **AND**
- ✓ Records of MIS quality control

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(e)(1)]
- 2) Clinical and Laboratory Standards Institute (CLSI). *Quality Control for Commercial Microbial Identification Systems*. CLSI document M50-A (ISBN 1-56238-675-1). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2008.

**MIC.21628 Antisera QC Phase I**

**Positive and negative controls are tested and results recorded for each new batch, lot number and shipment of antisera when prepared or opened and once every 6 months thereafter (eg, Salmonella/Shigella antisera).**

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003 (January 24):3708 [42CFR493.1261(a)(3)]

**MIC.21632 Beta-Lactamase QC Phase II**

**Positive and negative controls are tested and results recorded for beta-lactamase (other than Cefinase®) tests on each day of use.**

*NOTE: Beta lactamase tests using Cefinase® need be checked only with each batch, lot number and shipment.*

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003 (January 24):3708 [42CFR493.1261 (a) (1)]

**MIC.21812 Anaerobic Incubation Conditions QC Phase I**

**There are records that anaerobic incubation systems (eg, jars, chambers, bags) are checked for adequate anaerobic conditions with methylene blue strips, fastidious anaerobic organisms or other appropriate procedures.**

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Principles and Procedures for Detection of Anaerobes in Clinical Specimens; Approved Guideline*. CLSI document M56-A. Clinical and Laboratory Standards Institute, Wayne, PA; 2014

**MIC.21813 CO<sub>2</sub> Incubator Levels Phase I**

**CO<sub>2</sub> incubators are checked daily for adequate CO<sub>2</sub> levels, with recording of results.**

*NOTE: It is acceptable to monitor and record CO<sub>2</sub> levels from digital readouts; however, the laboratory must verify that the readout is accurate (by initial calibration, Fyrite, or other calibrated CO<sub>2</sub> meter). The frequency of verification of the digital readout must be defined and should be performed, at minimum, at the frequency recommended by the manufacturer.*




**\*\*REVISED\*\* 06/04/2020**

**MIC.21815 Campylobacter Incubation Conditions QC Phase I**

**Campylobacter incubation conditions are checked using QC organisms or other appropriate methods to ensure adequate environmental conditions to support growth of commonly isolated Campylobacter species.**

## BACTERIOLOGY SUSCEPTIBILITY TESTING

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of susceptibility test, QC and reporting policies and procedures</li> <li>• Sampling of susceptibility QC records</li> </ul>
	<ul style="list-style-type: none"> <li>• Susceptibility test set-up (standardized inoculum, pure culture)</li> </ul>
	<ul style="list-style-type: none"> <li>• How does your laboratory work with the pharmacy and medical staff to determine policies for reporting of antimicrobial agents?</li> </ul>

#### MIC.21820 Susceptibility Testing - Pure Cultures

Phase II

**Antimicrobial susceptibility testing of isolates must be performed using pure isolates or colonies (ie, susceptibility testing is not performed on mixed cultures).**

*NOTE: A purity check must be performed by subculturing an aliquot of the inoculum onto a blood agar plate or other non-selective media at the same time the inoculum is used for susceptibility testing with the following exceptions:*

- A separate purity plate is not required for disk diffusion testing from isolated colonies, as long as the disk diffusion plate is carefully examined for a mixed culture.
- When testing by gradient diffusion methods, the manufacturer's instructions must be followed.

#### Evidence of Compliance:

- ✓ Written procedure describing the use of isolated colonies or of pure cultures for susceptibility testing, including the use of purity plates

**\*\*REVISED\*\* 06/04/2020**

#### MIC.21835 Direct Identification and Susceptibility from Blood Culture Broth

Phase II

**If organism identification (ID) and/or antimicrobial susceptibility testing (AST) (phenotypic or genotypic) is performed directly from positive blood culture bottles, the broth from the bottle is inoculated onto solid media to assess for consistency with direct results.**

*NOTE: This checklist item is applicable to tests that detect bacteria and/or yeast in positive blood cultures that are culturable on standard bacteriological media such as sheep's blood agar and/or chocolate agar.*

*It is the responsibility of the laboratory director to determine the extent of confirmatory testing necessary by reviewing the manufacturer's recommendations and examining their verification/validation data.*

*The accuracy of antimicrobial resistance markers or rapid phenotypic AST results performed directly from positive blood culture broth must, at a minimum, be confirmed by traditional AST methods following recovery on solid media during the internal verification/validation of the assay.*

*This requirement applies only to testing performed for patient care/management, not to infection control or epidemiology testing.*

**Evidence of Compliance:**

- ✓ Written procedure describing the use of culture to confirm consistency with the direct results

**\*\*NEW\*\* 09/22/2021**

**MIC.21855 Antimicrobial Resistance Markers by Molecular Analysis - Clinical Validity Phase I**

**Detection of genotypic antimicrobial resistance markers (eg, *vanA*, *mecA*, *bla<sub>KPC</sub>*, etc.) is linked or attributed to a corresponding organism in the final laboratory report when molecular analysis is performed directly on patient specimens (eg, urine or bronchoalveolar lavage fluid). This can be accomplished through molecular detection of the corresponding organism or concurrent culture.**

*NOTE 1: The intent of this requirement is to ensure that detection of antimicrobial resistance has clinical validity. Ideally, genotypic antimicrobial resistance results will be correlated with other available results, such as identification of isolates in culture and their phenotypic AST results, with the goal of aiding in the assessment of clinical significance of such findings.*

*NOTE 2: This requirement does not include either screening tests (eg, rectal swab for carbapenemase gene detection) or surveillance tests (eg, testing performed to monitor for a community- or population-level occurrence and establish incidence or prevalence of that occurrence, if results do not go back to individual patients).*

**Evidence of Compliance:**

- ✓ Reports linking resistance determinants to specific organisms **AND**
- ✓ Policy for correlating genetic antimicrobial resistance markers to organisms

**MIC.21910 Susceptibility Test QC Frequency Phase II**

**For antimicrobial susceptibility testing by either disk or gradient diffusion strips or broth dilution (MIC) methods, quality control organisms are tested with each new lot number or shipment of antimicrobials or media before or concurrent with initial use, and each day the test is performed thereafter.**

*NOTE: The frequency of QC testing may be reduced to weekly (including the testing of new lots or batches of antimicrobials or media) if the laboratory director approves the use of an individualized quality control plan (IQCP), and the laboratory has records of satisfactory performance with daily QC tests as suggested by CLSI Standards. If multiple instruments are used for automated MIC testing, QC testing should be rotated equally among all testing instruments. Please refer to the IQCP section of the All Common Checklist for the requirements for implementation and ongoing monitoring of an IQCP. For this purpose, satisfactory performance criteria are defined as follows:*

*1. Records must show that all QC organisms are tested for 20 or 30 consecutive test days. For each drug/microorganism combination, no more than 1 of 20 or 3 of the 30 values may be outside the accepted QC ranges.*

*Or*

*2. Records must show that all QC organisms are tested in triplicate (using separate inoculum suspensions) for 5 consecutive test days. For each drug/microorganism combination, no more than 1 of the 15 values may be outside the accepted QC ranges.*



- *If 2 or 3 values are outside the accepted QC range during testing of 15 replicates, daily QC testing must be continued and performed in triplicate (using separate inoculum suspensions) for another 5 consecutive test days*
- *For each drug/microorganism combination, no more than 4 of the 30 values may be outside the accepted QC range*

*When a result is outside the accepted QC range during weekly QC testing, refer to the most recent CLSI Standards for the required corrective action.*

*If the laboratory performs QC on antimicrobial screening tests as defined by the CLSI Standard and manufacturer's instructions do not require QC on each day the test is performed, the laboratory must have an IQCP that meets all requirements defined in the All Common Checklist.*

#### **Evidence of Compliance:**

- ✓ Records of susceptibility QC results at defined frequency and meeting defined acceptability criteria

#### **REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7167 [42CFR493.1261(b)(1)]
- 2) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria*. 9th ed. CLSI standard M11. Clinical and Laboratory Standards Institute, Wayne, PA, 2018.
- 3) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 4) Clinical and Laboratory Standards Institute (CLSI). *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 5) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*; 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 6) Clinical and Laboratory Standards Institute. *Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems, 1st ed*. CLSI Document M52-ED1. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.

### **MIC.21940 Standardized Inoculum**

**Phase II**

**The inoculum used for antimicrobial susceptibility testing (ie, inoculum size) is controlled using a turbidity standard or other acceptable method.**

*NOTE: Antibiotic susceptibility may be substantially affected by inoculum size.*

#### **Evidence of Compliance:**

- ✓ Written procedure for standardizing susceptibility inoculum

#### **REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 2) Clinical and Laboratory Standards Institute (CLSI). *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 3) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*; 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 4) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria*. 9th ed. CLSI standard M11. Clinical and Laboratory Standards Institute, Wayne, PA, 2018.

### **MIC.21943 Selection of Antimicrobial Agents to Report**

**Phase II**

**There are written policies to ensure that only antimicrobial agents appropriate for the organism and body site are routinely reported.**

*NOTE: The microbiology department should consult with the medical staff and pharmacy to develop a list of antimicrobial agents to be reported for specific organisms isolated from various body sites. These lists may be based on the CLSI recommendations provided in the M100 Table 1, which suggests those agents that might be reported routinely (Group A) and that might be reported selectively (Group B). Selective reporting of antimicrobial agents should help improve the clinical relevance of antimicrobial reporting and help minimize overuse of broad-spectrum agents that might result in selection of multi-resistant organisms.*

*The antimicrobial reporting policy should include antibacterial, antifungal, and antimycobacterial agents tested in the laboratory. Where applicable, policies should be reviewed with the*

stakeholders involved in the antimicrobial stewardship in the institution annually and records of the review should be available in the laboratory. The same policies should be used in reporting proficiency testing susceptibility results, particularly for isolates from cerebrospinal fluid and urine.

**Evidence of Compliance:**

- ✓ Antimicrobial reporting policy **AND**
- ✓ Patient reports with reporting of antimicrobial agents for different body sites following written policy **AND**
- ✓ Records of annual antimicrobial reporting policy review by the antimicrobial stewardship committee **AND**
- ✓ Proficiency testing susceptibility results following written policy

**REFERENCES**

- 1) Poulter MD, Hindler JF. Challenges in Antimicrobial Susceptibility Testing and Reporting. *Lab Med*, November, 2002;11:33
- 2) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*; 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 3) CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at <http://cdc.gov/getsmart/healthcare/implementation/core-elements.html>.

**MIC.21944 Testing and Reporting Supplemental Antimicrobial Agents Phase I**

**There are written policies for testing supplemental agents when needed on isolates resistant to routinely tested antimicrobial agents.**

*NOTE: The policy may include submission of isolates to an outside referral laboratory if testing is not performed onsite.*

**Evidence of Compliance:**

- ✓ Patient testing reports demonstrating additional antimicrobial testing or referral

**MIC.21946 Cumulative Susceptibility Data Phase I**

**For hospital based microbiology laboratories, cumulative antimicrobial susceptibility test data are maintained and reported to the medical staff at least yearly.**

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline*. 4<sup>th</sup> ed. CLSI document M39-A4. Clinical and Laboratory Standards Institute, Wayne, PA, 2014

**\*\*REVISED\*\* 09/22/2021**

**MIC.21950 Inconsistent Antimicrobial Results Phase I**

**There is a written policy to address unusual or inconsistent antimicrobial testing results.**

*NOTE: Acceptable results derived from testing QC strains do not guarantee accurate results with all patient isolates. Results from testing patient isolates must be reviewed and unusual or inconsistent results must be investigated to ensure accuracy. Expert software can identify unusual or inconsistent results that might be due to technical errors and to identify emerging resistance. Additional resources for determining which antimicrobial testing results are unusual include the CLSI M100 Appendix A or the EUCAST Intrinsic Resistance and Unusual Phenotypes publication.*

*What is considered unusual (uncommonly found in the laboratory) antimicrobial susceptibility results may vary by local epidemiology. Examples of unusual antimicrobial susceptibility test results include:*

1. *Escherichia coli* resistant to carbapenems
2. *Klebsiella* spp. susceptible to ampicillin
3. *Staphylococcus aureus* resistant to vancomycin



*Actions must be taken to address unusual results. Actions may include consultation with a medical laboratory director, repeating antimicrobial susceptibility testing by the same or different method, confirming isolate identification, or referral of the isolate to a public health laboratory for confirmation. While confirming results, the laboratory must consider whether communication with treating clinicians is indicated to inform them that AST results are under investigation.*

**Evidence of Compliance:**




- ✓ Records of investigation for unusual/inconsistent results

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*; 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 2) European Committee on Antimicrobial Susceptibility Testing. *Intrinsic Resistance and Unusual Phenotypes*. Version 3.2. [https://www.eucast.org/expert\\_rules\\_and\\_intrinsic\\_resistance/](https://www.eucast.org/expert_rules_and_intrinsic_resistance/). February 2020. Accessed December 23, 2020.

## PROCEDURES AND TESTS

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of bacteriology test procedures of different source types</li> <li>• Sampling of patient worksheets/records</li> <li>• Sampling of patient reports</li> <li>• Records of blood culture specimen volume and contamination rate monitoring</li> </ul>
	<ul style="list-style-type: none"> <li>• How does your laboratory evaluate culture findings?</li> </ul>
	<ul style="list-style-type: none"> <li>• Follow a specimen from evaluation of culture findings, recording of results and reporting. Determine if practice follows test procedures.</li> </ul>

*ROUTINE PROCEDURES: The following requirements define minimum standards for evaluation of routine bacterial cultures. The outlined procedure (media used and incubation conditions) permits recovery of bacteria expected in the type of specimen used. This does not preclude the use of screening cultures (limited studies) and should not be construed to mean that all routine cultures require special media. Special media should be available if needed.*

## RESPIRATORY SPECIMENS

*Routine procedures from acceptable respiratory cultures should allow the isolation of *Streptococcus pneumoniae*, and *Haemophilus* species.*

**MIC.22100 Sputum Gram Stain**

**Phase I**

**A gram-stained smear is performed routinely on expectorated sputa to determine acceptability of a specimen for bacterial culture and as a guide for culture workup.**

*NOTE: An institution may define special policies to address patient needs at their institution in collaboration with providers. Examples include exceptions for patients with cystic fibrosis, suspected infection by legionellosis, and pediatric patients.*

**Evidence of Compliance:**

- ✓ Policy defining acceptable specimens

**REFERENCES**

- 1) Wilson ML. Clinically relevant, cost-effective clinical microbiology. Strategies to decrease unnecessary testing. *Am J Clin Pathol.* 1997;107:154-165
- 2) Church DL. Are there published standards for Gram stain results for sputa to establish specimen quality for culture? *College of American Pathologists CAP Today.* 2000;14(4):97
- 3) Jorgensen JH (ed), et al. *Manual of Clinical Microbiology.* 11th ed. Washington, DC: ASM Press; 2015.
- 4) Leber, AL (ed). *Clinical Microbiology Procedures Handbook.* 4th ed. Washington DC: ASM Press; 2016.

**MIC.22110 Unacceptable Sputum Specimens**

**Phase I**

**Specimens deemed unacceptable by Gram stain review are not cultured for routine bacteria (or cultured only by special request) and the health care provider or submitting laboratory is notified so another specimen can be collected without delay, if clinically indicated.**

*NOTE: It is suggested that the laboratory notify an appropriate caregiver about an inadequate specimen even when specimens are submitted from an outpatient setting, or submitted to a referral laboratory. Notification can be by phone or computer report. The laboratory may implement written agreements with particular providers or submitting laboratories defining policies for handling sputum samples.*

**Evidence of Compliance:**

- ✓ Records of specimen rejection such as rejection log or patient report

**REFERENCES**

- 1) Bartlett RC. *Medical microbiology: quality cost and clinical relevance.* New York, NY: Wiley, 1974:24-31
- 2) Carroll KC. Laboratory Diagnosis of Lower Respiratory Tract Infection: Controversy and Conundrums. *J Clin Microbiol.* 2002;3115-3120

**MIC.22140 Group A Streptococcus Direct Antigen Detection**

**Phase I**

**If group A Streptococcus direct antigen testing is performed on pediatric patients, confirmatory testing is performed on negative samples.**

*NOTE 1: Policies must be established for the use of cultures or other confirmatory tests on pediatric specimens that test negative when using antigen detection methods or if the manufacturer's guidelines include recommendations for culture follow-up. These policies should take into account the sensitivity of the assay in use, the age and clinical presentation of the patient, and other factors.*

*NOTE 2: Direct antigen tests should be performed and reported in a timely fashion, since their principal advantage (compared to culture) is rapid turn-around-time.*

**REFERENCES**

- 1) Shulman S, Bisno A, Clegg H, et al. Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2012;55(10). doi: 10.1093/cid/cis629.

## URINE SPECIMENS

**MIC.22200 Urine Colony Count**

**Phase II**

**Quantitative cultures (colony counts) are performed.**

*NOTE: Urine cultures should include an estimate of CFU/volume.*

**Evidence of Compliance:**

- ✓ Written procedure for colony counts

REFERENCES

- 1) Susan E. Sharp, *et al*, Cumitech 2C: Laboratory Diagnosis of Urinary Tract Infections, 2009. ASM Press, Washington, DC

**MIC.22210 Urine Culture Procedure**

**Phase II**

**The media and procedures used permit the isolation and identification of both gram-positive and gram-negative bacteria.**

*NOTE: This does not require the use of gram-positive selective media.*

REFERENCES

- 1) Susan E. Sharp, *et al*, Cumitech 2C: Laboratory Diagnosis of Urinary Tract Infections, 2009. ASM Press, Washington, DC

## GENITAL SPECIMENS

**\*\*REVISED\*\* 09/22/2021**

**MIC.22273 Group B Streptococcus Screen**

**Phase II**

**Group B streptococcus screens from pregnant women are collected and cultured in accordance with the current guidelines.**

*NOTE: Universal prenatal screening for vaginal and rectal Group B streptococcal (GBS) colonization of all pregnant women at 36 to 38 weeks gestation is recommended. The optimum specimen for this test is a vaginal/rectal swab and results may be compromised if only a vaginal swab is submitted. Detection of GBS in urine cultures in this population should also be addressed. Procedures for collecting and processing clinical specimens for GBS culture and performing susceptibility testing to clindamycin and erythromycin for highly penicillin allergic women are also included in the guidelines.*

REFERENCES

- 1) Filkins L, Hauser J, Robinson-Dunn B, Tibbetts R, Boyanton B, Revell P. American Society for Microbiology Clinical and Public Health Microbiology Committee, Subcommittee on Laboratory Practices. Guidelines for the Detection and Identification of Group B *Streptococcus*. March 10, 2020.

**MIC.22280 Bacterial Vaginosis**

**Phase I**

**When Gram stains are performed to make the laboratory diagnosis of bacterial vaginosis, the smear is scored and interpreted according to published criteria.**

*NOTE: Culture should not be used for the diagnosis of bacterial vaginosis. Bacterial vaginosis (BV) is a syndrome involving a shift in the concentrations of aerobic and anaerobic flora of the genitourinary tract flora from a predominant presence of *Lactobacillus* sp. to that of a mixture of anaerobes, *Gardnerella vaginalis* and other gram-negative bacteria. Culturing for a particular organism, such as *Gardnerella vaginalis*, or any single organism or combination of organisms is not specific for the diagnosis of BV. Use of a scored Gram stain that demonstrates whether there has been a shift in the vaginal flora from predominantly gram-positive *Lactobacillus* to a gram-negative flora has been shown to correlate well with the Amsel criteria for the diagnosis of BV. The primary reason for performing a Gram stain on vaginal secretions is to diagnose bacterial vaginosis.*

REFERENCES

- 1) Nugent RP, Krohn MA, Hillier SL. 1991. JCM 29:297-301
- 2) Forsum U, Hallen A, Larsson PG. Bacterial Vaginosis - a laboratory and clinical diagnostic enigma. Review article III. APMIS 113: 153-61. 2005

**MIC.22285 Genital Pathogens Phase II**

Written procedures are established to ensure the detection of genital pathogens such as *Neisseria gonorrhoeae*.

