August 2017 Changes

Histocompatibility Checklist

CAP Accreditation Program

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Using the Changes Only Checklist

This document contains new checklist requirements, major and minor requirement revisions, and changes to explanatory text. Changes appear in a track changes format that compares the previous checklist edition to the August 21, 2017 edition. Requirements with major revisions will display a "Revised" flag. These changes may affect your laboratory operations. Requirements with minor revisions will not display a "Revised" flag. They are editorial changes that are not likely to affect your laboratory operations.

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

### 2017 CHECKLIST EDITION CHANGES DELETED, MERGED, AND MOVED REQUIREMENTS *

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<th>2016 Requirement</th>
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*Merged – Combined the requirement with a similar requirement in the same or different checklist
*Moved – Relocated the requirement to another checklist or resequenced it within the same checklist

### PROFICIENCY TESTING

**REVISED** 08/17/2016

HSC.10475 PT Extent of Testing

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

**NOTE:** Proficiency testing samples are to be tested in the same way as regular, most comprehensive testing algorithm or pathway applied to patient samples. They should not receive more extensive testing than would be performed under routine testing conditions. For example, if a laboratory has a written procedure that calls for both low and high-resolution HLA analysis and sequence-based typing may be used only if they are regularly used in similar clinical circumstances. The level of resolution must reflect the certain patient population, then all PT samples are tested to the highest level of resolution that the laboratory performs for its patients.

### QUALITY MANAGEMENT AND QUALITY CONTROL

RESULTS REPORTING

**REVISED** 08/17/2016
Outside referral laboratories are accredited by appropriate histocompatibility agencies, and for 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.

RECORDS

Recipient and Donor Information Records

**REVISED** 08/21/2017
HSC.21382 Discrepancy Resolution

There is a written procedure to resolve HLA typing discrepancies within and between laboratories.

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

**NEW** 08/21/2017
HSC.21390 Donor Confidentiality

There are written policies and procedures to ensure 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 or donor information must be redacted.

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

PROCEDURES AND TEST SYSTEMS

RED CELL TYPING

**REVISED** 08/21/2017
HSC.29909 Antisera/Reagent Red Cell QC

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 directions for daily quality control are followed.

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

- Typing reagents, including antisera (e.g. 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 detection must be checked each day of use for reactivity of at least one antigen using antisera of 1+ or greater avidity.
- Typing reagents such as anti-D, anti-K, anti-Fy(a), etc., must be checked each day of use.
- Anti-IgG reactivity of antiglobulin reagents may be checked during antibody screening and crossmatching.
- Typing sera and reagent cells must be checked for reactivity and specificity on each day of use, including a check against known positive and negative cells or antisera.

This checklist requirement can be satisfied by testing one vial of each reagent lot each day of testing.

**MOLECULAR HLA TYPING TESTING**

If next generation sequencing methods are used for histocompatibility testing, the requirements in the Next Generation Sequencing section of the Molecular Pathology Checklist must be used in conjunction with these requirements for inspection.

**General Requirements for Molecular Testing**

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

**REVISED** 08/21/2017
HSC.36788 Daily Controls Phase II

Positive and negative controls are run included for each assay, when available and appropriate, in every run, and as specified in the manufacturer’s instructions (as applicable) and laboratory procedure.

**NEW** 07/28/2015
HSC.36795 Internal Controls - NAA Nucleic Acid Amplification Phase II

In all 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.

HSC.36975 DNA Contamination Phase II

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

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

**REVISED** 08/21/2017
HSC.3398338060 HLA Typing Level of Resolution Phase II

The level of resolution of HLA typing is adequate for the clinical programs supported and meets the requirements of relevant accrediting agencies.

NOTE: When performing HLA typing of deceased organ donors for the purpose of organ allocation (kidney, kidney-pancreas, pancreas, or pancreas islet donor transplants) in the United States, all of the following types are required to be reported for: A, B, Bw4, Bw6, C, DR, DR51, DR52, DR53, DQA, DQB, and DPB DRB1, DRB3/4/5, DQA1, DQB1, and DPB1.

For all other organs, HLA typing may be performed if required by the transplant program.

**REVISED** 08/21/2017
HSC.3622738070 Mendelian Inheritance Haplotype Reporting Phase I

Mendelian inheritance Reporting of the DNA system used haplotypes is validated supported by family studies.

