COLLEGE of AMERICAN PATHOLOGISTS

Master

Microbiology Checklist

CAP Accreditation Program

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Microbiology Checklist

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ON-LINE CHECKLIST AVAILABILITY

Participants of the CAP accreditation programs may download the checklists from the CAP website (www.cap.org) by logging into e-*LAB* Solutions. 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.

SUMMARY OF CHECKLIST EDITION CHANGES
Microbiology Checklist
08/21/2017 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 listing of requirements below is 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

Requirement	Effective Date
MIC.00375	08/17/2016
MIC.11395	08/17/2016
MIC.22675	08/17/2016
MIC.61060	08/21/2017

REVISED Checklist Requirements

Requirement	Effective Date
MIC.11025	08/17/2016
MIC.16605	08/17/2016
MIC.18976	08/17/2016
MIC.21240	08/17/2016
MIC.21813	08/17/2016
MIC.21910	08/17/2016
MIC.21943	08/21/2017
MIC.22140	08/17/2016

MIC.22610	08/17/2016
MIC.22640	08/17/2016
MIC.22700	08/17/2016
MIC.22830	08/17/2016
MIC.32100	08/17/2016
MIC.43100	08/17/2016
MIC.53050	08/21/2017
MIC.61140	08/21/2017
MIC.61210	08/17/2016
MIC.61310	08/17/2016
MIC.61370	08/21/2017
MIC.63220	08/17/2016
MIC.64760	08/21/2017
MIC.64770	08/21/2017
MIC.64960	08/21/2017
MIC.64968	08/21/2017
MIC.65120	08/21/2017
MIC.65130	08/21/2017
MIC.65140	08/21/2017
MIC.65200	08/17/2016
MIC.65320	08/17/2016
MIC.65330	08/21/2017
MIC.65340	08/21/2017
MIC.65550	08/21/2017
MIC.66120	08/21/2017

DELETED/MOVED/MERGED Checklist Requirements

Requirement	Effective Date
MIC.16275	08/20/2017
MIC.17000	08/20/2017
MIC.17050	08/20/2017
MIC.21840	08/16/2016
MIC.22710	08/20/2017
MIC.31660	08/16/2016
MIC.42450	08/16/2016
MIC.43150	08/16/2016
MIC.61330	08/20/2017
MIC.63282	08/16/2016
MIC.64631	08/16/2016
MIC.64730	08/20/2017
MIC.64810	08/20/2017
MIC.64815	08/20/2017
MIC.64840	08/20/2017
MIC.64860	08/20/2017
MIC.64880	08/20/2017
MIC.64884	08/20/2017
MIC.64886	08/20/2017
MIC.64920	08/20/2017
MIC.64926	08/20/2017
MIC.64938	08/20/2017
MIC.64952	08/20/2017
MIC.64964	08/20/2017
MIC.64972	08/16/2016
MIC.64976	08/16/2016
MIC.64980	08/20/2017
MIC.64984	08/16/2016

MIC.65000 08/20/2017

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.

Note for non-US laboratories: Checklist requirements apply to all laboratories unless a specific disclaimer of exclusion is stated in the checklist.

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:

	• Are proficiency testing samples tested to the same level as clinical specimens?
	• Select a representative clinical report of each culture type. Compare the extent of reporting for the relevant proficiency testing sample.

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 (e.g. "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.

*****NEW** 08/17/2016***
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 (e.g. bacteriology, mycology).

Evidence of Compliance:
- ✓ Records of proficiency testing performance

QUALITY MANAGEMENT AND QUALITY CONTROL

Inspector Instructions:

	• Sampling of QC policies and procedures • Sampling of QC records • Sampling of employee records of morphologic observation correlation
	• How do you determine when QC is unacceptable and when corrective actions are needed? • How do you ensure consistency among personnel performing microscopic morphology?
	• 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 • 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

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.

NOTE: The remaining requirements in this checklist on quality control do not apply to waived tests.

GENERAL ISSUES

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, recognizing that preanalytic and postanalytic variables may differ from those encountered with patients.

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.

NOTE: This includes, but is not limited to, antimicrobial susceptibility testing/identification (AST/ID) systems.

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**
- ✓ Evidence of corrective action taken when QC results are not acceptable

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 (e.g. 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 (e.g. trending for repeat failures, etc.).

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

*****REVISED** 08/17/2016***
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)].

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.11350 Morphologic Observation Assessment **Phase II**

The microbiology laboratory at least annually assesses morphologic observations among personnel performing Gram, trichrome and other organism stains, to ensure consistency.

NOTE: Suggested methods to accomplish this include:

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

Evidence of Compliance:

- ✓ Written procedure defining the method(s) and criteria used for evaluation of consistency **AND**
- ✓ Employee records of morphology assessment

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 incorporated into reporting patient and proficiency testing results even when commercial identification systems have not been updated.

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 Resource Committee provides periodic updates in taxonomy through educational challenges.

Additional information for specific specialties may be found 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://www.zipcodezoo.com
- 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/

REFERENCES
1) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline;* 2nd ed. CLSI document M45-ED3. Clinical and Laboratory Standards Institute, Wayne, PA, 2016.
2) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing;* 27th ed. CLSI supplement M100-S27. Clinical and Laboratory Standards Institute, Wayne, PA, 2017.

*****NEW** 08/17/2016***

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 (e.g. 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:

	• Sampling of specimen collection and handling policies and procedures • Sampling of requisitions for completeness
	• Sampling of microbiology specimens (transport media, timely delivery, labeling)
	• What is your course of action when you receive unacceptable microbiology specimens?

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 hrs 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 (*e.g.* CSF, wound cultures, anaerobes)**
6. **Method for preservation of specimens if processing is delayed (*e.g.* refrigeration of urines)**

NOTE: Manufacturer's recommendations must be followed when there is a delay in delivery or processing of specimens for automated instruments (e.g. 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; Approved Guideline.* CLSI document MM13-A (ISBN 1-56238-591-7). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2005.

REAGENTS - GENERAL

Inspector Instructions:

- Sampling of test procedures for QC
- Sampling of reagent QC records

Additional requirements are in the REAGENTS section of the All Common Checklist.

The following generic requirements apply to all subsections of the Microbiology Laboratory for nonwaived testing only.

MIC.14583 Direct Antigen Test QC **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 (e.g. 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 to address the use of the alternative control system. Please refer to the individualized Quality Control Plan 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)]

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)
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:

	• Sampling of pipette/diluter checks
	• Incubators (adequate space, maintained)

MIC.16150 Pipettors and Diluters **Phase II**

Pipettes, microtiter diluters or automatic dispensers that are used for quantitative dispensing of material are checked for accuracy and reproducibility at defined intervals (at least annually), with results recorded.

NOTE: Pipette checks must be performed following manufacturer's instructions, at minimum, and as defined in laboratory procedure.

This requirement is not applicable for precalibrated inoculation loops that are used in the direct plating of clinical specimens such as urine cultures.

Evidence of Compliance:

✓ Written procedure detailing method for checking the accuracy and reproducibility of pipettes

REFERENCES
1) Curtis RH. Performance verification of manual action pipets. Part I. *Am Clin Lab. 1994*;12(7):8-9
2) Curtis RH. Performance verification of manual action pipets. Part II. *Am Clin Lab. 1994*;12(9):16-17
3) Perrier S, *et al*. Micro-pipette calibration using a ratiometric photometer-reagent system as compared to the gravimetric method. *Clin Chem.* 1995;41:S183
4) Clinical and Laboratory Standards Institute. *Laboratory Instrument Implementation, Verification, and Maintenance; Approved Guideline.* CLSI Document GP31-A. Clinical and Laboratory Standards Institute, Wayne, PA; 2009.
5) Johnson B. Calibration to dye for: Artel's new pipette calibration system. *Scientist.* 1999;13(12):14
6) Connors M, Curtis R. Pipetting error: a real problem with a simple solution. Parts I and II. *Am Lab News.* 1999;31(13):20-22
7) Skeen GA, Ashwood ER. Using spectrophotometry to evaluate volumetric devices. *Lab Med.* 2000;31:478-479

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:

	• Sampling of mass spectrometer policies and procedures • Identification criteria compliance • Sampling of calibration and control records
	• How does your laboratory verify assay performance each day of use?

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 run each day of patient testing, with each change in target plate, or according to manufacturer's recommendations and these records are maintained.

NOTE: Acceptable tolerance limits for calibration parameters must be defined, and records maintained.