## STOOL SPECIMENS

**MIC.22330 *Clostridioides (Formerly Clostridium) difficile* Phase II**

There are written policies for the testing of stool for the detection and reporting of *C. difficile* or its toxins.

**REFERENCES**

- 1) Novak-Weekley SM, et al. *Clostridium difficile* testing in the Clinical Laboratory by Use of Multiple Testing Algorithms. *Journal of Clinical Microbiology* 2010; 48:889-893
- 2) Eastwood K, et al. Comparison of Nine Commercially Available *Clostridium difficile* Toxin Detection Assays, a Real-Time PCR Assay for *C. difficile tcdB* and a Glutamate Dehydrogenase Detection Assay to Cytotoxin Testing and Cytotoxigenic Culture Methods. *Journal of Clinical Microbiology* 2009; 47:3211-3217
- 3) Peterson LR and Robicsek A. Does my Patient have *Clostridium difficile* Infection? *Annals of Internal Medicine* 2009; 151:176-178

**MIC.22336 Stool Culture Reporting Phase I**

The final report for stool cultures submitted for routine bacterial pathogen examination lists the organisms for which the specimen was cultured (eg, *Salmonella*, *Shigella*, *Vibrio*).

**NOTE:**

1. It is inappropriate to report "No enteric pathogens isolated." The report should list the organisms whose presence was specifically sought (eg, No *Salmonella*, *Shigella*, or *Campylobacter* isolated).
2. When indicated, tests to detect Shiga toxin-producing *E. coli* (STEC) should be available at a referral laboratory if not performed onsite.

**REFERENCES**

- 1) Gilligan PH, et al. Laboratory diagnosis of bacterial diarrhea. Cumitech 12A, 1992. ASM Press; Washington DC

**MIC.22410 Stool Culture Enrichment/Selective Media Phase I**

Appropriate methods are used routinely to recover enteric pathogens.

*NOTE: Enrichment media may be used in addition to selective plating media to enhance recovery of pathogens, which may be present at low numbers.*

**MIC.22440 Stool Specimen Number/Timing Phase I**

There are written policies for the number and/or timing of collection of stool specimens submitted for routine bacterial testing.

*NOTE: The laboratory should consider developing policies with its clinicians for the number and/or timing of collection of stool specimens submitted for routine bacterial testing. Suggestions made by the authors of a 1996 CAP Q-Probes study (Valenstein et al) include:*

1. Accept no more than two specimens/patient without prior consultation with an individual who can explain the limited yield provided by additional specimens
2. Do not accept specimens from inpatients after the third hospital day, without prior consultation
3. Test stool for *Clostridioides difficile* toxin for all patients with clinically significant diarrhea and a history of antibiotic exposure. Consider *C. difficile* testing as an

*alternative to routine microbiologic studies for inpatients who have test requests for routine enteric pathogens*

4. *Positive test results for Clostridiodes difficile do not correlate well with disease in young children. Follow manufacturer's guidelines for guidance on the testing of pediatric patients.*

*These recommendations are for diagnostic testing. Different policies may apply to tests ordered for follow-up.*

#### REFERENCES

- 1) Yannelli B, *et al.* Yield of stool cultures, ova and parasite tests, and *Clostridium difficile* determinations in nosocomial diarrhea. *Am J Infect Control.* 1988;16:246-249
- 2) Siegel DL, *et al.* Inappropriate testing for diarrheal diseases in the hospital. *JAMA.* 1990;263:979-982
- 3) Asnis DS, *et al.* Cost-effective approach to evaluation of diarrheal illness in hospitals. *J Clin Microbiol.* 1993;31:1675
- 4) Fan K, *et al.* Application of rejection criteria for stool cultures for bacterial enteric pathogens. *J Clin Microbiol.* 1993;31:2233-2235
- 5) Valenstein P, *et al.* The use and abuse of routine stool microbiology. A College of American Pathologists Q-probes study of 601 institutions. *Arch Pathol Lab Med.* 1996;120:206-211
- 6) Wilson ML. Clinically relevant, cost-effective clinical microbiology. Strategies to decrease unnecessary testing. *Am J Clin Pathol.* 1997;107:154-165
- 7) Blackman E, *et al.* Cryptosporidiosis in HIV-infected patients: diagnostic sensitivity of stool examination, based on number of specimens submitted. *Am J Gastroenterol.* 1997;92:451-453
- 8) Wood M. When stool cultures from adult inpatients are not appropriate. *Lancet.* 2001;357:901-902
- 9) Bauer, TM, *et al.* Derivation and validation of guidelines for stool cultures for enteropathogenic bacteria other than *Clostridium difficile* in hospitalized patients. *JAMA.* 2001;285:313-319

## CEREBROSPINAL & OTHER BODY FLUID SPECIMENS

**MIC.22495 Centrifugation of Body Fluids Phase I**

**If only plated media are used for sterile body fluids, fluid is centrifuged and the sediment used to inoculate media unless the entire specimen is plated.**

*NOTE: If insufficient specimen is received for centrifugation/concentration when specified in the written procedure, the report should note that the culture results may be compromised by the limited volume of specimen received. Equivalent methods are acceptable, if validated by the laboratory.*

#### REFERENCES

- 1) Carroll KC, Pfaller MA, Landry ML, *et al.*, eds. *Manual of Clinical Microbiology.* 12th ed. Washington, DC: ASM Press; 2019.

**MIC.22500 CSF Processing Phase II**

**CSF specimens for culture are processed immediately on receipt.**

*NOTE: Bacterial meningitis is a critical condition that requires immediate attention. Samples must be processed upon receipt when meningitis is suspected. The laboratory may choose to handle surveillance cultures, eg, involving neurosurgical implants, differently.*

#### Evidence of Compliance:

- ✓ Policy and procedure for CSF processing **AND**
- ✓ Culture log or patient records

**MIC.22520 CSF Media/Incubation Phase II**

**The procedure (media and incubation conditions) permits recovery of fastidious bacteria expected in this type of specimen (*N. meningitidis*, *S. pneumoniae*, *H. influenzae*).**

**MIC.22550 CSF Back-Up Cultures Phase II**

**If bacterial antigen-detection methods are used, back-up cultures are performed on both positive and negative CSF specimens.**

*NOTE: Total dependence on a bacterial antigen test for the diagnosis of bacterial meningitis does NOT meet accreditation requirements. Meningitis may be caused by bacteria not detected by the antigen tests. Thus, culture is essential for proper evaluation of bacterial meningitis, and must be performed on the patient specimen - if not performed onsite by the laboratory, the inspector must seek evidence that culture is routinely performed in a referral laboratory if unable to be performed onsite.*

**Evidence of Compliance:**

- ✓ Written policy stating that CSF cultures are performed in conjunction with bacterial antigen tests **OR** policy describing testing at another location **AND**
- ✓ Records of back-up CSF cultures performed on-site **OR** records indicating that cultures are performed at another location **OR** records that the order for CSF bacterial antigen was blocked by the computer due to no order for a culture

**REFERENCES**

- 1) Forward KR. Prospective evaluation of bacterial antigen detection in cerebral spinal fluid in the diagnosis of bacterial meningitis in a predominantly adult hospital. *Diagn Micro Infect Dis*. 1988;11:61-63
- 2) Maxson S, et al. Clinical usefulness of cerebrospinal fluid bacterial antigen studies. *J Pediat*. 1994; 125:235-238
- 3) Finlay FO, et al. Latex agglutination testing in bacterial meningitis. *Arch Dis Child*. 1995;73:160-161
- 4) Rathore MH, et al. Latex particle agglutination tests on the cerebrospinal fluid. A reappraisal. *J Florida Med Assoc*. 1995;82:21-23
- 5) Kiska DL, et al. Quality assurance study of bacterial antigen testing of cerebrospinal fluid. *J Clin Micro*. 1995;33:1141-1144
- 6) Perkins MD, et al. Rapid bacterial antigen detection is not clinically useful. *J Clin Micro*. 1995;33:1486-1491

## BLOOD CULTURES

**MIC.22600 Blood Culture System**

**Phase II**

**The blood culture system is capable of detecting both aerobic and anaerobic organisms, when indicated.**

*NOTE: This criterion is not intended to imply that anaerobic cultures must be performed on all blood cultures, but be available when clinically indicated.*

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Blood Cultures; Approved Guideline*. CLSI Document M47-A (ISBN 1-56238-641-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2007.
- 2) Baron EJ, et al. *Blood Cultures IV, Cumitech 1C*, 2005, ASM Press; Washington, DC
- 3) Jorgensen JH (ed), et al. *Manual of Clinical Microbiology*. 11th ed. Washington, DC: ASM Press; 2015.
- 4) Leber, AL (ed). *Clinical Microbiology Procedures Handbook*. 4th ed. Washington DC: ASM Press; 2016.
- 5) Clinical and Laboratory Standards Institute. *Principles and Procedures for Detection of Anaerobes in Clinical Specimens; Approved Guideline*. CLSI document M56-A. Clinical and Laboratory Standards Institute, Wayne, PA; 2014

**MIC.22610 Manual Blood Culture Systems**

**Phase II**

**For non-automated systems, macroscopically negative aerobic blood cultures are stained and/or subcultured within 12-48 hours of incubation.**

**Evidence of Compliance:**

- ✓ Records of staining and/or subculture of macroscopically negative cultures

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Blood Cultures; Approved Guideline*. CLSI Document M47-A (ISBN 1-56238-641-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2007.
- 2) Baron EJ, et al. *Blood Cultures IV, Cumitech 1C*, 2005, ASM Press; Washington, DC
- 3) Jorgensen JH (ed), et al. *Manual of Clinical Microbiology*. 11th ed. Washington, DC: ASM Press; 2015.
- 4) Leber, AL (ed). *Clinical Microbiology Procedures Handbook*. 4th ed. Washington DC: ASM Press; 2016.



**MIC.22620 Blood Culture Examination****Phase II**

**Blood cultures are examined (macroscopically if manual method) for evidence of growth at least twice daily for the first two days of incubation, then at least daily for the remainder of the incubation period.**

*NOTE: The time to detection of positive blood cultures, whether processed by manual or automated methods, depends on the schedule of inspection for evidence of growth. The means of the inspection may include visual examination, gram staining, subculturing, or electronic analysis by continuous monitoring instruments. Because most significant positive blood cultures may be detected within 48 hours of incubation, it is recommended that blood cultures be examined for evidence of growth at least two times on the first two days of incubation, then at least once daily through the remainder of the laboratory's routine incubation period.*

**Evidence of Compliance:**

- ✓ Patient records/worksheet with result of examination for manual methods at defined frequency

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Blood Cultures; Approved Guideline*. CLSI Document M47-A (ISBN 1-56238-641-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2007.
- 2) Baron EJ, et al. *Blood Cultures IV, Cumitech 1C*, 2005, ASM Press; Washington, DC

**\*\*REVISED\*\* 06/04/2020****MIC.22630 Blood Culture Collection****Phase II**

**Sterile techniques for drawing and handling of blood cultures are defined, made available to individuals responsible for specimen collection and practiced.**

**Evidence of Compliance:**

- ✓ Written procedure for blood culture collection

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Blood Cultures; Approved Guideline*. CLSI Document M47-A (ISBN 1-56238-641-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2007.
- 2) Baron EJ, et al. *Blood Cultures IV, Cumitech 1C*, 2005, ASM Press; Washington, DC
- 3) Carroll KC, Pfaller MA, Landry ML, et al, eds. *Manual of Clinical Microbiology*. 12th ed. Washington, DC: ASM Press; 2019.
- 4) Leber, AL (ed). *Clinical Microbiology Procedures Handbook*. 4th ed. Washington DC: ASM Press; 2016.

**\*\*NEW/REVISED\*\* 09/22/2021****MIC.22635 Blood Culture Contamination****Phase II**

**The laboratory monitors blood culture contamination rates and has established an acceptable threshold.**

*NOTE: The laboratory must determine and regularly review the number of contaminated cultures. Tracking the contamination rate and providing feedback to units and persons drawing cultures has been shown to reduce contamination rates. Other measures for consideration in monitoring blood culture contamination include the types of skin disinfection used, line draws, and the use of diversion devices.*

*The threshold may be established in collaboration with other relevant institutional groups (eg, infection prevention). The laboratory must perform and record corrective action if the threshold is exceeded.*

**Evidence of Compliance:**

- ✓ Written procedure for monitoring blood culture contamination rates and threshold determination **AND**
- ✓ Records of contamination rates and corrective action if threshold is exceeded **AND**
- ✓ Records of feedback to responsible parties

## REFERENCES

- 1) Bekeris LG, Tworek JA, Walsh MD, Valenstein PN. Trends in blood culture contamination: a College of American Pathologists Q-TRACKS study of 365 institutions. *Arch Pathol Lab Med.* 2005;129:1222-5.
- 2) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Blood Cultures; Approved Guideline.* CLSI Document M47-A. Clinical and Laboratory Standards Institute. Wayne, PA, 2007.

**\*\*REVISED\*\* 09/22/2021****MIC.22640 Blood Culture Volume****Phase I**

**The laboratory monitors blood cultures from adults for adequate volume and provides feedback on unacceptable volumes to blood collectors.**

*NOTE: Larger volumes of blood increase the yield of true positive cultures. The volume collected must be in accordance with manufacturer instructions (in most systems it is 20 mL, but smaller volumes may be recommended in some systems).*

**Evidence of Compliance:**

- ✓ Written procedure for monitoring blood culture volume **AND**
- ✓ Records of monitoring of volume at a defined frequency **AND**
- ✓ Records of feedback to responsible parties

## REFERENCES

- 1) Novis DA, *et al.* Solitary blood cultures. A College of American Pathologists Q-Probes study of 132778 blood culture sets in 333 small hospitals. *Arch Pathol Lab Med.* 2001;125:1290-1294
- 2) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Blood Cultures; Approved Guideline.* CLSI Document M47-A (ISBN 1-56238-641-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2007.
- 3) Baron EJ, *et al.* *Blood Cultures IV*, Cumitech 1C, 2005, ASM Press; Washington, DC

## ANAEROBIC CULTURES

**MIC.22675 Anaerobic Cultures****Phase I**

**The laboratory has written policies defining when to culture for anaerobes.**

*NOTE: The policy must define criteria to determine if the submitted material is of sufficient quality to provide an interpretable result.*

*If the laboratory does not perform anaerobic cultures on-site, the laboratory must refer specimens to a referral laboratory for anaerobic culture when indicated.*

**MIC.22700 Anaerobic Cultures****Phase II**

**There are written procedures describing how to culture anaerobic organisms when indicated.**

*NOTE: For example, the minimum standards for the evaluation of deep wound cultures require adequate procedures for the collection, recovery and identification of clinically relevant pathogens, which includes aerobic, facultatively anaerobic, and strictly anaerobic organisms. Anaerobic organisms may be significant isolates from other specimen types as well. Suggested media for anaerobes include an anaerobic blood agar plate, a medium that inhibits gram-positive and facultative gram-negative bacilli such as KV blood agar, a differential or selective medium such as BBE (*Bacteroides bile-esculin*), and a gram-positive selective medium (colistin-nalidixic acid blood agar or phenylethyl alcohol blood agar). Provisions for adequate anaerobic incubation, with monitoring of the anaerobic environment, must be available. If specimens are referred to another laboratory, they must be transported in an expeditious fashion under appropriate conditions.*

## REFERENCES





- 1) Clinical and Laboratory Standards Institute. *Principles and Procedures for Detection of Anaerobes in Clinical Specimens; Approved Guideline*. CLSI document M56-A. Clinical and Laboratory Standards Institute, Wayne, PA; 2014

## WOUND SPECIMENS

### GAS CHROMATOGRAPHY (GC) FOR MICROBIAL IDENTIFICATION

#### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of gas chromatography policies and procedures</li> <li>• Sampling of QC records</li> </ul>
	<ul style="list-style-type: none"> <li>• Sampling of reagents (grade)</li> <li>• Chromatograph pattern controls</li> </ul>

#### MIC.22790 GC Calibrators/Standards

Phase II

**Appropriate calibrators or standards are run with each analytic batch.**

*NOTE: For GC, a calibrator mixture must be run approximately every tenth analysis. The calibrator mixture must contain acids that cover the entire analysis spectrum, that is, C-10 through C-20, as well as any labile acids such as hydroxyl fatty acids.*

##### Evidence of Compliance:

- ✓ Written procedure defining frequency and content of calibrator mixtures **AND**
- ✓ Records of calibration/calibration verification with each batch

#### MIC.22810 GC Controls

Phase II

**Appropriate controls are extracted and run through the entire procedure.**

*NOTE: For any GC system, positive controls must be run daily and include two organisms containing representative cellular fatty acids of all classes, ie, saturated, unsaturated, iso, cyclopropane and hydroxyl acids. If one is using the MIDI (or related system), the similarity index must be >0.6 for aerobic bacteria and >0.3 for anaerobes. This represents a procedure control, as opposed to a calibrator mixture, which is an instrument control. For all GC assays that are used for identification of microbes, a reagent blank must be run daily to evaluate reagent contamination and carry-over.*

##### Evidence of Compliance:

- ✓ Written policy defining QC requirements **AND**
- ✓ QC records at defined frequency

##### REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5232 [42CFR493.1256]
- 2) Winn W *et al*. The anaerobic bacteria in Koneman's color atlas and textbook of diagnostic microbiology. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:906-912

**MIC.22820 Chromatogram Controls Phase I**

**External chromatogram pattern controls are available.**

*NOTE: Patterns for known strains should be established. In addition, laboratories should have access to the standard method manuals containing comparable chromatographic patterns for comparison.*

**MIC.22830 GC Growth Conditions Phase II**

**Written policies define growth media and conditions acceptable for gas chromatography (GC) analysis.**

*NOTE: Final results can be influenced by conditions of growth. For reliable results, standard conditions of analysis must be met, including growth media.*

**REFERENCES**

- 1) Winn W *et al.* The anaerobic bacteria in Koneman's color atlas and textbook of diagnostic microbiology. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:906-912

**MIC.22840 Chromatographic Method Validation Phase II**

**The chromatographic method has been validated using known strains of bacteria, including strains expected to be encountered in routine clinical use.**

**Evidence of Compliance:**

- ✓ Record of method validation with appropriate strains

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5232 [42CFR493.1256]

**MIC.22850 Chromatographic Result Review Phase II**

**There is a written policy for review of chromatographic results in conjunction with other laboratory data, prior to reporting results.**

*NOTE: Chromatography is only one tool for microbial identification. When results of analysis conflict with growth characteristics, pigmentation, or the results of biochemical or molecular testing, identification must be based on all the information available.*

**REFERENCES**

- 1) Winn W *et al.* The anaerobic bacteria in Koneman's color atlas and textbook of diagnostic microbiology. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:906-912
- 2) Welch DF. Application of cellular fatty acid analysis. *Clin Micro Rev*. 1991;4:422-38

**MIC.22860 Chromatographic Analysis - Pure Isolates Phase II**

**There are procedures to check the purity of cultures used as a source for chromatographic analysis.**

*NOTE: Results of chromatographic analysis may be unreliable if mixed cultures are tested. If chromatography is performed on an isolate from liquid culture and an interpretable chromatogram is obtained, it is not necessary to await the results of the purity check before reporting results, but a purity check must still be performed.*

**\*\*REVISED\*\* 06/04/2020**

**MIC.22870 GC Reagent Grade Phase I**

**Reagents, solvents, and gases are of appropriate grade.**

**Evidence of Compliance:**

- ✓ Reagent logs

**MIC.22880 Instrument Operation****Phase II**





**There are written procedures for operation and calibration of the gas chromatography instrument.**

*NOTE: Basic principles of chromatographic analysis require continual monitoring of analysis conditions, including system calibration. System problems and corrective actions must be appropriately documented.*

## MYCOBACTERIOLOGY

### QUALITY CONTROL

#### Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Mycobacteriology specimen collection, transport and handling policy</li> <li>• Mycobacteriology reporting policy</li> <li>• Sampling of patient test reports</li> <li>• Sampling of mycobacteriology media/stain/reagent QC policies and procedures</li> <li>• Sampling of mycobacteriology QC records</li> </ul>
 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Patient mycobacteriology specimens (sealed, leak proof containers)</li> <li>• Sealed, safety centrifuge carriers</li> <li>• Sampling of media (expiration date, condition, contamination)</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• What is your policy for performing AFB stains on weekends and holidays?</li> </ul>
 <p>DISCOVER</p>	<ul style="list-style-type: none"> <li>• Review a sampling of QC data over the previous two-year period. Select several occurrences in which QC is out of range and follow records to determine if the steps taken follow the laboratory procedure for corrective action</li> </ul>

### SPECIMEN HANDLING

**\*\*REVISED\*\* 09/22/2021**

**MIC.31100 Specimen Collection/Transport****Phase I**

**Specimens for mycobacterial testing are collected appropriately, in sealed leak-proof containers, and transported to the laboratory without delay.**

*NOTE: The laboratory should recommend collecting three sputum specimens for acid-fast smears and culture in patients with clinical and chest x-ray findings compatible with tuberculosis.*

*These three samples should be collected at 8-24 hour intervals and should include at least one first morning specimen. Specimens must be delivered to the laboratory promptly; specimens that cannot be processed within one hour of the time of collection should be refrigerated during transport to and storage in the laboratory prior to processing. This will decrease overgrowth with contaminating organisms likely to be present.*

*Laboratories are encouraged to process acid-fast specimens in their laboratory or obtain results from referral laboratories as soon as possible so that smear results can be available within 24 hours of collection (see MIC.31200 below).*

**Evidence of Compliance:**

- ✓ Written policy describing specimen collection and handling requirements

**REFERENCES**

- 1) Toman K. How many bacilli are present in a sputum specimen found positive by smear microscopy [Chapter 4]. In: Frieden T, ed. Toman's tuberculosis case detection, treatment, and monitoring: questions and answers. 2nd ed. Geneva, Switzerland: World Health Organization; 2004:11-3
- 2) Siddiqui AH, Perl TM, Conlon M, Donegan N, Roghmann MC. Preventing nosocomial transmission of pulmonary tuberculosis: when may isolation be discontinued for patients with suspected tuberculosis? *Infect Control Hosp Epidemiol* 2002;23:141-4
- 3) CDC. "Treatment of Tuberculosis: American Thoracic Society, CDC, and Infectious Diseases Society of America" MMWR 2003:52 (No.RR-11)
- 4) Hopewell PC, Pai M, Maher D, *et al.* International Standards for Tuberculosis Care. *Lancet* 2006;6:710-25
- 5) Centers for Disease Control and Prevention. Guidelines for Preventing the Transmission of Mycobacterium Tuberculosis in Health-Care Settings. *MMWR*, 2005; 54(RR17);1-141.

