COLLEGE of AMERICAN PATHOLOGISTS

December 2024 Changes

Immunology Checklist

CAP Accreditation Program

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Using the Changes Only Checklist

This document contains new checklist requirements, major and minor requirement revisions, and changes to explanatory text**. Changes appear in a track changes format that compares the previous checklist edition to the December 26, 2024 edition.** Requirements with significant revisions will display a "Revised" flag. These changes may affect your laboratory operations. Requirements with minor revisions will not display a "Revised" flag. They are editorial changes that are not likely to affect your laboratory operations.

Information regarding requirements that are new or have been combined, moved, resequenced or deleted, as applicable, appears in table format below.

2024 CHECKLIST EDITION CHANGES
NEW, DELETED, MERGED, AND MOVED REQUIREMENTS *

2023 Requirement		Action Taken	2024 Requirement	
IMM	None			

*Deleted – Removed the requirement from the checklist edition
*Merged – Combined the requirement with a similar requirement in the same or different checklist
*Moved – Relocated the requirement to another checklist or resequenced it within the same checklist

ON-LINE CHECKLIST DOWNLOAD OPTIONS

Participants of the CAP accreditation programs may download the checklists ~~from the CAP website (cap.org)~~ by logging into cap.org and going to e-LAB Solutions Suite - Accreditation Checklists. 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.

INTRODUCTION

This checklist is used in conjunction with the All Common and Laboratory General Checklists to inspect an immunology 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.

Policy/Procedure icon - The placement of this icon next to a checklist requirement indicates that a written policy or procedure is required to demonstrate compliance with the requirement. The icon is not intended to imply that a separate policy or procedure is required to address individual requirements. A single policy or procedure may cover multiple checklist requirements.

Laboratories not subject to US regulations: *Checklist requirements apply to all laboratories unless a specific disclaimer of exclusion is stated in the checklist. When the phrase "FDA-cleared/approved test (or assay)" is*

used within the checklist, it also applies to tests approved by an internationally recognized regulatory authority (eg, CE-marking).

QUALITY MANAGEMENT

CALIBRATION AND STANDARDS

Calibration and Verification Processes - Nonwaived Tests

The ~~remaining~~ requirements in this checklist on CALIBRATION, CALIBRATION VERIFICATION, and ANALYTIC MEASUREMENT RANGE (AMR) VERIFICATION do not apply to waived tests.

~~The requirements for calibration, calibration verification and AMR verification in this section apply only to analyses that provide truly quantitative measurements expressed in mass units per unit volume (eg, gm/L or mg/ml) OR in units traceable to a reference preparation or standard that is calibrated in mass units per unit volume. If these criteria are not met, the measurement is NOT quantitative and this section is not applicable.~~

This introduction discusses the processes of calibration, calibration verification, and AMR verification.

CALIBRATION: The process of adjusting an instrument or test system to establish a relationship between the measurement response and the concentration or amount of the analyte that is being measured by the test procedure.

CALIBRATION VERIFICATION: The process of confirming that the current calibration settings for each analyte remain valid for a test system.

Each laboratory must define limits for accepting or rejecting results of the calibration verification process. Calibration verification can be accomplished in several ways. If the manufacturer provides a calibration validation or verification process, it should be followed. Other techniques include (1) assay of the current calibration materials as unknown specimens, and (2) assay of matrix-appropriate materials with target values that are specific for the test system.

ANALYTICAL MEASUREMENT RANGE (AMR): The range of analyte values that a method can directly measure on the specimen without any dilution, concentration, or other pretreatment that is not part of the usual assay process.

LINEARITY AND THE AMR
Linearity is a fundamental characteristic of many analytic measurement methods, whereby there is a straight-line relationship between "true" analyte concentrations and measured concentrations. In this context, linearity refers to the relationship between the predicted and observed measurement results and not to the relationship between instrument signal output and analyte concentration.

AMR VERIFICATION
Laboratories are required to verify that the appropriate relationship is maintained over the AMR. Laboratories may verify and use an AMR that is narrower than the range defined by the manufacturer. This may be appropriate when materials available for method validation and/or AMR verification are not available to verify the full range claimed by the manufacturer, or reporting values across the full range defined by the manufacturer is not clinically relevant. For many assays, results beyond the AMR can be reported through dilution or concentration studies (see IMM.33900 & IMM.33910). AMR verification is not required for calculated test results (refer to the Definition of Terms in the All Common Checklist) as long as the individual results contributing to the calculation have AMR verification.