Evidence of Compliance:
- ✓ Records of calibration

*****REVISED** 08/17/2016***
MIC.16605 Mass Spectrometer Controls **Phase II**

Appropriate control organisms or calibrators are tested on each day of patient testing.

NOTE: Appropriate controls would include at least one bacterium, with a representative yeast and mycobacterium also being run if these organisms are being tested for that day/routinely. For FDA-approved platforms, the organisms or calibrator(s) required by the manufacturer must be used.

For laboratory developed tests, choice 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. An extraction control should be included if any of the organisms being tested are run with extraction.

In formats of testing where a target is reused, a blank control needs to be run after each cleansing to assess the cleanliness of the target (demonstrating a lack of peaks prior to testing).

Evidence of Compliance:
- ✓ Written policy defining QC requirements **AND**
- ✓ QC records at defined frequency

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. This may be HPLC-grade or other reagent grades as indicated.

Evidence of Compliance:
- ✓ Reagent logs

MIC.16625 Mass Spectrometer Consumables **Phase II**

Consumables appropriate to the instrument and assay are required.

NOTE: For FDA-approved platforms, consumables utilized may be 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

BIOSAFETY

Items in this section apply to ALL areas of the microbiology laboratory. Additional items for specific subsections (bacteriology, mycobacteriology, mycology, parasitology, and virology) are found under the Laboratory Safety subsections for each of those areas.

Inspector Instructions:

READ	• Sampling of biosafety policies and procedures • Sampling of bench top decontamination logs • Records of biological safety cabinet certification
ASK	• How would you recognize a potential agent of bioterrorism? What action would you take if you encountered a suspect organism?

MIC.18968 Agents of Bioterrorism **Phase II**

The microbiology laboratory has 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 should 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 PatholLab 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) https://www.asm.org/index.php/guidelines/sentinel-guidelines

***REVISED** 08/17/2016*

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 PatholLab Med*. March 2002; 126
4) Morse SA. Bioterrorism: Laboratory Security. *Lab Med*. June 2001

MIC.18985 Spill Handling **Phase II**

There are written policies and procedures for handling spills of contaminated materials.

REFERENCES
1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009

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

There are records of daily decontamination of bench tops.

MIC.19035 Safe Specimen Processing **Phase II**

There are written policies and procedures for the safe handling and processing of specimens.

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 potential hazards of sniffing plates.

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 **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, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009
2) Richmond J. "Arthropod Borne Diseases", Anthology of Biosafety VI: American Biological Safety Association, Mundelein, IL April 2003

MIC.19160 Biosafety Levels **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, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009
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

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

A biological safety cabinet (BSC) or hood is available for handling specimens or organisms considered highly contagious by airborne routes.

Evidence of Compliance:

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

REFERENCES

1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009

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.

BACTERIOLOGY

MEDIA

Inspector Instructions:

	• Sampling of media QC policies and procedures • Sampling of media supplier records of QC • Sampling of records for QC performed by the laboratory
	• Sampling of media (expiration date, condition, contamination)
	• What is your QC procedure when receiving a new lot of media?
	• Follow a shipment of new media from receipt, examination and QC (if applicable). Determine if practice follows laboratory policy.

MIC.21220 Inspection of Media Shipments **Phase I**

The laboratory has records showing that each shipment of purchased media is examined for breakage, contamination, appearance, and evidence of freezing or overheating.

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.

***REVISED** 08/17/2016*

MIC.21240 Media QC - Purchased **Phase II**

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

1. **Sterility**
2. **Ability to support growth 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. This will ordinarily require that the

laboratory maintain a stock of reference organisms and test the media before or concurrent with use.

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/NCCLS Standard M22-A3, Quality Control for Commercially Prepared Microbiological Culture Media. The media supplier's records must be maintained and show that the QC performed meets the CLSI/NCCLS standard and checklist requirements. 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. 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 (e.g. 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/NCCLS Standard M22-A3, or are otherwise equivalent. The laboratory director may wish to have a signed contractual arrangement with his/her selected media supplier to cover all expected quality control and documentation thereof.

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 maintain records of such testing.

Evidence of Compliance:

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

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. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard. 12th ed.* CLSI document M02-A12. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.

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 growth 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

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**

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 (e.g. neutrophils or squamous epithelial cells). The policy should address correlation of direct Gram stain results with final culture results.

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

Evidence of Compliance:

✓ Written policy for Gram stain (laboratories may use the correlation of Gram stain results with the final culture results as a component of the QC program)

MIC.21540 Gram Stain QC **Phase II**

Quality control of Gram stain reagents is performed for intended reactivity and recorded for each new batch 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)]

REGENTS

Inspector Instructions:

READ	• Sampling of reagent QC policies and procedures • Sampling of reagent QC records • CO_2 monitoring procedure and CO_2 recording log • Anaerobic incubation condition monitoring records • Campylobacter incubation condition records
ASK	• What is your QC policy when receiving a new lot of identification system materials?

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) including all required elements of IQCP, may be implemented by the laboratory to allow for the use of streamlined QC for commercial microbial identification systems (MIS). Refer to the individualized Quality Control Plan section of the All Common Checklist for the requirements for implementation and ongoing monitoring of an IQCP. Streamlined QC must be performed, as specified by the manufacturer's instructions without modification. The laboratory may use additional 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, to assure appropriate reactivity.

Any test (e.g. 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 (*e.g.* 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 (*e.g.* 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

*****REVISED** 08/17/2016***
MIC.21813 CO_2 Incubator Levels **Phase I**

CO_2 incubators are checked daily for adequate CO_2 levels, with recording of results.

NOTE: Some organisms require CO_2 to grow sufficiently to form visible colonies. CO_2 monitoring is required in all CO_2 incubators, including those that adjust gas flow to maintain a set CO_2 level, to ensure that the environment is within an acceptable range for CO_2 content. It is acceptable to monitor and record CO_2 levels from digital readouts; however, the laboratory must verify that the readout is accurate (by initial calibration, Fyrite, or other calibrated CO_2 meter). The frequency of verification of the digital readout must be defined in the laboratory's equipment quality control procedure and should be performed, at minimum, at the frequency recommended by the manufacturer.

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 Campylobacter jejuni.

BACTERIOLOGY SUSCEPTIBILITY TESTING

Inspector Instructions:

	• Sampling of susceptibility test, QC and reporting policies and procedures • Sampling of susceptibility QC records
	• Susceptibility test set-up (standardized inoculum, pure culture)
	• How does your laboratory work with the pharmacy and medical staff to determine policies for reporting of antimicrobial agents?

MIC.21820 Susceptibility Testing - Pure Cultures **Phase II**

Only isolated colonies or pure cultures are used for performance of antimicrobial susceptibility testing (*i.e.* 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

*****REVISED** 08/17/2016***

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: If multiple instruments are used for automated MIC testing, QC testing should be rotated equally among all testing instruments. 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), including all required elements of IQCP, and the laboratory has records of satisfactory performance with daily QC tests as suggested by CLSI Standards. If the laboratory has multiple instruments for automated MIC testing, each individual instrument must be included as part of the IQCP. 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. For this purpose, satisfactory performance is defined as follows:

1. *There are records that all QC organisms were tested for 20 or 30 consecutive test days, and*
2. *For each drug/microorganism combination, no more than 1 of 20 or 3 of the 30 values (zone diameter or MICs) may be outside the accepted QC ranges. These*

accepted QC ranges may be those defined in the current CLSI guidelines or commercial device instructions or may be established by the laboratory

Or

1. *There are records that all QC organisms were tested in triplicate (using separate inoculum suspensions) for 5 consecutive test days*
2. *For each drug/microorganism combination, no more than 1 of the 15 values (zone diameter or MICs) may be outside the accepted QC range*
3. *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*
4. *For each drug/microorganism combination, no more than 4 of the 30 values (zone diameter or MICs) 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; Approved Standard—Eighth Edition.* CLSI document M11-A8 (ISBN 1-56238-626-3). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2012.
3) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard 12th ed*. CLSI Document M02-A12. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.
4) Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard 10th ed*. CLSI Document M07-A10. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.
5) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing;* 27th ed. CLSI Document M100-S27. Clinical and Laboratory Standards Institute, Wayne, PA; 2016.
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.21930 Susceptibility Test Endpoint Determination — Phase II

For antimicrobial susceptibility testing systems, there are written criteria for measuring and determining the MIC endpoint or zone size.