**\*\*REVISED\*\* 09/22/2021**

**MIC.31120 Centrifuge Safety**

**Phase II**

**Sealed screw-capped tubes are enclosed in sealed safety centrifuge carriers (ie, a double closure system) to minimize aerosol hazards when centrifuging specimens.**

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Laboratory Safety; Approved Guideline, Third Edition*. CLSI document GP17-A3 [ISBN 1-56238-797-9 (Print); ISBN 1-56238-798-7 (Electronic)]. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2012.

## REPORTING OF RESULTS

**MIC.31200 Acid Fast Stain Results**

**Phase I**

**When clinically indicated, results of acid-fast stains are reported within 24 hours of specimen receipt by the testing laboratory.**

**Evidence of Compliance:**

- ✓ Written policy defining turnaround time for reporting acid-fast stain results

**REFERENCES**

- 1) Huebner RE, *et al.* Current practices in mycobacteriology: results of a survey of state public health laboratories. *J Clin Microbiol.* 1993;31:771-775
- 2) Tenover FC, *et al.* The resurgence of tuberculosis: is your laboratory ready? *J Clin Microbiol.* 1993;31:767-770
- 3) Woods GL, *et al.* Mycobacterial testing in clinical laboratories that participate in the College of American Pathologists mycobacteriology surveys. Changes in practices based on responses to 1992, 1993, and 1995 questionnaires. *Arch Pathol Lab Med.* 1996;120:429-435

**MIC.31220 Susceptibility Test Results**

**Phase I**

**Susceptibility test results for *M. tuberculosis* are available in a timely manner.**

*NOTE: The rapid recognition of drug-resistant organisms is essential to the control of multidrug-resistant tuberculosis. For isolates of *M. tuberculosis* complex, the CDC and Prevention Laboratory work group recommends that laboratories use methods that may allow susceptibility test results to be available within 28 days of specimen receipt. From a CAP accreditation perspective, 28 days is a goal, not a requirement.*

## REFERENCES

- 1) Tenover FC, *et al.* The resurgence of tuberculosis: is your laboratory ready? *J Clin Microbiol.* 1993;31:767-770
- 2) College of American Pathologists position statement regarding rapid detection of *Mycobacterium tuberculosis*. *Arch Pathol Lab Med.* 1993;117:873
- 3) Woods GL, Witebsky FG. Current status of mycobacterial testing in clinical laboratories. *Arch Pathol Lab Med.* 1993;117:876-884
- 4) Huebner RE, *et al.* Current practices in mycobacteriology: results of a survey of state public health laboratories. *J Clin Microbiol.* 1993;31:771-775
- 5) Clinical and Laboratory Standards Institute (CLSI). *Susceptibility Testing for Mycobacteria, Nocardia spp., and Other Aerobic Actinomycetes.* 3rd ed. CLSI standard M24. Clinical and Laboratory Standards Institute, Wayne, PA; 2018.
- 6) Woods GL, *et al.* Mycobacterial testing in clinical laboratories that participate in the College of American Pathologists mycobacteriology surveys. Changes in practices based on responses to 1992, 1993, and 1995 questionnaires. *Arch Pathol Lab Med.* 1996;120:429-435
- 7) Woods GL, Witebsky FG. Susceptibility testing of *Mycobacterium avium* complex in clinical laboratories. Results of a questionnaire and proficiency test performance by participants in the College of American Pathologists mycobacteriology E survey. *Arch Pathol Lab Med.* 1996;120:436-439
- 8) Howanitz JH, Howanitz PJ. Timeliness as a quality attribute and strategy. *Am J Clin Pathol.* 2001;116:311-315

## MEDIA

**\*\*REVISED\*\* 09/22/2021**

**MIC.31380 Media QC - Purchased/Acquired**

**Phase II**

**An appropriate sample from each lot and shipment of each purchased/acquired medium is checked before or concurrent with initial use for each of the following:**

- 1. Sterility**
- 2. Ability to support the growth of organisms intended to be isolated on the media by means of stock cultures or by parallel testing with previous lots and shipments**
- 3. Biochemical reactivity, where appropriate**

*NOTE: The laboratory must have records showing that all media are sterile, able to support growth, and are appropriately reactive biochemically. End user quality control must be performed on media not listed on Table 2 of M22-A3 (eg, dermatophyte test medium), regardless of the exempt status.*

*This checklist requirement does not apply to commercially prepared additives that are reconstituted when added to mycobacterial media.*

*An individualized quality control plan (IQCP), including all required elements of IQCP, may be implemented by the laboratory to allow for the acceptance of the quality control performed by the media supplier for media listed as "exempt" in the CLSI Standard M22-A3, Quality Control for Commercially Prepared Microbiological Culture Media. The media supplier's records must be retained and show that the QC performed meets the CLSI standard and checklist requirements. Please refer to the IQCP section of the All Common Checklist for the requirements for implementation and ongoing monitoring of an IQCP.*

*Laboratories receiving media from media suppliers must have records showing that the quality control activities performed by the media supplier meet the CLSI Standard M22-A3, or are otherwise equivalent. Problems with media deterioration or loss of reactivity in properly-stored media prior to the expiration date must be reported to the manufacturer, with records retained by the laboratory as part of corrective action.*

*Laboratories using exempt media that have not implemented an IQCP or are using media that do not qualify for an IQCP must continue to test each lot and shipment of media and retain records of such testing.*

**Evidence of Compliance:**

- ✓ Written procedure for QC on new lot numbers or shipments of purchased/acquired medium  
**AND**
- ✓ Individualized quality control plan for the media approved by the laboratory director, as applicable **AND**

- ✓ Records of media quality control **AND**
- ✓ Records of reports of media problems/defects to manufacturers

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Quality Control for Commercially Prepared Microbiological Culture Media; Approved Standard*; 3rd ed. CLSI document M22-A3. Clinical and Laboratory Standards Institute, Wayne, PA, 2004.
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)].

**MIC.31400 Media QC - Laboratory Prepared****Phase II**

**For microbiology media prepared by the laboratory, there are records showing that an appropriate sample of each medium and additive is checked before or concurrent with initial use for each of the following:**

1. **Sterility**
2. **Ability to support the growth of organisms intended to be isolated on the media by means of stock cultures or by parallel testing with previous lots and shipments**
3. **Biochemical reactivity (where appropriate)**

**Evidence of Compliance:**

- ✓ Records of media QC for laboratory-prepared media and additives

## REFERENCES

- 1) Sharp SE, et al. Lowenstein-Jensen media. No longer necessary for mycobacterial isolation. *Am J Clin Pathol*. 2000;113:770-773
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)].

**MIC.31460 Media Visual Examination****Phase II**

**All media are in satisfactory condition (adequately hydrated, tubed media not dried or loose from sides).**

## CONTROLS AND STANDARDS

**MIC.31640 AFB Stain QC****Phase II**

**Acid-fast bacillus stains are checked each day of use with appropriate positive and negative controls, and results recorded.**

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(e)(2)]

**MIC.31650 Fluorescent Stain QC****Phase II**

**Fluorescent stains are checked with positive and negative controls each time of use and results recorded.**

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(e)(3)]

**MIC.31670 Nucleic Acid Probe QC****Phase II**

**If nucleic acid probes are used for identification of mycobacteria grown in culture, appropriate positive and negative controls are tested on each day of use.**

**Evidence of Compliance:**

- ✓ Records of nucleic acid probe QC at defined frequency

## REFERENCES

- 1) Woods GL. Molecular methods in the detection and identification of mycobacterial infections. *Arch Pathol Lab Med.* 1999;123:1002-1006

**\*\*REVISED\*\* 09/22/2021**

**MIC.31680 Susceptibility QC**

**Phase II**

**If the laboratory performs susceptibility testing of *mycobacterial isolates*, a control strain susceptible to all antimycobacterial agents is run each week of patient testing, and with each new batch/lot number of media and antimycobacterial agents.**

**Evidence of Compliance:**





- ✓ Records of routine and new lot QC results at defined frequency

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):3708 [42CFR493.1262(b)]

## PROCEDURES AND TESTS

### Inspector Instructions:

<p><b>READ</b></p> 	<ul style="list-style-type: none"> <li>• Sampling of mycobacteriology test procedures/identification schemes</li> <li>• Sampling of mycobacteriology QC policies and procedures</li> <li>• Sampling of patient worksheets/records</li> <li>• Sampling of mycobacteriology QC records</li> <li>• Sampling of HPLC policies and procedures</li> <li>• Sampling of HPLC QC records</li> <li>• New HPLC column verification</li> </ul>
<p><b>OBSERVE</b></p> 	<ul style="list-style-type: none"> <li>• Chromatograph pattern controls</li> <li>• Sampling of reagents (storage, grade, solvent purity)</li> </ul>
<p><b>ASK</b></p> 	<ul style="list-style-type: none"> <li>• What specimens are concentrated before AFB examination and culture?</li> <li>• What testing process is used for rapid detection of <i>Mycobacterium tuberculosis</i> complex?</li> </ul>
<p><b>DISCOVER</b></p> 	<ul style="list-style-type: none"> <li>• Follow a positive patient worksheet from receipt and processing to identification and reporting</li> </ul>

## RAPID METHODS

*The College of American Pathologists encourages laboratories in areas of the country where the incidence of tuberculosis has increased over the past several years and laboratories in other parts of the country that have experienced an increased rate of recovery of mycobacteria to utilize the most rapid and reliable methods available for detection and identification of mycobacteria, especially *M. tuberculosis*, and the most rapid and reliable methods available for susceptibility testing of isolates of *M. tuberculosis*.*



**MIC.32100 Fluorochrome Stain****Phase II**

**Fluorochrome staining is performed on mycobacterial smears prepared from primary respiratory specimens, either in the laboratory or by the referral laboratory.**

*NOTE: Such smears are easier to read than those stained with a conventional carbol-fuchsin based stain. Fluorescing organisms stand out prominently against the background of the smear, and the smears can be examined at a lower power than conventionally-stained smears, so that a larger amount of material can be examined in a given period of time. As with the interpretation of Ziehl-Neelsen- and Kinyoun-stained smears, expertise is needed for interpretation of smears stained with a fluorescent stain; not everything that fluoresces in such a stain is necessarily a mycobacterium. Particularly when only a few organism-like structures are seen, it is important to pay careful attention to their morphology before interpreting them as mycobacteria.*

*This requirement does not apply to laboratories outside of the United States where local regulations prevent fluorochrome staining.*

**Evidence of Compliance:**

- ✓ Written policy for including fluorochrome staining on primary respiratory specimens for mycobacterial culture **OR** written policy for referral of specimens to a referral laboratory for fluorochrome staining **AND**
- ✓ Patient reports/worksheets with fluorochrome stain results **OR** referral laboratory reports with results

**REFERENCES**

- 1) Narain R, *et al.* Microscopy positive and microscopy negative cases of pulmonary tuberculosis. *Am Rev Resp Dis.* 1971;103:761-773
- 2) Lipsky BA, *et al.* Factors affecting the clinical value of microscopy for acid-fast bacilli. *Rev Infect Dis.* 1984;6:214-222
- 3) Witebsky FG. Q&A. *College of American Pathologists CAP TODAY*, 1999;13(1):72
- 4) Somoskovi A, *et al.* Lessons from a proficiency testing event for acid-fast microscopy. *Chest.* 2001;120:250-257

**\*\*REVISED\*\* 06/04/2020****MIC.32140 Rapid Method****Phase I**

**A rapid method (nucleic acid probes, chromatography, the NAP test, matrix-assisted laser description ionization time-of-flight (MALDI-TOF) mass spectrometry, nucleic acid amplification, or sequencing) is employed for identification of mycobacterial isolates.**

**Evidence of Compliance:**

- ✓ Written policy defining method(s) in use for identification of mycobacterial isolates

**REFERENCES**

- 1) Smith MB, *et al.* Evaluation of the enhanced amplified Mycobacterium tuberculosis direct test for direct detection of *Mycobacterium tuberculosis* complex in respiratory specimens. *Arch Pathol Lab Med.* 1999;123:1101-1103
- 2) Driscoll JR, *et al.* How and why we fingerprint tuberculosis. *RT J Resp Care Pract.* 2001:Feb/Mar

**\*\*NEW\*\* 06/04/2020****MIC.32150 Rapid Detection of *Mycobacterium tuberculosis* Complex - Laboratories Subject to US Regulations****Phase I**

**A nucleic acid amplification test is available, either in the laboratory or by a referral laboratory, for the rapid detection of *Mycobacterium tuberculosis* complex on at least one respiratory specimen submitted to the laboratory (preferably the first diagnostic specimen) for mycobacteria culture.**

*NOTE: The US Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) algorithms for diagnosis of Mycobacterium tuberculosis complex infections recommend performing a diagnostic nucleic acid amplification test (NAAT) on the initial respiratory specimen from patients suspected of having pulmonary tuberculosis. This can include physician requests for patients with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered, but has not yet been established, and for whom the test result would alter case management or TB control activities (high index of clinical suspicion).*

**Evidence of Compliance:**

- ✓ Written policy for availability of *M. tuberculosis* complex NAAT testing **AND**
- ✓ Patient reports/worksheets with NAAT testing results **OR** referral laboratory reports with results

## REFERENCES

- 1) Forbes BA, Hall SH, Miller MB, et al. Practical Guidelines for clinical microbiology laboratories: Mycobacteria. *Clin Microbiol Rev.* 2018;31(2). Doi: 10.1128/CMR.00038-17.
- 2) Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. *Clin Infect Dis.* 2017;64(2):111-115. Doi: 10.1093/cid/ciw778.
- 3) World Health Organization. Implementing tuberculosis diagnostics: Policy framework. 2015 [Tuberculosis Diagnostics](#)

**\*\*NEW\*\* 06/04/2020**

**MIC.32170 Rapid Detection of *Mycobacterium Tuberculosis* Complex - Laboratories Phase I**  
**Not Subject to US Regulations**

**Appropriate testing is available, either in the laboratory or by a referral laboratory, for the rapid detection of *Mycobacterium tuberculosis* complex on at least one respiratory specimen submitted to the laboratory (preferably the first diagnostic specimen) for mycobacterial culture that includes a nucleic acid amplification test or follows an established testing algorithm for that country or region.**

*NOTE: The US Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) algorithms for diagnosis of Mycobacterium tuberculosis complex infections recommend performing a diagnostic nucleic acid amplification test (NAAT) on the initial respiratory specimen from patients suspected of having pulmonary tuberculosis. This can include physician requests for patients with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered, but has not yet been established, and for whom the test result would alter case management or TB control activities (high index of clinical suspicion).*

**Evidence of Compliance:**

- ✓ Written policy for availability of tests for rapid detection of *M. tuberculosis* that aligns with public health authority recommendations in the country or region **AND**
- ✓ Patient reports/worksheets with *M. tuberculosis* testing results **OR** referral laboratory reports with results

## REFERENCES

- 1) Forbes BA, Hall SH, Miller MB, et al. Practical Guidelines for clinical microbiology laboratories: Mycobacteria. *Clin Microbiol Rev.* 2018;31(2). Doi: 10.1128/CMR.00028-17.
- 2) Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. *Clin Infect Dis.* 2017;64(2):111-115. Doi: 10.1093/cid/ciw778.
- 3) World Health Organization. Implementing tuberculosis diagnostics: Policy framework. 2015 [Tuberculosis Diagnostics](#)

## CONCENTRATION, INOCULATION, INCUBATION

**MIC.32200 AFB Concentration Phase II**

**There is a written policy defining those specimens (eg, sputum) requiring concentration before AFB smear examination and culture.**

**MIC.32250 Specimen Inoculation Phase I**

**Specimens (other than blood) are routinely inoculated on media that support optimal growth of the majority of clinically relevant mycobacterial species.**

*NOTE: The use of two types of media (for specimens other than blood), including one liquid medium (when possible) or a comparable culture method, is recommended for optimal isolation of mycobacteria.*

#### REFERENCES

- 1) Clinical and Laboratory Standards Institute (CLSI). *Laboratory Detection and Identification of Mycobacteria; Approved Guideline*. CLSI document M48-A (ISBN 1-56238-659-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2008.