Minimum requirements for AMR verification can be met by using matrix appropriate materials, which include low, mid and high concentration or activity range of the AMR with recovery of results that fall within a defined range of the target value. Records of AMR verification must be available.

CLOSENESS OF SAMPLE CONCENTRATIONS OR ACTIVITIES TO THE UPPER AND LOWER LIMITS OF THE AMR
When verifying the AMR, it is required that materials used are near the upper and lower limits of the AMR. Factors to consider in verifying the AMR are the expected analytic imprecision near the limits, the clinical impact of errors near the limits, and the availability of test specimens near the limits. It may be difficult to obtain specimens with values near the limits for some analytes. In such cases, reasonable procedures should be adopted based on available specimen materials. The closeness of sample concentrations or activities to the upper and lower limits of the AMR are defined at the laboratory director's discretion. The method manufacturer's instructions for verifying the AMR must be followed, when available. The laboratory director must define limits for accepting or rejecting verification tests of the AMR.

PROCEDURES AND TEST SYSTEMS

BLOOD TYPE, GROUP, AND/OR ANTIBODY SCREENS

***REVISED** 12/26/2024*
IMM.40755 Historical Record Check **Phase II**

ABO/Rh results are compared with historical result records for each patient for at least the preceding 12 months.

NOTE: The purpose of this comparison is to detect sample/patient identification errors or other errors that might lead to the attribution of an incorrect blood type or antibody screen result to a patient. The historical record search can be performed manually by qualified laboratory personnel or with a validated computer system capable of performing historical checks. Acceptable ABO and Rh historical records for transfusion purposes are only those generated or entered by laboratory personnel into the health system's laboratory information system and performed by an accredited laboratory/certified by the relevant government agency in its jurisdiction. If the laboratory performing the testing does not maintain records that would allow this check to be performed, the testing shall be reported with a disclaimer alerting the ordering physician that the check has not been performed and that verifications of the sample's identity and the test results are strongly recommended.

Evidence of Compliance:
✓ Records of historical checks **OR**
✓ Records of LIS historical check validations

SYPHILIS SEROLOGY

***REVISED** 12/26/2024*
IMM.41420 ~~Anti-Treponemal~~Syphilis Antibody Screening **Phase II**

If the laboratory ~~uses anti-treponemal antibody testing as a~~ offers screening ~~test~~ for syphilis~~ infection, all specimens with an initial positive result have a non-treponemal test (eg, RPR, VDRL) performed. If results of the two~~, a complete screening algorithm is followed including appropriate confirmatory/secondary tests~~ are discordant, a second treponemal test on a different platform (eg, TPPA) is required~~.

NOTE: Screening for ~~syphilis~~infection by ~~starting~~Treponemal pallidum can be performed by initial testing with ~~an anti-~~either a nontreponemal (lipoidal antigen) antibody test (ie, traditional syphilis

screening) or a treponemal antibody test ~~first~~ (ie, ~~the~~ reverse sequence syphilis screening ~~algorithm~~). ~~has been shown to be an effective way to screen for infection with Treponema pallidum. It is still acceptable to use RPR or VDRL assays to test for active syphilis (forward algorithm).~~ The reverse ~~algorithm~~screening algorithm (with anti-treponemal antibody testing performed initially) may be preferred in cases of recent infection ~~and~~ or in cases of late latent or tertiary syphilis when ~~non-treponemal~~nontreponemal antibodies may not be detectable ~~or have disappeared over time~~ (even in the absence of adequate treatment)~~, respectively~~.

Regardless of the method used, a positive (reactive) result in the primary screening assay must be reflexively tested by at least one secondary test method. In the traditional syphilis screening algorithm, a nontreponemal (lipoidal antigen) antibody screening assay must be reflexively tested by an anti-treponemal assay (such as EIA or TPPA).

In the reverse sequence screening algorithm, a treponemal antibody screening assay must be tested by a nontreponemal (lipoidal antigen) assay (such as RPR or VDRL). When discordant results are obtained (screening anti-treponemal antibody positive, nontreponemal (lipoidal antigen) negative), an additional anti-treponemal test (eg, TPPA or EIA) must be performed g~~G~~iven the possibility of false positive results in anti-treponemal antibody screening assays ~~however, in cases where the second tier non-treponemal test is negative (non-reactivity), a second anti-treponemal test (eg, TPPA) must be performed. This reflex~~.

Reflex testing in either algorithm may be performed on site or by a referral laboratory.