NOTE: The laboratory may use CLSI criteria, but the use of other validated criteria, such as the FDA or European Committee on Antimicrobial Susceptibility Testing (EUCAST) is acceptable.

REFERENCES

1) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard 12th ed*. CLSI Document M02-A12. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.
2) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing;* 27th ed. CLSI Document M100-S27. Clinical and Laboratory Standards Institute, Wayne, PA; 2016.
3) Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard 10th ed*. CLSI Document M07-A10. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.
4) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition.* CLSI document M11-A8 (ISBN 1-56238-626-3). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2012.

MIC.21940 Standardized Inoculum — Phase II

The inoculum used for antimicrobial susceptibility testing (*i.e.* 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. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard 12th ed*. CLSI Document M02-A12. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.
2) Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard 10th ed*. CLSI Document M07-A10. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.
3) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing;* 27th ed. CLSI Document M100-S27. Clinical and Laboratory Standards Institute, Wayne, PA; 2016.
4) Clinical and Laboratory Standards Institute (CLSI). *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition.* CLSI document M11-A8 (ISBN 1-56238-626-3). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2012.

*****REVISED** 08/21/2017***

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. 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. *Performance Standards for Antimicrobial Susceptibility Testing;* 27th ed. CLSI Document M100-S27. Clinical and Laboratory Standards Institute, Wayne, PA; 2016.
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. 4th ed.* CLSI document M39-A4. Clinical and Laboratory Standards Institute, Wayne, PA, 2014

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 should 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. Each laboratory should have a policy such as that provided by CLSI for confirming unusual or inconsistent 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. Some examples include:

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

Evidence of Compliance:

✓ Records of investigation for unusual/inconsistent results

REFERENCES
1) Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing;* 27th ed. CLSI Document M100-S27. Clinical and Laboratory Standards Institute, Wayne, PA; 2016.

PROCEDURES AND TESTS

Inspector Instructions:

READ	• Sampling of bacteriology test procedures of different source types • Sampling of patient worksheets/records • Sampling of patient reports
ASK	• How does your laboratory evaluate culture findings?
DISCOVER	• Follow a specimen from evaluation of culture findings, recording of results and reporting. Determine if practice follows test procedures.

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.

Evidence of Compliance:

✓ Policy defining acceptable specimens

REFERENCES
1) Valenstein PN. Semiquantitation of bacteria in sputum Gram stains. *J Clin Microbiol.* 1988;26:1791-1794
2) Wilson ML. Clinically relevant, cost-effective clinical microbiology. Strategies to decrease unnecessary testing. *Am J Clin Pathol.* 1997;107:154-165
3) 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
4) Jorgensen JH (ed), et al. *Manual of Clinical Microbiology*. 11th ed. Washington, DC: ASM Press; 2015.
5) 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

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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

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 35-37 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) Center for Disease Control and Prevention, 2010. Prevention of perinatal Group B streptococcal disease MMWR 59(RR-10);1-32

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 *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 *Colostridium 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 Specimen Reporting **Phase I**

The final report for stool cultures submitted for routine bacterial pathogen examination lists the organisms for which the specimen was cultured (*e.g.* 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 (e.g. 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 Clostridium 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 Clostridium 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: When inadequate volume is received, 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) Versalovic, James. *Manual of Clinical Microbiology - 10th Edition.* Washington, DC: ASM Press. 2011

MIC.22500 CSF Processing **Phase II**

CSF samples 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, e.g. 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 a culture has been performed in a referral laboratory.

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 in use is designed to recover both aerobic and, when indicated or if intended to be part of the routine procedure, anaerobic organisms.

NOTE: This criterion is not intended to imply that anaerobic cultures must be performed on all blood cultures if circumstances where anaerobic cultures are not indicated are specifically delineated (e.g. on neonates where volume is of concern).

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

***REVISED** 08/17/2016*

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

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.

NOTE: It is recommended that blood culture statistics, including number of contaminated cultures, be maintained and reviewed regularly by the laboratory director. The laboratory should establish a threshold for an acceptable rate of contamination. Tracking the contamination rate and providing feedback to phlebotomists or other persons drawing cultures has been shown to reduce contamination rates. Other measures to monitor include types of skin disinfection, volume of blood drawn, number of culture sets drawn, number of single cultures and line draws.

REFERENCES

1) Gibb AP, *et al.* Reduction in blood culture contamination rate by feedback to phlebotomists. *Arch Pathol Lab Med.* 1997;121:50-507
2) Schifman RB, *et al.* Blood culture contamination. A College of American Pathologists Q-probes study involving 640 institutions and 497 134 specimens from adult patients. *Arch Pathol Lab Med.* 1998;122:216-221
3) DesJardin JA, *et al.* Clinical utility of blood cultures drawn from indwelling central venous catheters in hospitalized patients with cancer. *Ann Int Med.* 1999;131:641-647
4) Ernst DJ. Controlling blood culture contamination rates. *Med Lab Observ.* 2000;32(5):36-47
5) Ruge DG, *et al.* Reduction of blood culture contamination rates by establishment of policy for central intravenous catheters. *Lab Med.* 2002;33:797-800
6) 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.
7) Baron EJ, *et al.* Blood Cultures IV, Cumitech 1C, 2005, ASM Press; Washington, DC

8) Jorgensen JH (ed), et al. *Manual of Clinical Microbiology*. 11th ed. Washington, DC: ASM Press; 2015.
9) Leber, AL (ed). Clinical Microbiology Procedures Handbook. 4th ed. Washington DC: ASM Press; 2016.

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MIC.22640 Blood Culture Volume **Phase I**

The laboratory has a written policy and procedure for monitoring blood cultures from adults for adequate volume and providing feedback on the results to blood collectors.

NOTE: Larger volumes of blood increase the yield of true positive cultures. In adults, optimally 20 mL of blood per culture set (two bottles) should be collected for culture. The laboratory should periodically monitor collected blood volumes and provide feedback to clinical staff. Automated blood culture systems approved or cleared by the FDA may use smaller volumes per culture set and are acceptable.

Evidence of Compliance:

- ✓ Records of monitoring of volume at a defined frequency **AND**
- ✓ Records of feedback to the clinical staff

REFERENCES

1) Kellogg JA, *et al.* Justification and implementation of a policy requiring two blood cultures when one is ordered. *Lab Med.* 1994;25:323-330
2) Li J, *et al.* Effects of volume and periodicity on blood cultures. *J Clin Microbiol.* 1994;32:2829-2831
3) Schiffman RB, *et al.* Blood culture quality improvement. A College of American Pathologists Q-probes study involving 909 institutions and 289 572 blood culture sets. *Arch Pathol Lab Med.* 1996;120:999-1002
4) Arendup M, *et al.* Diagnosing bacteremia at a Danish hospital using one early large blood volume for culture. *Scand J Infect Dis.* 1996;28:609-614
5) Wilson ML. Clinically relevant, cost-effective clinical microbiology. Strategies to decrease unnecessary testing. *Am J Clin Pathol.* 1997;107:154-165
6) 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
7) 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.
8) Baron EJ, *et al.* Blood Cultures IV, Cumitech 1C, 2005, ASM Press; Washington, DC

ANAEROBIC CULTURES

***NEW** 08/17/2016*

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.

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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:

READ	• Sampling of gas chromatography policies and procedures • Sampling of QC records
OBSERVE	• Sampling of reagents (grade) • Chromatograph pattern controls

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, i.e. 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.

*****REVISED** 08/17/2016***

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.

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

Reagents 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.

LABORATORY SAFETY

Inspector Instructions:

	• Hazardous waste disposal policy
	• How does your laboratory dispose of specimens and contaminated media?

NOTE TO THE INSPECTOR: The inspector should review relevant requirements from the Safety section of the Laboratory General checklist, to assure that the bacteriology laboratory is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

The following requirement pertains specifically to the bacteriology laboratory.

MIC.23200 Hazardous Waste Disposal **Phase II**

Microbiology specimen residuals and contaminated media are disposed of in a manner to minimize hazards to all personnel handling the material.

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.

MYCOBACTERIOLOGY

QUALITY CONTROL

Inspector Instructions:

	• Mycobacteriology specimen collection, transport and handling policy • Mycobacteriology reporting policy • Sampling of patient test reports • Sampling of mycobacteriology media/stain/reagent QC policies and procedures • Sampling of mycobacteriology QC records
	• Sampling of media (expiration date, condition, contamination)
	• What is your policy for performing AFB stains on week-ends and holidays?