## CULTURES

*Laboratories providing complete identification must provide a sufficient variety of differential tests to accurately identify and differentiate the different types of mycobacteria, including temperature growth requirements and photoreactivity studies. Laboratories not providing complete identification are encouraged to at least provide photoreactivity studies.*

### MIC.32320 Incubation Temperature

Phase II

**Mycobacterial cultures are maintained at suitable temperatures.**

*NOTE: The optimal incubation temperature for most mycobacterial specimens is 35 to 37°C. Exceptions to this include specimens obtained from skin or soft tissue suspected to contain *M. marinum* or one of the rapidly growing mycobacteria. These specimens should be incubated at both 30 to 32°C and 35 to 37°C.*

#### Evidence of Compliance:

- ✓ Temperature records

## DIFFERENTIAL BIOCHEMICAL PROCEDURES

### MIC.32420 Differential Biochemical Test

Phase II

**Differential biochemical tests are appropriate for the extent and manner of mycobacterial identification.**

*NOTE: The number and types of biochemical tests needed depend upon (a) the extent to which mycobacteria are identified (eg, "*Mycobacterium kansasii*" or "photochromogen"), (b) the particular species which a laboratory attempts to identify (eg, does it attempt to identify *Mycobacterium terrae* complex, or the species and subspecies of the *Mycobacterium chelonae-Mycobacterium fortuitum* complex), and (c) the degree to which biochemical testing is ancillary to other methods such as nucleic acid probes and HPLC. Useful biochemical tests include, but are not limited to, arylsulfatase, 68° C catalase, semiquantitative catalase, iron uptake, MacConkey agar, 5% NaCl, niacin accumulation, nitrate reductase, Tween 80 hydrolysis, and urease. These tests are particularly useful for the following identifications and discriminations:*

TEST	UTILITY
<i>Arylsulfatase</i>	<i>Helps distinguish pathogenic from non-pathogenic rapid growers; also useful for M. marinum, M. szulgai, M. xenopi, M. triviale.</i>
<i>68°C catalase</i>	<i>Helpful for identification of M. tuberculosis</i>
<i>Semiquantitative catalase</i>	<i>Helpful in certain circumstances. M. tuberculosis complex, MAC, M. xenopi, and a few other species produce &lt;45 mm of bubbles.</i>
<i>Iron uptake</i>	<i>Helps distinguish M. chelonae from M. fortuitum.</i>
<i>MacConkey agar</i>	<i>Helps with identification of rapid growers.</i>
<i>5% NaCl</i>	<i>Helps with identification of rapid growers and M. triviale.</i>
<i>Niacin accumulation</i>	<i>Helps with identification of M. tuberculosis, M. simiae, some strains of M. bovis.</i>
<i>Nitrate reductase</i>	<i>Helpful in identifying many mycobacterial species.</i>
<i>Tween 80 hydrolysis</i>	<i>Helps distinguish some usually pathogenic from some usually non-pathogenic mycobacterial species.</i>
<i>Urease</i>	<i>Helpful in identifying many mycobacterial species.</i>

**Evidence of Compliance:**

- ✓ Written procedure detailing tests performed and identification scheme appropriate for the extent of testing

## REFERENCES

- 1) Kent PT, Kubica GP. Public health mycobacteriology: a guide for the level III laboratory. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control, 1985

**MIC.32480 Biochemical Test QC****Phase II**

**All biochemical tests employed are checked each day of use with appropriate positive and negative controls and results recorded.**

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1262(a)]

## HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) FOR MICROBIAL IDENTIFICATION

**MIC.32518 HPLC Calibrators/Standards****Phase II**

**Appropriate calibrators or standards are run with each analytic batch.**

*NOTE: Either calibration standards or organisms of known identity must be run with each analytic batch, and criteria must exist for acceptance of runs based on mobility of internal standards, ability to identify significant peaks, baseline noise, peak symmetry of internal standards, detection of low-quantity peaks, and similar criteria.*

**Evidence of Compliance:**

- ✓ Written policy defining calibrators/standards appropriate for the test system used **AND**
- ✓ Records of calibration/calibration verification with each batch

## REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32556 HPLC Controls****Phase II**

**Appropriate controls are extracted and run through the entire procedure.**

*NOTE: Control organisms must be extracted and carried through the entire procedure with each run or batch. Appropriate positive (eg, mycobacterial) and negative controls (organisms such as Candida from which no mycolic acids are expected) must be included with each run.*

**Evidence of Compliance:**

- ✓ Written policy defining QC requirements **AND**
- ✓ QC records at defined frequency

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5232 [42CFR493.1256]
- 2) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32594 Chromatogram Controls****Phase I**

**External chromatogram pattern controls are available.**

*NOTE: Patterns for known strains should be established in those laboratories using HPLC. In addition laboratories should have access to the standard method manuals containing comparable chromatographic patterns for comparison.*

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32632 Column Verification****Phase II**

**New columns are verified for performance before use.**

*NOTE: Column verification must include assessment of flow, consistency, and carryover. If the HPLC-method interpretive software uses a peak-naming table, it must be calibrated with each change of column. Generally the basic performance of new columns is certified by the manufacturer. HPLC analysis requires columns be equilibrated with about 10 column volumes of solvent followed with a blank run to test pressure and solvent flow.*

**Evidence of Compliance:**

- ✓ Written procedure for column verification **AND**
- ✓ Records of column verification

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32670 Column/Detector Monitoring****Phase II**

**The performance of the column and detector are monitored on each day of use.**

*NOTE: Unextracted standard organisms and extracted calibrators or controls, typically containing a range of mycolic acids (or other appropriate targets) of known relative retention times, may be analyzed to monitor critical aspects of HPLC performance. Appropriate criteria for evaluating such parameters as retention time of specific standards, relative retention compounds time, separation of closely eluting peaks of interest, detection of known low-quantity peaks, column pressure, chromatography quality and detector response should be established and monitored. Column temperatures and pump pressures are monitored with each run to ensure they met specified criteria for analysis. The column and detector operations are monitored with a blank run prior to use and during batch runs. Positive and negative control samples supplement the blank run when samples are analyzed.*

**Evidence of Compliance:**

- ✓ Records for column and detector monitoring at defined frequency

## REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32708 Carryover Detection****Phase II**

**There is a written procedure for the detection and evaluation of potential carryover.**

*NOTE: No matter what type of injection is used, the written procedure must address criteria for the evaluation of potential carryover from a preceding elevated (high concentration) sample to the following sample, either periodically, or in each analytical batch analysis.*

**Evidence of Compliance:**

- ✓ Records of reassessment of samples with potential carryover

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Preliminary Evaluation of Quantitative Clinical Laboratory Methods; Approved Guideline.* 3<sup>rd</sup> ed. CLSI Document EP10-A3-AMD. Clinical and Laboratory Standards Institute, Wayne, PA; 2014.
- 2) Society of Forensic Toxicologists/American Academy of Forensic Sciences. *Forensic Toxicology Laboratory Guidelines.* 2002; 8.2.8:13
- 3) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32746 HPLC Growth Media****Phase II**

**The laboratory policies define which growth media may be used for organisms to be analyzed by HPLC.**

*NOTE: Final results can be influenced by conditions of growth. For reliable results, standard conditions of analysis must be met, including growth media.*

## REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32784 Peak Verification****Phase II**

**There is a procedure for verifying calibration of the peak-naming table, if used.**

*NOTE: In order to insure that peaks are correctly identified by interpretive software, the table must be verified at least annually with standard materials or organisms with known characteristics.*

## REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32822 HPLC Method Validation****Phase II**

**The HPLC method has been validated using known strains of bacteria, including strains expected to be encountered in routine clinical use.**

**Evidence of Compliance:**

- ✓ Record of method validation with appropriate strains

## REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

**MIC.32860 HPLC Result Review****Phase II**



**There is a policy for review of HPLC results in conjunction with other laboratory data prior to reporting results.**

*NOTE: HPLC is only one tool for microbial identification. When results of HPLC analysis conflict with growth characteristics, pigmentation, or the results of biochemical or molecular testing, identification decisions must be based on all the information available.*

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

### MIC.32898 HPLC Analysis - Pure Isolates

Phase II

**There are procedures to check the purity of cultures used as a source for HPLC analysis.**

*NOTE: Results of HPLC analysis may be unreliable if mixed cultures are tested. If HPLC is performed on an isolate from liquid culture and an interpretable chromatogram is obtained, it is not necessary to await the results of the purity check before reporting results, but a purity check must still be performed.*

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

### MIC.32936 HPLC Reagent Grade

Phase I

**Reagents and solvents are of appropriate grade, and solvent purity is assessed when needed.**

*NOTE: Only HPLC grade solvents are recommended for this procedure. Degradation begins once ultra-pure solvents are opened. Degradation can be slowed by storing solvents in tightly capped, amber bottles in the dark. Solvent purity verification is suggested when a degradation-related problem is suspected.*

#### Evidence of Compliance:

- ✓ Reagent logs

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996

### MIC.32974 Instrument Operation

Phase II

**There are written procedures for operation and calibration of the HPLC instrument.**

*NOTE: Basic principles of HPLC analysis require continual monitoring of analysis conditions, including standard operating procedures, and system calibration. System problems and corrective actions must be appropriately recorded.*

#### REFERENCES




- 1) Department of Health and Human Services, Centers for Disease Control and Prevention, Steering Committee of the HPLC User's Group. Standardized Method for HPLC Identification of Mycobacteria, 1996



# MYCOLOGY

## QUALITY CONTROL

### Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of mycology media/stain/reagent QC policies and procedures</li> <li>• Sampling of mycology QC records</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• How do you determine when QC is unacceptable and when corrective actions are needed?</li> </ul>
 <p>DISCOVER</p>	<ul style="list-style-type: none"> <li>• Review a sampling of QC data over the previous two-year period. Select several occurrences in which QC is out of range and follow records to determine if the steps taken follow the laboratory policy for corrective action</li> </ul>

## MEDIA

**\*\*REVISED\*\* 09/22/2021**

**MIC.41200 Media QC - Purchased/Acquired**

**Phase II**

**An appropriate sample from each lot and shipment of each purchased/acquired medium is checked before or concurrent with initial use for each of the following:**

- 1. Sterility**
- 2. Ability to support the growth of organisms intended to be isolated on the media by means of stock cultures or by parallel testing with previous lots and shipments**
- 3. Biochemical reactivity, where appropriate**

*NOTE: The laboratory must have records showing that all media used are sterile, able to support growth, and are appropriately reactive biochemically. End user quality control must be performed on media not listed on Table 2 of M22-A3 (eg, dermatophyte test medium), regardless of the exempt status.*

*An individualized quality control plan (IQCP), including all required elements of IQCP, may be implemented by the laboratory to allow for the acceptance of the quality control performed by the media supplier for media listed as "exempt" in the CLSI Standard M22-A3, Quality Control for Commercially Prepared Microbiological Culture Media. The media supplier's records must be retained and show that the QC performed meets the CLSI standard and checklist requirements. Please refer to the IQCP section of the All Common Checklist for the requirements for implementation and ongoing monitoring of an IQCP.*

Laboratories receiving media from media suppliers must have records showing that the quality control activities performed by the media supplier meet the CLSI Standard M22-A3, or are otherwise equivalent.

Problems with media deterioration or loss of reactivity in properly-stored media prior to the expiration date must be reported to the manufacturer, with records retained by the laboratory as part of corrective action.

Laboratories using exempt media that have not implemented an IQCP or are using media that do not qualify for an IQCP must continue to test each lot and shipment of media and retain records of such testing.

**Evidence of Compliance:**

- ✓ Written procedure for QC on new lot numbers and shipments of medium **AND**
- ✓ Records of media QC **AND**
- ✓ Individualized quality control plan for the media approved by the laboratory director, as applicable **AND**
- ✓ Records of reports of media problems/defects to manufacturers

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Quality Control for Commercially Prepared Microbiological Culture Media; Approved Standard*; 3rd ed. CLSI document M22-A3. Clinical and Laboratory Standards Institute, Wayne, PA, 2004.
- 2) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Detection of Fungi in Clinical Specimens-Direct Examination and Culture*. 2nd ed. CLSI guideline M54. Clinical and Laboratory Standards Institute, Wayne, PA; 2021.
- 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)].

**MIC.41215 Media QC - Laboratory Prepared**

**Phase II**

**For microbiology media prepared by the laboratory, there are records showing that an appropriate sample of each medium is checked before or concurrent with initial use for each of the following:**

1. **Sterility**
2. **Ability to support the growth of organisms intended to be isolated on the media by means of stock cultures or by parallel testing with previous batches**
3. **Biochemical reactivity (where appropriate)**

**Evidence of Compliance:**

- ✓ Written procedure for testing media prepared by the laboratory
- ✓ Records of media quality control

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1256(e)]

## CONTROLS AND STANDARDS

*Good laboratory practice includes checking all media either at the time of receipt or concurrently with use. This applies to purchased media as well as media prepared by the laboratory.*

**MIC.41250 Reference Organisms**

**Phase II**

**Reference cultures or control organisms are used to check stains and reagents at appropriate intervals.**

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7167 [42CFR493.1261(b)]

**MIC.41270 Nucleic Acid Probe/Exo-antigen QC**

**Phase II**

If nucleic acid probes or exo-antigen tests are used for identification of fungi isolated from culture, appropriate positive and negative controls are tested on each day of use.

**Evidence of Compliance:**

- ✓ Written policy defining QC for nucleic acid probe or exo-antigen tests **AND**
- ✓ Records of nucleic acid probe or exo-antigen QC at defined frequency

**MIC.41370 Direct Smear Stain QC**

**Phase II**

**Direct patient specimen stains (eg, acid fast, PAS, Giemsa, Gomori's methenamine silver, India ink) are checked with positive and negative controls on each day of patient sample testing.**

*NOTE: For certain stains such as GMS and Giemsa, the slide itself serves as the negative control. Controls for KOH preparations are not required.*

**Evidence of Compliance:**

- ✓ Records of stain QC at defined frequency

**REFERENCES**

- 1) Carey RB, Bhattacharyya S, Kehl SC, et al. Practical Guidance for Clinical Microbiology Laboratories: Implementing a Quality Management System in the Medical Microbiology Laboratory. *Clin Microbiol Rev.* 2018;31(3): e00062-17.
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):7166 [42CFR493.1256(e)(2); 493.1256(e)(3); 493.1273(a)]
- 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):3709 [42CFR493.1263(a)]

**MIC.41390 Fluorescent Stain QC**

**Phase II**

**Fluorescent stains (such as calcofluor white) are checked with positive and negative controls each time of use and records retained.**

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):3708 [42CFR493.1256(e)(3)]

**MIC.41400 Lactophenol Cotton Blue QC**

**Phase II**

**Lactophenol cotton blue is checked for intended reactivity with a control organism with each new batch, lot number, and shipment of reagent.**

**Evidence of Compliance:**

- ✓ Records of QC at defined frequency




## PROCEDURES AND TESTS

*The intent of this series of requirements is to ensure the use of an appropriate variety of media and growth conditions to isolate the significant pathogens with minimal interference from contaminants.*

### Inspector Instructions:



- Sampling of mycology specimen handling procedures, test procedures, and identification schemes
- Sampling of patient worksheets/records

 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>Safe work practices (taping of culture plates, procedures performed under BSC)</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>What tests or procedures are used to identify dimorphic fungi? Filamentous fungi?</li> </ul>
 <p>DISCOVER</p>	<ul style="list-style-type: none"> <li>Follow a mycology patient worksheet from receipt and processing to culture evaluation, identification, and reporting</li> </ul>

**MIC.42025 Cryptococcal Antigen****Phase II**

**If cryptococcal antigen-detection methods are used on CSF, back-up cultures are performed on positive CSF specimens submitted for diagnosis.**

*NOTE: It is important to recover the causative organism for precise identification (*C. neoformans* vs. *C. gattii*) and potential susceptibility testing. Back-up cultures of follow-up specimens used for trending the antigen titer are not required. If culture is not performed onsite by the laboratory, the laboratory must show evidence that it has been performed in a referral laboratory.*

**Evidence of Compliance:**

- ✓ Written policy stating that CSF cultures are performed in conjunction with initial positive cryptococcal antigen tests **OR** policy describing testing at another location **AND**
- ✓ Records of back-up CSF cultures performed on-site **OR** records indicating that cultures are performed at another location

**MIC.42050 Selective Media****Phase II**

**Suitable selective media are used for the growth and isolation of dermatophytes and/or systemic fungi.**

**Evidence of Compliance:**

- ✓ Written policy for mycology culture defining the media used for growth and isolation

**MIC.42100 Selective Media****Phase II**

**Media with antimicrobial agents are used to suppress the growth of contaminants.**

*NOTE: Antimicrobial agents may inhibit some yeasts and the yeast phase of dimorphic organisms. Both types of media (with and without antimicrobials) should be available and used when indicated.*

**Evidence of Compliance:**

- ✓ Written policy for mycology culture defining the use of media to suppress contaminants

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Detection of Fungi in Clinical Specimens-Direct Examination and Culture; Approved Guideline*. CLSI document M54-A (ISBN 1-56238-857-6 [Print] ISBN 1-56238-858-4 [Electronic]). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2012.

**\*\*REVISED\*\* 09/22/2021****MIC.42110 Mycology Plate Culture Media Safety****Phase II**

**If plate culture media is used in mycology, appropriate safety precautions are taken (such as taping lid to plate on both sides when not in use or other appropriate measures) to prevent the accidental opening of a plate.**

*NOTE: Some authorities recommend the transfer of growing colonies from plate to tubed media, if the former is routinely used for initial inoculation.*

**Evidence of Compliance:**

- ✓ Written policy defining safety precautions for handling mycology culture plates

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Detection of Fungi in Clinical Specimens-Direct Examination and Culture; Approved Guideline*. CLSI document M54-Ed2 (ISBN 1-56238-857-6 [Print] ISBN 1-56238-858-4 [Electronic]). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2012.

**\*\*REVISED\*\* 09/22/2021****MIC.42120 Mycology Culture Safety****Phase II**

**When working with a colony exhibiting mycelial growth, all transfers are performed within a biologic safety cabinet, and the use of slide culture techniques is limited, whenever possible, to work with low virulence organisms.**

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Principles and Procedures for Detection of Fungi in Clinical Specimens-Direct Examination and Culture; Approved Guideline*. CLSI document M54-Ed2 (ISBN 1-56238-857-6 [Print] ISBN 1-56238-858-4 [Electronic]). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2012.

**\*\*REVISED\*\* 09/22/2021****MIC.42130 Mycology Teased Preparation Safety****Phase II**

**When preparing teased preparations or "scotch" tape preps, mycelia are always submerged in liquid medium (such as lactophenol cotton blue).**

**MIC.42150 Incubation Temperature****Phase II**

**Incubation temperatures for the growth and isolation of dermatophytes and systemic fungi are defined and followed under culture conditions.**

**Evidence of Compliance:**

- ✓ Temperature records

**MIC.42200 Incubation Temperature****Phase II**

**If cultures are incubated at room temperatures, actual ambient temperature (22 to 26 °C) is recorded daily to determine if proper growth conditions are being maintained.**

**MIC.42250 Differential Tests****Phase II**

**Procedures for the differentiation and identification of fungi (differential tests) are adequate for the needs of the laboratory.**

*NOTE: Laboratories offering full identification must have sufficient procedures to do so. Smaller laboratories with limited services should have an arrangement with an approved referral laboratory for back-up and complete identification of mycology specimens.*

**Evidence of Compliance:**

- ✓ Written procedure detailing tests performed and identification scheme appropriate for the extent of testing

## REFERENCES

- 1) Riddle DL, *et al.* Clinical comparison of the Baxter Microscan yeast identification panel and the Vitek yeast biochemical card. *Am J Clin Pathol.* 1994;101:438-442
- 2) Love GL. Mycology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Fungi. Northfield, IL: College of American Pathologists; 2013.

**\*\*REVISED\*\* 06/04/2020****MIC.42350 Differential Tests****Phase II**

**Differential tests include biochemical tests (eg, urease, carbohydrate assimilation and/or fermentation), when appropriate.**

**MIC.42400 Differential Tests****Phase I**

**Differential tests include slide cultures (when appropriate).**

## REFERENCES

- 1) Love GL. Mycology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Fungi. Northfield, IL: College of American Pathologists; 2013.

**\*\*REVISED\*\* 09/22/2021****MIC.42550 Dimorphic Fungi****Phase I**

**The identification of dimorphic fungal isolates is confirmed by exo-antigen, molecular, yeast-mold conversion, MALDI-TOF mass spectrometry (MS), or tissue phase detection tests.**




*NOTE: Exo-antigen tests, DNA probes, DNA sequencing, or MALDI-TOF MS are recommended. Laboratories should ensure adequate inactivation prior to testing by methods that occur outside a biological safety cabinet and have risk for aerosol generation (eg, MALDI-TOF MS).*

## REFERENCES

- 1) Love GL. Mycology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Fungi. Northfield, IL: College of American Pathologists; 2013.
- 2) U.S. Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH). Biosafety in Microbiological and Biomedical Laboratories (BMBL). 6th Edition. June 2020.
- 3) American Society for Microbiology (ASM). Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases Biological Safety, October 2018.