**REVISED** 08/21/2017
HSC.3585338100 Result Reporting - HLA Typing and Engraftment Phase II

For HLA typing and engraftment tests, there is sufficient information available on the nature of all restriction enzymes, probes, or primers used in an assay to permit interpretation and troubleshooting of test results.

NOTE: Items that must be defined are:

-1. The oligonucleotide sequence of probes and primers, the complementary sequence recognized, and the target HLA locus and alleles
-2. The HLA locus and allele designations recognized by the WHO for each combination of positive results (hybridization for SSOP and PCR product for SSP)
-3. Ambiguous allele combinations
-4. The HLA sequence database used

Stem Cell Engraftment Monitoring

**REVISED** 08/17/201621/2017
HSC.3828438120 Stem Cell Engraftment Procedure Phase II

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

**NEW** 08/21/2017
HSC.38140 Negative Control

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

**NEW** 08/21/2017
HSC.38150 Sensitivity Control

A sensitivity control is used and evaluated with each run.

**REVISED** 08/21/2017
HSC.38171 Internal Controls

Internal For stem 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.

**NEW** 08/21/2017
HSC.38180 Preferential Amplification

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.

**REVISED** 08/21/2017
HSC.38438200 Stem Cell Engraftment Testing

For stem cell engraftment, samples from patient pre-transplant, patient (recipient), pre-transplant donor, patient(s), post-transplant patient, and an appropriate control are amplified and 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.

**NEW** 08/21/2017
HSC.38205 Engraftment Analysis

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.

**NEW** 08/21/2017
HSC.38220  Minimal Number of Informative Loci  Phase II
For stem 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.

HSC.38471  Stem Cell Engraftment  Phase II

For stem cell engraftment, independent segregation (e.g. location on separate
chromosomes) is recorded for all single locus probes tested in the DNA system used.

**REVISED** 08/21/2017
HSC.38658  Result Reporting  Phase II

For stem cell engraftment or other individual identity purposes, the final report includes
an appropriate summary of the methods, probes and endonucleases used, the loci
tested, the objective findings and a clinical interpretation in a readily interpretable format.

number of informative loci used, the percent donor cells, an indication of any trace cells,
and the sensitivity of the assay.

**NEW** 08/21/2017
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 Rh
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.
DONOR-RECIPIENT HISTOCOMPATIBILITY

**NEW/REVISED** 08/17/2016 21/2017

HSC.39430 Written Agreements

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

NOTE: Written agreements must be reviewed annually 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 supports a program that is accepted through the Foundation for the Accreditation of Cellular Therapy (FACT), the agreements must contain the requirements defined in the 6th edition of the FACT Standards.

If a laboratory supports a program that is participating in the National Marrow Donor Program (NMDP)/Be The Match, the agreement must contain the provisions defined in the November 2015 NMDP U.S. Transplant Center Participation Criteria.

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 most current version of the Organ Procurement and Transplantation Network (OPTN) Bylaws. The following elements are defined in the March 1, 2016 OPTN Bylaws:

The agreement with transplant programs and OPOs must include the following:

- Specimen requirements for typing and crossmatching
- Loci and level of resolution typed
- Process for requesting extended HLA typing
- Process for reporting HLA typing results to UNOS
- Process for resolving HLA discrepancies and errors
- Turnaround time from sample receipt to reporting to transplant program or OPO
- Length of specimen retention for repeat or future testing

Agreements with the transplant program must also include the following:

- Process for reporting and verifying HLA and other data at the time of registration on the waiting list and where there are changes
- Process to obtain sensitization history
- Frequency of periodic sample collection
- Frequency for antibody screening
- Criteria for crossmatch
- Assay format used for antibody screening and crossmatching
- Criteria for determining unacceptable antigens used during organ allocation
- Protocol for monitoring antibody levels if desensitization is used
- Process for blood type verification if the laboratory registers candidates for the transplant program
- Protocol for monitoring antibody levels is post-transplant monitoring is performed

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
**REVISIONS** 08/17/2016

Section Director/Technical Supervisor Qualifications  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 chemical, physical, biological or clinical laboratory science from an accredited institution, AND
2. Laboratory training and experience: 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 stem cell transplantation, records of training or relevant experience in histocompatibility appropriate to the supported transplant program(s)

NOTE: If the histocompatibility laboratory participates as a member of the United Network for Organ Sharing (UNOS) and there has been a change in the HLA Section Director (Technical Supervisor) in the last two years, the inspector must review the new section director’s curriculum vitae and portfolio. The review should include at least 10 solid organ transplant cases from the portfolio.

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