SPECIMEN HANDLING

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

Specimens for mycobacterial testing are collected appropriately 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.

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, and Other Aerobic Actinomycetes; Approved Standard - Second Edition*. CLSI document M24-A2. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400 Wayne, PA 19087-1898, USA, 2011.
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

MIC.31380 Media QC - Purchased — Phase II

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

1. Sterility

2. **Ability to support growth 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. This will ordinarily require that the laboratory maintain a stock of reference organisms and test the media before or concurrent with use. End user quality control must be performed on media not listed on Table 2 of M22-A3 (e.g. 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/NCCLS Standard M22-A3, Quality Control for Commercially Prepared Microbiological Culture Media. The media supplier's records must be maintained and show that the QC performed meets the CLSI/NCCLS standard and checklist requirements. 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.

Laboratories receiving media from media suppliers must have a copy of the CLSI/NCCLS Standard M22-A3 as a reference source. The media supplier must provide records showing that the quality control activities meet the CLSI/NCCLS Standard M22-A3, or are otherwise equivalent. The laboratory director may wish to have a signed contractual arrangement with his/her selected media supplier to cover all expected quality control and documentation thereof.

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 maintain records of such testing.

Evidence of Compliance:

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

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.

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 growth by means of stock cultures or by parallel testing with previous batches**
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

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

MIC.31680 Susceptibility QC **Phase II**

If the laboratory performs susceptibility testing of *M. tuberculosis*, 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 antimicrobial 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:

	• Sampling of mycobacteriology test procedures/identification schemes • Sampling of mycobacteriology QC policies and procedures • Sampling of patient worksheets/records • Sampling of mycobacteriology QC records • Sampling of HPLC policies and procedures • Sampling of HPLC QC records • New HPLC column verification
	• Chromatograph pattern controls • Sampling of reagents (storage, grade, solvent purity)
	• What specimens are concentrated before AFB examination and culture?
	• Follow a positive patient worksheet from receipt and processing to identification and reporting

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.

*****REVISED** 08/17/2016***

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

MIC.32140 Rapid Method — Phase I

Nucleic acid probes, chromatography, the NAP test, or other rapid method (*e.g.* 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

CONCENTRATION, INOCULATION, INCUBATION

MIC.32200 AFB Concentration — Phase II

There is a written policy defining those specimens (*e.g.* 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 35 to 37°C.

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 (incubate at 30 to 32°C) or M. xenopi (incubate at 42°C). These specimens should be held at 35 to 37°C in addition to the lower or higher temperature.

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 (e.g. "Mycobacterium kansasii" or "photochromogen"), (b) the particular species which a laboratory attempts to identify (e.g. 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*
Arylsulfatase	*Helps distinguish pathogenic from non-pathogenic rapid growers; also useful for M. marinum, M. szulgai, M. xenopi, M. triviale.*
68°C catalase	*Helpful for identification of M. tuberculosis*
Semiquantitative catalase	*Helpful in certain circumstances. M. tuberculosis complex, MAC, M. xenopi, and a few other species produce <45 mm of bubbles.*
Iron uptake	*Helps distinguish M. chelonae from M. fortuitum.*
MacConkey agar	*Helps with identification of rapid growers.*
5% NaCl	*Helps with identification of rapid growers and M. triviale.*
Niacin accumulation	*Helps with identification of M. tuberculosis, M. simiae, some strains of M. bovis.*
Nitrate reductase	*Helpful in identifying many mycobacterial species.*
Tween 80 hydrolysis	*Helps distinguish some usually pathogenic from some usually non-pathogenic mycobacterial species.*
Urease	*Helpful in identifying many mycobacterial species.*

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 (e.g. 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.* 3rd 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

LABORATORY SAFETY

NOTE TO THE INSPECTOR: The inspector should review relevant requirements from the Safety section of the Laboratory General checklist, to assure that the mycobacteriology laboratory is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

The following requirements pertain specifically to the mycobacteriology laboratory.

Inspector Instructions:

	• Mycobacteriology specimen collection, transport and handling policy • Records of biological safety cabinet certification
	• Patient mycobacteriology specimens (sealed, leak proof containers) • Sealed, safety centrifuge carriers

MIC.33050 Specimen Collection **Phase II**

All specimens for mycobacterial testing are collected and/or received in sealed leak-proof containers.

MIC.33100 Centrifuge Safety **Phase II**

Sealed screw-capped tubes are enclosed in sealed safety centrifuge carriers (*i.e.* 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.

MIC.33300 Biological Safety Cabinet **Phase II**

The biological safety cabinet meets minimum requirements for mycobacterial work.

NOTE: Exhaust air from a class I or class II biological safety cabinet 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 every 12 months. It may 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 (e.g. 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**
- ✓ Maintenance schedule of BSC function checks **AND**
- ✓ Records of testing and certification **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, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009
2) Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline.* 4th ed. CLSI Document M29-A4. Clinical and Laboratory Standards Institute, Wayne, PA; 2014.
3) NSF/ANSI Standard 49-2012 Biosafety Cabinetry: Design, Construction, Performance and Field Certification. Ann Arbor, MI: NSF; 2012.
4) Kruse RH, Puckett WH, Richardson JH. Biological safety cabinetry. *Clin Microbiol Rev.* 1991;4(2):207-241.
5) 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.

MYCOLOGY

QUALITY CONTROL

Inspector Instructions:

READ	• Sampling of mycology media/stain/reagent QC policies and procedures • Sampling of mycology QC records
ASK	• How do you determine when QC is unacceptable and when corrective actions are needed?
DISCOVER	• 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

MEDIA

MIC.41200 Media QC - Purchased Phase II

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

1. **Sterility**
2. **Ability to support growth 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. This will ordinarily require that the laboratory maintain a stock of reference organisms and test the media before or concurrent with use. End user quality control must be performed on media not listed on Table 2 of M22-A3 (e.g. 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/NCCLS Standard M22-A3, Quality Control for Commercially Prepared Microbiological Culture Media. The media supplier's records must be maintained and show that the QC performed meets the CLSI/NCCLS standard and checklist requirements. 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.

Laboratories receiving media from media suppliers must have a copy of the CLSI/NCCLS Standard M22-A3 as a reference source. The media supplier must provide records showing that the quality control activities meet the CLSI/NCCLS Standard M22-A3, or are otherwise equivalent. The laboratory director may wish to have a signed contractual arrangement with his/her selected media supplier to cover all expected quality control and documentation thereof.

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 maintain 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

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; 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.

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 growth 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

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 (*e.g.* 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) 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):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 maintained.

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 test procedures/identification schemes • Sampling of patient worksheets/records
	• What tests or procedures are used to identify dimorphic fungi? Filamentous fungi?
	• Follow a mycology patient worksheet from receipt and processing to culture evaluation, identification and reporting

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.

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.

MIC.42350 Differential Tests **Phase II**

Differential tests include biochemical tests (*e.g.* urease, carbohydrate assimilation and/or fermentation).

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.

MIC.42550 Dimorphic Fungi **Phase I**

The identification of dimorphic fungal isolates is confirmed by exo-antigen, molecular, yeast-mold conversion or tissue phase detection tests.

NOTE: Exo-antigen tests, DNA probes, or DNA sequencing are recommended.

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

MYCOLOGY SUSCEPTIBILITY TESTING

Inspector Instructions:

	• Sampling of susceptibility test, QC and reporting policies and procedures • Sampling of susceptibility QC records
	• Susceptibility test set-up (standardized inoculum, pure culture)
	• How does your laboratory work with the pharmacy and medical staff to determine guidelines for reporting of antimicrobial agents?

MIC.42600 Susceptibility Testing QC **Phase II**

For antifungal susceptibility testing, quality control is performed on each new batch, lot number and shipment of disks, antimicrobial strips, antimicrobial agents, media, minimum inhibitory concentration (MIC) panels, and susceptibility testing plates before or concurrent with initial use with appropriate QC organisms.

Evidence of Compliance:

✓ Records of new lot susceptibility QC for media, disk, and MIC panels

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)].

MIC.42620 Susceptibility Testing QC Frequency **Phase II**

For antifungal susceptibility testing by either disk, strip or MIC methods, quality control organisms are tested with each new lot number and/or shipment 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)].
2) Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard.* 3rd ed. CLSI Document M27-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.
3) Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi; Approved Standard.* 2nd ed. CLSI Document M38-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.
4) Clinical and Laboratory Standards Institute. *Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts; Approved Guideline.* 2nd ed. CLSI Document M44-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2009.

