Summary of Proposed Revisions to the 2020 Standards  
December 15, 2021

The following revisions are proposed to the 2020 ASHI Standards.

The following changes were made to the Table of Contents:

D.5.2.13 Immunophenotyping and/or single antigen typing by flow cytometry

D.5.2.13 D.5.2.14 Typing of non-classical HLA loci, etc.

D.5.3.2 Renal and/or pancreas transplantation  
Solid organ transplantation

D.5.3.6 Platelet and granulocyte transfusion  
Transfusion support

The following changes were made to A.3 Definitions:

Definitions

Qualitative method: An assay that detects the presence or absence of a specific analyte, but does not determine the specific concentration of the analyte.

Quantitative method: An assay that measures the amount of an analyte in a specimen and reports the results in units traceable to a recognized standard.

Re: C.1.3 - Any laboratory that receives a proficiency testing sample from another laboratory for testing must notify CMS and ASHI of the receipt of that sample regardless of whether the referral was made for reflex or confirmatory testing, or any other reason.

Re: D.4.1.8.6.2.2 – For Assays other than molecular assays, eEven when the manufacturer’s instructions for use of a qualitative procedure do not specify that a positive and negative control be included in the test run, the laboratory is required to include an external positive and negative control at least once each day that the test is run. The manufacturer’s instructions do not obviate this minimum requirement. For molecular assays, laboratories must define and review quality parameters that ensure test accuracy for each test run.

D.5.2.7.17 Laboratories performing antibody analysis for non-HLA antigens must:

D.5.2.7.17.1 Define the target antigens in the assay.

D.5.2.7.17.2 Ensure that the antigens targeted by the assay are appropriate for the clinical application.

D.5.2.7.17.3 For multiplexed assays, ensure the specificity of antibodies to individual target proteins.
D.5.2.12.2 If genotyping of glycosyltransferases for prediction of ABO/RhD antigen typing: If performed using molecular techniques, exclusively for donor registry screening:

D.5.2.12.2.1 ABO/RhD typing by molecular methods must only be used as predicted phenotype and may not be used as an independent method for patient transfusion and transplant compatibility evaluations.

D.5.2.14 Laboratories performing genotyping of loci other than classical HLA and ABO/RhD antigen genes (e.g., non-classical HLA loci, KIR loci) must:

D.5.2.14.1 Define the target loci genotyped by the assay.

D.5.2.14.2 Ensure that the level of resolution (gene presence, SNP and/or allele genotype, etc.) is appropriate for the clinical application.

D.5.2.14.3 Have written criteria and protocols for:

D.5.2.14.3.1 Isolation, preparation, and quality control of nucleic acids for analysis.

D.5.2.14.3.2 Selection, use, and quality control of all reagents, data handling, and analyses.

D.5.2.14.4 Use standardized terminology when available.

D.5.3.2.1.1 Prospectively type living donors and transplant patient for HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQA1, -DQB1, -DPA1, -DPB1 and -Bw4/Bw6. HLA-A, -B, -Bw4/Bw6 and -DRB1. It is highly recommended that laboratories also type for HLA-C, -DRB3, -DRB4, -DRB5, -DQA1, -DQB1, -DPA1, and -DPB1 loci.

D.5.3.2.1.1.1 For kidney, pancreas, or islet donors, or multi-organ transplants including a renal organ, typing must be completed prior to organ offers.

D.5.3.2.1.1.2 For heart or lung donors, or multi-organ transplants including a thoracic organ, typing must be completed prior to final organ acceptance.

D.5.3.2.1.1.3 For donors of other organs or vascularized composite allografts, typing must be completed within the period specified in the transplant agreement.

D.5.3.2.1.2 Prospectively type recipients of kidney, pancreas, or islet transplants, or multi-organ transplants including a renal organ, for HLA-A, -B, -DRB1, and -Bw4/Bw6.

D.5.3.2.1.23 All UNOS histocompatibility laboratories prospectively typing deceased donors for OPTN matchruns must use a molecular method to type donors at the antigen level of resolution needed to meet the most recent OPTN/UNOS tables of antigen and unacceptable antigen equivalencies. Reporting of HLA typing must be sent to the OPTN contractor and OPO within the period specified by the written agreement with the OPO.