If the nontreponemal (lipoidal antigen) antibody test is performed to monitor treatment of patients with known syphilis infection (not as a screening tool), anti-treponemal antibody testing is not required. Because anti-treponemal antibodies persist after successful treatment, ~~guidelines recommend performing a non-treponemal test (RPR or VDRL) to help determine if infection~~testing patients with previously diagnosed syphilis using a reverse algorithm approach is ~~current or past. RPR and VDRL are also the assays that~~discouraged; therefore, laboratories should ~~be used to monitor~~ provide a clear option for providers to order nontreponemal (lipoidal antigen) titers directly for following serologic response to treatment.

This checklist requirement only applies to testing serum/plasma specimens. For testing CSF specimens, stand-alone anti-treponemal (eg, FTA-ABS or TPPA) and ~~non-treponemal (~~/or nontreponemal (lipoidal antigen) (eg, VDRL) tests may be used at the discretion of the laboratory director.

Evidence of Compliance:

✓ Records of ~~non-treponemal test confirmation~~confirmatory testing of positive ~~anti-treponemal~~screening antibody results with appropriate secondary assays

REFERENCES

1) ~~Workowski KA~~Papp JR, Park IU, Fakile Y, Pereira L, Pillay A, Bolan GA. ~~Sexually transmitted disease guidelines, 2015. *MMWR*,~~ CDC laboratory recommendations for syphilis testing, United States, 2024. *MMQR Recomm Rep.* ~~2015;64(~~2024;73 (No. RR-~~03):1-37~~): 1-32.

2) Rhoads DD, et al. Prevalence of traditional and reverse-algorithm syphilis screening in laboratory practice. A survey of participants in the College of American Pathologists syphilis serology proficiency testing program. *Arch Pathol Lab Med.* 2017;141(1):93-97.

HIV PRIMARY DIAGNOSTIC TESTING

IMM.41450 HIV Primary Diagnostic Testing - Supplemental and Confirmatory Testing Phase I

The laboratory follows public health recommendations or guidelines for HIV primary diagnostic testing, including primary screening and additional (supplemental and/or confirmatory) testing.

NOTE: If additional testing after a primary screening test is recommended by public health authorities, the laboratory:

- *Performs additional testing reflexively if the specimen is suitable and the test is performed in house, or*
- *Sends additional testing to a referral laboratory if the specimen is suitable, or*
- *Provides guidance to providers on submission of additional specimens, if needed for supplemental or confirmatory testing.*

The US Centers for Disease Control and Prevention (CDC) and Association of Public Health Laboratories (APHL) provide recommendations for HIV testing. Guidelines and recommended algorithms can be found on the CDC and APHL websites.

~~*This checklist item does not apply to the testing of individuals from whom human derived products for therapeutic use are being derived or other types of testing performed for the monitoring of HIV infection (eg, viral load, CD4 counts). Reporting HIV results to public health is not within the scope of this checklist item.*~~

Evidence of Compliance:

✓ Patient reports with initial screening results and reflexive testing results and/or guidance

REFERENCES

1) Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Available at http://stacks.cdc.gov/view/cdc/23447. Published June 27, 2014. Accessed 11/19/2019.
2) National Center for HIV/AIDS, Viral Hepatitis, and TB Prevention (US). Divisions of HIV/AIDS Prevention; Association of Public Health Laboratories. 2018 Quick reference guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens, Available at: https://stacks.cdc.gov/view/cdc/50872. Published January 2018. Accessed 4/2/2023.
3) Association of Public Health Laboratories. Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm. January 2019. Available at APHL Publications. Accessed 11/19/2019.

DIRECT ANTIGEN TESTING

IMM.41820 ***Clostridioides (formerly Clostridium) difficile*** **Phase II**

The laboratory defines criteria for the rejection of specimens for *C. difficile* and/or *C. difficile* toxin testing in stool.

NOTE: The laboratory, in collaboration with institutional stakeholders (eg, infection prevention and control, antimicrobial stewardship, infectious ~~diseases~~disease physicians), must develop criteria for rejection of inappropriate specimens submitted to the laboratory for C. difficile testing. For example, these criteria may include stool consistency (eg, test only unformed stool), repeat testing (eg, do not perform repeat testing during the same episode of diarrhea), and any exceptions. Reference or commercial laboratories may not have the ability to collaborate with stakeholders, but still need to define rejection criteria.

Evidence of Compliance:

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

REFERENCES

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