COLLEGE of AMERICAN PATHOLOGISTS

Master

Histocompatibility Checklist

CAP Accreditation Program

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Histocompatibility Checklist

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ON-LINE CHECKLIST DOWNLOAD OPTIONS

Participants of the CAP accreditation programs may download the checklists 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.

CHECKLIST ACCREDITATION RESOURCES

CAP accredited laboratories have access to additional checklist accreditation tools and resources found on the CAP website (cap.org) by logging into e-LAB Solutions Suite - Accreditation Resources. Content found in Accreditation Resources includes:

- A library of past Focus on Compliance webinars and laboratory inspection preparation videos
- Answers to the most common checklist questions
- Customizable templates and forms (eg, competency assessment, personnel, validation/verification, quality management)
- Proficiency testing (PT) frequently asked questions, forms, and troubleshooting guides
- IQCP eligibility, frequently asked questions, forms, templates, and examples
- Laboratory director education and resources
- Quality management resources
- Inspector training and inspection tip sheets
- Self and post inspection toolbox

SUMMARY OF CHECKLIST EDITION CHANGES
Histocompatibility Checklist
12/26/2024 Edition

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

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

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

Previously Cited Checklist Requirements

- The **inspector's version** of the checklist contains a listing of previously cited checklist requirements. Specific information on those citations, including the inspection date and inspector comments, is included following each related requirement within the checklist.
- Laboratories can access data on previously cited deficiencies by logging into e-LAB Solutions Suite on cap.org and going to Accreditation Reports - Inspection Summation Report.

NEW Checklist Requirements

Requirement	Effective Date
HSC.20985	12/26/2024
HSC.21340	12/26/2024
HSC.38098	12/26/2024

REVISED Checklist Requirements

Requirement	Effective Date
HSC.20200	12/26/2024
HSC.21130	12/26/2024
HSC.21275	12/26/2024
HSC.21382	12/26/2024
HSC.21800	12/26/2024
HSC.22531	12/26/2024
HSC.22775	12/26/2024
HSC.34357	12/26/2024
HSC.34731	12/26/2024
HSC.34918	12/26/2024
HSC.38658	12/26/2024
HSC.39430	12/26/2024
HSC.40000	12/26/2024
HSC.40100	08/24/2023
HSC.45000	12/26/2024

DELETED/MOVED/MERGED Checklist Requirements

Requirement	Effective Date
HSC.24446	08/23/2023
HSC.24633	08/23/2023
HSC.35105	12/25/2024
HSC.38100	12/25/2024

INTRODUCTION

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

Histocompatibility inspectors must be pathologists, clinical scientists or medical technologists who have extensive experience in the practice of histocompatibility testing, are knowledgeable about current CAP Checklist and CLIA requirements, and have completed CAP Inspector Training. Inspectors should, to the greatest extent possible, be peers of the laboratory being inspected.


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).*

APPLICABILITY

The Histocompatibility Checklist covers clinical testing for clinical transplantation support, HLA cellular functional tests, HLA flow cytometry, HLA serology, HLA solid phase assays, and HLA molecular testing.

For histocompatibility testing performed by ***next generation sequencing (NGS) methods,*** *the requirements in the Molecular Pathology Checklist (eg, assay validation, quality control, specimen handling) must be used in conjunction with the Histocompatibility Checklist for inspection.*

DEFINITION OF TERMS

Common, intermediate and well-documented (CIWD) alleles - Common alleles have frequencies of at least 1 in 10,000; intermediate alleles are found at frequencies less than 1 in 10,000 but at least 1 in 100,000; well-documented alleles have been observed five or more times in unrelated individuals but not at the common or intermediate levels.

High resolution typing - A high-resolution typing is defined as an allele or a set of alleles (G or P groups) that encode the same protein sequence for the region of the HLA molecule called the antigen binding site, with the exception of common, intermediate, or well-documented null alleles (CIWD) version 3.0.0, Hurley CL, et al. *HLA.* 2020;95:516-531), which need to be resolved. The high-resolution genotype must include only one unambiguously assigned genotype; however, alternative genotypes can be listed if they do not contain common or intermediate alleles (CIWD) version 3.0.0, Hurley CK, et al. *HLA.* 2020;95:516-531).

Low resolution typing - A low-resolution HLA genotype result provides sufficient information to identify serological splits or their equivalent. In some cases, this may require two-field genotyping results. A list of serological splits can be accessed at: http://hla.alleles.org/nomenclature/index.html.

PROFICIENCY TESTING

Inspector Instructions:

	• Are proficiency testing samples tested with the same cut-offs for clinical HLA antibody determination as clinical specimens? • Are proficiency testing samples for HLA antigens tested to the same level of resolution as clinical specimens?
	• Select a representative clinical report from each service area. Compare the extent of reporting for the relevant proficiency testing sample.

HSC.10475 PT Extent of Testing **Phase II**

Proficiency testing specimens are tested to the same extent as clinical specimens.

NOTE: Proficiency testing samples must be tested using the most comprehensive testing algorithm or pathway applied to patient samples. For example, if a laboratory has a written procedure that calls for both low and high-resolution HLA analysis for a certain patient population, then all PT samples are tested to the highest resolution level.

Evidence of Compliance:

✓ Comparison of patient and proficiency testing work records demonstrating identification to the same extent

QUALITY MANAGEMENT

PROCEDURE MANUAL

Inspector Instructions:

	• Representative sample of procedures for completeness. Current practice must match contents of procedures.

***REVISED** 12/26/2024*

HSC.20200 Procedure Manual **Phase II**

The procedure manual contains specific instructions for test performance, preparation of reagents, control methods, specimen requirements, limitations of the method, and criteria for accepting/rejecting runs and reporting of results for each of the following procedures, as applicable:

1. **Lymphocyte isolation or identification, as applicable**
2. **HLA serologic typing**
3. **HLA molecular typing**
4. **Crossmatching-T cells**
5. **Crossmatching-B cells**
6. **Antibody screening and identification**
7. **Engraftment monitoring**
8. **ABO grouping**
9. **Complement titration**
10. **Environmental 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 2024): [42CFR493.1251(b)(1) and (8)].

SPECIMEN COLLECTION AND HANDLING

Inspector Instructions:

READ	• Sampling of histocompatibility specimen collection/handling/tracking retrieval policies and procedures • Evaluation records (specimen collection containers/anticoagulants) for preservation of sample integrity
ASK	• What are the specimen acceptability criteria for each specimen type? • What is your course of action when you receive unacceptable/sub-optimal histocompatibility specimens? • How does your laboratory ensure preservation of antibody integrity in recipient sera?
DISCOVER	• Review records of unacceptable specimens and follow up. Determine if practice matches procedure.

HSC.20982 Specimen Collection Procedures Evaluation Phase II

The laboratory evaluates its specimen collection procedures to ensure that the anticoagulant/preservation medium in use does not contribute to analytic interference in the assays to be performed, and that it preserves sample integrity as necessary.

NOTE: This may be done through some combination of direct testing by the laboratory, review of the clinical literature, and evaluation of information from manufacturers. It does not mandate exhaustive testing by each laboratory.

Evidence of Compliance:

✓ Records of the evaluation of specimen collection procedures and anticoagulants in collection containers

***NEW** 12/26/2024*

HSC.20985 Extracted Nucleic Acid Specimens **Phase II**

If extracted nucleic acid is accepted as a specimen type, the laboratory ensures that isolation of nucleic acids for clinical testing occurs in a CLIA-certified laboratory or a laboratory meeting equivalent requirements as determined by the CAP and/or the CMS. This policy is clearly displayed to ordering clients.

NOTE: All clinical testing must be performed in CLIA-certified laboratories or laboratories meeting equivalent requirements (refer to GEN.41350 and MOL.35840). This includes all components of testing that may impact the quality of the test result, including isolation or extraction of nucleic acids. Laboratories may choose to have referring clients formally attest that extracted nucleic acid submitted for testing has been isolated or extracted in an appropriately qualified laboratory.

Evidence of Compliance:

- ✓ Written statement on the test requisition, test catalog, or policy available to referring clients stating that the laboratory only accepts isolated or extracted nucleic acids for which extraction or isolation is performed in an appropriately qualified laboratory

HSC.20988 Specimen Integrity - Flow Cytometry **Phase II**

The laboratory has a defined process to evaluate the integrity of flow cytometry specimens.

NOTE: The yield of lymphocytes from blood samples is affected by a number of factors. If specimens are not processed immediately after collection, the laboratory should verify that its anticoagulant, holding temperature and preparation method maintain specimen integrity. Selective loss of cell subpopulations and/or the presence of dead cells may lead to spurious results. Routine viability testing is not necessary on specimens of whole blood that are analyzed within 24 hours of drawing. Analyses on older samples are possible if the laboratory has verified the absence of statistical differences between the fresh and aged specimen phenotype fractions being evaluated.

REFERENCES

1) Clinical and Laboratory Standards Institute. *Enumeration of Immunologically Defined Cell Populations by Flow Cytometry; Approved Guideline.* 2nd ed. CLSI Document H42-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.21050 Recipient Sera **Phase II**

The most appropriate recipient sera are employed for final crossmatching or final selection of donor.

NOTE: There must be a written policy defining an appropriate specimen to utilize in transplantation or final donor selection that takes into consideration the potential recipient's past pregnancies, past transplants, recent blood transfusions, and sensitization history. The specimens must have been properly handled and appropriately stored to preserve antibody integrity.

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee ISCT and EBMT (JACIE). FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration. 8th Edition, December 14, 2021.

***REVISED** 12/26/2024*

HSC.21130 Specimen Storage **Phase II**

Stored specimens are retained in a way which allows for prompt retrieval for further 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.* 2023(Dec 28):[42CFR493.1278(a)(2)].

RESULTS REPORTING

Inspector Instructions:

	• Sampling of patient reports for completeness, use of appropriate nomenclature, and review prior to release • Sampling of referral laboratory accreditation records
	• How are urgent results communicated?

HSC.21250 Patient Reports **Phase II**

Patient results are reported in a legible, easy to interpret format that clearly indicates the test method and delineates the clinical implications of the results.

NOTE: For patient test results that include an interpretative analysis narrative or statement, the name of the individual(s) responsible for the interpretation must be included.

***REVISED** 12/26/2024*

HSC.21275 Final Report **Phase II**

The final report includes the following:

- **Summary of the methods used**
- **Loci tested**
- **Objective findings***
- **Limitations of the methods, when applicable**
- **Interpretation.**

NOTE: For donor registries, aggregate reports may be provided for a group of donors.

When performing testing by next generation sequencing (NGS), the loci tested are not required to be listed on the report.

** For high resolution HLA typing, there is no need to list unresolved non-common, intermediate, or well-documented (CIWD version 3.0.0) alleles or G and P group alleles or codes if stated in the report, client agreement, or client request in writing.*

REFERENCES
1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Hurley CK, et al. Common, intermediate and well-documented HLA alleles in world populations: CIWD version 3.0.0. *HLA.* 2020;95(6):516-531.

HSC.21277 Nomenclature **Phase II**

The HLA antigen and allele assignments and their written designation conform to the current World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System for histocompatibility antigens.