## MYCOLOGY SUSCEPTIBILITY TESTING

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of susceptibility test, QC and reporting policies and procedures</li> <li>• Sampling of susceptibility QC records</li> </ul>
	<ul style="list-style-type: none"> <li>• Susceptibility test set-up (standardized inoculum, pure culture)</li> </ul>
	<ul style="list-style-type: none"> <li>• How does your laboratory work with the pharmacy and medical staff to determine guidelines for reporting of antimicrobial agents?</li> </ul>

**\*\*REVISED\*\* 09/22/2021**

**MIC.42600 Susceptibility Testing QC Frequency**

**Phase II**

**For antifungal susceptibility testing by either disk, gradient diffusion strips, or broth dilution (MIC) methods, appropriate quality control organisms are tested with each new lot number or shipment of susceptibility test reagents and media before or concurrent with initial use, and each day the test is performed thereafter.**

*NOTE: The frequency of QC testing may be reduced to weekly (and whenever any reagent component of the test is changed) if the laboratory director approves the use of an individualized quality control plan (IQCP), including all required elements of IQCP, and the laboratory has records of satisfactory performance with daily QC tests as suggested by CLSI Standards and Guidelines (M27, M44, and M38). Please refer to the Individualized Quality Control Plan section of the All Common Checklist for the requirements for implementation and ongoing monitoring of an IQCP.*

#### **Evidence of Compliance:**

- ✓ Records of susceptibility QC results recorded at defined frequency and meeting defined acceptability criteria

#### **REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services, Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):[42CFR493.1263(b)].
- 2) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts*. 4th ed. CLSI standard M27. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.
- 3) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi*. 3rd ed. CLSI standard M38. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.
- 4) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts*. 3rd ed. CLSI guideline M44. Clinical and Laboratory Standards Institute, Wayne, PA, 2018.
- 5) Clinical and Laboratory Standards Institute (CLSI). *Epidemiological Cutoff Values for Antifungal Susceptibility Testing*. 3rd ed. CLSI supplement M59. Clinical and Laboratory Standards Institute, Wayne, PA, 2020.
- 6) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antifungal Susceptibility Testing of Yeasts*. 1st ed. CLSI supplement M60. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.
- 7) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antifungal Susceptibility Testing of Filamentous Fungi*. 2nd ed. CLSI supplement M61. Clinical and Laboratory Standards Institute, Wayne, PA, 2020.



**MIC.42640 Susceptibility Testing - Pure Cultures Phase II**

**Only isolated colonies or pure cultures are used for performance of antifungal susceptibility testing (ie, susceptibility testing is not performed on mixed cultures).**

**Evidence of Compliance:**

- ✓ Written procedure describing the use of isolated colonies or of pure cultures for susceptibility testing, including the use of purity plates

**MIC.42660 Standardized Inoculum Phase II**

**The inoculum size of both QC strains and test organisms is standardized using a turbidity standard or another acceptable method.**

**Evidence of Compliance:**

- ✓ Written procedure for standardizing susceptibility inoculum

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts*. 4th ed. CLSI standard M27. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.
- 2) Clinical and Laboratory Standards Institute. *Performance Standards for Antifungal Susceptibility Testing of Yeasts; 1st ed.* CLSI Supplement M60. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.

**MIC.42700 Antifungal Agents to Test/Report Phase II**

**There are written policies to ensure that only antifungal agents appropriate for the organism and body site are routinely tested and reported.**

*NOTE: The microbiology department should consult with the medical staff and pharmacy to develop a list of antifungal agents to be reported for specific organisms isolated from certain body sites, instead of indiscriminate susceptibility testing and reporting of all fungal isolates or reporting of all antifungal agents that might be included on a test panel. Isolates from body sites for which susceptibility might be routinely tested and reported include Candida spp. isolates from blood cultures.*

**Evidence of Compliance:**

- ✓ Patient records showing selection and testing of fungal isolates and reporting of fungal agents for certain body sites **AND**
- ✓ Records of review of antimicrobial reporting policies on an annual basis **AND**
- ✓ Proficiency testing susceptibility reporting following policy

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts*. 4th ed. CLSI standard M27. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.
- 2) Clinical and Laboratory Standards Institute (CLSI). *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi*. 3rd ed. CLSI standard M38. Clinical and Laboratory Standards Institute, Wayne, PA; 2017.
- 3) Clinical and Laboratory Standards Institute (CLSI). *Epidemiological Cutoff Values for Antifungal Susceptibility Testing*. 3rd ed. CLSI supplement M59. Clinical and Laboratory Standards Institute, Wayne, PA, 2020.
- 4) Clinical and Laboratory Standards Institute (CLSI). *Epidemiological Cutoff Values for Antifungal Susceptibility Testing*. 3rd ed. CLSI supplement M59. Clinical and Laboratory Standards Institute, Wayne, PA, 2020.
- 5) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antifungal Susceptibility Testing of Yeasts*. 1st ed. CLSI supplement M60. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.
- 6) Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antifungal Susceptibility Testing of Filamentous Fungi*. 2nd ed. CLSI supplement M61. Clinical and Laboratory Standards Institute, Wayne, PA, 2020.

**MIC.42720 Inconsistent Antifungal Susceptibility Reports Phase I**

**There is a written policy to address unusual or inconsistent antifungal testing results.**

*NOTE: Acceptable results obtained when testing QC organisms do not guarantee accurate results on patient isolates. Results from testing of patient isolates should be reviewed, and unusual or inconsistent results should be investigated. Each laboratory should have a policy for confirming unusual or inconsistent results. For yeasts and molds, the time of endpoint reading (particularly for the echinocandins) and the effect of trailing growth (particularly for the azoles*

and flucytosine) can be significant factors impacting susceptibility results. In some cases, it may be necessary to repeat susceptibility testing and/or identification procedures to confirm initial results. This may involve using alternative testing methods or sending the isolate to a referral laboratory. Options also include retrospectively reviewing individual patient data or cumulative data for unusual resistance patterns. Some examples of inconsistent antifungal testing results include:

1. *Candida albicans* resistant to all azoles
2. *Candida* spp. susceptible to azoles but resistant to echinocandins
3. *Candida albicans* resistant to echinocandins
4. *Candida krusei* susceptible to fluconazole



**Evidence of Compliance:**

- ✓ Records of investigation for unusual or inconsistent results

## PARASITOLOGY

### QUALITY CONTROL

#### Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of parasitology stain/reagent QC policies and procedures</li> <li>• Sampling of parasitology QC records</li> </ul>
 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Reference materials (permanent mounts, photomicrographs or atlas available)</li> <li>• Zinc sulfate solution (tightly-stoppered)</li> </ul>

#### MIC.51000 Reference Materials

#### Phase I

**Reference materials, such as permanent mounts, photomicrographs, CLSI documents M15-A and M28-A2, or printed atlases are available at the work bench to assist with identifications.**

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.
- 2) Garcia LS, Shimizu R. Diagnostic parasitology: parasitic infections and the compromised host. *Lab Med*. 1993;24:205-215
- 3) Ash R, Orihel TC. *Atlas of human parasitology*, 4th ed. Chicago, IL: American Society of Clinical Pathology, 1996
- 4) Clinical and Laboratory Standards Institute (CLSI). *Procedures for the Recovery and Identification of Parasites From the Intestinal Tract; Approved Guideline—Second Edition*. CLSI document M28-A2 (ISBN 1-56238-572-0). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2005
- 5) Garcia LS. *Diagnostic medical parasitology*. 4th ed. Washington, DC: ASM Press, 2001
- 6) Colmer-Hamood JA, Fecal microscopy. Artifacts mimicking ova and parasites. *Lab Med*. 2001;32:80-84
- 7) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24); [42CFR493.1264(a)]
- 8) Pritt BS. *Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites*. Northfield, IL: College of American Pathologists; 2014.

## REAGENTS

**MIC.51120 Reagents Phase II**

If zinc sulfate is used, the solution is stored in a tightly-stoppered bottle and checked for specific gravity (1.18 for fresh specimens and 1.20 for formalin-fixed specimens) with a hydrometer whose scale is large enough to differentiate the two values.

**Evidence of Compliance:**

- ✓ Records for specific gravity checks on the zinc sulfate solution

**MIC.51160 Permanent Stool Parasitology Stain QC Phase II**

All permanent parasitology stains (eg, trichrome, iron hematoxylin) are checked for intended reactivity with controls or reference materials at least monthly (or with each test if performed less frequently than every month).

*NOTE: PVA fixative solutions thoroughly mixed with fresh fecal material that has been seeded with buffy coat leukocytes usually provides reliable controls for permanent stains.*

**Evidence of Compliance:**

- ✓ Records of permanent stain QC at defined frequency

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7167 [42CFR493.1264(c)]
- 2) Garcia LS, Diagnostic medical parasitology, 4th ed. Washington, DC: ASM Press, 2001

**MIC.51170 Special Stain QC Phase II**

Stains that are used to detect specific parasites (eg, acid fast, fluorescent, Giemsa) are checked with appropriate control organisms each time of use.

*NOTE: Laboratories may check stains used for blood parasites (eg, Giemsa, Wright-Giemsa) by confirming the intended reactivity of the stain on the cellular elements on the slide (eg, WBC, RBC, platelets). A slide prepared from a normal specimen can be used in lieu of a positive parasite slide.*

**Evidence of Compliance:**



- ✓ Records of special stain QC each time of use

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.

## PROCEDURES AND TESTS

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of parasitology test procedures</li> <li>• Sampling of patient worksheets/records</li> </ul>
	<ul style="list-style-type: none"> <li>• Follow a parasitology patient worksheet from receipt and processing to identification and reporting</li> </ul>

## STOOLS FOR OVA AND PARASITES

### MIC.52100 Ova/Parasite Exam

### Phase II

**The microscopic examination of all stools submitted for an ova and parasite (O&P) examination includes a concentration procedure and a permanent stain.**

*NOTE: When a stool specimen is submitted fresh, the usual approach would be to perform a direct wet preparation (looking for motility), a concentration (helminth eggs/larvae/protozoan cysts), and the permanent stained smear (identification of protozoa missed by concentration and confirmation of suspect organisms). As a minimum (and certainly if the stool is submitted in preservatives), the standard O&P examination would include the concentration procedure and a permanent stained smear. The main point is to ensure that the permanent stained smear is performed on all stool specimens, regardless of what was or was not seen in the concentration wet preparation. Often, intestinal protozoa will be seen in the permanent stained smear, but may be missed in the concentration examination. If the laboratory does not perform both a concentration procedure and a permanent stain, it must refer the testing that is not completed to a referral laboratory so that testing may be completed.*

#### Evidence of Compliance:

- ✓ Written procedures for stool for O&P **AND**
- ✓ Patient reports/worksheets with concentration and permanent stain results

#### REFERENCES

- 1) Garcia LS. Diagnostic medical parasitology, 4th edition. Washington, DC: ASM Press, 2001
- 2) Clinical and Laboratory Standards Institute (CLSI). *Procedures for the Recovery and Identification of Parasites From the Intestinal Tract; Approved Guideline—Second Edition*. CLSI document M28-A2 (ISBN 1-56238-572-0). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2005
- 3) Pritt BS. Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites. Northfield, IL: College of American Pathologists; 2014.

### MIC.52190 Stool Number/Timing

### Phase I

**There are written policies for the number and/or timing of collection of stool specimens submitted for routine parasitology testing.**

*NOTE: The laboratories should consider developing policies with its clinicians for the number and/or timing of collection of stool specimens submitted for routine parasitology testing.*

*Suggestions made by the authors of a 1996 CAP Q-Probes study (Valenstein et al) include:*

1. *Accept no more than two or three specimens/patients without prior consultation with an individual who can explain the limited yield provided by additional specimens*
2. *Do not accept specimens from inpatients after the fourth hospital day, without prior consultation*

*These recommendations are for diagnostic testing. Different policies may apply to tests ordered for follow-up.*

#### REFERENCES

- 1) Yannelli B, et al. Yield of stool cultures, ova and parasite tests, and *Clostridium difficile* determinations in nosocomial diarrhea. *Am J Infect Control*. 1988;16:246-249
- 2) Morris AJ, et al. Application of rejection criteria for stool ovum and parasite examinations. *J Clin Microbiol*. 1992;30:3213-3216
- 3) Valenstein P, et al. The use and abuse of routine stool microbiology. A College of American Pathologists Q-probes study of 601 institutions. *Arch Pathol Lab Med*. 1996;120:206-211
- 4) Cartwright CP. Utility of multiple-stool-specimen ova and parasite examinations in high-prevalence setting. *J Clin Microbiol*. 1999;37:2408-2411

## BLOOD FILMS FOR MALARIA AND OTHER PARASITES

### MIC.52193 Blood Parasite Detection

Phase II

**The microscopic examination of blood films submitted for detection of blood parasites allows for detection of parasites responsible for malaria, babesiosis, trypanosomiasis and filariasis.**

#### REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.
- 2) Pritt BS. *Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites*. Northfield, IL: College of American Pathologists; 2014.

**\*\*REVISED\*\* 06/04/2020**

### MIC.52195 Parasite Load Reporting

Phase I

**When blood films are positive for malaria parasites (*Plasmodium* spp.), the parasite load (provided as percentage parasitemia or the number of parasites per  $\mu\text{L}$  of blood) is reported along with the organism identification.**

*NOTE: It is important to determine the parasite load when blood films are reviewed and found to be positive for malaria parasites because this information may be used to guide treatment decisions and monitor the response to therapy. Due to the potential for drug resistance in some of the Plasmodium species, particularly P. falciparum, it is important that every positive smear be assessed and the parasite load reported exactly the same way on follow-up specimens as on the initial specimen. This allows the parasite load to be monitored after therapy has been initiated. The parasite load will usually drop very quickly within the first 24 hours; however, in cases of drug resistance, the level may not decrease, but actually increase over time.*

*Although there are currently no requirements for reporting parasite load when blood films are positive for Babesia species, physicians may ask for these data to guide treatment decisions and monitor the response to therapy.*

#### Evidence of Compliance:

- ✓ Written procedure for performing and reporting parasite load with identification

#### REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.
- 2) Garcia LS. *Diagnostic Medical Parasitology*. Washington, DC, ASM Press, 2001.
- 3) Pritt BS. *Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites*. Northfield, IL: College of American Pathologists; 2014.
- 4) World Health Organization. Recording and Reporting Microscopy Results: Malaria Microscopy Standard Operating Procedure - MM-SOP-6B. Version i. [http://www.wpro.who.int/mvp/lab\\_quality/2096\\_oms\\_gmp\\_sop\\_06b\\_rev.pdf](http://www.wpro.who.int/mvp/lab_quality/2096_oms_gmp_sop_06b_rev.pdf). Effective January 1, 2016. Accessed September 12, 2019.
- 5) World Health Organization. Malaria Parasite Counting. Malaria Microscopy Standard Operating Procedure - MM-SOP-9. Version 1. g [http://www.wpro.who.int/mvp/lab\\_quality/2096\\_oms\\_gmp\\_sop\\_09\\_rev1.pdf](http://www.wpro.who.int/mvp/lab_quality/2096_oms_gmp_sop_09_rev1.pdf). Effective January 1, 2016. Accessed August 12, 2019.

### MIC.52200 Thick and Thin Films

Phase II

**Both thick and thin films (routine blood films and/or buffy coat films), or methods of equivalent sensitivity, are made to provide thorough examination for blood parasites.**

#### REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.
- 2) Thomson S, et al. External quality assessment in the examination of blood films for malarial parasites within Ontario, Canada. *Arch Pathol Lab Med*. 2000;124:57-60
- 3) Pritt BS. *Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites*. Northfield, IL: College of American Pathologists; 2014.

**MIC.52220 Malaria Stain Procedure****Phase I**

**There are records that malaria stains are washed with a buffer of a pH appropriate for the stain used (eg, pH 6.8-7.2 for Giemsa), or the range specified by the manufacturer.**

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.
- 2) Garcia LS, *Diagnostic medical parasitology*. 4th ed. Washington, DC: ASM Press, 2001
- 3) Pritt BS. *Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites*. Northfield, IL: College of American Pathologists; 2014.

**MIC.52260 Slide Review Procedure****Phase II**

**An adequate number of fields are examined under oil immersion using the 100X oil immersion objective (eg, 300 fields).**

**Evidence of Compliance:**

- ✓ Written procedure defining criteria for assessment of malaria slides including objective and number of fields examined




## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline*. CLSI document M15-A. CLSI, Wayne, PA, 2000.
- 2) Pritt BS. *Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites*. Northfield, IL: College of American Pathologists; 2014.

## VIROLOGY

### QUALITY CONTROL

#### Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of virology test procedures</li> <li>• Sampling of virology cell culture system and reagent QC policies and procedures</li> <li>• Sampling of virology QC records and cell line checks</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• How are cell lines checked for contamination?</li> </ul>
 <p>DISCOVER</p>	<ul style="list-style-type: none"> <li>• Follow a virology patient worksheet from receipt and processing to identification and reporting</li> </ul>

## REAGENTS

**MIC.61000 Breakage****Phase I**

**The laboratory has records that each shipment of commercial cell culture tubes, flasks, shell vials or cluster trays is examined for breakage.**



## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline*. CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.
- 2) Ginocchio, CC. Quality Assurance in Clinical Virology. In: Spector S, Hodinka RL, Young SA, editors. *Clinical Virology Manual*. Fourth Edition. Washington: ASM Press; 2009.p. 3-17

**MIC.61050 Acceptance of Materials****Phase II**

**There are written policies for the acceptance and rejection of cell culture tubes, flasks, shell vials or cluster trays used for virus isolation.**

*NOTE: Cell cultures should be observed microscopically to confirm that the cells are attached to the substratum, the confluency of the monolayer is appropriate for the method and cell line (75%-90%) and cell appearance is typical. Confluent or overgrown monolayers may obscure viral cytopathic effect (CPE) in tube or flask cell cultures and can adversely affect the recovery of some more fastidious viruses, such as RSV. The cell culture media should be free of contamination (clear) and should be near a neutral pH (salmon pink in color). Cell culture tubes, flasks, vials or plates not meeting the expected criteria should be observed or rejected, depending on the observation and laboratory policies.*

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline*. CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.
- 2) Ginocchio, CC. Quality Assurance in Clinical Virology. In: Spector S, Hodinka RL, Young SA, editors. *Clinical Virology Manual*. Fourth Edition. Washington: ASM Press; 2009.p. 3-17
- 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1242(a)]

**MIC.61060 Cell Culture System Growth Checks****Phase II**

**The cell culture system is checked for the ability to support growth.**

*NOTE: For systems using shell vials and/or co-cultivated cell lines that detect multiple viruses, laboratories can evaluate both the ability of the cell lines to support the growth of the virus(es) and the reactivity of the detection reagents (MIC.61370) by rotating growth controls that include the viruses tested for which the test is performed. By using this method over the course of a week, the cell culture system lot and detection reagents will be checked for all viruses. While rotation of viral culture controls for all viral targets is desirable, certain viruses may be difficult to maintain by serial propagation (for example varicella zoster virus). In these cases, integrity of the cell culture system may be demonstrated through the use of other, more easily propagated viruses.*

**Evidence of Compliance:**

- ✓ Written procedure for cell culture system QC **AND**
- ✓ Records of quality control

## REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1265(a)].

**MIC.61140 Cell Culture Media and Diluent Checks****Phase II**

**Cell culture media and diluents are checked for sterility and pH.**

*NOTE: Entering the media to remove aliquots for refeeding, etc. does not generate the need for repeat sterility testing. It is satisfactory to test either the individual components or the final product.*

**Evidence of Compliance:**

- ✓ Written procedure for cell culture media QC **AND**
- ✓ Records of media sterility and pH QC

## REFERENCES



- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):[42CFR493.1265(a)].