MIC.42640 Susceptibility Testing - Pure Cultures — Phase II

Only isolated colonies or pure cultures are used for performance of antifungal susceptibility testing (i.e. 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. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard.* 3rd ed. CLSI Document M27-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.
2) Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts;* 4th Informational Supplement. CLSI Document M27-S4. Clinical and Laboratory Standards Institute, Wayne, PA; 2012.

MIC.42680 Susceptibility Testing Endpoint Determination — Phase II

For antifungal susceptibility testing, there are written criteria for measuring and determining the MIC endpoint or zone size.

NOTE: The laboratory may use CLSI criteria, but the use of other validated criteria such as the FDA or European Committee on Antimicrobial Susceptibility Testing (EUCAST) is acceptable.

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)(1)].
2) Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard.* 3rd ed. CLSI Document M27-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.
3) Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi; Approved Standard.* 2nd ed. CLSI Document M38-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.
4) Clinical and Laboratory Standards Institute. *Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts; Approved Guideline.* 2nd ed. CLSI Document M44-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2009.

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 indiscriminant 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. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard.* 3rd ed. CLSI Document M27-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.
2) Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi; Approved Standard.* 2nd ed. CLSI Document M38-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2008.

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

LABORATORY SAFETY

NOTE TO THE INSPECTOR: The inspector should review relevant requirements from the Safety section of the Laboratory General checklist, to assure that the mycology laboratory is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

The following requirements pertain specifically to the mycology laboratory.

Inspector Instructions:

READ	• Sampling of mycology safety policies and procedures • Records of biological safety cabinet certification
OBSERVE	• Safe work practices (taping of culture plates, procedures performed under BSC)

MIC.43050 Safety Precautions **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-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** 08/17/2016***

MIC.43100 Safety Precautions **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-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.

MIC.43200 Safety Precautions **Phase II**

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

MIC.43250 Biological Safety Cabinet **Phase II**

A biological safety cabinet (BSC) or hood is available for handling specimens or organisms considered to be highly contagious by airborne routes.

Evidence of Compliance:

✓ Maintenance schedule of BSC function checks **AND**

✓ Records of testing and certification

REFERENCES

1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009

MIC.43300 Biological Safety Cabinet **Phase II**

The biological safety cabinet (BSC) is certified 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

MIC.43350 Biological Safety Cabinet **Phase II**

The BSC meets minimum requirements for mycologic work.

NOTE: Exhaust air from a class I or class II BSC must be filtered through HEPA filters. Air from Class I and IIB 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 every 12 months. It may 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 (e.g. thimble connection) that avoids any interference with the air balance of the BSC or building exhaust system.

Evidence of Compliance:
- ✓ Written policy defining the types of safety cabinets, filtration systems and exhaust systems used **AND**
- ✓ Maintenance schedule of BSC function checks **AND**
- ✓ Records of testing and certification **AND**
- ✓ Records of HEPA filters used for filtration of all BSC classes **AND**
- ✓ Records of exhaust mechanism **OR** recirculation, if appropriate

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.
4) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009

PARASITOLOGY

QUALITY CONTROL

Inspector Instructions:

READ	• Sampling of parasitology stain/reagent QC policies and procedures • Sampling of parasitology QC records • Ocular micrometer calibration procedure and records
OBSERVE	• Reference materials (permanent mounts, photomicrographs or atlas available) • Zinc sulfate solution (tightly-stoppered) • Ocular micrometer

MIC.51000 Reference Materials **Phase I**

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

REFERENCES
1) NCCLS. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline.* NCCLS document M15-A. NCCLS, 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 Stain QC — Phase II

All permanent parasitology stains 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 (*e.g.* acid fast, fluorescent) are checked with appropriate control organisms each time of use.

Evidence of Compliance:
- ✓ Records of special stain QC each time of use

INSTRUMENTS AND EQUIPMENT

MIC.51210 Ocular Micrometer — Phase II

An ocular micrometer is available for determining the size of eggs, larvae, cysts, trophozoites, and microfilaria or other bloodborne parasites.

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(b)]

MIC.51220 Calibration/Recalibration - Ocular Micrometer **Phase II**

The ocular micrometer has been calibrated for the microscope(s) in which it is used and it is recalibrated each time the eyepieces or objectives are changed.

NOTE: Calibrations can be checked against a micrometer or other objects of known dimensions. If there are no changes to a particular microscope's optical components, there is no need to recheck calibration.

Evidence of Compliance:

✓ Records of initial calibration and recalibration if applicable

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(b)]

PROCEDURES AND TESTS

Inspector Instructions:

READ	• Sampling of parasitology test procedures • Sampling of patient worksheets/records
DISCOVER	• Follow a parasitology patient worksheet from receipt and processing to identification and reporting

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.

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 (developed with clinicians) for the number and/or timing of collection of stool specimens submitted for routine parasitology testing.

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

MIC.52195 Percentage Parasitemia Reporting — Phase I

When blood films are positive for malaria parasites (Plasmodium spp.), the percentage parasitemia is reported along with the organism identification.

NOTE: It is important to report the percentage of parasitemia when blood films are reviewed and found to be positive for malaria parasites. Because of 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 parasitemia reported exactly the same way on follow-up specimens as on the initial specimen. This allows the parasitemia to be followed after therapy has been initiated.

The parasitemia 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 percent parasitemia when blood films are positive for Babesia species, physicians may ask for these data to monitor the response to therapy.

Evidence of Compliance:

✓ Written procedure for performing and reporting parasitemia percentage with identification

REFERENCES
1) NCCLS. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline.* NCCLS document M15-A. NCCLS, Wayne, PA, 2000.
2) Garcia LS, *Diagnostic Medical Parasitology*. Washington, DC, ASM Press, 2001
3) http://www.dpd.cdc.gov/DPDx/HTML/DiagnosticProcedures.htm
4) Pritt BS. Parasitology Benchtop Reference Guide: An Illustrated Guide for Commonly Encountered Parasites. Northfield, IL: College of American Pathologists; 2014.

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) NCCLS. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline.* NCCLS document M15-A. NCCLS, 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 (*e.g.* pH 6.8-7.2 for Giemsa), or the range specified by the manufacturer.

REFERENCES
1) NCCLS. *Laboratory Diagnosis of Blood-borne Parasitic Diseases; Approved Guideline.* NCCLS document M15-A. NCCLS, 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 (*e.g.* 300 fields).

Evidence of Compliance:

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

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

LABORATORY SAFETY

NOTE TO THE INSPECTOR: The inspector should review relevant requirements from the Safety section of the Laboratory General checklist, to assure that the parasitology laboratory is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

The following requirements pertain specifically to the parasitology laboratory.

Inspector Instructions:

READ

- Formalin monitoring procedure and records of monitoring

***REVISED** 08/21/2017*

MIC.53050 Formaldehyde and Xylene Safety **Phase II**

Formaldehyde and xylene vapor concentrations are maintained below the following maxima, expressed as parts per million.

NOTE: Formaldehyde and xylene vapor concentrations must be monitored in all areas where these reagents are used. Initial monitoring involves identifying all employees who may be exposed at or above the action level or at or above the STEL and accurately determining the exposure of each employee identified. Once an initial monitoring procedure has been performed, further periodic formaldehyde monitoring is mandated at least every six months if the initial monitoring result equals or exceeds 0.5 ppm (8 hr time-weighted exposure, the "action level") or at least once per year if the results exceed the short term exposure limit (STEL) 2.0 ppm. The laboratory may discontinue periodic formaldehyde monitoring if results from two consecutive sampling periods taken at least seven days apart show that employee exposure is below the action level and the short-term exposure limit, and 1) no change has occurred in production, equipment, process or personnel or control measures that may result in new or additional exposure to formaldehyde, and 2) there have been no reports of conditions that may be associated with formaldehyde exposure.

Formaldehyde monitoring must be repeated any time there is a change in production, equipment, process, personnel, or control measures which may result in new or additional exposure to formaldehyde for an employee involved in the activity. If any personnel report signs or symptoms of respiratory or dermal conditions associated with formaldehyde exposure, the laboratory must promptly monitor the affected person's exposure.