*NOTE: For example: Phenotype is HLA-A1,2; B51,B44; Cw3; DR1,4; DR53; DQ4,8. Genotype is HLA-A*01:01, *02:01; HLA-B*51:07, B*44:03, HLA-C*03:01; HLA-DRB1*01:01, DRB1*04:01; DRB4*01:01; DQB1*04:01, DQB1*03:02. Haplotypes should not be assigned unless all haplotypes can be identified, uniquely, by pedigree analysis. For example, solid organ transplant typings are reported as antigens compatible with UNOS/OPTN requirements and hematopoietic progenitor cell transplant typings are reported at the allele level compatible with National Marrow Donor Program (NMDP) requirements.*

All genotype and phenotype designations must also conform to WHO Nomenclature Committee for Factors of the HLA System recommendations. The laboratory must maintain a list of antigens and alleles defined by the reagents used.

Evidence of Compliance:

- ✓ Appropriate antigen and allele assignments to support the transplant program

REFERENCES
1) http://www.ebi.ac.uk/imgt/hla
2) Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2023(Dec 28):[42CFR493.1278(b)(1)].

HSC.21281 Accreditation of Referral Laboratories — Phase II

Outside referral laboratories are accredited by appropriate histocompatibility agencies. US laboratories are CLIA certified or meet equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS).

NOTE: Laboratories that are members of the United Network for Organ Sharing (UNOS) may only refer histocompatibility testing to other laboratories that are OPTN-approved.

Refer to GEN.41350 for additional information on requirements for referral laboratory selection.

Evidence of Compliance:

- ✓ Records verifying referral laboratory certification/accreditation in histocompatibility

REFERENCES
1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.21287 Result Review — Phase II

All laboratory results (excluding reports from outside referral laboratories) have two levels of independent review, including review by the section director (technical supervisor) or designee prior to release.

NOTE: The initial review may be performed by validated automated analysis or by a qualified individual. The data output results must be reviewed by a qualified individual before release.

Evidence of Compliance:

- ✓ Records of result review

HSC.21295 Critical Reporting — Phase I

The laboratory communicates critical findings when test results meet defined criteria (eg, an unexpected positive crossmatch or development of a de novo donor-specific antibody).

Evidence of Compliance:

- ✓ Records of critical report communications

RECORDS

The records listed below must be kept to the extent of services provided by the laboratory.

Inspector Instructions:

	• Record retention policy • Sampling of stored specimen inventory records/log • Sampling of transplant donor and recipient records • Verification of patient data policy (interval of review is defined) • Sampling of patient histocompatibility data review and verification • Sampling of policies and procedures for donor confidentiality
	• How does your laboratory resolve inter-laboratory HLA typing discrepancies? • How do you store results for comparison with subsequent reports?
	• Review all records of a sampling of patient and donor histocompatibility results and reports to ensure completion of all steps in the process from specimen requisitions to final disposition. Determine if records provide an adequate audit trail of all activities.

HSC.21316 Record and Material Retention - Histocompatibility **Phase II**

A copy of each final report, all records of results, reagent lots, gel images, *in situ* hybridization slides, and histograms used for interpretation and determination of test results are retained in compliance with existing laws.

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.21332 Stored Specimen Log **Phase II**

A log of all stored specimens is maintained to enable prompt retrieval for further testing.

Evidence of Compliance:

✓ Electronic or paper inventory log of stored specimens

*****NEW** 12/26/2024***

HSC.21340 Laboratory Records **Phase II**

Methods, instruments, and reagent lot and shipment numbers used for processing and analyzing each specimen (or batch of specimens) can be identified and traced in the laboratory's records.

RECIPIENT AND DONOR INFORMATION RECORDS

HSC.21350 Clinical Transplant Registries and Transplant Data Retention **Phase II**

The institution participates in and retains records of patient and donor transplant information in the United Network for Organ Sharing (UNOS) Clinical Transplant Registry or its equivalent.

NOTE: The laboratory and/or transplant coordinator must retain records on transplant recipients, including a history of prior transfusion, pregnancy, and prior transplants as well as HLA antibody history, date of transplant(s) and outcome. In addition, there must be records of donor and recipient age, race, sex, ABO, and HLA types. The source of the donor organ or donor hematopoietic stem cells must be recorded. This information can be retained as part of an institutional registry.

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.21366 Record Review **Phase II**

There are records of periodic review and verification of patient histocompatibility data.

NOTE: Histocompatibility tests performed for organ transplantation (HLA typing, HLA antibody sensitization, unacceptable antigens during prior transplants or sensitization, and any pretransplant screening results) must be reviewed and verified when patients are placed on organ waiting lists. Changes or additions to the waiting lists must be verified. These records must be readily available for review and retained for at least two years.

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

****REVISED** 12/26/2024***

HSC.21382 Discrepancy Resolution **Phase II**

The laboratory has a defined process to resolve HLA typing discrepancies within and between laboratories.

NOTE: There must be records of the steps taken to resolve discrepancies.

This requirement applies to HLA testing performed by all testing methods, including next generation sequencing.

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee ISCT and EBMT (JACIE). FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration. 8th Edition, December 14, 2021.

HSC.21390 Donor Confidentiality **Phase II**

The laboratory ensures confidentiality of all donor records, including releasing or sharing donor information for clinical purposes.

NOTE: For example, if identifiable donor information will be shared with the recipient, appropriate donor informed consent must be obtained, donor information must be redacted, or other appropriate action taken.

Refer to the Laboratory General Checklist for specific requirements on patient privacy and patient data accessibility.

REFERENCES

1) Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee ISCT and EBMT (JACIE). FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration. 8th Edition, December 14, 2021.

REAGENTS

Inspector Instructions:

	• Reagent inventory log • Sampling of procedures for reagent and patient sample storage and handling • Sampling of typing/screening tray records for completeness • Validation studies for modified reagents
	• What are your laboratory's criteria for mixing components from one lot number of reagent kit with components from another lot number of kit? • How do you ensure that all reagents are acceptable and in date? • How does your laboratory manage and control reagent inventory?

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

HSC.21612 Reagent Tracking **Phase II**

The laboratory records the reagent lot numbers and shipments used for each assay.

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2004(Oct 1): 1038 [42CFR493.1256(a)]

HSC.21675 Reagent Kit Components **Phase II**

Combinations of reagents from different lots are checked against old reagent lots or with suitable reference material before or concurrently with being placed in service.

Evidence of Compliance:

✓ Records of checks performed on combinations of reagents from different lots

*****REVISED** 12/26/2024***

HSC.21800 Reagent and Specimen Storage **Phase II**

Optimal storage conditions for reagent and specific types of patient specimens are defined and followed.

NOTE 1: Written procedures must include storage and retention requirements for specific types of patient specimens, including lymphocytes, RNA, DNA, and sera.

NOTE 2: Use of continuous monitoring and alert systems and back-up storage plans must be specified as applicable.

Evidence of Compliance:

✓ Records of storage and retention at defined conditions

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(a)(1) and (a)(2)].

2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.21805 Histocompatibility Reagent Confirmation of Acceptability **Phase II**

New typing reagents are checked using suitable reference materials prior to use.

NOTE: Suitable materials for checking typing reagents include the use of previously typed cells or known archived DNA. Suitable materials for checking reagents for engraftment monitoring include the use of previously tested or archived admixtures.

Evidence of Compliance:

✓ Records of acceptability studies for new reagents prior to use

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(a)(3)].

HSC.21810 Specimen Handling - Typing/Screening Trays **Phase II**

If typing trays and antibody screening trays are prepared locally, the records indicate source, bleeding date, donor, identification, and available volume for sera and a means of identifying, locating and collecting fresh donor cells.

HSC.21835 Modified Reagent Use **Phase II**

If reagents are used in a manner different than manufacturer's instructions, there are records of validation studies.

Evidence of Compliance:

✓ Validation study data

CONTROLS

Inspector Instructions:

READ	• Sampling of QC policies and procedures • Sampling of lymphocyte preparation viability checks • Sampling of QC records
OBSERVE	• Control material (labeling)
ASK	• How do you determine when QC is unacceptable and corrective actions are needed? • What is your course of action when QC for compatibility testing is not acceptable?

DISCOVER

- Review a sampling of QC data over the previous two-year period. Select several occurrences in which QC is out of range and follow documentation to determine if the steps taken follow the laboratory procedure for corrective action

HSC.21850 Daily Controls **Phase II**

The laboratory performs positive and negative controls daily, using positive controls for specific cell types (T cells, B cells, etc.), where available.

NOTE: Positive and negative controls must be run with each test procedure where appropriate. This must include daily positive controls for specific cell type (T cells, B cells, etc.), as well as appropriate antibody isotypes as needed for each assay. This must also include one positive control serum that is historically reactive to all Class I and/or Class II positive cells at the same dilutional titer as appropriate for the methodology utilized.

Evidence of Compliance:

✓ Records of control results

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):7168 [42CFR493. 1256(d)(3)(iii)]

HSC.21950 Viability Checks **Phase II**

Viability checks on lymphocyte preparations are performed by recording negative control results or by performing and recording a separate test each time they are used.

NOTE: For cytotoxicity procedures, cell viability after initial incubation should be greater than 80% in the negative control well.

Evidence of Compliance:

✓ Records of viability checks on lymphocyte preparations

HSC.22070 Compatibility Testing Controls **Phase II**

The laboratory includes control material for each phase of compatibility testing.

NOTE: Results of patient testing must not be reported until control values are reviewed and found acceptable.

HSC.22140 QC Handling **Phase II**

The laboratory tests control specimens in the same manner and by the same personnel as patient/client samples.

NOTE: Personnel who routinely perform patient testing must analyze QC specimens; however, this does not imply that each operator must perform QC daily. Personnel must participate in QC on a regular basis. To the extent possible, all steps of the testing process must be controlled.

Evidence of Compliance:

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

REFERENCES

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

HSC.22150 Alternative Control Procedures Phase II

If the laboratory performs test procedures for which control materials are not commercially available, the laboratory performs and records alternative control procedures to detect immediate errors and monitor test system performance over time.

NOTE: "Performance" includes elements of accuracy, precision, and clinical discriminating power. The following are examples of alternative procedures: 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:

✓ Records of alternative control procedures

REFERENCES

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

HSC.22160 QC Confirmation of Acceptability Phase II

Personnel review control results for acceptability before reporting patient/client results.

NOTE: If the positive and negative controls do not give the expected outcome, the results are not reportable. The negative control serum is one that historically has been negative with all tested cells.

The negative control may also originate from a non-sensitized male whose serum has been shown to be totally negative for cell death in cytotoxicity systems.

Evidence of Compliance:

✓ Records of control result approval

REFERENCES

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

HSC.22170 QC Corrective Action Phase II

The laboratory performs and records corrective action when control results exceed defined acceptability limits.

NOTE: The actions taken must be consistent with the laboratory's quality control program (GEN.30000). 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. For example, evaluation could include comparison of patient means for the run in question to historical patient means, and/or review of selected patient results against previous results to see if there are consistent biases (all results higher or lower currently than previously) for the test(s) in question.