**MIC.61150 Cell Line QC****Phase II****Continuous cell lines are checked for mycoplasma contamination.**

*NOTE: An alternative method to culturing for mycoplasma is the monitoring of a negative, uninoculated control. If cell lines are provided by a commercial vendor, documentation of mycoplasma screening by the vendor is acceptable. Vendor records must be retained by the laboratory.*

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline*. CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.
- 2) Lennette DA. General Principles for Laboratory Diagnosis for Viral, Rickettsial, and Chlamydial Infections. In: Lennette EH, Lennette DA, Lennette ET, editors. *Diagnostic Procedures for Viral, Rickettsial, and Chlamydial Infections*. Seventh Edition ed. Washington: American Public Health Association; 1995 p. 3-25

**MIC.61155 Cell Line QC****Phase II****Continuous cell lines are checked for endogenous viral contamination.**

*NOTE: Upon receipt in the laboratory and during the period of use, cell lines must be monitored for the presence of endogenous contamination due to viruses such as foamy virus and monkey viruses.*

*Endogenous viral contamination must be recorded. Individual laboratories may decide to reject all cell lines with contamination. Alternatively, cell lines may be monitored to determine if the contamination will prohibit the isolation and identification of patient viral isolates. Endogenously contaminated cell cultures can be evaluated by considering conditions such as the degree (percent) of contamination of the monolayer, the specificity of the contamination CPE, the effect of the contamination on the quality of the culture system, and the condition of the culture cell to support virus growth. If such contamination will affect the ability to recover patient isolates, cell lines must be rejected.*

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline*. CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.
- 2) Lennette DA. General Principles for Laboratory Diagnosis for Viral, Rickettsial, and Chlamydial Infections. In: Lennette EH, Lennette DA, Lennette ET, editors. *Diagnostic Procedures for Viral, Rickettsial, and Chlamydial Infections*. Seventh Edition ed. Washington: American Public Health Association; 1995 p. 3-25

**MIC.61160 Media QC****Phase II****Animal sera used for cell growth media are checked for absence of toxicity to cells.****Evidence of Compliance:**

- ✓ Written procedure for checks of animal sera for toxicity **AND**
- ✓ Records of animal sera checks

**MIC.61180 Cell Line Availability****Phase II****The laboratory has the appropriate minimal cell line(s) available for all types of specimens tested and for all viruses reported by the laboratory.**

*NOTE: The following is a suggested list of cell lines for the intended purpose:*

ORGANISM	CELL LINE
<i>Chlamydia</i>	McCoy or Buffalo Green Monkey Kidney
<i>Herpes simplex</i>	HDF, Primary or First Pass Rabbit Kidney, MRC-5, or A549, CV-1/ MRC-5, transgenic BHK
<i>Varicella zoster</i>	HDF, Primary Monkey Kidney, CV-1/MRC-5
<i>Influenza</i>	Primary Monkey Kidney or MDCK, Mink lung /A549
<i>Parainfluenza</i>	Primary Monkey Kidney, Mink lung/A549
RSV	HEp-2 or Primary Monkey Kidney, Mink lung/A549
<i>Enteroviruses</i>	Primary Monkey Kidney, A549, HDF, MRC-5, GGMK+Daf/A549
<i>Adenoviruses</i>	HEp-2, Human Embryonic Kidney, A549, Mink lung/A549, MDCK/ A549
Human metapneumovirus	LLC-MK2, Mink lung/A549
Cytomegalovirus	HDF, MRC-5

## REFERENCES

- 1) McCarter YS, Robinson A. Comparison of MRC-5 and primary rabbit kidney cells for the detection of *Herpes simplex* virus. *Arch Pathol Lab Med.* 1997;121:122-124
- 2) McCarter YS, Ratkiewicz IN. Comparison of virus culture and direct immunofluorescent staining of cytocentrifuged virus transport medium for detection of Varicella-Zoster virus in skin lesions. *Am J Clin Pathol.* 1998;109:631-633
- 3) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline.* CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.

## MIC.61210 Incubation Time

## Phase II

**Viral cultures are incubated for a sufficient time to recover the viruses for which service is offered.**

NOTE: The following is a suggested list of minimum incubation times for the intended purpose:

ORGANISM	INCUBATION TIME
<i>Herpes simplex (genital)</i>	5 days
<i>Herpes simplex (other)</i>	7 days
<i>Respiratory viruses</i>	10 days - 14 days
<i>Other viruses</i>	14 to 28 days

**Evidence of Compliance:**

- ✓ Written procedure indicating length of incubation for each virus cultured

## REFERENCES

- 1) Clinical and Laboratory Standards Institute. *Viral Culture; Approved Guideline.* CLSI document M41-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2006.
- 2) Leland DS, Ginocchio CC. Role of cell culture for virus detection in the age of technology. *Clin Microbiol Rev* 2007 January; 20(1):49-78
- 3) Landry ML, Hsiung GD. Primary Isolation of Viruses. In: Specter S, Hodinka RL, Young SA, editors. *Clinical Virology Manual.* Third Edition ed. Washington: ASM Press; 2000. p. 27-42
- 4) Leland DS, Emanuel D. Laboratory diagnosis of viral infections of the lung. *Semin Respir Infect* 1995 December;10(4):189-98

## MIC.61300 Work Records

## Phase II

**Records are kept of cell types, passage number, source, and media that are used for specimen testing, virus culture or propagation and maintenance of control organisms.**

## CONTROLS AND STANDARDS

**MIC.61310 Cytopathic Effect Phase II**

**Inoculated cultures are checked for cytopathic effect in a fashion that optimizes the time to detection of viral pathogens.**

*NOTE: Primary cultures must be checked at least every other working day for cytopathic effect at least for the first two weeks of incubation.*

**Evidence of Compliance:**

- ✓ Written policy defining the frequency of CPE checks **AND**
- ✓ Work records reflecting CPE examination at defined frequency

**MIC.61320 Media QC Phase II**

**Uninoculated cell monolayers or monolayers that have been inoculated with sterile material are available for comparison with cultures of clinical material.**

*NOTE: Uninoculated cell culture controls must be included on each inoculation day of cell culture tubes in order to detect non-specific degeneration; or to detect extraneous infection of the cell culture with endogenous viral agents capable of producing cytopathic effects.*

**Evidence of Compliance:**

- ✓ Records of uninoculated/sterile cell monolayer checks documented at defined frequency

**REFERENCES**

- 1) Ginocchio, CC. Quality Assurance in Clinical Virology. In: Spector S, Hodinka RL, Young SA, editors. *Clinical Virology Manual*. Fourth Edition. Washington: ASM Press; 2009.p. 3-17
- 2) Lennette DA. General Principles for Laboratory Diagnosis for Viral, Rickettsial, and Chlamydial Infections. In: Lennette EH, Lennette DA, Lennette ET, editors. *Diagnostic Procedures for Viral, Rickettsial, and Chlamydial Infections*. Seventh Edition ed. Washington: American Public Health Association; 1995 p. 3-25
- 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1265(a)]

**MIC.61325 Unusual Cytopathic Effect Phase I**

**There are written policies for the handling of cell cultures with unusual cytopathic effect.**

*NOTE: Unusual CPE can be detected in cell culture from samples positive for viruses not commonly detected by the laboratory (ie, monkey pox, vaccinia, variola, etc.) Policies should include the extent of further manipulation of the cell culture and notification of the appropriate regulatory agency (ex. Department of Health, CDC).*

**MIC.61340 Standardized Red Cell Suspensions Phase I**

**Red cell suspensions that are used for quantitative serologic procedures are standardized (photometrically or with some other equivalent procedure).**

**Evidence of Compliance:**

- ✓ Written procedure for standardization of red cell suspensions

**MIC.61350 Agglutination/Lysis Criteria Phase I**

**Criteria for degrees of agglutination and lysis are defined for quantitative serologic procedures.**

**MIC.61360 Work Records Phase I**

**Worksheets and/or records indicate actual titers, when known, of reagents and control sera.**

**MIC.61370 Serologic Reaction Controls Phase II**

**Reactive and nonreactive controls are analyzed in serologic reactions for detection of antigens.**

*NOTE: Positive and negative controls must be run daily for immunofluorescent and immunochromatic testing when using pool reagents and for virus specific reagents, if performed.*

**Evidence of Compliance:**

- ✓ Written procedure for serological QC **AND**
- ✓ Records of serological QC results

**MIC.61380 Reagent Verification Phase II**

**Each new lot and shipment of reagents that detect multiple viruses are verified for each individual virus component prior to patient testing**

*NOTE: A pool reagent cannot be verified using only a pool control, as the reactivity of each virus specific component cannot be individually assessed. After initial verification, pool controls can be used for daily quality control of the pool reagent.*

**Evidence of Compliance:**

- ✓ Records of IF reagent verification, as applicable

**REFERENCES**

- 1) Ginocchio, CC. Quality Assurance in Clinical Virology. In: Spector S, Hodinka RL, Young SA, editors. *Clinical Virology Manual*. Fourth Edition. Washington: ASM Press; 2009.p. 3-17

## TESTS AND PROCEDURES

### Inspector Instructions:



- Sampling of virology test procedures
- Sampling of virology patient reports

**MIC.62400 Order Information Phase I**

**For viral screening tests by direct antigen detection (direct immunofluorescence or EIA), rapid cell culture or molecular methods, reports and test order information indicates the specific viruses sought/detected by the assay.**

*NOTE: For example, if the rapid cell culture method is used to detect seven different respiratory viruses, then the report must specifically indicate which viruses are included in the screening. While the cell lines in use may permit the growth of other viruses, such as enterovirus, these need not be specifically enumerated in the report, unless detected in a given sample.*

**MIC.62500 Isolation Policies Phase I**

**There are written policies for viral testing based upon such criteria as specimen source, diagnosis, suspected virus(es) and season.**

*NOTE: Testing algorithms can vary depending on specimen type, virus(es) suspected, immune status of the patient, and season. For example, routine rapid EIA testing for influenza is not recommended outside of the respiratory virus season due to low specificity.*

#### REFERENCES

- 1) Leland DS, Ginocchio CC. Role of cell culture for virus detection in the age of technology. *Clin Microbiol Rev* 2007 January; 20(1):49-78

#### MIC.62550 CMV Antigenemia

Phase I

**There are written policies for the acceptance and rejection of samples for CMV antigenemia testing.**

*NOTE: Policies must be in place to deal with suboptimal specimens, such as those whose receipt in the laboratory exceeds the time frame for optimal test sensitivity, or those samples with low cellularity. If it is not possible to recollect a sample, and such specimens are tested, results must be accompanied by a comment noting the potential reduction in test reliability due to inappropriate sample storage and/or delay in processing.*

#### REFERENCES

- 1) Boeckh M, Boivin G. Quantitation of cytomegalovirus: methodologic aspects and clinical applications. *Clin Microbiol Rev* 1998 July;11(3):533-54

#### MIC.62560 Tzanck Test

Phase I

**Slides for the Tzanck test are of sufficient quality for diagnosis.**

*NOTE: Slides must be of adequate technical quality to be diagnostically useful. The laboratory should have access to a photographic atlas appropriate to the diagnostic purpose and method (eg, Papanicolaou or Giemsa) in use.*

## MOLECULAR MICROBIOLOGY

*All requirements in this checklist section apply to nonwaived molecular-based infectious disease testing. The following requirements apply to waived molecular-based infectious disease testing: MIC.63252, MIC.63318, MIC.65620, and MIC.66100.*

Laboratories that use this section of the checklist must also comply with all applicable requirements included in the General section of the Microbiology checklist.

## QUALITY MANAGEMENT

### Inspector Instructions:



- Sampling of QM statistics/turnaround time data



- What is your course of action when monitored statistics increase above the expected positive rate?

**MIC.63252 Quality Monitoring****Phase I**

**There are written procedures to monitor for the presence of false positive results (eg, due to nucleic acid contamination) for all molecular microbiology tests.**

*NOTE: Examples of this may include review of summary statistics (eg, monitoring percentage of results that are positive for Chlamydia trachomatis and/or Neisseria gonorrhoeae for an increase above historical positive rate within a run or over multiple runs), unexpected increase in positive results for seasonal pathogens outside of the standard epidemiology, performance of wipe testing, review and investigation of physician complaints on false positive results, use of process controls to minimize risk of contamination.*

**Evidence of Compliance:**

- ✓ Written procedure for monitoring for presence of false positive results **AND**
- ✓ Records of data review, wipe testing, statistical data, and, evaluation and corrective action if indicated

**REFERENCES**

- 1) Borst A, Box AT, Fluit AC. False-positive results and contamination in nucleic acid amplification assays: suggestions for a prevent and destroy strategy. *Eur J Clin Microbiol Infect Dis.* 2004; 23(4):289-99.
- 2) Cone RW, Hobson AC, Huang ML, Fairfax MR. Polymerase chain reaction decontamination: the wipe test. *Lancet.*1990; 336:686-687.
- 3) McCormack JM, Sherman ML, Maurer DH. Quality control for DNA contamination in laboratories using PCR- based class II HLA typing methods. *Hum Immunol.* 1997;54:82-88.

**MIC.63256 Turnaround Times****Phase I**

**The laboratory has defined sample turnaround times that are appropriate for the intended purpose of the test and performs ongoing monitoring for compliance.**




*NOTE: There are certain clinical situations in which rapid completion is essential. An example is detection of HSV in CSF.*

**Evidence of Compliance:**

- ✓ Written procedure defining turnaround time and mechanism for monitoring **AND**
- ✓ Records showing that defined turnaround times are routinely met

## SPECIMEN HANDLING & PROCESSING

### Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of molecular microbiology specimen handling and processing policies and procedures</li> </ul>
 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Patient specimens/aliquots (storage, labeling)</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• What is your process for identification of patient specimens and aliquots?</li> </ul>

#### MIC.63318 Specimen Handling Procedures

Phase II

**There are written procedures to prevent specimen loss, alteration, or contamination during collection, transport, processing and storage.**

*NOTE: Specimen collection, processing and storage must follow manufacturer's instructions and limit the risk of preanalytical error. For example, there must be a procedure to ensure absence of cross-contamination of samples during processing/testing for amplified molecular testing using liquid based cervical cytology (LBC) specimens; alternatively, an aliquot can be removed for amplified molecular testing prior to LBC processing.*

*NOTE: The remaining items in this section do not apply to waived testing.*

#### MIC.63324 Residual Samples

Phase II

**If residual samples are used for amplification-based testing, policies and procedures ensure absence of cross-contamination of samples.**

*NOTE: An example of a residual sample is a liquid based cytology sample that is tested post-cytologic processing using amplified *C. trachomatis* or *N. gonorrhoeae* tests.*

#### MIC.63327 Derivative Material Identification

Phase II

**There is a system to positively identify derivative material (eg, nucleic acid extracts) from patient specimens from nucleic acid extraction through all phases of subsequent testing and storage.**

#### MIC.63328 Specimen Processing/Storage

Phase II



**Patient samples are processed promptly or stored appropriately to minimize degradation of nucleic acids.**

*NOTE: Frost-free freezers may not be used to store patient samples unless freezer temperature is monitored by a continuous monitoring system, or a maximum/minimum thermometer.*

**Evidence of Compliance:**

- ✓ Written procedure for processing and storage of specimens

**REFERENCES**

- 1) Farkas DH, Kaul KL, Wiedbrauk DL, *et al.* Specimen Collection and Storage for Diagnostic Molecular Pathology Investigation. *Arch Pathol Lab Med.* 1996;120:591-596
- 2) Kiechle FL, Kaul KL, Farkas DH. Mitochondrial Disorders: Methods and Specimen Selection for Diagnostic Molecular Pathology. *Arch Pathol Lab Med.* 1996;120:597-603
- 3) Farkas DH, Drevon AM, Kiechle FL, *et al.* Specimen Stability for DNA-based Diagnostic Testing. *Diag Molec Pathol.* 1996;5(4):227-235

**\*\*NEW\*\* 09/22/2021**

**MIC.63340 Extracted Nucleic Acid Specimens**

**Phase II**

**If extracted nucleic acid is accepted as a specimen type, the laboratory has a written policy that isolation of nucleic acids for clinical testing occurs in a CLIA-certified laboratory or a laboratory meeting equivalent requirements as determined by the CAP and/or the CMS. This policy is clearly displayed to ordering clients.**

*NOTE: All clinical testing must be performed in CLIA-certified laboratories or laboratories meeting equivalent requirements (refer to GEN.41350). This includes all components of testing that may impact the quality of the test result, including isolation or extraction of nucleic acids. Laboratories may choose to have referring clients formally attest that extracted nucleic acid submitted for testing has been isolated or extracted in an appropriately qualified laboratory.*

**Evidence of Compliance:**



- ✓ Written statement on the test requisition, test catalog, or policy available to referring clients stating that the laboratory only accepts isolated or extracted nucleic acids for which extraction or isolation is performed in an appropriately qualified laboratory

## ASSAY VALIDATION AND VERIFICATION - NONWAIVED TESTS

*Additional requirements and details for validation and verification of nonwaived methods are found in the Test Method Validation and Verification - Nonwaived Test section of the All Common Checklist.*

*For waived tests, refer to the Waived Test Implementation section of the All Common Checklist.*

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of assay verification and validation studies</li> </ul>
	<ul style="list-style-type: none"> <li>• How does your laboratory validate assay performance for use of different specimen types or collection devices?</li> <li>• If specimens are tested in pools, how do you ensure the appropriateness of the pooling strategy?</li> </ul>

**\*\*REVISED\*\* 09/22/2021**

**MIC.64770 Validation Studies - Specimen Type/Collection Device****Phase II**

**If the laboratory tests specimen types or uses collection devices other than those listed in the package insert, the laboratory performs validation studies to document adequate performance of the test with those specimen types or collection devices.**

*NOTE: Any change to the manufacturer's supplied or recommended specimen collection devices, solutions, or reagents or modifications to the assay as set forth in the manufacturer's labeling and instructions is considered a modification. It may include a change to specimen type, instrumentation or procedure that could affect its performance specifications for sensitivity, specificity, accuracy, or precision or any change to the stated purpose of the test, its approved test population, or any claims related to interpretation of the results. Refer to the section Test Method Validation and Verification in the All Common Checklist for additional details.*

*Results from tests performed on specimen types not listed in the package insert may be reported without complete validation only if the specimen type is encountered rarely, precluding an adequate number for validation studies. Under these circumstances, the test report must include a disclaimer stating that the specimen type has not been validated*

**Evidence of Compliance:**

- ✓ Records of validation studies for modified FDA-cleared/approved assays for different specimen types and collection devices

**REFERENCES**

- 1) Lawrence Jennings, Viviana M. Van Deerlin, Margaret L. Gulley (2009) Recommended Principles and Practices for Validating Clinical Molecular Pathology Tests. *Archives of Pathology & Laboratory Medicine*: Vol. 133, No. 5, pp. 743-755.
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1253(b)(2)].

**MIC.64790 Validation of Specimen Pooling****Phase II**

**If the laboratory chooses to pool specimens for tests performed using test systems that have not been FDA-cleared/approved for that purpose (eg, *Chlamydia trachomatis*/*Neisseria gonorrhoeae* NAAT on pooled urine specimens), the laboratory validates the testing procedure for pooled specimens, including limit of detection (sensitivity), reproducibility, and accuracy (method comparison).**

*NOTE: As part of the method comparison, the results for pooled specimens must be compared to the single (non-pooled) results using an adequate number of clinical specimens covering the entire range of organism concentration seen in clinical specimens (ie, low and high positive specimens).*

*Any clinical claim regarding the efficacy of pooling must be validated (see COM.40640).*

**REFERENCES**

- 1) Centers for Disease Control and Prevention. Screening Tests to Detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Infections—2002. *MMWR* 2002;51(No. RR-15).