D.5.3.2.1.34 All UNOS histocompatibility laboratories prospectively typing deceased donors for OPTN matchruns must distinguish the following null alleles: A*24:09N (associated with B*40 or B*27), B*51:11N (associated with A*02:01, C*15:02/15:13 and DRB1*04:02), C*04:09N (associated with B*44:03); DRB4*01:03:01:02N (associated with DRB1*07 and DQB1*03:03 (DQ9) and DRB5*01:08:01N/01:08:02N (associated with DRB1*15:02).

D.5.3.2.1.25 Follow policies and procedures established by a joint agreement with the transplant program to Screen test transplant patients for the presence of anti-HLA antibodies at initial evaluation, at intervals consistent with established clinical transplant protocols, and following sensitizing events.
D.5.3.2.1.36 Perform crossmatching using samples and an assay with the sensitivity appropriate for the clinical protocols established with the transplant center.

D.5.3.2.1.36.1 Have results of final crossmatches available before renal transplantation or combined organ and tissue transplants in which a kidney is to be transplanted, except for emergency situations. If emergency transplants are performed before the crossmatch results are available, information provided by the transplant candidate’s physician to the laboratory as to the reason for the emergency transplant must be documented. Crossmatch testing for kidney transplantation, including multi-organ transplants including kidneys, must be performed prospectively, with the testing results available prior to transplantation.

D.5.3.2.1.47 Have a policy for selection of sera for crossmatching of allosensitized patients that addresses the impact of historic and current sensitizing events.

D.5.3.2.1.5 When feasible, incorporate a serum sample obtained post-sensitization in the final crossmatch if a transplant patient receives a blood transfusion, has an allograft that is rejected or removed, or experiences any other potentially sensitizing event.

D.5.3.2.1.8 All UNOS histocompatibility laboratories must review and verify the data they completed and entered into the UNet Waitlist. There must be documentation of review by the laboratory of UNOS HLA data within one month of entry. Documentation of such review must be kept for at least three years or the interval required by local, state and federal regulations, whichever is longer, and must be available for audit by UNOS.

D.5.3.2.1.9 All UNOS histocompatibility laboratories must use a solid phase method for antibody identification that can identify HLA antibody specificities even in very highly sensitized transplant patients.

D.5.3.2.2 Laboratories performing testing for solid organ transplantation from deceased donors must also:

D.5.3.2.2.1 U.S. based laboratories must report HLA typing for deceased organ donors, based on the molecular typing results, report the following assignments to the OPTN contractor: HLA-A, B, Bw4/Bw6, C, DR, DR51/52/53, DQA1, DQB1, and DPB1. Reporting of HLA typing must be sent to the OPTN contractor and OPO within the period specified by the written agreement with the OPO.

D.5.3.2.2.2 Follow policies and procedures established by a joint agreement with the transplant program to have periodic (e.g., monthly) serum samples submitted from potential transplant patient for HLA antibody screening and crossmatching.

D.5.3.2.2.3 Have results of final crossmatches available before renal transplantation or combined organ and tissue transplants in which a kidney is to be transplanted, except for emergency situations. If emergency transplants are performed before the crossmatch test results are available, information provided by the transplant candidate’s physician to the laboratory as to the reason for the emergency transplant must be documented.

D.5.3.2.2.4 All UNOS histocompatibility laboratories must review and verify the UNet Waitlist histocompatibility data for each patient for whom the laboratory performed testing. There must be documentation of review by the laboratory of UNOS HLA data within one month of entry. Documentation of such review must be kept for at least three years or the interval required by local, state and federal regulations, whichever is the longer, and must be available for audit by UNOS.
D.5.3.2.2.5 All UNOS histocompatibility laboratories must use a method for antibody identification that can identify HLA antibody specificities even in very highly sensitized transplant patients. A solid phase method must be used if unacceptable antigens based on antibody screening are listed.