Evidence of Compliance:

✓ Records of corrective action for unacceptable control results

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1445(e)]
2) Department of Health and Human Services, Centers for Medicare and Medicaid Serivces. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Oct 1): [42CFR493.1282(b)].

HSC.22190 Monthly QC Review **Phase II**

The laboratory director or designee reviews and assesses quality control data at least monthly.

NOTE: The reviewer must record follow-up for outliers, trends, or omissions that were not previously addressed.

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

Evidence of Compliance:
- ✓ Records of QC review **AND**
- ✓ Records of corrective action taken when acceptability criteria are not met

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.

TEMPERATURE-DEPENDENT EQUIPMENT

Inspector Instructions:

READ	• Sampling of thermocycler monitoring logs • Sampling of alert system checks • Sampling of LN2 monitoring records
ASK	• What back-up options are available in the event of an electrical power failure? • How is the storage unit alert system monitored? How was the response time validated? • How does the laboratory ensure the individual wells of the thermocycler are maintaining accurate temperature?

*****REVISED** 12/26/2024***

HSC.22531 Alarm System **Phase II**

All sample and reagent storage units are monitored continuously (24 hours per day) with an in laboratory or remote alarm system.

NOTE: All storage units must have a continuous monitoring and alert system (in laboratory or remote). The laboratory must be able to demonstrate how this system works, and that there is a process to ensure a timely response to an alarm.

Evidence of Compliance:
- ✓ Records of continuous monitoring that includes alarms

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(a)(1)].

HSC.22562 Alarm System Checks **Phase II**

Alarm systems are checked for functionality initially and at specified periodic intervals.

NOTE: The alarm system must be checked at specified periodic intervals to ensure proper function.

Evidence of Compliance:
- ✓ Records of alarm testing

HSC.22593 Power Failure Back-up **Phase II**

The alarms continue to function if the power is interrupted.

NOTE: Alarm systems must have a source of power separate from the house current, in order to allow proper monitoring during power failures. This can be accomplished by a separate circuit, power failure alarm, or battery power.

HSC.22625 Cell Freezers **Phase II**

The laboratory monitors and maintains adequate liquid nitrogen (LN2) levels in cell freezers.

NOTE: The system must ensure that an adequate supply of liquid nitrogen is present to maintain optimal cell storage temperature.

Evidence of Compliance:
- ✓ Records of monitoring of LN2 levels

*****REVISED** 12/26/2024***
HSC.22775 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 preventative maintenance.

Evidence of Compliance:
- ✓ 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) 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): [42CFR1252(b)].

COLORIMETERS, SPECTROPHOTOMETERS, AND FLUOROMETERS

The following requirements apply to stand-alone instruments; they are not applicable to instruments embedded in automated equipment for which the manufacturer's instructions must be followed.

Inspector Instructions:

	• Spectrophotometer policy or procedure • Sampling of manufacturer required system checks
	• Filters (clean, not scratched or deteriorated)

HSC.23137 Absorbance/Linearity **Phase II**

Absorbance and/or linearity fluorescence is checked and recorded at least annually or as often as specified by the manufacturer, with filters or standard solutions.

Evidence of Compliance:

✓ Records of absorbance and linearity checks at required frequency

HSC.23324 Filter Photometers **Phase II**

Filters (filter photometers) are checked at least annually to ensure they are in good condition (eg, clean, free of scratches).

Evidence of Compliance:

✓ Records of filter checks at defined frequency

HSC.23511 Spectrophotometer Checks **Phase II**

Spectrophotometer (including ELISA plate readers) wavelength calibration, absorbance and linearity are checked at least annually (or as often as specified by the manufacturer), with appropriate solutions, filters or emission line source lamps, and the results recorded.

NOTE: Some spectrophotometer designs, eg, diode array, have no moving parts that can alter wavelength accuracy and do not require routine verification. The manufacturer's instructions must be followed.

Evidence of Compliance:

✓ Records of spectrophotometer checks at required frequency

HSC.23698 Stray Light **Phase II**

Stray light is checked at least annually with extinction filters or appropriate solutions, if required by the instrument manufacturer.

Evidence of Compliance:

✓ Records of stray light checks at required frequency

ELECTROPHORESIS EQUIPMENT

Inspector Instructions:

	• Sampling of voltage check records
	• Electrophoresis equipment (clean, properly maintained)

HSC.25007 Electrophoresis Equipment **Phase II**

All electrophoretic apparatus in the laboratory is clean and properly maintained (electrodes and buffer tank intact, power supply electrodes fit snugly, no build-up of dried buffer).

HSC.25194 Voltage Reading **Phase II**

The displayed voltage reading is confirmed at least annually by a voltmeter or other suitable means for all power supplies in the laboratory.

Evidence of Compliance:

✓ Records of annual voltage checks

PROCEDURES AND TEST SYSTEMS

Inspector Instructions:

	• If problems are identified during the review of the procedures and test systems, or when asking questions, further evaluate the laboratory's responses, corrective actions and resolutions • Select a representative assay and follow the entire process from specimen receipt to final result reporting

LYMPHOCYTE ISOLATION

Inspector Instructions:

	• Lymphocyte isolation policies and procedures

HSC.27438 Lymphocyte Source **Phase II**

The source of the lymphocytes is recorded.

NOTE: These may include blood, bone marrow, lymph nodes, spleen, or cultured cells.

SEROLOGICAL PROCEDURES

GENERAL

Inspector Instructions:

READ	• Sampling of complement reagent validation records
ASK	• How does your laboratory ensure cell death is appropriately measured?

HSC.27625 Scoring System **Phase II**

A scoring system is used for measuring cell death in cytotoxicity tests.

NOTE: There must be established limits for defining positive and negative results by approximate percentage of cell death.

HSC.27812 QC - Complement **Phase II**

Each lot, batch and/or shipment of complement is checked for effectiveness before or during use for each specific target cell and each test method.

NOTE: Each lot, batch and/or shipment of complement must be evaluated to determine that it can mediate cytotoxicity when a specific antibody is present, and is not cytotoxic in the absence of a specific antibody. For each specific target cell (T cell, B cell, monocyte, etc.), complement cytotoxicity studies must be performed to determine optimal dilution for each type of cell tested by cytotoxicity. Two HLA antibodies should have variable antibody strengths when utilized in complement testing against 2 different known antigen-containing cells that are reactive to the antibodies. Alternatively, one antibody may be utilized at variable dilutions for complement testing.

Evidence of Compliance:

- ✓ Records of validation of complement reagents

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(e)]
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(a)(3)].

HLA CLASS I AND II ANTIGEN TYPING

Inspector Instructions:

READ	• Sampling of HLA Class I & Class II Ag typing policies and procedures. Procedures should specify the level of resolution of HLA typing required for each tissue or organ transplanted. • Sampling of HLA typing of solid organ and hematopoietic progenitor cell transplantation policies and procedures • List of antigens defined by reagents used • Sampling of typing reagent validation records • Sampling of typing tray QC records
ASK	• How does your laboratory select target cells to ensure the detection of antigens recognized by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System? • What is your laboratory's course of action when a donor cannot be reliably HLA typed?

HSC.28186 Serologic Typing - Class I **Phase II**

Target cells are defined for serological determination of HLA Class I antigens, and selected to permit typing the antigens officially recognized by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System for which reagents are readily available.

NOTE: HLA Typing for all hematopoietic progenitor cell donors and recipients, and deceased organ donors must be performed by molecular methods. Serological determination of HLA Class I antigens should be performed on T cells or mononuclear cell preparations. Local serological typing reagents must be supported by appropriate documentation of HLA specificity, using cells of known HLA types. The test must detect WHO recognized specificities.

REFERENCES
1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(b)].

HSC.28373 Serologic Typing - Class II **Phase II**

The methodology for serological Class II antigen typing defines the proportion of B-cells needed for optimal testing, and the specificities that are officially recognized by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System and for which reagents are readily available.

NOTE: The method should produce at least 80% B-cell enriched preparations. Documentation of B cell enrichment may not be necessary when procedural techniques already distinguish T- and B-lymphocytes, or when well-characterized antibodies are used that can only discriminate and identify Class II antigens. HLA typing for all hematopoietic progenitor cell donors and recipients, and deceased organ donors must be performed by molecular methods.

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(b)].
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.28560 Class I Antigen Defined **Phase II**

The minimum number of Class I antisera used are defined by the laboratory.

HSC.28747 Class II Antigen Defined **Phase II**

The minimum number of Class II antisera used is defined by the laboratory.

HSC.28934 Typing Trays **Phase I**

The typing trays used for disease association testing permit characterization of at least those antigens accepted by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System for which sera are readily available.

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):7170 [42CFR493. 1278(a) through (c)]

HSC.28996 Controls - Typing Trays **Phase II**

Each typing tray contains both a positive and a negative control.

NOTE: The positive control must be known to react with all cells expressing the class of antigens being tested at a titer comparable with the typing reagents. Each typing tray must also contain one negative control. Cell viability in the negative control must be sufficient to accurately interpret the results. The use of sufficiently discriminatory positive and negative controls also applies to assays in which cell viability is not required.

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(a)(3)].

CYTOTOXICITY CROSSMATCH

Inspector Instructions:

READ

- Sampling of cytotoxicity crossmatch policies and procedures including method sensitivity

HSC.29308 HLA Crossmatch Sensitivity **Phase II**

The method used in the HLA crossmatch procedure is more sensitive than the basic complement dependent micro-lymphocytotoxicity crossmatch and is able to distinguish between reactions with T and B lymphocytes, such that crossmatches with donor T-lymphocytes identify Class I anti-HLA antibodies and crossmatches with donor B-lymphocytes identify Class I and Class II anti-HLA antibodies.

Evidence of Compliance:

- ✓ Records of method sensitivity **AND**
- ✓ Peer-reviewed published literature on method sensitivity

HSC.29495 Crossmatch **Phase II**

The laboratory defines the patient sera and donor cells utilized for final crossmatch testing.

NOTE: Cellular targets for transplant crossmatches must include donor T-cells, and may include donor B-cells when appropriate.

REFERENCES
1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(e)].

HSC.29682 Specimen Handling **Phase II**

Patient samples for crossmatch testing are used undiluted, and kept frozen for a defined time post-transplantation.

REFERENCES
1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.29869 Final Crossmatch Results Availability **Phase II**

The laboratory defines criteria for availability of final crossmatch results for renal transplant patients (before transplantation) and for presensitized extrarenal transplant patients.

NOTE: Laboratories supporting solid organ transplants must be capable of performing prospective crossmatches and must have a written policy describing in what situations pre- or post-transplant crossmatching is performed for all types of solid organ transplants. Results of the final crossmatch must be available before a kidney transplant is performed. The policy for presensitized extrarenal transplant patients must describe if and when crossmatches are performed. Crossmatches may be physical or virtual crossmatches as defined in the policy.

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(e)].
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.29874 Virtual Crossmatch **Phase II**

The eligibility criteria and process used to perform a prospective virtual crossmatch are defined for each transplant program the laboratory serves.