Xylene must be monitored initially, but there is no requirement for periodic monitoring of xylene. Repeat monitoring should be considered when there is a change in production, equipment, process, personnel, or control measures likely to increase exposure levels.

	8 hr Time-Weighted Exposure Limit in ppm	Action Level (8 hr Time-Weighted Exposure) in ppm	15 min Short-Term Average Exposure Limit (STEL) in ppm
Formaldehyde	**0.75**	**0.5**	**2.0**
Xylene	**100**		**150**

Evidence of Compliance:

- ✓ Written safety policy for formalin and xylene safety including action limits, criteria for discontinuation of monitoring and criteria for resumption of monitoring **AND**
- ✓ Record of initial formalin and xylene monitoring and repeat monitoring when indicated **AND**
- ✓ Records of corrective action when exposure limits are exceeded

REFERENCES

1) Montanaro A. Formaldehyde in the workplace and in the home. Exploring its clinical toxicology. *Lab Med.* 1996;27:752-757
2) Goris JA. Minimizing the toxic effects of formaldehyde. *Lab Med.* 1997;29:39-42
3) Occupational Safety and Health Administration, 1998(Jul 1) [29CFR1910.1048]

MIC.53150 Ether Safety **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.

VIROLOGY

QUALITY CONTROL

Inspector Instructions:

READ	• Sampling of virology test procedures • Sampling of virology cell culture system and reagent QC policies and procedures • Sampling of virology QC records and cell line checks
ASK	• How are cell lines checked for contamination?
DISCOVER	• Follow a virology patient worksheet from receipt and processing to identification and reporting

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)]

*****NEW** 08/21/2017***

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)].

*****REVISED** 08/21/2017***

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 virus.

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*
Chlamydia	*McCoy or Buffalo Green Monkey Kidney*
Herpes simplex	*HDF, Primary or First Pass Rabbit Kidney, MRC-5, or A549, CV-1/ MRC-5, transgenic BHK*
Varicella zoster	*HDF, Primary Monkey Kidney, CV-1/MRC-5*
Influenza	*Primary Monkey Kidney or MDCK, Mink lung /A549*
Parainfluenza	*Primary Monkey Kidney, Mink lung/A549*
RSV	*HEp-2 or Primary Monkey Kidney, Mink lung/A549*
Enteroviruses	*Primary Monkey Kidney, A549, HDF, MRC-5, GGMK+Daf/A549*
Adenoviruses	*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.

***REVISED** 08/17/2016*

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*
Herpes simplex (genital)	*5 days*
Herpes simplex (other)	*7 days*
Respiratory viruses	*10 days - 14 days*
Other viruses	*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

***REVISED** 08/17/2016*

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 uninnoculated/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 (i.e. monkey pox, vaccina, 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.

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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 (e.g. Papanicolaou or Giemsa) in use.

LABORATORY SAFETY

NOTE TO THE INSPECTOR: The inspector should review relevant requirements from the Safety section of the Laboratory General checklist, to assure that the virology laboratory is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

The following requirements pertain specifically to the virology laboratory.

Inspector Instructions:

- Sampling of virology specimen handling and processing policies
- Records of biological safety cabinet certification

MIC.63050 Biological Safety Cabinet **Phase II**

A biological safety cabinet (BSC) or hood is available for handling specimens or organisms considered to be highly contagious by airborne routes.

Evidence of Compliance:

✓ Maintenance schedule of BSC function checks **AND**

- ✓ Records of testing and certification

REFERENCES
1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009
2) Biological Safety, Principles and Practices, 4th ed. Fleming DO, Hunt DL, Ed. (ISBN 978-1-55581-339-0) ASM Press; Washington DC., 2006
3) Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline.* 4th ed. CLSI Document M29-A4. Clinical and Laboratory Standards Institute, Wayne, PA; 2014.

MIC.63100 Biological Safety Cabinet **Phase II**

The BSC is certified 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

MIC.63150 Biological Safety Cabinet **Phase II**

The BSC meets minimum requirements for virology work.

NOTE: Exhaust air from a class I or class II BSC must be filtered through HEPA filters. Air from Class I and IIB 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 every 12 months. It may 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 (e.g. thimble connection) that avoids any interference with the air balance of the BSC or building exhaust system.

Evidence of Compliance:
- ✓ Written policy defining the types of safety cabinets, filtration systems and exhaust systems used **AND**
- ✓ Maintenance schedule of BSC function checks **AND**
- ✓ Records of testing and certification **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, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009
2) Biological Safety, Principles and Practices, 4th ed. Fleming DO, Hunt DL, Ed. (ISBN 978-1-55581-339-0) ASM Press; Washington DC., 2006
3) NSF/ANSI Standard 49-2012 Biosafety Cabinetry: Design, Construction, Performance and Field Certification. Ann Arbor, MI: NSF; 2012.
4) Kruse RH, Puckett WH, Richardson JH. Biological safety cabinetry. *Clin Microbiol Rev.* 1991;4(2):207-241.
5) 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.

MIC.63200 Specimen Handling/Processing **Phase II**

There are written policies for the safe handling and processing of virology specimens.

Evidence of Compliance:
- ✓ Written policies for safe handling/processing of specimens

REFERENCES
1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009
2) Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline.* 4th ed. CLSI Document M29-A4. Clinical and Laboratory Standards Institute, Wayne, PA; 2014.

*****REVISED** 08/17/2016***
MIC.63220 Specimen Handling/Processing **Phase II**

There are written policies for the safe handling and processing of samples that are suspected to contain highly infectious emerging pathogens.

NOTE: Laboratories should review State and Federal guidelines for the handling of samples from patients suspected to have high risk pathogens such as avian influenza, MERS coronavirus, or SARS coronavirus.

REFERENCES
1) Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Washington, DC: HHS Publishing No. (CDC) 21-1112, December 2009

MIC.63250 Hazardous Waste Disposal **Phase II**

Specimens and used media are disinfected, sterilized or contained in a manner to minimize the hazard of an accident during transportation to a remote autoclave or incinerator.

Evidence of Compliance:

✓ Written procedure 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.

MOLECULAR MICROBIOLOGY

This checklist section does not apply to tests using direct non-amplified nucleic acid probes to identify organisms from a positive culture. Such tests may be inspected with the Mycobacteriology, Mycology or other appropriate section of this checklist.

This checklist section applies to all other molecular microbiology tests, including FDA-cleared/approved tests, as well as tests not cleared/approved by the FDA (including FDA-cleared/approved tests modified by the laboratory, and laboratory-developed tests). A database of FDA-cleared/approved tests can be found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA/Search.cfm

When specimens are referred to outside referral laboratories for sequence analysis or other testing, such laboratories must meet the requirements in GEN.41350 and other applicable requirements in the "Reporting of Results" section of the Laboratory General checklist.

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:

READ

- Sampling of QM statistics/turnaround time data

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

MIC.63252 Statistics **Phase I**

When appropriate, statistics (*e.g.* percentage of results that are positive for *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*) are maintained and monitored.

NOTE: An increase above the expected positive rate within a run or over multiple runs should prompt investigation for potential false positive results.

Evidence of Compliance:
- ✓ Written procedure for calculating statistics including thresholds **AND**
- ✓ Records of statistical data, evaluation and corrective action if indicated

MIC.63256 Turnaround Times **Phase I**

There is evidence that the laboratory monitors sample turnaround times and that they are appropriate for the intended purpose of the test.

NOTE: There are certain clinical situations in which rapid completion is essential. An example is detection of HSV in CSF.

Evidence of Compliance:
- ✓ Written policy defining turnaround time and mechanism for monitoring **AND**
- ✓ Records showing that times defined in the policy are routinely met

SPECIMEN HANDLING & PROCESSING

Inspector Instructions:

- Sampling of molecular microbiology specimen handling and processing policies and procedures

- Patient specimens/aliquots (storage, labeling)

- What is your process for identification of patient specimens and aliquots?

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. For example, for amplified molecular testing using liquid based cervical cytology (LBC) specimens, there must be a procedure in place to ensure absence of cross contamination of samples during the LBC processing steps; alternatively, an aliquot can be removed for amplified molecular testing prior to LBC processing.

MIC.63322 Specimen Aliquots **Phase II**

If aliquoting of specimens is performed, there is a written procedure that prevents cross-contamination of the aliquot containers.

NOTE: Although in some cases it may be appropriate to aliquot a specimen, the laboratory must have a policy that no aliquot is ever returned to the original container.