**\*\*REVISED\*\* 06/04/2020****MIC.64960 Validation or Verification Studies - Specimen Selection****Phase II**

**Validation or verification studies were performed with an adequate number and representative (reasonable) distribution of samples for each type of specimen (eg, blood, fresh/frozen tissue, paraffin-embedded tissue).**

*NOTE: The number of specimens to be included in a verification study for each specimen type is to be determined by the laboratory director. Verification studies must include the following:*

- *Evaluation of adequate numbers of positive and negative specimens across the specimen types to be used in the assay (eg, urine, genital swabs, rectal swabs, pharyngeal swabs), even if they are obtained with the same collection device*

- *Evaluation of local specimens representing the strains or genotypes, as appropriate, if geographic variations are known or expected in the strains or genotype of organisms tested*

*Validation studies, by definition, are more rigorous assessments of non-FDA cleared/approved tests or specimens, requiring multiple positive and negative specimens representing all specimen types and strain/genotype variations.*

*For qualitative tests, a verification or validation study includes comparison of positive and negative test results to a comparable test method. For quantitative tests, the manufacturer's limit of detection, reportable range and precision must be validated or verified by the laboratory, as well as a comparison of patient test results across the reportable range of the test. Specimens for the validation or verification study can include quantitative external control material, cultured organisms (quantified) and proficiency testing material, and must include patient specimens.*

*Refer to the section "Test Method Validation and Verification" in the All Common Checklist for additional details.*

**Evidence of Compliance:**

- ✓ Records of validation and verification studies

**MIC.64975 Modified Cut-Off**

**Phase II**

**If the laboratory has modified the manufacturer's cut off-value for a positive result, the new cut-off value has been validated.**

**Evidence of Compliance:**

- ✓ Records of cut-off validation when different cut-off values are utilized

## **QUANTITATIVE ASSAYS: CALIBRATION & STANDARDS - NONWAIVED TESTS**

*This section of the checklist only applies to quantitative tests for which appropriate external materials exist.*

*This introduction discusses the processes of calibration, calibration verification, and analytic measurement range (AMR) verification.*

*CALIBRATION: The process of adjusting an instrument or test system to establish a relationship between the measurement response and the concentration or amount of the analyte that is being measured by the test procedure.*

*CALIBRATION VERIFICATION: The process of confirming that the current calibration settings for each analyte remain valid for a test system.*

*Each laboratory must define limits for accepting or rejecting results of the calibration verification process. Calibration verification can be accomplished in several ways. If the manufacturer provides a calibration validation or verification process, it must be followed. Other techniques include (1) assay of the current calibration materials as unknown specimens, and (2) assay of matrix-appropriate materials with target values that are specific for the test system.*

### **MATERIALS SUITABLE FOR CALIBRATION VERIFICATION**

*Materials for calibration verification must have a matrix appropriate for the clinical specimens assayed by that method, and target values appropriate for the measurement system. Suitable materials may include, but are not limited to:*

1. *Calibrators used to calibrate the analytical measurement system*
2. *Materials provided by the analytical measurement system vendor for the purpose of calibration verification*

3. *Previously tested unaltered patient/client specimens*
4. *Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method,*
5. *Proficiency testing material or proficiency testing validated material with matrix characteristics and target values appropriate for the method*

*In general, routine control materials are not suitable for calibration verification, except in situations where the material is specifically designated by the method manufacturer as suitable for verification of the method's calibration process.*

*ANALYTICAL MEASUREMENT RANGE (AMR): The range of analyte values that a method can directly measure on the specimen without any dilution, concentration, or other pretreatment that is not part of the usual assay process.*

#### **LINEARITY AND THE AMR**

*Linearity is a fundamental characteristic of many analytic measurement methods, whereby there is a straight-line relationship between "true" analyte concentrations and measured concentrations. In this context, linearity refers to the relationship between the predicted and observed measurement results and not to the relationship between instrument signal output and analyte concentration. For most assays, this relationship is linear within the AMR.*

#### **AMR VERIFICATION**





*Laboratories are required to verify that the appropriate relationship is maintained over the AMR. Laboratories may verify and use an AMR that is narrower than the range defined by the manufacturer. This may be appropriate when materials available for method validation and/or AMR verification are not available to verify the full range claimed by the manufacturer, or reporting values across the full range defined by the manufacturer is not clinically relevant. For many assays, results beyond the AMR can be reported through dilution studies (see CHM.13720).*

*Minimum requirements for AMR verification can be met by using matrix appropriate materials, which include low, mid and high concentration or activity range of the AMR with recovery of results that fall within a defined range of the target value. Records of AMR verification must be available.*

#### **CLOSENESS OF SAMPLE CONCENTRATIONS OR ACTIVITIES TO THE UPPER AND LOWER LIMITS OF THE AMR**

*When verifying the AMR, it is required that materials used are near the upper and lower limits of the AMR. Factors to consider in verifying the AMR are the expected analytic imprecision near the limits, the clinical impact of errors near the limits, and the availability of test specimens near the limits. It may be difficult to obtain specimens with values near the limits for some analytes. In such cases, reasonable procedures should be adopted based on available specimen materials. The closeness of sample concentrations or activities to the upper and lower limits of the AMR are defined at the laboratory director's discretion. The method manufacturer's instructions for verifying the AMR must be followed, when available. The laboratory director must define limits for accepting or rejecting verification tests of the AMR.*

## Inspector Instructions:

 <p>READ</p>	<ul style="list-style-type: none"> <li>• Sampling of calibration and AMR policies and procedures</li> <li>• Sampling of calibration/calibration verification records</li> <li>• Sampling of AMR verification records</li> </ul>
 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Sampling of calibration materials (labeling, storage, quality)</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• What is your course of action if calibration is unacceptable?</li> <li>• When was the last time you performed a calibration procedure and how did you verify the calibration?</li> <li>• What is your course of action when results fall outside the AMR?</li> </ul>
 <p>DISCOVER</p>	<ul style="list-style-type: none"> <li>• Further evaluate the responses, corrective actions, and resolutions for unacceptable calibration, unacceptable calibration verification, and results outside the AMR</li> </ul>

### MIC.65100 Calibration Procedures

Phase II

**Calibration procedures for each test system are appropriate, and the calibration records are reviewed for acceptability.**

*NOTE: Calibration must be performed following manufacturer's instructions, at minimum, including the number, type, and concentration of calibration materials, frequency of calibration, and criteria for acceptable performance. Calibration procedures are typically specified in the manufacturer's instructions but may also be established by the laboratory.*

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare & Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7165 [42CFR493.1217]
- 2) Department of Health and Human Services, Centers for Medicare & Medicaid Services. Medicare, Medicaid and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications; final rule. *Fed Register*. 2003(Jan 24):3707 [42CFR493.1255]
- 3) Clinical and Laboratory Standards Institute. *Evaluation of Matrix Effects; Approved Guideline*. 3<sup>rd</sup> ed. CLSI Document EP14-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2014
- 4) Miller WG. Quality Control In: Henry's Clinical Diagnosis and Management by Laboratory Methods, 21st Edition, ed. by McPherson RA and Pincus MR, Saunders Elsevier 2007, p99-111

### MIC.65120 Test Calibration - FDA-Cleared/Approved Tests

Phase II

**For FDA-cleared/approved quantitative tests, test calibration is performed according to the manufacturer's specifications.**

*NOTE: Calibrators must be run following the manufacturer's recommendations. Some systems may use electronic calibration data.*

#### Evidence of Compliance:

- ✓ Records of calibration

### MIC.65130 Calibration Materials - LDT and Modified FDA-Cleared/Approved Tests

Phase II

**High quality materials with test system and matrix-appropriate target values are used for calibration and calibration verification for laboratory-developed (LDT) and modified FDA-cleared/approved tests whenever possible.**

*NOTE: If a different matrix is used for recalibration of subsequent (different) reagent lots, its equivalence to the test sample matrix must be established.*

*For example, if multiple specimen types are tested in a quantitative test, the test calibration must encompass the range for all expected values for each specimen type.*

**Evidence of Compliance:**

- ✓ Written policy defining the use of appropriate calibration/calibration verification materials

**REFERENCES**

- 1) Clinical and Laboratory Standards Institute. *Evaluation of Matrix Effects; Approved Guideline*. 3<sup>rd</sup> ed. CLSI Document EP14-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2014
- 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1255]

**MIC.65140 Calibration Materials - Laboratory Developed Tests**

**Phase II**

**The quality of all calibration materials used for laboratory-developed tests is evaluated and recorded.**

*NOTE: Commercial standards used to prepare calibrators require certificates of analysis. The laboratory must evaluate the accuracy of a new lot of calibrators by checking the new lot against the current lot.*

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988, final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1255]

**MIC.65145 Recalibration/Calibration Verification Criteria**

**Phase II**

**Criteria are established for frequency of recalibration or calibration verification, and the acceptability of results.**

*NOTE: Laboratories must either recalibrate or perform calibration verification at least every six months and if any of the following occur:*

1. *At changes of reagent lots unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client results*
2. *If QC shows an unusual trend or shift or is outside acceptable limits and the system cannot be corrected to bring control values into the acceptable range*
3. *After major preventive maintenance or change of a critical instrument component*
4. *When recommended by the manufacturer*

*Single use devices, and other test devices that do not allow user calibration, do not require calibration verification.*

**Evidence of Compliance:**

- ✓ Written policy defining the method, frequency and limits of acceptability of calibration verification for each instrument/test system **AND**
- ✓ Records of calibration verification at defined frequency

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3707[42CFR493.1255(b)(3)]
- 2) Miller WG. Quality control. In: Henry's Clinical Diagnostic and Management by Laboratory Methods, 21st Edition, ed McPherson RA, Pincus MR. Saunders Elsevier, 2007: 99-111.



**MIC.65150 Recalibration****Phase II**

**The system is recalibrated when calibration verification fails to meet the established written criteria of the laboratory.**

*NOTE: An indication of a potential calibration failure would be external or kit controls with values that repeatedly fall outside of the established control range.*

**Evidence of Compliance:**

- ✓ Written policy defining criteria for recalibration **AND**
- ✓ Records of recalibration, if calibration or calibration verification has failed

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3707[42CFR493.1255(b)(3)].

**MIC.65160 AMR Verification****Phase II**

**Verification of the analytical measurement range (AMR) is performed at least every six months and following defined criteria. Records are retained.**

*NOTE: The AMR must be verified at least every six months after a method is initially placed in service and if any of the following occur:*

1. *At changes of reagent lots unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client results, and the range used to report patient/client test data*
2. *If QC shows an unusual trend or shift or is outside acceptable limits, and the system cannot be corrected to bring control values into the acceptable range*
3. *After major preventive maintenance or change of a critical instrument component*
4. *When recommended by the manufacturer*

*It is not necessary to independently verify the AMR if the calibration of an assay includes calibrators that span the full range of the AMR, with low, midpoint and high values (ie, three points) and the system is calibrated at least every six months. A one-point or two-point calibration does not include all of the necessary points to validate the AMR.*

**Evidence of Compliance:**

- ✓ Written policy defining the method and frequency performed **AND**
- ✓ Records of AMR verification at least every six months

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1255]

**MIC.65170 AMR Verification Materials****Phase II**

**Verification of the analytical measurement range (AMR) is performed with matrix-appropriate materials, which at a minimum, include low, mid and high range of the AMR, and appropriate acceptance criteria are defined.**

*NOTE: The matrix of the sample (ie, the environment in which the sample is suspended or dissolved) may influence the measurement of the analyte. In many cases, the method manufacturer will recommend suitable materials. Other suitable materials for AMR verification include the following:*

1. *Linearity material of appropriate matrix, eg, CAP CVL Survey-based or other suitable linearity verification material*
2. *Previously tested patient/client specimens, that may be altered by admixture with other specimens, dilution, spiking in known amounts of an analyte, or other technique*



3. *Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method*
4. *Patient samples that have reference method assigned target values.*
5. *Control materials, if they adequately span the AMR and have method specific target values*

#### Evidence of Compliance:

- ✓ Written policy for AMR verification defining the types of materials used and acceptability criteria

#### REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3707 [42CFR493.1255]
- 2) Shah VP, Midha KK, Dighe S, et al. Bioanalytical Method Validation - *Pharm Res*.1992;9(4):588–92.
- 3) Hartmann C, Smeyers-Verbeke J, Massart DL, McDowall RD. Validation of bioanalytical chromatographic methods. *J Pharm Biomed Anal*. 1998;17(2):193–218.
- 4) Findlay JW, et al. Analytical Methods Validation - Bioavailability, Bioequivalence and Pharmacokinetic Studies. *Pharm Res*. 2000;17(12):1551-7.
- 5) Killeen AA, Long T, Souers R, Styler P, Ventura CB, Klee GG. Verifying Performance Characteristics of Quantitative Analytical Systems: Calibration Verification, Linearity, and Analytical Measurement Range. *Arch Pathol Lab Med*. 2014;138(9): 1773-81.




## QUALITY CONTROL - NONWAIVED TESTS

*Controls are samples that act as surrogates for patient/client specimens. They are processed like a patient/client sample to monitor the ongoing performance of the entire analytic process in every run.*

*Qualitative molecular tests typically include positive and negative controls and, in some instances, a sensitivity control to show that low level target is detectable. Quantitative tests typically include a negative control and at least two levels of control at relevant decision points to verify that calibration status is maintained within acceptable limits.*

*For waived tests, refer to the Quality Control - Waived Tests section of the checklist.*

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of molecular microbiology QC policies and procedures</li> <li>• Sampling of molecular microbiology QC records</li> </ul>
	<ul style="list-style-type: none"> <li>• How would you investigate results of negative controls that test as positive or equivocal?</li> <li>• What is your course of action when monthly precision data changes significantly from the previous month's data?</li> </ul>
	<ul style="list-style-type: none"> <li>• Review a sampling of QC data over the previous two-year period. Select several occurrences in which QC is out of range and follow records to determine if the steps taken follow the laboratory procedure for corrective action</li> <li>• Use QC data to identify tests that utilize internal quality control processes to confirm that any individualized quality control plan (IQCP) is used as approved by the laboratory director</li> </ul>

**\*\*REVISED\*\* 09/22/2021**

**MIC.65200 Daily QC - Molecular-based Testing - Nonwaived Tests**

**Phase II**

**For molecular-based quantitative and qualitative tests, controls are run at least daily, or more frequently if specified in manufacturer's instructions, laboratory procedure, or the CAP Checklist, and when changes occur that may impact patient results.**

*NOTE: The laboratory must define the number and type of quality control used and the frequency of testing in its quality control procedures. Control testing is not required on days when patient testing is not performed.*

*Controls must be run prior to resuming patient testing when changes occur that may impact patient results, including after a change of analytically critical reagents, major preventive maintenance, change of a critical instrument component, or with software changes, as appropriate.*

*Daily quality control must be run as follows:*

- *Quantitative tests - three controls at least daily, including a negative control, a low-positive control and a high-positive control, except where a specific exception is given in this checklist*
- *Qualitative tests - a positive and negative control at least daily*

*Controls should verify assay performance at relevant decision points. The selection of these points may be based on clinical or analytical criteria.*

*If an internal quality control process (eg, electronic/procedural/built-in) is used instead of an external control material to meet daily quality control requirements, the laboratory must have an individualized quality control plan (IQCP) approved by the laboratory director defining the control process, including the frequency and use of external and internal controls. At a minimum, external control materials must be analyzed with new lots and shipments of reagents or more frequently if indicated in the manufacturer's instructions. Please refer to the IQCP section of the All Common Checklist for the eligibility of tests for IQCP and requirements for implementation and ongoing monitoring of an IQCP.*

*Controls must assess adequacy of extraction and amplification, eg, positive and negative controls that go through the entire testing process.*

- *Laboratories performing tests using an IQCP may define their own quality control procedures to monitor the extraction and amplification phases based on the risk assessment performed by the laboratory and the manufacturer's instructions.*
- *If an IQCP is not in place that monitors the extraction and amplification processes, the following must be followed:*
  1. *An extraction control must be used for each run with the positive control(s).*
  2. *If the samples from an extraction batch are tested over multiple amplification runs, each amplification run must have its own amplification control. A single extraction control need only be tested in one of the amplification runs.*
  3. *If samples from multiple extraction batches are tested in a single amplification run, each extraction batch needs an extraction control. All extraction controls must be tested in a single amplification run. A single amplification control is sufficient.*

#### **Evidence of Compliance:**

- ✓ *Written QC procedures*
- ✓ *Records of QC results including external and electronic/procedural/built-in control systems **AND***
- ✓ *Manufacturer's product insert or manual*

#### **REFERENCES**

- 1) *Clinical and Laboratory Standards Institute (CLSI). **Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline.** 4th ed. CLSI document C24-ED4. Clinical and Laboratory Standards Institute, Wayne, PA, 2016.*
- 2) *Ye JJ, et al. Performance evaluation and planning for patient/client-based quality control procedures. **Am J Clin Pathol.** 2000;113:240-248*
- 3) *Department of Health and Human Services, Centers for Medicare and Medicaid Services. **S & C: 16-20-CLIA: Policy Clarification on Acceptable Control Materials Used when Quality Control (QC) is Performed in Laboratories.** April 8, 2016.*

**MIC.65220 Multiplex QC - Nonwaived Tests** **Phase II**

**For multiplex tests, controls for each analyte are either included in each run or rotated so that all analytes are tested periodically.**

*NOTE: If an internal quality control process (eg, electronic/procedural/build-in) is used instead of an external control material to meet daily quality control requirements, the laboratory must have an individualized quality control plan (IQCP) approved by the laboratory director defining the control process, including the frequency and use of external and internal controls. At a minimum, external control materials must be analyzed with new lots and shipments of reagents or more frequently if indicated in the manufacturer's instructions. Please refer to the IQCP section of the All Common Checklist for the eligibility of tests for IQCP and requirements for implementation and ongoing monitoring of an IQCP.*

See also MIC.65200 Daily QC - Molecular-based Testing.

**Evidence of Compliance:**

- ✓ Written policy defining multiplex test QC **AND**
- ✓ Records of multiplex test QC

**REFERENCES**

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. S & C: 16-20-CLIA: Policy Clarification on Acceptable Control Materials Used when Quality Control (QC) is Performed in Laboratories. April 8, 2016.

**MIC.65230 Control and Standard Acceptability Limits** **Phase II**

**Acceptability limits are defined for all control procedures, control materials, and standards.**

*NOTE: These controls must be appropriate for the range of sensitivities tested and should, ideally, focus on result ranges that are near clinical decision points.*

**Evidence of Compliance:**

- ✓ Written policy defining acceptability limits

**MIC.65240 QC Statistics** **Phase I**

**For quantitative assays, quality control statistics are calculated monthly to define analytic imprecision and to monitor trends over time.**

*NOTE: The laboratory must use statistical methods such as calculating SD and CV monthly to evaluate variance in numeric QC data.*

**Evidence of Compliance:**

- ✓ Written policy for monitoring of analytic imprecision including statistical analysis of data

**REFERENCES**

- 1) Mukherjee KL. Introductory mathematics for the clinical laboratory. Chicago, IL: American Society of Clinical Pathology, 1979:81-94
- 2) Barnett RN. Clinical laboratory statistics, 2nd ed. Boston, M; Little, Brown, 1979
- 3) Weisbrodt IM. Statistics for the clinical laboratory. Philadelphia, PA: JB Lippincott, 1985
- 4) Matthews DF, Farewell VT. Understanding and using medical statistics. NY, NY: Karger, 1988
- 5) Department of Health and Human Services, CMS. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7146 [42CFR493.1256(d)(10)(i)]
- 6) Ross JW, Lawson NS. Analytic goals, concentrations relationships, and the state of the art of clinical laboratory precision. *Arch Pathol Lab Med*. 1995;119:495-513
- 7) Clinical and Laboratory Standards Institute (CLSI). *Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline*. 4th ed. CLSI document C24-ED4. Clinical and Laboratory Standards Institute, Wayne, PA, 2016.
- 8) Brooks ZC, et al. Critical systematic error used of varied QC rules in routine chemistry. *Clin Chem*. 2000;46:A70

**MIC.65250 Inhibition Assessment** **Phase II**

**For assays without an internal control, the laboratory has a procedure to assess inhibition for each specimen type.**

*NOTE: Documentation of an acceptable inhibition rate may be provided by the manufacturer. If not, laboratories may test for inhibition by spiking an aliquot of the clinical specimen with target nucleic acid. This practice can be discontinued once the laboratory accumulates sufficient data showing that the inhibition rate falls within acceptable limits.*

*This requirement does not apply to probe-based solution hybridization methods (eg, Gen-Probe AccuProbe) performed without nucleic acid amplification.*

#### REFERENCES

- 1) Ballagi-Pordany A, Belek S. *Mol Cell Probes* 1996 Jun 10(3):159-64

### MIC.65260 Isolation/Preparation

Phase II

**The adequacy of nucleic acid isolation/preparation procedures is evaluated.**

*NOTE: Adequacy of nucleic acid isolation/preparation procedures (manual or automated) must be evaluated with each assay by the use of positive and negative controls run in parallel with patient samples. To the extent possible, controls must be processed through all steps of the assay, including the extraction phase.*

#### Evidence of Compliance:

- ✓ Written procedure for evaluating adequacy of nucleic acid **AND**
- ✓ Records of controls used to assess adequacy