NOTE: The laboratory must define the following, as applicable:
1. *Patient eligibility criteria (eg, sensitization level)*
2. *Sample date eligibility criteria*
3. *Evaluation of known sensitizing events since the last sample date*
4. *Requirement for recipient solid phase antibody testing and donor molecular HLA typing*
5. *Description of antibody interpretation (eg, consideration of locus, cutoff value, cross-reactivity, epitome, etc.) utilized in the virtual crossmatch*
6. *Situations requiring additional testing (eg, donor high resolution typing, DPA1 typing, up-to-date antibody testing)*
7. *Process for reporting the virtual crossmatch results.*

The virtual crossmatch eligibility criteria and procedure must be addressed within each transplant program agreement.

If a prospective physical crossmatch is performed, the above eligibility criteria are not applicable.

REFERENCES
1) Bray RA, Nolen JD, Larsen C, et al. Transplanting the highly sensitized patient: The emory algorithm. *Am J Transplant.* 2006 Oct;6(10):2307-15. doi: 10.1111/j.1600-6142.2006.01521.x. Epub 2006 Aug 25. PMID: 16939516.
2) Jackson AM. The Virtual Crossmatch: An Essential Tool for Transplanting Sensitized Patients. *Clin Transpl.* 2014:131-6. PMID: 26281137.

RED CELL TYPING

Inspector Instructions:

READ	• Sampling of blood type/antibody screen policies and procedures • Sampling of current typing sera/reagent package inserts, for consistency with written procedures • Sampling of typing sera/reagent cell reactivity/anti-D QC records • Sampling of patient records with forward and reverse grouping • Record retention policy • Sampling of historical record checks
DISCOVER	• If there has been an instance where the ABO and Rh typing results were not in agreement with the patient's historical record, further evaluate the laboratory's responses, corrective actions and resolutions

HSC.29877 Reagent Handling - Red Cell Typing Reagents — Phase II

Typing sera and reagent cells are used according to the manufacturer's instructions; or, if alternative procedures are used, validation records confirm that they perform as intended.

NOTE: Testing methods used for ABO, Rh and antibody screening that are different from the manufacturer's instructions, are acceptable provided they are not prohibited by the manufacturer, have been demonstrated to be satisfactory, or, for laboratories subject to US regulations, have been approved by the Centers for Biologics Evaluation and Research (CBER).

Evidence of Compliance:

✓ Records of validation if instructions have been modified

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):[42CFR493.1271(a)(1)]

HSC.29885 Package Inserts/Manufacturer's Instructions - Red Cell Typing — Phase II

Current package inserts/manufacturer's instructions are available for the red cell typing reagents used by the laboratory.

NOTE: The laboratory must have a procedure that assures that:
- *The most current manufacturer's instructions/package inserts are in use*
- *The relevant procedures are updated when changes to the instructions occur.*

Although it is not required to retain discontinued instructions, the laboratory must have a process to obtain expired package inserts from the manufacturer, if requested.

HSC.29893 Forward/Reverse Typing — Phase II

For each patient, red blood cells are tested with anti-A, anti-B, and anti-D, and serum/plasma is tested using A1 and B reagent red cells.

NOTE: The ABO/Rh type of the patient's red blood cells must be determined by an appropriate test procedure. Tests on each sample must include forward and reverse grouping. Discrepancies between cell and serum groups must be resolved before ABO group is assigned.

Evidence of Compliance:

✓ Logs or computer records with forward and reverse grouping

HSC.29901 A1 Red Cell Subgrouping **Phase II**

There is evidence of the specificity of A1 subgroup testing in the ABO system to distinguish A1 from other red cell subgroups.

NOTE: If the organ donor has been transfused with red blood cells in the past three months, ABO subgroup typing must be performed on a pretransfusion sample. This is due to the possibility of misinterpretation of ABO subgroup typing.

HSC.29909 Antisera/Reagent Red Cell QC **Phase II**

There are records of acceptable reactivity and specificity of typing sera and reagent red cells on each day of use, including a check against known positive and negative cells or antisera, or manufacturer's instructions for daily quality control are followed.

NOTE: Unless manufacturer's instructions state otherwise, the following apply:

- *Typing reagents, including antisera (eg, anti-D, anti-K, anti-Fy(a)) and reagent red cells must be checked for reactivity and specificity on each day of use. Typing antisera must be checked with known positive and negative cells; reagent red cells must be checked with known positive and negative antisera.*
- *Each cell used for antibody screening must be checked each day of use for reactivity of at least one antigen using antisera of 1+ or greater avidity.*
- *Anti-IgG reactivity of antiglobulin reagents may be checked during antibody screening and crossmatching.*

This checklist requirement can be satisfied by testing one vial of each reagent lot each day of 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*. 1992(Feb 28):7171 [42CFR493.1256]

HSC.29925 Historical Record Check - Red Cell Typing **Phase II**

ABO, Rh, and antibody screen test results are compared with results of the same tests performed previously to detect discrepancies.

Evidence of Compliance:

✓ Records of historical result comparisons

HSC.29941 Results Reporting - ABO Antibody Titers **Phase I**

The laboratory defines how to perform and interpret ABO antibody titers.

HSC.29949 Anti-D Controls **Phase II**

Appropriate control(s) are used for anti-D testing.

NOTE: If an anti-D reagent contains a potentiating diluent, the appropriate control is the diluent alone. Controls used must be consistent with the manufacturer's instructions.

Evidence of Compliance:
- ✓ Records of anti-D control results

FLOW CYTOMETRY

INSTRUMENTATION AND PHENOTYPING

Inspector Instructions:

READ	• Sampling of flow cytometry policies and procedures • Sampling of QC policies and procedures (includes acceptable control type/frequency for each flow cytometric application) • Sampling of QC records • Sampling of optical alignment/laser output checks
ASK	• How does your laboratory monitor instrument reproducibility? • How does your laboratory ensure each fluorochrome is appropriately calibrated? • How does your laboratory determine appropriate color compensation settings? • How does your laboratory ensure nucleic acid dye specificity?

HSC.29957 QC - Quantitative Assays **Phase II**

The laboratory analyzes at least two levels of positive cellular controls for quantitative assays (eg, CD4+, CD34+ cell concentrations) each day of patient testing or after an instrument restart to verify the performance of reagents, preparation methods, staining procedures, and the instrument.

NOTE: One of the levels of these controls should be at (or near) clinical decision levels (eg, low CD34).Control testing is not necessary on days when testing is not performed.

Evidence of Compliance:
- ✓ Records of QC results

HSC.29965 Optical Alignment **Phase II**

The laboratory monitors optical alignment (where applicable) and instrument reproducibility on each day of use or after each time the flow cytometer is started.

NOTE: Instrument performance must be monitored under the same conditions used to run test samples.

Evidence of Compliance:
- ✓ Records for monitoring optical alignment (where applicable) and instrument reproducibility

REFERENCES
1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Flow Cytometric Analysis of Neoplastic Hematolymphoid Cells; Approved Guideline—Second Edition*. CLSI document H43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.29973 Fluorochrome Standards **Phase II**

Appropriate standards for each fluorochrome (eg, fluorescent beads) are run each day that the instrument is used as part of the calibration.

NOTE: These steps are necessary to optimize the flow system and the optics of the instrument.

Evidence of Compliance:

✓ Records of calibration results using appropriate fluorochrome standards

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Enumeration of Immunologically Defined Cell Populations by Flow Cytometry; Approved Guideline—Second Edition*. CLSI document H42-A2 (ISBN 1-56238-640-9). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2007

HSC.29981 Color Compensation Settings — Phase II

The laboratory defines appropriate color compensation settings.

NOTE: For two or more color analysis there must be a procedure to ensure that cells co-labeled with more than one fluorescent reagent can be accurately distinguished from cells labeled only with one reagent. Cells stained with mutually exclusive antibodies bearing the relevant fluorochromes are the proper reference material for establishing appropriate compensation settings.

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Flow Cytometric Analysis of Neoplastic Hematolymphoid Cells; Approved Guideline—Second Edition*. CLSI document H43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.29989 Laser Performance — Phase I

The laboratory ensures acceptable and constant laser instrument performance.

NOTE: For some instruments, current is a better gauge of laser performance than is power output, which may be relatively constant.

HSC.29997 Gating Techniques — Phase II

Appropriate gating techniques are used to select the cell population for analysis.

NOTE: This may involve a combination of light scatter and/or fluorescence measurements. This is particularly important if the cell samples have a low lymphocyte count and/or a relatively high monocyte-granulocyte count. Lymphocyte gates may be validated using linear forward angle light scatter and 90-degree side scatter, and/or by using monoclonal antibodies to markers, such as CD45 and CD14.

REFERENCES

1) Clinical and Laboratory Standards Institute. *Enumeration of Immunologically Defined Cell Populations by Flow Cytometry; Approved Guideline.* 2nd ed. CLSI Document H42-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.30005 Markers/Cursors — Phase II

The laboratory has defined criteria for setting markers (cursors) to distinguish fluorescence negative and fluorescence positive cell populations.

NOTE: Each laboratory must have a set of objective criteria to define the appropriate placement of markers (cursors) to delineate the population of interest. Isotypic controls may not be necessary in all cases, and cursor settings for the isotype control may not be appropriate for all markers. Cursor settings must be determined based on the fluorescence patterns from the negative and positive populations for CD3, CD4, and CD8.

REFERENCES

1) National Institute of Allergy and Infectious Diseases/Division of AIDS flow cytometry guidelines, sec 3.09B and 5.03A
2) Sreenan JJ, *et al*. The use of isotypic control antibodies in the analysis of CD3+ and CD3+, CD4+ lymphocyte subsets by flow cytometry. Are they really necessary? *Arch Pathol Lab Med.* 1997;121:118-121

HSC.30013 Cellular Viability — Phase II

The laboratory defines when the percentage of viable cells in each test specimen is measured.

NOTE: Selective loss of cell subpopulations and/or the presence of dead cells may lead to spurious results. This does not mean that all specimens with low viability must be rejected. Finding an abnormal population in a specimen with poor viability may be valuable but the failure to find an abnormality should be interpreted with caution. If specimen viability is below the established laboratory minimum, test results may not be reliable and this should be noted in the test report. Routine viability testing may not be necessary. However, viability testing of specimens with a high risk of loss of viability, such as disaggregated lymph node specimens, is required.

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Flow Cytometric Analysis of Neoplastic Hematolymphoid Cells; Approved Guideline—Second Edition*. CLSI document H43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.30021 Immunoglobulin Staining Phase II

The laboratory ensures that immunoglobulin binding is specific.

NOTE: Many cell types will bind serum immunoglobulin nonspecifically via Fc receptors, and steps may have to be taken to ensure that immunoglobulin staining detected by flow cytometry is specific rather than non-specific.

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Flow Cytometric Analysis of Neoplastic Hematolymphoid Cells; Approved Guideline—Second Edition*. CLSI document H43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.30029 Cell Population Distinction Phase II

The laboratory distinguishes fluorescence-negative and fluorescence-positive cell populations.