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 (e.g. 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

ASSAY VALIDATION AND VERIFICATION

Additional requirements and details for validation and verification of methods are found in the "Test Method Validation and Verification" and "Method Performance Specifications - Nonwaived Test" sections of the All Common Checklist.

Inspector Instructions:

	• Sampling of assay verification and validation studies
	• How does your laboratory verify or validate assay performance prior to test implementation? • How do you ensure that the modified FDA-cleared/approved test exhibits equal or superior performance?

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MIC.64760 Validation or Verification Study **Phase II**

There are records that the laboratory has performed a validation or verification study prior to reporting patient results.

NOTE: Refer to the section "Test Method Validation and Verification" in the All Common Checklist for additional details.

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MIC.64770 Validation Studies - Specimen Type/Collection **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.

NOTE: If the use of an alternative specimen type or collection device requires any part of the test procedure to be modified (including, for example, a preprocessing step), the test must be validated.

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

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 (e.g. *Chlamydia trachomatis/ Neisseria gonorrhoeae* NAAT on pooled urine specimens), the testing procedure for pooled specimens must be validated, 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 (i.e. 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).

MIC.64956 Modified FDA-Cleared/Approved Assay **Phase II**

If the laboratory modifies an FDA-cleared/approved assay, the modified procedure has been validated to yield equivalent or superior performance.

Evidence of Compliance:

✓ Records of validation studies for modified FDA-cleared/approved assays

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Fluorescence In Situ Hybridization Methods for Clinical Laboratories; Approved Guideline—Second Edition*. CLSI document MM07-A2 (ISBN 1-56238-885-1] Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2013.
2) Lawrence Jennings, Vivianna 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
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): [42CFR493.1253](b)(2)]

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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 (*e.g.* blood, fresh/frozen tissue, paraffin-embedded tissue).

NOTE: Validation or verification studies must include specimens representing each strain or genotype, as appropriate, and an adequate number of positive and negative specimens representing the specimen types used in the assay (e.g. plasma, blood, CSF). Specimens may be spiked (suspensions of target added to appropriate matrix), if patient specimens are not available or inadequate in number across the dynamic range of a quantitative assay.

For qualitative tests this includes comparison of positive and negative test results to a comparable test method. For quantitative tests, the manufacturer's limit of detection, linearity, 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

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MIC.64968 Validation Study Comparison - Laboratory-Developed Test **Phase II**

For laboratory-developed tests, the results of each validation study were compared to another valid test method or to results of a specimen exchange with a laboratory performing the same type of test in a similar fashion.

NOTE: There may not be a closely related test to be used for comparison. In such cases, the test performance (sensitivity and specificity) should be assessed in relation to the patient's clinical diagnosis and in addition assessed by exchanges of specimens with a laboratory that performs the test in a similar fashion.

Evidence of Compliance:

✓ Records of comparison and evaluation of each validation study to another test method **OR** records of comparison using specimen exchange with another laboratory

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

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.

DEFINITIONS:
CALIBRATION is the set of operations that establish, under specified conditions, the relationship between reagent system/instrument response and the corresponding concentration/activity values of an analyte. Calibration procedures are typically specified in the manufacturer's instructions, but may also be established by the laboratory.

CALIBRATION VERIFICATION denotes the process of confirming that the current calibration settings for each analyte remain valid for a test system. If calibration verification confirms that the current calibration settings for each analyte are valid, it is not necessary to perform a complete calibration or recalibration of the test system. Each laboratory must define limits for accepting or rejecting tests of calibration verification. Calibration verification can be accomplished in several ways. If the manufacturer provides a calibration validation or verification process, it should be followed. Other techniques include (1) assay of the current method calibration materials as unknown specimens, and determination that the correct target values are recovered, 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) is the range of analyte values that a method can directly measure on the specimen without any dilution, concentration, or other pretreatment not part of the usual assay process.

AMR VERIFICATION is the process of confirming that the assay system will correctly recover the concentration or activity of the analyte over the AMR. The materials used for verification must be known to have matrix characteristics appropriate for the method. The matrix of the sample (i.e. the environment in which the analyte is suspended or dissolved) may influence the measurement of the analyte. The method manufacturer may recommend suitable materials. The test specimens must have analyte values that, at a minimum, are near the low, midpoint, and high values of the AMR. Specimen target values can be established by comparison with peer group values for reference materials, by assignment of reference or comparative method values, and by

dilution or admixture ratios of one or more specimens with known values. Each laboratory must define limits for accepting or rejecting verification tests of the AMR.

MATERIALS SUITABLE FOR AMR VERIFICATION
Materials for AMR verification should have a matrix appropriate for the clinical specimens assayed by that method, and target values appropriate for the measurement system. Materials may include, but are not limited to:

1. *Linearity material of appropriate matrix, e.g. CAP Survey-based or other suitable linearity verification material*
2. *Proficiency testing survey material or proficiency testing survey-validated material*
3. *Previously tested patient/client specimens, unaltered*
4. *Previously tested patient/client specimens, altered by admixture with other specimens, dilution, spiking in known amounts of an analyte, or other technique*
5. *Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method*
6. *Calibrators used to calibrate the analytic measurement system*
7. *Control materials, if they adequately span the AMR.*

RECALIBRATION/CALIBRATION VERIFICATION and AMR VERIFICATION INTERVAL:
Recalibration or calibration verification, and AMR verification must be performed at least once every six months. Successful calibration verification certifies that the calibration is still valid; unsuccessful calibration verification requires remedial action, which usually includes recalibration. The performance of recalibration or a calibration verification procedure resets the calendar to a new maximum six-month interval before the next required reassessment. Test systems that are recalibrated more frequently than every six months do not require a separate calibration verification procedure.

In addition to the every six-month requirement, laboratories must perform recalibration or calibration verification and AMR verification at changes in major system components and at changes of lots of chemically or physically active reagents unless the laboratory can demonstrate that changing reagent lot numbers does not affect the range used to report patient/client test results. The director should determine what constitutes a verification of the AMR. Manufacturers' instructions should be followed.

The laboratory should establish other criteria, as appropriate, for recalibration/calibration verification. These include but are not limited to failure of quality control to meet established criteria, and major maintenance or service to the instrument.

Inspector Instructions:

	• Sampling of calibration and AMR policies and procedures • Sampling of calibration records • Sampling of AMR verification records
	• Sampling of calibration materials (labeling, storage, quality)
	• What is your course of action if calibration is unacceptable? • When was the last time you performed a calibration procedure and how did you verify the calibration? • What is your course of action when results fall outside the AMR?
	• Further evaluate the responses, corrective actions, and resolutions for unacceptable calibration, unacceptable calibration verification, and results outside the AMR

MIC.65100 Calibration Procedures **Phase II**

Calibration procedures for each test system are appropriate, and the calibration records are reviewed for acceptability.

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) Kroll MH, Emancipator K. A theoretical evaluation of linearity. *Clin Chem.* 1993;39:405-413
4) Clinical and Laboratory Standards Institute. *Evaluation of Matrix Effects; Approved Guideline.* 3rd ed. CLSI Document EP14-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2014
5) Miller WG. "Quality control." Professional Practice in Clinical Chemistry: A Companion Text, ed. DR Dufour. Washington, DC: AACC Press, 1999:12-1 to 12-22
6) Kroll MH, *et al*. Evaluation of the extent of non linearity in reportable range studies. *Arch Pathol Lab Med.* 2000;124:1331-1338
7) 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

*****REVISED** 08/21/2017***

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

*****REVISED** 08/21/2017***

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.* 3rd 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]

*****REVISED** 08/21/2017***

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.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 Criteria **Phase II**

There is a written policy for the verification of the analytical measurement range and records maintained.

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. *A change of reagent lots for chemically or physically active or critical components, unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client test results, and the range used to report patient/client test data*

2. *If QC materials reflect an unusual trend or shift or are outside of the laboratory's acceptable limits and other means of assessing and correcting unacceptable control values fail to identify and correct the problem*
3. *After major preventive maintenance or change of a critical instrument component*
4. *When recommended by the manufacturer*

Evidence of Compliance:

✓ Written policy defining the method, frequency and acceptability criteria for AMR verification

MIC.65170 AMR Verification **Phase II**

Verification of the analytical measurement range (AMR) is performed with matrix-appropriate materials, which at a minimum, include the low, mid and high range of the AMR, and the process is documented.