### MIC.65270 Qualitative Cut-Off - Laboratory-Developed Test

Phase II

**For qualitative tests that use a cut-off value to distinguish positive from negative, the cut-off value is established initially, and verified with every change in lot or at least every six months.**

*NOTE: The limit of detection that distinguishes a positive from a negative result must be established or verified when the test is initially placed in service, and verified with every change in lot (eg, new master mix), instrument maintenance, or at least every six months thereafter. Note that a low-positive control that is close to the limit of detection can satisfy this checklist requirement, but must be external to the kit (eg, weak-positive patient sample or reference material prepared in appropriate matrix).*



#### Evidence of Compliance:

- ✓ Written procedure for initial establishment and verification of the cut-off value **AND**
- ✓ Records of initial establishment and verification at defined frequency

## REAGENTS

*For waived tests, refer to the Reagents section of the All Common Checklist.*

## Inspector Instructions:

 <p>OBSERVE</p>	<ul style="list-style-type: none"> <li>• Sampling of reagents/controls (storage, designated pre- and post-amplification)</li> </ul>
 <p>ASK</p>	<ul style="list-style-type: none"> <li>• How do you verify new multiplex lots/shipments?</li> </ul>

### MIC.65300 Reagent Storage

Phase II

**All test reagents and controls are stored properly and in a manner which minimizes target DNA/RNA contamination and degradation.**

*NOTE: Pre- and post-amplification reagents and controls must be stored under appropriate temperature and conditions in designated pre- and post-amplification areas. Temperature-sensitive reagents and/or controls may not be stored in frost-free freezers, unless either of the following conditions are met: 1) Reagent/control materials are kept in thermal containers and the laboratory can demonstrate that the function of these materials is not compromised; or 2) Freezer temperature is monitored by a continuous monitoring system, or a maximum/minimum thermometer.*

*Patient samples may be stored in a frost-free freezer only if the temperature is monitored in accordance with (2), above.*

#### Evidence of Compliance:

- ✓ Written policy defining storage requirements for reagents and controls

#### REFERENCES

- 1) Borst A, Box AT, Fluit AC. False-positive results and contamination in nucleic acid amplification assays: suggestions for a prevent and destroy strategy. *Eur J Clin Microbiol Infect Dis*. 2004 Apr;23(4):289-99. Epub 2004 Mar 10. Review. PMID: 15015033 [[PubMed](#) - indexed for MEDLINE]

### MIC.65320 New Reagent Lot - Multiplex Tests

Phase II

**For multiplex tests, at least two analytes are individually verified for each new shipment and lot, and the analytes verified are periodically rotated.**

*NOTE: A multiplex test simultaneously detects a defined set of analytes (eg, two or more pathogen-specific nucleic acid sequences) from a single run or cycle of the assay. Although a sample of analytes (at least two) may be used to verify each lot and shipment, the analytes verified must be rotated periodically as defined in laboratory procedure to assess all analytes in the multiplex test over time.*

#### Evidence of Compliance:

- ✓ Written procedure for new lot/shipment verification of each multiplex test **AND**
- ✓ Records of new lot and shipment verification

### MIC.65330 Current Primers/Probes - Laboratory-Developed Test

Phase II

**For tests developed by the laboratory, there are written policies and procedures to evaluate nucleic acid tests for compatibility with currently circulating microbial strains.**

*NOTE: This can include, but is not limited to in silico analysis of compatibility of primers and probes with their intended targets, surveying the literature for evidence of problems with the assay or description of a discovered target variation that might affect test performance of the assay. The performance of the assays in use should be assessed against newly described variants (eg, Influenza H1N1, EV-D68) if they occur in the patient population served by the laboratory.*

**MIC.65340 Probe Characteristics - Laboratory-Developed Test**

**Phase II**

**Information regarding the nature of any probe or primer used in a laboratory-developed test is sufficient to permit interpretation and troubleshooting of test results.**

*NOTE: Sequence and size data may not be available for commercially-obtained tests when this information is considered proprietary.*

**Evidence of Compliance:**

- ✓ Records of probe details including oligonucleotide sequence, target, concentration, or purity, as applicable

## INSTRUMENTS

Refer to the All Common Checklist for additional requirements on instrument and equipment.

### Inspector Instructions:



- Sampling of thermocycler well accuracy records

**MIC.65400 Thermocycler Temperature Checks**

**Phase II**

**Individual wells (or a representative sample thereof) of thermocyclers are checked for temperature accuracy before being placed in service and at least annually thereafter.**

*NOTE: A downstream measure of well-temperature accuracy (such as productivity of amplification) may be substituted to functionally meet this requirement. For closed systems this function should be performed as a component of the manufacturer-provided preventive maintenance.*

**Evidence of Compliance:**

- ✓ Written procedure for verification of thermocycler accuracy **AND**
- ✓ Records of thermocycler verification




**REFERENCES**

- 1) Saunders GC, *et al.* Interlaboratory study on thermal cycler performance in controlled PCR and random amplified polymorphic DNA analyses. *Clin Chem.* 2001;47:47-55
- 2) Clinical and Laboratory Standards Institute. *Establishing Molecular Testing in Clinical Laboratory Environments; Approved Guideline.* CLSI Document MM19-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2011.



## PROCEDURES & TESTS

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of test policies and procedures</li> <li>• Sampling of temperature incubation logs</li> <li>• Sampling of molecular microbiology policies for analytic interpretation</li> <li>• Sampling of HIV result reports</li> </ul>
	<ul style="list-style-type: none"> <li>• Physical containment practices (frequent glove change, separate manipulation of pre- and post-specimens, dedicated pipettes)</li> </ul>
	<ul style="list-style-type: none"> <li>• What is your course of action when the incubation temperature is out of range?</li> <li>• What follow-up action is taken when a negative result is obtained for Group B strep tests using direct DNA probes?</li> </ul>

#### MIC.65500 Carryover

#### Phase II

**Nucleic acid amplification procedures (eg, PCR) use appropriate physical containment and procedural controls to minimize carryover (false positive results).**

*NOTE: This item is primarily directed at ensuring adequate physical separation of pre- and post-amplification samples to avoid amplicon contamination. The extreme sensitivity of amplification systems requires that the laboratory take special precautions. For example, pre- and post-amplification samples should be manipulated in physically separate areas; gloves must be worn and frequently changed during processing; dedicated pipettes (positive displacement type or with aerosol barrier tips) must be used; and manipulations must minimize aerosolization. Enzymatic destruction of amplification products is often helpful, as is real-time measurement of products to avoid manual manipulation of amplification products.*

#### Evidence of Compliance:

- ✓ Written procedure that defines the use of physical containment and procedural controls as applicable to minimizing carryover

#### REFERENCES

- 1) Kwok S, Higuchi R. Avoiding false positives with PCR. *Nature* 1989;339:237-238
- 2) Clinical and Laboratory Standards Institute (CLSI). *Collection, Transport, Preparations, and Storage of Specimens for Molecular Methods*. 2nd ed. CLSI guideline MM13. Clinical and Laboratory Standards Institute, Wayne, PA; 2020.
- 3) Clinical and Laboratory Standards Institute. *Establishing Molecular Testing in Clinical Laboratory Environments; Approved Guideline*. CLSI Document MM19-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2011.
- 4) Clinical and Laboratory Standards Institute. *Molecular Diagnostic Methods for Infectious Diseases; Approved Guideline*. 3<sup>rd</sup> ed. CLSI document MM03-ED3. Clinical and Laboratory Standards Institute, Wayne, PA, 2015.

#### MIC.65520 Temperature Range Defined

#### Phase II

**For each step of the procedure all incubation temperatures are defined and recorded.**

*NOTE: For some instruments this function is performed automatically by software provided by the manufacturer.*



**MIC.65530 Incubations - Manufacturer's Specifications Phase II**

**Incubations (reactions) performed using baths/blocks/instruments meet manufacturer's specifications.**

*NOTE: Bath/blocks/instruments must be able to maintain the appropriate temperature throughout the incubation (reaction) within the range specified by the manufacturer of the assay.*

**Evidence of Compliance:**

- ✓ Written procedure to monitor incubation performance consistent with manufacturer's specifications

**MIC.65540 Nucleic Acid Extraction/Purification Phase II**

**Nucleic acids are extracted and purified by validated methods.**

*NOTE: These can include methods reported in the literature, an established commercially available kit or instrument, or a laboratory-developed method.*

**Evidence of Compliance:**

- ✓ Records to support nucleic acid extraction/purification is performed by a validated method

**MIC.65550 Melting Temperature - Laboratory-Developed Test Phase II**

**For laboratory-developed tests that generate a result based on a melting temperature (T<sub>m</sub>), appropriately narrow temperature ranges (+/- 2.5°C) are defined and recorded each day of use.**

**MIC.65560 Analytic Interpretation Phase II**

**There are written policies for analytic interpretation of results, as applicable.**

**MIC.65570 Calculating Quantitative Values Phase II**

**For quantitative molecular tests, methods for calculating quantitative values are adequately described and units clearly documented.**

**MIC.65580 Group B Screening - Non-amplified DNA Probe Phase II**

**Negative results obtained for Group B streptococcus intrapartum screening by a non-amplified DNA probe are followed up with a selective broth culture method.**

*NOTE: Direct DNA probing is insufficiently sensitive to detect light colonization and is therefore not adequate to replace culture based prenatal screening or to use in place of risk based approaches when culture results are unknown at the time of labor. An adequate rapid intrapartum test must be as sensitive as culture of vaginal and rectal swabs inoculated into selective broth media.*

**Evidence of Compliance:**

- ✓ Written policy requiring follow-up testing for negative Group B performed by non-amplified DNA probe

**REFERENCES**

- 1) Filkins L, Hauser J, Robinson-Dunn B, Tibbetts R, Boyanton B, Revell P. American Society for Microbiology Clinical and Public Health Microbiology Committee, Subcommittee on Laboratory Practices. Guidelines for the Detection and Identification of Group B *Streptococcus*. March 10, 2020.
- 2) The American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 485: Prevention of early-onset group B streptococcal disease in newborns. 2011;117(4):1019-27. doi: 10.1097/AOG.0b013e318219229b.

**\*\*REVISED\*\* 09/22/2021****MIC.65590 Group B Screening - Amplified Method****Phase II**

**A pre-enrichment step using a selective broth enrichment culture is performed for antepartum (36 to 38 weeks gestation) vaginal/rectal swab screening for Group B streptococci (GBS) colonization by nucleic acid amplification testing (NAAT).**

*NOTE: If direct sample testing is performed, without the broth enrichment step, all antepartum samples testing negative for GBS must be followed up with a selective enrichment broth step in conjunction with culture or NAAT testing.*

*The utility of NAAT assays for intrapartum testing (ie, during active labor) remains unsettled. If used, it is recommended that testing only be considered for women not appropriately screened at 36 to 38 weeks and for whom no other clinical risk factors related to neonatal GBS infection are present during labor.*

**REFERENCES**

- 1) Filkins L, Hauser J, Robinson-Dunn B, Tibbetts R, Boyanton B, Revell P. American Society for Microbiology Clinical and Public Health Microbiology Committee, Subcommittee on Laboratory Practices. Guidelines for the Detection and Identification of Group B *Streptococcus*. March 10, 2020.

**MIC.65600 M. tuberculosis Molecular Testing****Phase II**

**When performing molecular testing for the detection of *M. tuberculosis* directly from clinical specimens, culture is performed on all samples regardless of the molecular test result.**

**Evidence of Compliance:**

- ✓ Patient reports or worksheets

**\*\*NEW\*\* 06/04/2020****MIC.65620 HIV Primary Diagnostic Testing - Supplemental and Confirmatory Testing****Phase I**

**The laboratory follows public health recommendations or guidelines for HIV primary diagnostic testing, including primary screening and additional (supplemental and/or confirmatory) testing.**

*NOTE: If additional testing after a primary screening test is recommended by public health authorities, the laboratory:*

- Performs additional testing reflexively if the specimen is suitable and the test is performed in house, or
- Sends additional testing to a referral laboratory if the specimen is suitable, or
- Provides guidance to providers on submission of additional specimens, if needed for supplemental or confirmatory testing.

*The US Centers for Disease Control and Prevention (CDC) and Association of Public Health Laboratories (APHL) provide recommendations for HIV testing. Guidelines and recommended algorithms can be found on the [CDC](#) and [APHL](#) websites.*

*This checklist item does not apply to the testing of individuals from whom human derived products for therapeutic use are being derived or other types of testing performed for the monitoring of HIV infection (eg, viral load, CD4 counts). Reporting HIV results to public health is not within the scope of this checklist item.*

**Evidence of Compliance:**

- ✓ Written policy for the performance of HIV testing **AND**
- ✓ Patient reports with initial screening results and reflexive testing results and/or guidance




**REFERENCES**

- 1) Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Available at <http://stacks.cdc.gov/view/cdc/23447>. Published June 27, 2014. Accessed 11/19/2019.

- 2) Association of Public Health Laboratories. Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm. January 2019. Available at [APHL Publications](#). Accessed 11/19/2019.

## ELECTROPHORESIS

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of electrophoresis test procedures</li> <li>• Sampling of melting temperature record monitoring</li> </ul>
	<ul style="list-style-type: none"> <li>• Autoradiographs/gel photographs (low background, clear signal absence of bubbles)</li> </ul>
	<ul style="list-style-type: none"> <li>• How is the endpoint of gel electrophoresis determined?</li> <li>• What criteria are used to interpret electrophoretic gels?</li> </ul>

#### MIC.65700 Molecular Weight Markers

Phase II

**Known molecular weight markers that span the range of expected bands are used for each electrophoretic run.**

#### Evidence of Compliance:

- ✓ Records of appropriate markers for each run



#### MIC.65720 Visual/Fluorescent Markers

Phase II

**Visual or fluorescent markers are used to determine the endpoint of gel electrophoresis.**

## MICROBIAL *IN SITU* HYBRIDIZATION (ISH)

### Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of ISH QC policies and procedures</li> <li>• Sampling of ISH QC records</li> </ul>
	<ul style="list-style-type: none"> <li>• What is your course of action when ISH results do not correlate with culture findings?</li> </ul>

**MIC.65800 ISH QC****Phase II**

**Appropriate positive and negative controls are run in parallel and results recorded for each microbial *in situ* hybridization (ISH) analysis.**

*NOTE: Laboratories should refer to the manufacturer's guidelines for the selection of appropriate controls. Quality control must be performed with every run, independent of the number of samples tested (ie, one sample or batch of several samples)*

**Evidence of Compliance:**

- ✓ Written policy for ISH QC consistent with manufacturer's guidelines

**REFERENCES**

- 1) Stefano, K., and J. J. Hyldig-Nielsen. 1997. Diagnostic applications of PNA oligomers. *In* S. A. Minden and L. M. Savage (ed.), Diagnostic gene detection & quantification technologies. IBC Library Series, Southborough, Mass
- 2) Perry-O'Keefe, H., S. Rigby, K. Oliveira, D. Sorensen, H. Stender, J. Coull, and J. J. Hyldig-Nielsen. 2001. Identification of indicator microorganisms using a standardized PNA FISH method. *J. Microbiol. Methods* 47:281-292. [[CrossRef](#)][[Medline](#)]
- 3) Oliveira, K., S. M. Brecher, A. Durbin, D. S. Shapiro, D. R. Schwartz, P. C. De Girolami, J. Dakos, G. W. Procop, D. Wilson, C. S. Hanna, G. Haase, H. Peltroche-Llacsahuanga, K. C. Chapin, M. C. Musgnug, M. H. Levi, C. Shoemaker, and H. Stender. 2003. Direct identification of *Staphylococcus aureus* from positive blood culture bottles. *J. Clin. Microbiol.* 41:889-891. [[Abstract/Free Full Text](#)]

**MIC.65820 QC Corrective Action****Phase II**

**Corrective action is documented when microbial ISH (*in situ* hybridization) results do not correlate with culture findings.**

*NOTE: Discordant findings should be promptly investigated for potential false positive or false negative results from reagent failure, technical error, interpretive error or cross-reactivity of probes.*




**REFERENCES**

- 1) Stefano, K., and J. J. Hyldig-Nielsen. 1997. Diagnostic applications of PNA oligomers. *In* S. A. Minden and L. M. Savage (ed.), Diagnostic gene detection & quantification technologies. IBC Library Series, Southborough, Mass
- 2) Perry-O'Keefe, H., S. Rigby, K. Oliveira, D. Sorensen, H. Stender, J. Coull, and J. J. Hyldig-Nielsen. 2001. Identification of indicator microorganisms using a standardized PNA FISH method. *J. Microbiol. Methods* 47:281-292. [[CrossRef](#)][[Medline](#)]
- 3) Oliveira, K., S. M. Brecher, A. Durbin, D. S. Shapiro, D. R. Schwartz, P. C. De Girolami, J. Dakos, G. W. Procop, D. Wilson, C. S. Hanna, G. Haase, H. Peltroche-Llacsahuanga, K. C. Chapin, M. C. Musgnug, M. H. Levi, C. Shoemaker, and H. Stender. 2003. Direct identification of *Staphylococcus aureus* from positive blood culture bottles. *J. Clin. Microbiol.* 41:889-891. [[Abstract/Free Full Text](#)]

## SEQUENCING

*The requirements in this section apply to a variety of methods that can be used for sequencing (eg, Sanger sequencing, pyrosequencing, next generation sequencing (NGS)). If NGS methods are used for infectious disease related testing (eg, sequences for specific organisms or taxonomic groups, assignment of drug resistance sequences, assignment of pathogenicity markers, or assignment of host response markers), the requirements in the Next Generation Sequencing section of the Molecular Pathology Checklist must be used in conjunction with these requirements for inspection.*

## Inspector Instructions:

	<ul style="list-style-type: none"> <li>• Sampling of sequencing policies and procedures</li> </ul>
	<ul style="list-style-type: none"> <li>• Manufacturer's interpretive software (most current version)</li> </ul>
	<ul style="list-style-type: none"> <li>• How does your laboratory detect cross-contamination of samples/amplicons? What action would you take if cross contamination is suspected?</li> </ul>

**MIC.65900 Sequencing Data Criteria Phase II**

**There are written criteria for the acceptability and interpretation of primary sequencing data.**

**MIC.65920 Sequencing Data Interpretation Phase II**

**There is a policy to assure that appropriate databases are used and updated for the interpretation of sequencing data.**

*NOTE: Data bases should be comprehensive and current.*

**MIC.65940 Alternative Sequencing Interpretive Databases Phase II**

**If the laboratory uses alternative sequence interpretive databases, either alone or in conjunction with manufacturer's software, the alternative databases have been validated for the interpretation of the sequence data.**

*NOTE: This validation can be completed using published literature that evaluates the interpretation of the sequence data (for example the ISA-USA resistance interpretation guidelines). If the use of alternative data bases is done by the clinician after laboratory reporting of sequence interpretation, this validation is not necessary.*

**Evidence of Compliance:**

- ✓ Records of validation study if alternative interpretive databases are utilized, if applicable

**MIC.65960 Sample/Amplicon Contamination Phase II**

**Procedures prevent or detect potential cross-contamination of samples and/or amplicons.**

*NOTE: Examples are the use of negative controls in each batch, the manufacturer's use of Uracil N-glycosylase (UNG), or the fingerprinting program provided by the manufacturer.*

**MIC.65980 Sample/Amplicon Contamination Phase II**

If results of fingerprint analysis or negative control indicate a potential for sample and/or amplicon contamination, the laboratory has a written procedure in place to investigate and resolve the problem.

**MIC.66000 Sequence Data Correlation****Phase II**

The sequence data are correlated with available phenotypic data.

**Evidence of Compliance:**

- ✓ Records of result review including correlation with phenotypic data

## RESULTS REPORTING

### Inspector Instructions:

**OBSERVE**

- Sampling of test reports (test methodology, clinical interpretation)

**MIC.66100 Final Report****Phase I**

The final report includes a summary of the test method and information regarding clinical interpretation if appropriate.

*NOTE: For example, when a test may be performed by either direct antigen or PCR, including the test method in the report is important information for interpreting the results.*