NOTE: This does not imply that a separate negative control sample must be run. It is possible to coordinate panels of monoclonal antibodies to compare the binding of monoclonal antibodies of the same subclass that typically have mutually exclusive patterns of reactivity of subsets of hematopoietic cells. In this way, test antibodies may also double as control reagents.

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Flow Cytometric Analysis of Neoplastic Hematolymphoid Cells; Approved Guideline—Second Edition*. CLSI document H43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

HSC.30037 Staining Methodology Phase II

The staining and analytical processes described in the procedure manual are based upon established methodology (reference cited).

NOTE: Many different variables need to be controlled to ensure proper stoichiometry of dye binding to DNA. Therefore, it is essential that procedures adopted by a laboratory are based on published work.

HSC.30045 Specimen Treatment Phase II

Specimen treatment with nucleic acid dye includes treatment with RNAse if the dye is not specific for DNA.

NOTE: Certain dyes used to stain fixed cells, (eg, ethidium and propidium iodide) bind to RNA. Prior treatment with RNAse eliminates artifactual broadening of the DNA content distributions that would result from fluorescence of complexes of the dye with RNA.

REFERENCES
1) Shapiro HA. Practical flow cytometry. New York, NY: Alan R. Liss, 1985

FLOW CYTOMETRY CROSSMATCH

Inspector Instructions:

	• Sampling of flow cytometry crossmatch policies and procedures • Sampling of QC policies and procedures • Sampling of QC records • Sampling of positive cutoff validation records
	• How has your laboratory established the cutoff for positive crossmatch results? • Are cutoffs for crossmatches reviewed with the clinical transplant service? • Have the cutoffs been correlated with signal strength or other measure of antibody concentration in the HLA antibody screen and detection methods used? • How does your laboratory ensure separation of Class I & Class II antibodies?

HSC.30056 Crossmatch **Phase II**

The flow cytometry crossmatch identifies antibodies to T and B-cells.

NOTE: Two or multiple color techniques must be used to identify antibodies to T cells. Antibodies to B cells and other target cells must also be identified properly.

HSC.30243 IgG Antibody Identification **Phase II**

IgG antibodies are identified by appropriately labeled heavy chain-specific F(ab')2 reagents.

HSC.30430 Sensitivity **Phase II**

There is a record of the number of cells and volume of serum used for optimal sensitivity.

HSC.30617 Negative Control - Normal Human Serum **Phase II**

Normal human serum with demonstrated lack of reactivity against any potential target cell is used as a negative control.

Evidence of Compliance:
✓ Records of control results

HSC.30804 Positive Control - Diluted Human Serum **Phase II**

The positive control is an appropriately diluted human serum containing suitable HLA antibodies of appropriate immunoglobulin class known to react with lymphocytes from all donors.

Evidence of Compliance:
✓ Records of control results

HSC.30991 Antibody Reagents **Phase II**

The antibody reagents (anti IgG, IgM, IgA, etc.) are used at a selected dilution for optimal sensitivity and class specificity.

HSC.31178 Positive Crossmatch Results Cut-off **Phase II**

The cut-off for positive crossmatch results is determined by testing an appropriate number of sera from non-alloimmunized individuals and established for all pertinent target cells (T-cells, B-cells, etc.).

Evidence of Compliance:

✓ Records for the validation of the positive cut-off

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.31552 HLA Class II Antibody Procedure **Phase II**

The procedure for HLA Class II antibodies readily separates Class I from Class II specificity.

HLA ANTIBODY SCREENING

Inspector Instructions:

READ	• Sampling of HLA antibody screening policies and procedures, including protocol for screening for each organ transplanted or hematopoietic progenitor cell recipient and the frequency of such screening • Agreement for reflex testing using more sensitive screening method, if applicable • Sampling of antibody identification QC records • Sampling of initial and subsequent recipient sera screening records
ASK	• What is your laboratory's course of action for antibody identification/crossmatching for high risk patients? • How does the laboratory determine cutoffs for identification of HLA antibody based on the clinical programs supported? • How does the laboratory determine the assignment of unacceptable antigens for organ transplantation?

HSC.32487 Immunizing Event **Phase II**

There is a system to record any potential immunizing event that could cause sensitization in a patient.

NOTE: There must be a policy that encourages timely blood sample collection at 14 days after the potential immunizing event in a patient. This new sample should be available for use in antibody screening and crossmatch studies.

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1278(c)].
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.32674 HLA Antibody Detection **Phase II**

The laboratory has the capability to detect HLA antibodies with sufficient sensitivity and to distinguish HLA antibodies from IgM autoantibodies or non-HLA antibodies.

NOTE: Methods to detect HLA antibodies must be more sensitive than the basic/NIH technique. There must be written procedures to differentiate HLA antibodies from autoantibodies.

REFERENCES
1) Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee ISCT and EBMT (JACIE). FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration. 8th Edition, December 14, 2021.
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2023(Dec 28): [42CFR1278(d)(1)].
3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2023(Dec 28): [42CFR1278(e)(1)].

HSC.32861 Antigenic Diversity and Targets — Phase II

There is sufficient antigenic diversity (individual antigens and/or crossreactive groups) for HLA Class I and II, and sufficient numbers of antigenic targets for optimal HLA antibody detection and specificity determination.

NOTE: There must be sufficient diversity for Class I and II HLA antigens and cross reactive groups, as well as sufficient numbers of well-characterized panel cells or HLA-purified protein targets for antibody detection and specificity determinations, and strength/avidity of the antibody when applicable.

Evidence of Compliance:
- ✓ Listing of antigenic targets for each panel cell

HSC.33048 Antibody Detection and Specificity QC — Phase II

For HLA antibody detection and specificity determinations, positive and negative controls are used, and sera tested undiluted and diluted when appropriate.

Evidence of Compliance:
- ✓ Records of QC for antibody detection and identification

HSC.33235 Target Source for Class I/II Antibody Determination — Phase II

There are records that the appropriate target sources are used for separate HLA Class I and II antibody determination including appropriate methods to distinguish antibody mixtures.

NOTE: There must be records that the appropriate target sources are used for HLA Class I and II antibody determination. The targets for HLA Class I antibody determination should be blood, spleen, lymph nodes, and cell lines. In addition, well-characterized purified HLA protein targets may also be used. Class II antibodies are best detected utilizing B-lymphocytes, B-lymphoblastoid cell lines, CLL cells or specific Class II purified HLA protein. Mixtures must be defined by methods shown to distinguish Class I from Class II reactivity.

Evidence of Compliance:
- ✓ Records of target sources used for HLA Class I/II antibody determination and to differentiate antibody mixtures

HSC.33422 Recipient Sera Screening — Phase II

All recipient sera are screened for HLA antibodies including, at minimum, an initial sample at the time of HLA typing, after sensitizing events and upon request.

Evidence of Compliance:

- ✓ Defined criteria for screening recipient sera **AND**
- ✓ Records showing initial screening of recipient sera and all subsequent screening results

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2023(Dec 28): [42CFR1278].

HSC.33475 Antibody Identification/Crossmatching **Phase I**

The laboratory performs antibody identification and crossmatching as defined by the transplantation programs supported by the laboratory (includes solid organ and hematopoietic progenitor cell transplantation).

MOLECULAR TESTING

If next generation sequencing (NGS) methods *are used for histocompatibility testing, the applicable requirements in the Molecular Pathology Checklist (eg, assay validation, quality control, specimen handling, NGS section) must be used in conjunction with the Histocompatibility Checklist for inspection.*

Inspector Instructions:

	• Sampling of molecular HLA typing policies and procedures • Specimen storage/handling procedure • Sampling of QC records • Sampling of HLA typing and hematopoietic progenitor cell engraftment reports for completeness • Sampling of the following records: molecular weight marker, in-house probe labeling validation, nucleic acid measurement, electrophoretic gel interpretation, and chimerism measurement
	• Raw data (eg, gel images, sequencer histograms, flow microbead fluorescence intensity histograms) • Current databases of known sequences for all alleles recognized by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System (available) • Pre/post amplification areas (adequate physical separation)
	• What is your laboratory's process for assessing the quality (intactness) of high molecular weight DNA or RNA? • How does your laboratory avoid cross-contamination when performing amplification procedures? • How does the laboratory ensure the level of HLA typing resolution is adequate for each transplant service or registry supported (eg, allele-level resolution for hematopoietic progenitor cell transplants)?

GENERAL REQUIREMENTS FOR MOLECULAR TESTING

The requirements in this section are intended to apply to all molecular-based histocompatibility testing.

***REVISED** 12/26/2024*

HSC.34357 Nucleic Acid Extraction/Isolation/Purification **Phase II**

Nucleic acids are extracted, isolated, and purified by methods reported in the literature, by an established commercially available kit or instrument, or by a method validated by the laboratory.

NOTE: Extraction procedures may combine purification or isolation of nucleic acids according to the level of purity needed for downstream applications.

Evidence of Compliance:

- ✓ Records to support nucleic acid extraction/isolation/purification is performed by a validated method

REFERENCES
1) Sambrook J, *et al*. Molecular cloning: A laboratory manual, second edition. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1989:E.3-E.4

HSC.34544 Reverse Transcription **Phase II**

For RNA amplification methods, appropriate controls are used for reverse transcription.

***REVISED** 12/26/2024*

HSC.34731 Specimen Preservation/Storage **Phase II**

The laboratory uses established methods for specimen preservation and storage before testing.

NOTE: Patient samples may be stored in a frost-free freezer only if protected from thawing.

- *Repeated freeze-thaw cycles contribute to biomolecular degradation and are detrimental to biospecimen quality.*
- *It is prudent to avoid freeze-thaw altogether by aliquoting specimens before freezing.*
- *Peripheral blood specimens should not be frozen, unless otherwise validated, because induced hemolysis can result in PCR inhibition through the presence of contaminating hemoglobin.*

REFERENCES
1) Rainen L, *et al.* Stabilization of mRNA expression in whole blood samples. *Clin Chem.* 2002;48:1883-1890

HSC.34760 Dedicated Pipettes **Phase II**

Dedicated pipettors are used for pre-amplification procedures.

***REVISED** 12/26/2024*

HSC.34918 Nucleic Acid Quantity and Quality Determination **Phase II**

The quantity and quality of nucleic acids are determined, when appropriate.

NOTE: The quantity and quality of nucleic acids (DNA or RNA) must be measured prior to use in a procedure whose success depends on accurately determining the quantity, concentration, integrity, and/or purity of the nucleic acids. Techniques commonly used to assess nucleic acid quantity and/or quality include electrophoresis, UV/VIS spectrophotometry and fluorescence spectroscopy.

Evidence of Compliance:

- ✓ Defined conditions under which quantity and/or quality of nucleic acid are measured **AND**
- ✓ Records of nucleic acid quantity and/or quality determinations

HSC.35292 Loading Analytical Gels **Phase II**

Standard amounts of nucleic acid are loaded on analytical gels, when possible.

HSC.35479 Gel Images **Phase II**

Gel images are of sufficient resolution and quality (low background, clear signal, absence of bubbles, etc.) to permit the reported interpretation.