NOTE: If the materials used for calibration or for calibration verification include low, midpoint, and high values that are near the stated AMR, and if calibration verification data are within the laboratory's acceptance criteria, the AMR has been verified; no additional studies are required. If the calibration and/or calibration verification materials do not span the full AMR, or the laboratory extends the AMR beyond the manufacturer's stated range, the AMR must be verified by assaying materials reasonably near the lowest and highest values of the AMR.

Calibration, calibration verification, and verification of the analytical measurement range (AMR) are required to substantiate the continued accuracy of a test method. The CLIA regulations use the term "calibration verification" to refer to both verification of correct method calibration and verification of the analytical measurement range. This Checklist uses separate terms to identify two distinct processes that are both required for good laboratory practice.

Evidence of Compliance:

✓ Written procedure for AMR verification defining the types of materials used and acceptability criteria consistent with manufacturer's instructions

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]

QUALITY CONTROL

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.

Inspector Instructions:

- Sampling of molecular microbiology QC policies and procedures
- Sampling of molecular microbiology QC records

	• How would you investigate results of negative controls that test as positive or equivocal? • What is your course of action when monthly precision data changes significantly from the previous month's data?
	• 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 • 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

*****REVISED** 08/17/2016***

MIC.65200 Daily QC - Molecular-based Testing **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 (e.g. 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 to address the use of the alternative control system. Please refer to the Individualized Quality Control Plan 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, e.g. positive and negative controls that go through the entire testing process.

- *Laboratories performing tests using an IQCP approved by the laboratory director 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 (positive controls fulfill this requirement).*
  2. *If the samples from an extraction batch are tested over multiple amplification runs, each amplification run (as defined by the laboratory) 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

MIC.65220 Multiplex QC — Phase II

For multiplex tests, controls for each analyte are either included in each run or rotated so that all analytes are tested periodically.

Evidence of Compliance:

- ✓ Written policy defining multiplex test QC **AND**
- ✓ Records of multiplex test QC

MIC.65230 QC Acceptability Limits — Phase II

Acceptability limits are defined for all control materials and standards.

NOTE: Acceptability limits must be defined for all control materials and standards. 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 QC policy(s) 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 (e.g. 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 (e.g. 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 (e.g. 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

Inspector Instructions:

	• Sampling of reagents/controls (storage, designated pre- and post-amplification)
	• How do you verify new multiplex lots/shipments?

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]

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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 (e.g. 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

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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 (e.g. Influenza H1N1, EV-D68) if they occur in the patient population served by the laboratory.

***REVISED** 08/21/2017*

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.

Evidence of Compliance:

✓ Records of probe details including oligonucleotide sequence, target, concentration, or purity, as applicable

INSTRUMENTS

Inspector Instructions:

READ

- 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:

	• Sampling of test policies and procedures • Sampling of temperature incubation logs • Sampling of molecular microbiology policies for analytic interpretation
	• Physical containment practices (frequent glove change, separate manipulation of pre- and post-specimens, dedicated pipettes)
	• What is your course of action when the incubation temperature is out of range? • What follow-up action is taken when a negative result is obtained for Group B strep tests using direct DNA probes?

MIC.65500 Carryover **Phase II**

Nucleic acid amplification procedures (*e.g.* 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. *Collection, Transport, Preparations, and Storage of Specimens for Molecular Methods; Approved Guideline.* CLSI Document MM13-A. Clinical and Laboratory Standards Institute, Wayne, PA, 2005.
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. 3rd 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

*****REVISED** 08/21/2017***

MIC.65550 Melting Temperature - Laboratory-Developed Test **Phase II**

For laboratory-developed tests that generate a result based on a melting temperature (Tm), appropriately narrow temperature ranges (+/- 2.5ºC) 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) Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines form the CDC, 2010. Morbidity and Mortality Weekly Report http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm
2) Prevention of Early-Onset Group B Streptococcal Disease in Newborns. 2011. The American College of Obstetricians and Gynecologists Committee on Obstetric Practice Opinion 485. http://www.acog.org/~/media/Committee%20Opinions/Committee%20on%20Obstetric%20Practice/co485.pdf?

MIC.65590 Group B Screening - Amplified Method **Phase II**

A pre-enrichment step using a selective broth enrichment culture is performed for antepartum (35-37 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 (i.e. during active labor) remains unsettled. If used, it is recommended that testing only be considered for women not appropriately screened at 35-37 weeks and for whom no other clinical risk factors related to neonatal GBS infection are present during labor.

REFERENCES
1) Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines form the CDC, 2010. Morbidity and Mortality Weekly Report http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm.
2) Prevention of Early-Onset Group B Streptococcal Disease in Newborns. 2011. The American College of Obstetricians and Gynecologists Committee on Obstetric Practice Opinion 485. http://www.acog.org/~/media/Committee%20Opinions/Committee%20on%20Obstetric%20Practice/co485.pdf?

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

ELECTROPHORESIS

Inspector Instructions:

READ	• Sampling of electrophoresis test procedures • Sampling of melting temperature record monitoring
OBSERVE	• Autoradiographs/gel photographs (low background, clear signal absence of bubbles)
ASK	• How is the endpoint of gel electrophoresis determined? • What criteria are used to interpret electrophoretic gels?

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:

	• Sampling of ISH QC policies and procedures • Sampling of ISH QC records
	• What is your course of action when ISH results do not correlate with culture findings?

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 (i.e. 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.
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 (e.g. Sanger sequencing, pyrosequencing, next generation sequencing (NGS). If NGS methods are used for infectious disease related testing (e.g. 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:

	• Sampling of sequencing policies and procedures
	• Manufacturer's interpretive software (most current version)
	• How does your laboratory detect cross-contamination of samples/amplicons? What action would you take if cross contamination is suspected?

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:

- Sampling of test reports (test methodology, clinical interpretation)
- Sampling of patient tests reports performed with Class I analyte specific reagents (ASRs) including appropriate disclaimer

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, HIV-1 viral load results may vary significantly depending upon the test method used; including the test method in the report is important information for interpreting the results.

*****REVISED** 08/21/2017***

MIC.66120 ASR Disclaimer **Phase II**

If patient testing is performed using Class I analyte-specific reagents (ASRs) obtained or purchased from an outside vendor, the patient report includes the disclaimer statement required by federal regulations.

NOTE: ASRs are antibodies, both polyclonal and monoclonal, specific receptor proteins, ligands, nucleic acid sequences, and similar reagents which, through specific binding or chemical reaction with substances in a specimen, are intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens.

An ASR is the active ingredient of a laboratory-developed test system. Class I ASRs are not subject to preclearance by the US Food and Drug Administration (FDA) or to special controls by the FDA.

If the laboratory performs patient testing using Class I ASRs, federal regulations require that the following disclaimer accompany the test result on the patient report: "This test was developed and its performance characteristics determined by (laboratory name). It has not been cleared or approved by the US Food and Drug Administration."

The CAP recommends additional language, such as "The FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing."

The disclaimer is not required for tests using reagents that are sold in kit form with other materials and/or an instrument, and/or with instructions for use, and/or when labeled by the manufacturer as Class I for in vitro diagnostic use (IVD), Class II IVD, or Class III IVD.

The laboratory must establish the performance characteristics of tests using Class I ASRs in accordance with the Method Performance Specifications section of the All Common Checklist.

The laboratory may put a single ASR disclaimer on the patient report for all microbiology studies collectively used in a particular case. Separately tracking each reagent used for a case and selectively applying the disclaimer to only the class I ASRs is unnecessary.

REFERENCES
1) Department of Health and Human Services, Food and Drug Administration. Medical devices; classification/reclassification; restricted devices; analyte specific reagents. Final rule. Fed Register. 1997(Nov 21);62243-45 [21CFR809, 21CFR864]
2) Caldwell CW. Analyte-specific reagents in the flow cytometry laboratory. Arch Pathol Lab Med. 1998;122:861-864
3) Graziano. Disclaimer now needed for analyte-specific reagents. Northfield, IL: College of American Pathologists CAP Today. 1998;12(11):5-11

LABORATORY SAFETY

The inspector should review relevant requirements from the Safety section of the Laboratory General checklist, to assure that the molecular testing section is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

The following requirement pertains specifically to the molecular microbiology section.

Inspector Instructions:

READ

- Sampling of molecular microbiology specimen handling and processing policies

MIC.66200 Specimen Handling/Processing **Phase II**

There are written policies for the safe handling and processing of samples from patients with suspected infections due to avian influenza, SARS, or similar emerging pathogens.