D.5.3.2.2.6 All UNOS histocompatibility laboratories prospectively typing deceased donors for OPTN matchruns must use a molecular method to assign HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQA1, -DQB1, -DPB1 and -Bw4/Bw6 at the antigen level of resolution needed to meet the most recent OPTN/UNOS tables of antigen and unacceptable antigen equivalencies.

Re: D.5.3.2.2.6 Verify prospective molecular typing of donors for HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQA1, -DQB1, and DPB1.

D.5.3.2.2.7 All UNOS histocompatibility laboratories prospectively typing deceased donors for OPTN matchruns must distinguish common null alleles from expressed genes (antigens) as appropriate for solid organ allocation and transplantation.

Re: D.5.3.2.2.7 There are many null alleles on the lists in the ASHI Ad Hoc Committee’s report on Common and Well Documented Alleles (Mack et al., Tissue Antigens 81: 2013). Laboratories must be able to distinguish the following alleles: A*24:09N (associated with B*40 or B*27), B*51:11N (associated with A*02:01, C*15:02/15:13 and DRB1*04:02), C*04:09N (associated with B*44:03); DRB4*01:03N (associated with DRB1*07 and DQB1*03:03 (DQ9) and DRB5*01:08N (associated with DRB1*15:02).

Re: D.5.3.5.21 - Laboratories must have and follow joint-agreement policies for each organ type transplanted including policies that require no testing for specific organ types.

D.5.3.8.1.1.4 When Situations for which additional donor typing (such as DQA1, -DPA1 allele-level typing) is required to determine for any locus/allele against which the patient has documented antibody reactivity.

D.6.2.2.11 All phenotype terminology using WHO approved nomenclature where it exists.

D.6.2.2.11.1 The laboratory must have a written policy for assignment of serologic equivalents outside of WHO terminology. This applies to the assignment of serologic equivalents for alleles and loci that do not have WHO approved serologic nomenclature, and/or assignment of serologic epitopes.

Re: D.6.2.2.11.1 When assigning serological equivalents for which WHO terminology is not available, laboratories must indicate on their report when they are not using WHO nomenclature.

D.6.2.2.12 HLA antibody specificities when clinically relevant:

D.6.2.2.12.1 The laboratory must have a written policy for reporting anti-HLA antibody specificities that are not WHO-recognized serologic antigens.

D.6.2.2.4.21 A list of unresolved alleles appropriate to the clinical use of the results as defined in each transplant program or OPO agreement, and as required by regulatory agencies governing solid organ or hematopoietic cell transplantation (HCT).
Re: D.6.2.2.1213 – All approved WHO nomenclature codes and/or multiple allele (NMDP) codes must be fully defined by either listing the ambiguity string or providing a link to a published reference to the clinicians. Low resolution typing does not require consultation of the CWIWD catalog.

D.6.2.2.1213.1 Results reported using G or P group codes do not need to list unresolved alleles that are within the G or P group listed.

D.6.2.2.1213.2 Results reported may exclude non-common, intermediate, or well-documented (CIWD 3.0.0) alleles found in alternative genotypes if stated in the report, transplant agreement, or client written request.

D.6.2.2.1213.3 Typing results reported using NMDP codes must define all unresolved alleles represented by the allele code.

D.6.2.2.14 The virtual crossmatch analysis report used for final organ allocation must be documented, and must contain:

D.6.2.2.14.1 The recipient identifier.

D.6.2.2.14.2 The donor identifier.

D.6.2.2.14.3 The sample date for the patient antibody testing results used, and the source of donor typing information.

D.6.2.2.1315 For U.S. laboratories using a test method and reagents that are not FDA-approved, a statement to the effect that “This test was developed in and its performance characteristics determined by [laboratory name]. It has not been cleared or approved by the U.S. FDA.”

Re: D.6.2.2.1315 - Non-U.S. laboratories do not need to have this on reports.

Re: D.6.3.1.1 - Examples of tests performed using more than one method or instrument include typing by cytotoxicity and DNA, antibody tests by cytotoxicity and solid phase, and crossmatching using two different flow cytometers. Relationships can be evaluated by using the same proficiency test samples.