HSC.35666 Specimen Handling **Phase II**

The laboratory uses appropriate processes to prevent specimen loss, alteration, or contamination.

HSC.36040 Carryover - Enzymatic Amplification **Phase II**

Enzymatic amplification procedures (eg, PCR) use appropriate physical containment and procedural controls to minimize carryover (false positive results).

NOTE: This item is primarily directed at ensuring adequate physical separation of pre- and post-amplification samples to avoid amplicon contamination. The extreme sensitivity of amplification systems requires that the laboratory take special precautions. For example, pre- and post-amplification samples should be manipulated in physically separate areas; gloves must be worn and frequently changed during processing; dedicated pipettes (positive displacement type or with aerosol barrier tips) must be used; manipulations must minimize aerosolization; following complete reagent addition to the reaction tubes, the patient samples should be added one at a time. The best way to avoid cross-contamination is to use the following order of preparation within an amplification run: actual samples, followed by positive controls, followed by negative controls.

REFERENCES
1) Kwok S, Higuchi R. Avoiding false positives with PCR. *Nature* 1989;339:237-238
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.

HSC.36414 Electrophoretic Gel Interpretation **Phase II**

Electrophoretic gels are interpreted independently by at least two qualified readers using an objective method.

Evidence of Compliance:
- ✓ Patient testing records or worksheets

HSC.36601 End-Point Amplification QC **Phase II**

For end-point amplification assays such as sequence-specific priming, adequate internal controls are used, and criteria defined for a positive reaction.

HSC.36788 Daily Controls **Phase II**

For qualitative and quantitative tests, positive and negative controls are included for each assay, where appropriate, in every run, and as specified in the manufacturer's instructions (as applicable) and laboratory procedure.

Evidence of Compliance:
- ✓ Records of QC results, including external and internal control processes **AND**
- ✓ Manufacturer's product insert or manual, as applicable

REFERENCES
1) Clinical and Laboratory Standards Institute (CLSI). *Establishing Molecular Testing in Clinical Laboratory Environments; Approved Guideline.* CLSI document MM19-A. Clinical and Laboratory Standards Institute, Wayne, PA; 2011.
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): [42CFR1256(d)(3)(i) and (ii)].

HSC.36795 Internal Controls - Nucleic Acid Amplification — Phase II

In nucleic acid amplification procedures, internal controls are run to detect a false negative reaction secondary to extraction failure or the presence of an inhibitor, when appropriate.

NOTE: The laboratory should be able to distinguish a true negative result from a false negative due to failure of extraction or amplification. Demonstration that another sequence can be successfully amplified in the same specimen should be sufficient to resolve this issue. For quantitative amplification assays, the effect of partial inhibition must also be addressed.

The internal control should not be smaller than the target amplicon.

Evidence of Compliance:
- ✓ Records of assay validation and monitoring statistics for test result trends

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

HSC.36975 DNA Contamination — Phase II

There is a process to detect and control for DNA contamination.

NOTE: Contamination must be monitored in different areas by wipe tests using the regular detection for testing. There are records of the results of monitoring and corrective action taken when contamination is detected.

HSC.37162 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 with each run

HSC.37349 Amplification Quality — Phase II

For hybridization techniques, there are records that the different components and steps are monitored and acceptable, including the amount and integrity of amplified product and the signal intensity produced by each probe.

REFERENCES
1) Clark JR, Scott SD, Jack AL, et al. Monitoring of chimerism following allogeneic haematopoietic stem cell transplantation (HSCT): Technical recommendations for the use of short tandem repeat (STR) based techniques, on behalf of the United Kingdom National External Quality Assessment Service for Leucocyte Immunophenotyping Chimerism Working Group. *Br J Haematol.* 2015;168(1):26-37.

HSC.37536 Pre-Analytic Testing Requirements — Phase II

The conditions (temperature, salt concentration, probe concentration, etc.) for pre-hybridization, hybridization, and solid-phase support systems are optimized to consistently produce accurate results.

HSC.37723 Probe Labeling Validation — Phase II

The method of probe labeling is validated to detect the target sequence without a false positive signal for non-target sequences.

Evidence of Compliance:
- ✓ Records of in-house validation study data

HSC.37910 Re-Probing **Phase II**

If re-probing a solid-phase nucleic acid sample is performed, there are records of complete stripping of the previous probe before re-probing.

MOLECULAR HLA TYPING

HSC.38060 HLA Typing Level of Resolution **Phase II**

The level of resolution of HLA typing is adequate for the clinical programs, including donor registries, and the type of cell, tissue, or organ to be transplanted and meets the requirements of relevant accrediting agencies.

NOTE: Laboratories performing testing for NMDP donors must follow NMDP policies for resolution of typing ambiguities. Alternative allele combinations must be resolved when they contain one or more alleles in the common or intermediate categories of the CIWD 3.0.0 catalog.

For hematopoietic progenitor cell transplant, the laboratory must perform HLA typing at the level of resolution and including the loci required by the agreements with the transplant center and/or donor registry. For example, high resolution typing of HLA-A, B, C, DRB1 and DPB1 is mandatory for patient and unrelated donor matching per NMDP.

When performing HLA typing of deceased donors for the purpose of solid organ allocation in the United States, report the following loci as required by OPTN policies: A, B, Bw4, Bw6, C, DRB1, DRB3/4/5, DQA1, DQB1, and DPB1.

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Policies. Policy 4: Histocompatibility. US Department of Health and Human Services. Effective Date: December 5, 2022.
2) Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee ISCT and EBMT (JACIE). FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration. 8th Edition, December 14, 2021.
3) National Marrow Donor Program (NMDP)/Be The Match. US Transplant Center Participation Criteria. Document #A00228. Effective January 30, 2023.
4) National Marrow Donor Program. NMDP Policy for HLA Confirmatory Typing Requirements for Unrelated Adult Donors and HLA Typing Requirement for Patients. Document Number: P00079. Effective date: February 27, 2021.
5) Hurley CK, et al. Common, intermediate and well-documented HLA alleles in world populations: CIWD version 3.0.0. *HLA.* 2020;95(6):516-531.

HSC.38097 Sequence-Based Typing **Phase II**

For sequence-based typing, there are records of the following:

- **Templates with sufficient specificity for a locus or allele**
- **Appropriate monitoring of all steps**
- **Adequate electrophoretogram quality to support the sequence results**
- **Definition of a sequence following a procedure for accurate assignment of HLA alleles**

NOTE: Records must include the HLA locus and allele specificity of the template, the source of the sequence data base used (annually updated), and procedures to resolve ambiguous combinations. Assignment of alleles for HLA loci must be done by comparing the sequence data with the sequences of all alleles that are recognized by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System.

Laboratories must recognize ambiguous allele combination(s) and resolve these as appropriate for the clinical use as defined by the transplant agreement.

***NEW** 12/26/2024*

HSC.38098 IPD-IMGT/HLA Database **Phase I**

For molecular HLA typing, when applicable, the laboratory maintains records that include the IPD-IMGT/HLA or similar database version number at the time of testing.

NOTE: IPD-IMGT/HLA or similar database for HLA type reporting must be reviewed at least annually and updated if applicable.

REFERENCES

1) European Molecular Biology Laboratory-European Bioinformatics Institute (EMBL-EBI). IPD-IMGT/HLA. EMBL-EBI website. Accessed January 26, 2024. https://www.ebi.ac.uk/ipd/imgt/hla/
2) Marsh SGE, Albert ED, Bodmer WF, et al. HLA Nomenclature. HLA Alleles website. Updated January 11, 2024. Accessed January 26, 2024. https://hla.alleles.org/nomenclature/index.html

HEMATOPOIETIC PROGENITOR CELL ENGRAFTMENT MONITORING

HSC.38120 Hematopoietic Progenitor Cell Engraftment **Phase II**

For hematopoietic progenitor cell engraftment, the polymorphic nature and independent segregation (eg, location on separate chromosomes) of the DNA system used is detailed and recorded in the literature.

REFERENCES

1) Clark JR, Scott SD, Jack AL, et al. Monitoring of chimerism following allogeneic haematopoietic stem cell transplantation (HSCT): Technical recommendations for the use of short tandem repeat (STR) based techniques, on behalf of the United Kingdom National External Quality Assessment Service for Leucocyte Immunophenotyping Chimerism Working Group. *Br J Haematol.* 2015;168(1):26-37.

HSC.38130 Chimerism **Phase II**

There are records of the accuracy of quantitative methods used to measure chimerism.

NOTE: The accuracy of quantitative methods used to measure chimerism must be verified at least annually by controlled blood mixing or other suitable method. If results on cell subpopulations are reported, there must be records of periodic testing of the purity of such cell subsets.

HSC.38140 Negative Control **Phase II**

A negative control is used and evaluated for non-specific background with each run.

REFERENCES

1) Clark JR, Scott SD, Jack AL, et al. (2015), Monitoring of chimerism following allogeneic haematopoietic stem cell transplantation (HSCT): Technical recommendations for the use of Short Tandem Repeat (STR) based techniques, on behalf of the United Kingdom National External Quality Assessment Service for Leucocyte Immunophenotyping Chimerism Working Group. *Br J Haematol.* 2015;168:26-37.

HSC.38150 Sensitivity Control **Phase II**

A sensitivity control is used and evaluated with each run.

NOTE: A low positive control may be used to meet this requirement.

HSC.38171 Internal Controls **Phase II**

For hematopoietic progenitor cell engraftment assays, internal controls are used to determine appropriate genotypes or at least to distinguish patient from donor(s) with each run.

NOTE: There must be criteria for the acceptance and rejection of the amplification of a particular genetic locus or individual sample.

HSC.38180 Preferential Amplification **Phase II**

Reactions are optimized to avoid preferential amplification. The minimum amount of DNA is determined to obtain optimal sensitivity.

NOTE: Method validation must include a dilution study to evaluate the concentration of DNA to determine minimum sensitivity of the assay.

HSC.38190 Cell Subset Purity **Phase II**

If cell subset enrichment is performed, the patient report includes the actual or approximate purity of the cell subset.

NOTE: The determination of the actual or approximate purity of the cell subset does not imply that the purity determined in validation studies can be used without further evaluation. An actual measurement may be performed at the time of sample testing. Some isolation methods and cell subpopulations (eg, CD56) may not produce enough cells to test purity and run the monitoring engraftment test. At a minimum, the purity can be determined for each lot of reagent used to isolate the cell subset and then be reported as an approximate purity for that specific lot.

HSC.38200 Hematopoietic Progenitor Cell Engraftment Testing **Phase II**

For hematopoietic progenitor cell engraftment, samples from pre-transplant patient (recipient), pre-transplant donor(s), post-transplant patient, and an appropriate control are analyzed concurrently.

NOTE: Previously generated data from pre-transplant specimens may be used to compare to post-transplant results if a validated system is used to identify and link the appropriate data files for concurrent analysis.

Evidence of Compliance:
- ✓ Records of HPC testing

HSC.38205 Engraftment Analysis **Phase II**

Prior to evaluating post engraftment specimens, the laboratory evaluates a specimen from the donor(s) and a pre-transplant specimen from the patient to determine the number of informative loci to test in order to meet the minimum number of loci needed for calculations.

Evidence of Compliance:
- ✓ Records of hematopoietic progenitor cell engraftment testing

HSC.38208 Preferential Allele Amplification **Phase II**

Preferential allele amplification is considered in the interpretation of hematopoietic progenitor cell engraftment tests.

HSC.38220 Minimal Number of Informative Loci **Phase II**

For hematopoietic progenitor cell engraftment testing, a minimum of three informative loci are routinely used in the calculations.

NOTE: There are exceptions to this rule. Informative loci refer to loci that can distinguish between donor(s) and recipient. An exception for the number of informative loci used may occur in syngeneic twins (donor(s) and recipient) and rarely in closely related donor(s) and recipient.

***REVISED** 12/26/2024*

HSC.38658 Result Reporting **Phase II**

For hematopoietic progenitor cell engraftment, the final report includes an appropriate summary of the methods, the loci tested, the number of informative loci used, the percent donor cells, an indication of any trace cells, and the sensitivity of the assay.

NOTE: For hematopoietic progenitor cell engraftment, when performing testing by next generation sequencing (NGS), the loci tested are not required to be listed on the report.

REFERENCES
1) Clark JR, Scott SD, Jack AL, et al. Monitoring of chimerism following allogeneic haematopoietic stem cell transplantation (HSCT): Technical recommendations for the use of short tandem repeat (STR) based techniques, on behalf of the United Kingdom National External Quality Assessment Service for Leucocyte Immunophenotyping Chimerism Working Group. *Br J Haematol.* 2015;168(1):26-37.
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

ADDITIONAL MOLECULAR TESTING METHODS

HSC.38690 ABO and RhD Typing by Molecular Methods **Phase II**

ABO and RhD typing performed by molecular methods is used for presumptive ABO and RhD typing only. Donor-recipient ABO and RhD typing for transfusion and transplant compatibility evaluations is performed using FDA-cleared or approved serologic methods.

*NOTE: Transplant donor registries often collect samples from potential donors using buccal swabs or saliva. These samples cannot be used for traditional serological ABO/RhD blood group typing because fresh intact red blood cells (RBCs) are not available. Molecular ABO and RhD typing may be performed to predict the presumptive ABO and RhD phenotype to aid in finding an appropriate donor. Because the ABO and Rh genes are complex, prediction of ABO and Rh phenotype by molecular methods is currently used in immunohematology red cell reference laboratories that focus on blood typing complications, for research, or for providing **preliminary** information that can be confirmed by FDA-cleared or approved methods.*

The use of molecular based screening assays is not acceptable for ABO and RhD blood type assignment for the purposes of transfusion or transplantation. ABO and RhD typing by FDA-cleared or approved serologic methods must be used for the purpose of transfusion or donor and recipient ABO and RhD typing for transplantation.

Evidence of Compliance:

✓ Donor-recipient compatibility records with serologic ABO and RhD typing results

DONOR-RECIPIENT HISTOCOMPATIBILITY

Inspector Instructions:

	• Sampling of donor recipient histocompatibility policies and procedures • Sampling of cell typing records • Staffing/on call schedule
	• What evidence, from family studies, does your laboratory use to support haplotype or other genetic reporting conclusions (four distinct haplotypes must be identified in a pedigree analysis for haplotype assignment)?

HSC.38845 HLA Identity Confirmation for Hematopoietic Progenitor Cell Transplantation **Phase II**

HLA identity is confirmed in both donor and recipient hematopoietic progenitor cell transplantation.

NOTE: For laboratories performing typing to support hematopoietic progenitor cell (HPC) transplants facilitated by NMDP, NMDP policy for patient typing and confirmatory typing of unrelated donors must be followed.

For laboratories performing typing to support HPC transplantation, repeat HLA typing of the transplant patient using a new sample is performed to verify the individual's HLA type prior to final donor selection for both related and unrelated transplants.

Similarly, repeat HLA typing of the related HPC donor is performed using a new sample prior to HPC collection. For purposes of verification testing, results from donor registry or another laboratory is acceptable as the first of the two samples required. For example, lower resolution is acceptable for verifying the original high-resolution typing of recipients and related donors.

Evidence of Compliance:

✓ Records of testing to confirm HLA identity

REFERENCES

1) Nunes E., *et al*. Definitions of histocompatibility typing terms: Harmonization of Histocompatibility Typing Terms Working Group. *Hum Immunol*. 2011; 72(12):1214-6; *Blood*. 2011; 118:e180-3
2) National Marrow Donor Program. NMDP Policy for HLA Confirmatory Typing Requirements for Unrelated Adult Donors and HLA Typing Requirement for Patients. Document Number: P00079. Effective date: February 27, 2021.

HSC.39032 Haplotype Reporting **Phase II**

Haplotype assignments are supported by sufficient evidence.

NOTE: When reporting haplotypes, homozygosity, blanks, recombination, or other genetic information, there must be sufficient evidence from family studies to support such conclusions. If probable haplotypes are reported, the report must indicate clearly that they are "probable". Reliable haplotype frequencies of the appropriate ethnic groups must be used.

If haplotypes are assigned, this can be done by testing both the parents or clearly defined segregation of the four haplotypes or may be based upon population frequencies. Haplotype assignments based on population frequency, must be clearly stated on the report and include the relevant source (including the version) or reference.

HSC.39219 Donor Typing for Solid Organ Transplant **Phase I**

Donor materials obtained pre-organ recovery are used whenever possible for donor HLA typing and recipient serum screening.

NOTE: Organ donors should be HLA-typed from any acceptable source of viable lymphocytes. Whenever possible, pre-organ recovery HLA testing and screening crossmatches should be done.

Evidence of Compliance:

✓ Record of typing and screening on pre-organ donor materials, when possible

HSC.39406 Donor and Recipient HLA Typing **Phase II**

The HLA laboratory types all potential recipients and donors referred to the laboratory, and follows policies defining when HLA retyping and redefinition are required.

Evidence of Compliance:

✓ Records of all HLA typing

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):7170 [42CFR493.1278]

HSC.39410 HLA Typing Post Transfusion **Phase II**

The laboratory has a defined process for actions to be taken when a donor or patient cannot be reliably HLA typed after transfusion.

NOTE: Transfusions may result in detection of additional HLA antigens and/or alleles in donor or patient samples. Alternative source typing material (eg, buccal swab, lymph node or spleen) may be considered if more than two antigens are detected for a locus or alleles cannot be discriminated. Typing must be performed at the level of resolution required for the transplant service being supported.

HSC.39415 HLA Typing Level **Phase II**

The laboratory performs HLA typing at least to the minimal resolution appropriate for the individual transplant program supported (*eg,* 2-field typing for hematopoietic progenitor cell transplantation, when appropriate, and the level of serological splits for solid organ transplantation).

Evidence of Compliance:

✓ Patient reports and typing records

REFERENCES

1) Nunes E., et al. Definitions of histocompatibility typing terms: Harmonization of Histocompatibility Typing Terms Working Group. *Hum Immunol.* 2011; 72(12):1214-6; *Blood* 2011; 118:e180-3.
2) Organ Procurement and Transplantation Network (OPTN) Policies. Policy 4: Histocompatibility. US Department of Health and Human Services. Effective Date: December 5, 2022.
3) National Marrow Donor Program. NMDP Policy for HLA Confirmatory Typing Requirements for Unrelated Adult Donors and HLA Typing Requirement for Patients. Document Number: P00079. Effective date: February 27, 2021.

*****REVISED** 12/26/2024***

HSC.39430 Written Agreements **Phase II**

There are written agreements for histocompatibility testing with each transplant program, organ procurement organization (OPO), or donor registry served by the laboratory, unless clinical urgency prevents such an agreement.

NOTE: Written agreements must be reviewed biennially by the histocompatibility section director/ technical supervisor, and/or clinical consultant, and the clinical transplant program director, and be revised as necessary.

If the laboratory participates as a member of the United Network for Organ Sharing (UNOS), the written agreements must address all elements defined in the Organ Procurement and Transplantation Network (OPTN) Bylaws when applicable:

- *The sample requirements for typing and crossmatching*
- *The loci and level of resolution typed*
- *A process for requesting extended HLA typing*
- *A process for reporting and verifying HLA and unacceptable antigen data at the time of registration on the waiting list and any time there are changes*
- *A process for reporting HLA typing results to the OPTN Contractor*
- *A process for resolving HLA typing discrepancies and errors*
- *The maximum turnaround time from receipt of sample to reporting of results to the transplant program*
- *A process to obtain sensitization history for each patient*
- *The frequency of periodic sample collection*
- *The frequency of antibody screenings*
- *The criteria for crossmatching including the optimal time limits between recipient testing and crossmatch performance*
- *The assay format that will be used for antibody screening and for crossmatching*
- *The criteria for determining unacceptable antigens used during organ allocation*
- *The duration for which specimens need to be stored for repeat or future testing*
- *If desensitization is performed, a protocol for monitoring antibody levels*
- *If the laboratory registers candidates for the transplant process, a process for blood type verification*
- *If post-transplant monitoring is performed, a protocol for monitoring antibody levels.*

If the laboratory supports a program or donor registry that is accepted through the Foundation for the Accreditation of Cellular Therapy (FACT), the agreements must contain the requirements defined in the 7th edition of the FACT Standards.

If a laboratory supports a program or donor registry that is participating in the National Marrow Donor Program (NMDP)/Be The Match, the agreement must contain the provisions defined in the November 2017 NMDP U.S. Transplant Center Participation Criteria.

Agreements with OPOs must also include the following:

- *Process for prioritizing donors for histocompatibility testing*
- *All methods used for crossmatching, interpretation, and reporting of results if crossmatching is done by the OPO*

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.
2) Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee ISCT and EBMT (JACIE). FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration. 8th Edition, December 14, 2021.
3) National Marrow Donor Program (NMDP)/Be The Match. US Transplant Center Participation Criteria. Document #A00228. Effective January 30, 2023.

HSC.39450 Histocompatibility Testing Requests — Phase II

There are records of histocompatibility testing requests not covered by the transplant program support agreement.

NOTE: The laboratory has records of HLA testing requests which deviate from or are not covered in the existing transplant program support agreement (eg, the use of serum for a final crossmatch that is "too old" or "no final crossmatch" for a patient who would normally require a crossmatch within a previously defined time before transplant).

HSC.39499 Laboratory Coverage Plan **Phase II**

The laboratory coverage plan for staffing ensures that qualified testing personnel and key personnel are available to perform histocompatibility testing for organ transplantation and to facilitate organ acceptance and transplantation as needed.

NOTE: For laboratories that are members of the United Network for Organ Sharing (UNOS), the following staff availability requirements from the OPTN Bylaws apply:

- *Key personnel include the laboratory director, technical supervisor, general supervisor, and the clinical consultant*
- *The plan must include coverage at all times, including when changes occur in key personnel, and address coverage when key personnel serve more than one laboratory*
- *If the laboratory performs testing on deceased organ donors, key personnel and qualified testing personnel must be available 24-hours a day, seven days a week, unless an alternative coverage plan has been approved by UNOS/OPTN Membership and Professional Standards Committee*

Evidence of Compliance:

✓ Staffing schedule **OR** on-call schedule if 24-hour staffing is not available

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

NON-RENAL ORGAN TRANSPLANTS

Inspector Instructions:

READ

- Sampling of non-renal organ transplant policies and procedures
- Sampling of antibody screening records
- Sampling of crossmatch records

HSC.39593 Recipient Screening **Phase II**

Solid organ transplant recipients are screened for HLA Class I and Class II antibodies by a solid phase method.

NOTE: The frequency of testing is determined by the transplant program support agreement.

Evidence of Compliance:

✓ Records of antibody screening on transplant recipients

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.39780 Prospective Crossmatch **Phase II**

Non-renal sensitized transplant recipients are prospectively crossmatched with their potential donor, whenever possible, before transplantation.

NOTE: The technique used for crossmatching in these patients must be one of enhanced sensitivity for antibody detection.

Evidence of Compliance:

✓ Crossmatch records

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.39850 CD34 Cellular Viability - Apheresis and Cord Blood Products Phase II

The laboratory measures the viability of CD34 positive cells in samples aliquoted at the time of processing of hematopoietic progenitor cells, apheresis products and cord blood products.

NOTE: CD34 cell viability testing of cord blood products must be done on a sample aliquoted prior to the addition of cryoprotectant.

For any hematopoietic progenitor cell product, CD34 cell viability testing during or after storage should be considered as an additional quality control.

The viability dye 7-amino actinomycin-D (7-AAD) yields excellent results in this analysis. The viability assay must be performed using a flow cytometric method with the viability dye included in the same tube with the CD34 and CD45 monoclonal antibodies for the CD34+ viability determination. Estimates of total cellular viability (for example, trypan blue exclusion) may not be used as an alternative because the method can overestimate the viability of the CD34 stem cell population.

REFERENCES

1) Owens M, Loken M. Peripheral blood stem cell quantitation, In Flow Cytometry Principles for Clinical Laboratory Practice. New York, NY: Wiley-Liss, 1995:111-127
2) Keeney M., *et al.* Single platform flow cytometry absolute CD34+ cell counts based on the ISHAGE guidelines. *Cytometry.* 1998; 34:61-70
3) Hubl W., *et al.* Measurement of absolute concentration and viability of CD34+ cells in cord blood and cord blood products using fluorescent beads and cyanine nucleic acid dyes. *Cytometry.* 1998; 34:121-127
4) Gratama J., *et al.* Flow cytometric enumeration of CD34+ hematopoietic stem and progenitor cells. *Cytometry.* 1998;34:128-145
5) Lee S., *et al.* Post-thaw viable CD34+ cell count is valuable predictor of haematopoietic stem cell engraftment in autologous peripheral blood stem cell transplantation. *Vox Sang* Feb: 2008; 94:46-152
6) Riech-Slotky R., *et al.* Determining post-thaw CD34+ cell dose of cryopreserved haematopoietic progenitor cells demonstrates high recovery and confirms their integrity. *Vox Sang* 2008: May; 94(4):351-357
7) Clinical and Laboratory Standards Institute. *Enumeration of Immunologically Defined Cell Populations by Flow Cytometry; Approved Guideline.* 2nd ed. CLSI Document H42-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

PERSONNEL

Inspector Instructions:

READ	• Records of section director (technical supervisor), testing personnel, and clinical consultant education and experience • Continuing education policy • Sampling of continuing education records
ASK	• Has there been any changes in the histocompatibility section director or key personnel in the last two years?

***REVISED** 12/26/2024*

HSC.40000 Section Director/Technical Supervisor Qualifications - Histocompatibility Phase II

The section director (technical supervisor) of the histocompatibility section has the following qualifications.

1. MD or DO licensed to practice (if required) in the jurisdiction where the laboratory is located, OR doctoral degree in biological, clinical or medical laboratory science,

or medical technology from an accredited institution, OR meet the educational requirement found in CLIA regulation §42CFR493.1443(b)(3)(i)(B); AND

2. **Four years training and experience in histocompatibility, OR two years training and experience in general immunology plus two years in histocompatibility. For section director/technical supervisors supporting solid organ and/or hematopoietic progenitor cell transplantation, records of training or relevant experience in histocompatibility appropriate to the supported transplant program(s)**

NOTE: The training and experience must relate to testing of human specimens for the purpose of diagnosing, treating, and monitoring an individual's condition. Individuals qualified and serving as a technical supervisor for high complexity testing in a CLIA-certified laboratory as of December 28, 2024, may continue to fill this role if they have done so continuously since December 28, 2024. More detailed information on Section Director/ Technical Supervisor qualifications can be found in the CAP Personnel Guidance Document located in e-LAB Solutions Suite on cap.org (log-in required) under Accreditation Resources - Accreditation Checklists.

If more stringent state or local regulations are in place for supervisory qualifications, including requirements for state licensure, they must be followed.

If there is a change in the histocompatibility section director, the laboratory must notify the CAP as required in HSC.40100. If the new section director has not been previously accepted by the CAP (either by CAP evaluation or by evidence of prior directorship of a CAP-accredited histocompatibility laboratory for the same types of services), the laboratory must submit records to the CAP for review, including the new section director's curriculum vitae and portfolio, or evidence that the portfolio has been reviewed and approved by a certifying board (eg, ACHI). If the new section director is accepted by the CAP, a letter is sent to the laboratory director. The letter must be retained and be provided to inspectors upon request. If the CAP does not accept the section director, another section director meeting CAP qualifications must be assigned.

The CAP's review of a new section director includes an evaluation of the individual's education, training, and experience for acceptability with the laboratory's scope of service (activity menu). Where indicated, the CAP may require submission of a portfolio of cases consistent with the laboratory's scope of service, which includes cases covered during the previous five years demonstrating analytical skills, ability to recognize and resolve testing and interpretation issues, and instances where recommendations were made for additional testing or clinical care including:

- *At least 20 solid organ transplant cases for solid organ transplant (10 in detail and a log of 20 total)*
- *If the laboratory participates as a member of UNOS/OPTN, at least 50 cases for solid organ transplantation (10 in detail and a log of 50 total)*
- *At least 20 hematopoietic progenitor cell transplant cases representative of the program mix of related and unrelated transplants (10 in detail and a log of 20 total) and/or*
- *At least 10 cases for other histocompatibility testing (eg, pharmacogenomics, disease association, transfusion support).*

If the laboratory participates as a member of the United Network for Organ Sharing (UNOS), the CAP may require submission of additional records based on the qualifications of the new section director to demonstrate compliance with the Organ Procurement and Transplantation Network (OPTN) Bylaws: Appendix C for approval, including the following:

- *Proof of active interaction with transplant professionals*
- *A statement explaining all experience in immunology and clinical histocompatibility testing, including a summary of time spent in the laboratory, technologies used, level of responsibility, and specific tasks performed*
- *A current curriculum vitae*
- *Participation in transplant or clinical laboratory professional conferences or publications in peer-reviewed journals*

Evidence of Compliance:

- ✓ Records of section director/technical supervisor qualifications including diploma, transcript(s), primary source verification report, equivalency evaluation (eg, ACHI certified Fellow/Affiliate,

previously ASHI-DTRC approved laboratory director), board certification (eg, Diplomate ACHI (ABHI), ABMLI), or current license (if required) **AND**
- ✓ Work history in related field **AND**
- ✓ CAP letter of acceptance for new histocompatibility section directors

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1449(h)].
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

***REVISED** 08/24/2023*

HSC.40100 Notification of Change in Key Personnel **Phase II**

The laboratory notifies the CAP's Laboratory Accreditation Program when there is a change in the histocompatibility director (technical supervisor) and other key personnel, as applicable.

NOTE: All laboratories must notify the CAP when there is a change of histocompatibility section director and submit records for review by the CAP as requested.

Histocompatibility testing laboratories that participate as a member of the United Network for Organ Sharing (UNOS) must also notify the CAP when there is a change in other key personnel, including the general supervisor and/or clinical consultant.

Notification must occur no later than 30 days prior to the change; or in the case of an unexpected change, no later than 2 working days afterwards. For changes in laboratory directorship, refer to GEN.26791.

REFERENCES
1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

***REVISED** 12/26/2024*

HSC.45000 Testing Personnel Qualifications - Histocompatibility **Phase II**

Personnel performing the technical work of histocompatibility have at least one year of training and/or experience in histocompatibility and qualify as high complexity testing personnel with a minimum of the following:

1. **Bachelor's degree in a chemical, biological, clinical or medical laboratory science, or medical technology from an accredited institution; or**
2. **Associate degree in a laboratory science or medical laboratory technology from an accredited institution, or equivalent laboratory training and experience meeting the requirements defined in GEN.54750 for high complexity testing.**

NOTE: A more detailed listing of personnel qualifications can be found in the CAP Personnel Guidance Document located in e-LAB Solutions Suite on cap.org (log-in required) under Accreditation Resources - Accreditation Checklists.

Persons with less than one year of training and/or experience must work under the supervision of persons who are qualified.

Evidence of Compliance:
- ✓ Records of section director/technical supervisor qualifications including diploma, transcript(s), primary source verification report, equivalency evaluation, board certification, or current license (if required) **AND**
- ✓ Work history in related field

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1489].
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.46250 General Supervisor Qualifications - Histocompatibility **Phase II**

The general supervisor has a minimum of three years of experience in histocompatibility/ transplantation.

Evidence of Compliance:

- ✓ Records of work history in personnel file

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.47500 Continuing Education Program **Phase II**

There is a continuing clinical laboratory education program that addresses the areas of service offered by the laboratory, identifies the need for remedial training, where appropriate, and provides continuing education to improve skills in histocompatibility.

NOTE: The laboratory must have a complete continuing clinical laboratory education program that meets the needs of the various types of laboratory personnel and addresses the areas of service offered by the laboratory, including a predefined minimum number of contact hours annually. This program may be provided locally, regionally/nationally, through scientific article review and discussion, or some combination of the above.

Evidence of Compliance:

- ✓ Records of continuing education

REFERENCES

1) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.

HSC.48750 Clinical Consultant Qualifications - Histocompatibility **Phase II**

The section director or other individual fulfills the responsibilities of clinical consultant.

NOTE: The clinical consultant must be an MD or DO licensed to practice medicine in the jurisdiction where the laboratory is located (if required) with appropriate training and experience in the interpretation of histocompatibility / transplantation immunology test results, or a doctoral level clinical scientist certified by a CLIA-approved specialty board.

Evidence of Compliance:

- ✓ Records of section director/technical supervisor qualifications including diploma, transcript(s), primary source verification report, equivalency evaluation, board certification, or current license (if required) **AND**
- ✓ Work history in related field **AND**
- ✓ Job description defining responsibilities of clinical consultant

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28):[42CFR493.1449(h)] and [42CFR493.1455].
2) Organ Procurement and Transplantation Network (OPTN) Bylaws. Appendix C. Membership Requirements for Histocompatibility Laboratories. US Department of Health and Human Services. December 5, 2022.