**Summary of Proposed Revisions to the 2019 Standards**
**July 28, 2020**

The following revisions are proposed to the 2019 ASHI Standards.

**The following changes were made to A.3 Definitions:**

**Definitions**

**Common, Intermediate, and Well-Documented (CIWD)**: Version 3.0.0 of the CIWD catalog categorizes HLA alleles according to population frequencies, based on data from several donor registries (Hurley CK, et al. 2020. HLA. 1-16. Doi. 10.1111/tan.13811). Common alleles have a frequency of ≥ 1 in 10,000, intermediate alleles ≥ 1 in 100,000, and well-documented alleles have ≥ 5 occurrences in at least one population studied.

**Control material:** a reagent or biological sample that tests the accuracy, precision or functionality of a test system.

**Control procedure:** a process to monitor and assure the reliability of a test system.

**High resolution typing:** A high-resolution HLA genotype is defined as an allele or set of alleles that encode the same protein sequence for the region of the HLA molecule called the antigen binding site. The high resolution HLA genotype results must contain only one unambiguously assigned genotype or may contain multiple alternative genotypes if only one combination includes ~~two~~ common ~~and well-documented (CWD) alleles. https://protect2.fireeye.com/url?k=48d5e2bd-14958feb-48d5c5a0-0cc47adb57f0-bf6293e266775110&u=http://igdawg.org/cwd.html~~ and/or intermediate alleles (CIWD version 3.0.0), with the exception of null alleles; alternative genotype combinations containing a null allele listed as either common, intermediate, or well-documented must be resolved.

**Individual Quality Control Plan (IQCP):** An inclusive quality control approach that enables flexibility for laboratories to develop quality control plans that address risks and meet CLIA regulations. Detailed requirements can be found: https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Individualized_Quality_Control_Plan_IQCP

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**D.2.4.1** The laboratory must have a system in place to ensure that it documents all complaints and problems reported to the laboratory. All complaints must be investigated and corrective action must be taken when necessary.

**D.2.9.5** Every procedure must be reviewed every two years by the ASHI Laboratory Director and relevant Technical Supervisor.~~, and ẅ~~Written or electronic evidence of this review must be readily available.

**Re: D.2.9.5** –The CLIA lab director must review and sign any new and revised procedures. This initial review cannot be delegated. Ongoing biennial review can be performed by the ASHI Director or Technical Supervisor. ~~Individual procedures must be reviewed and signed.~~

**Re: D.4.1.7.4** - Actual temperature checks in at least selected individual wells must be performed ~~at least twice a year~~ every six months. Not every well needs to be tested.

For Quantitative ~~q~~PCR instruments (i.e. real time instruments), ~~and real time PCR instruments,~~ perform functional checks ~~in lieu of~~ using ~~temperature monitoring instruments until such time as these become readily available~~ Spectral and Normalization calibration trays, at least every six months.

**Re: D.4.1.8.6.2.2** – When controls are not indicated by the manufacturer's recommendation, and the lab is not performing negative and positive controls, then the lab's IQCP plan must be documented in the lab's procedures.

**D.4.1.8.6.3** ~~For each e~~Electrophoretic procedures of clinical specimens must~~,~~ include~~, concurrent with patient specimens,~~ at least one control material containing the substances being identified or measured (e.g., molecular weight markers).

**D.4.1.8.8** Laboratories may fulfill quality control requirements using alternative individual quality control plans (IQCP) that meet CLIA IQCP requirements.

**Re: D.5.2.2.15** – Alternative ambiguous allele combinations must be recognized and resolved when the alternatives include more than one common and well documented type* at the resolution required for the clinical use of the test results. Laboratories performing confirmatory testing for NMDP donors must follow NMDP policies for resolution of typing ambiguities referenced at (https://bioinformatics.bethematchclinical.org/workarea/downloadasset.aspx?id=21474837267).

* Hurley CK, et al. 2020. HLA. 1-16. Doi. 10.1111/tan.13811 ~~*Cano et al, Human Immunology 68, 392-417 (2007) through 2014 or Mack et al., Tissue Antigens, 81, 194-203 (2013) effective January 2015~~

**D.5.2.5.1** Ensure that the method for preparing sequencing templates reliably generates appropriate ~~length sequencing~~ templates that are free of inhibitors ~~of subsequent reactions (e.g., residual primer extension)~~ and ~~free of~~ contaminants ~~that cause~~ capable of causing sequencing artifacts (e.g., residual primers) ~~sequencing artifacts~~.

**D.5.2.5.8** Laboratories must ~~D~~determine the sequences of both sense and anti-sense DNA strands~~,~~ if a sequence suggests a novel allele ~~or a rare combination of alleles~~

**D.5.2.9.4** Laboratories must ~~U~~use the dilution and/or volume of reagents that have been locally validated prior to use.

**Re: D.5.2.11.9 & D.5.11.10** - If part of testing is performed by a lab with a different CLIA #, and this lab is not ASHI accredited, then this lab must provide documentation of personnel qualifications, competency, instrument PM, QA/QC, etc. that ASHI requires. If part of testing is performed by a lab section not covered by ASHI but under the same CLIA#, this section would also be required to provide documentation of personnel qualifications, competency, instrument PM, QA/QC, etc.

Laboratories must also adhere to local government regulations first, as some locations restrict referring portions of patient testing.

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

**D.5.3.2.1** Laboratories performing testing for solid organ ~~renal~~ transplantation must:

**D.5.3.2.2** Laboratories performing testing for solid organ ~~renal and/or pancreas~~ transplantation from deceased donors must also:

**D.5.3.2.2.1** ~~Prospectively type transplant patient for HLA-Bw4/Bw6. All UNOS histocompatibility laboratories typing deceased donors for kidney, Heart, Heart-Lung or Lung must~~ 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.5.3.5.2** All UNOS histocompatibility laboratories prospectively typing deceased donors for nonrenal transplantation must use a molecular method to assign HLA-A, -B, -Bw4/Bw6, -C, -DRB1, - DRB3, -DRB4, -DRB5, -DQA1, -DQB1, and -DPB1 at the level of resolution needed to meet the most recent OPTN/UNOS tables of antigen and unacceptable antigen equivalencies.~~

~~**D.5.3.5.3** All UNOS histocompatibility laboratories typing deceased donors for non-renal transplantation must distinguish common null alleles from expressed genes (antigens) as appropriate for solid organ allocation and transplantation.~~

~~**D.5.3.5.4** All UNOS histocompatibility laboratories typing deceased donors for Heart, Heart-Lung or Lung must report HLA typing to the OPO prior to final acceptance, if required by the transplant program.~~

~~**D.5.3.5.5** All UNOS histocompatibility laboratories typing deceased donors for Liver must report HLA typing to the OPO within the period specified by the transplant program.~~

**D.5.2.11.9** Have a protocol for monitoring any element of NGS testing referred to another laboratory. Standards for NGS-based testing cover the entire testing process including sample handling, target DNA enrichment, library generation, DNA sequencing, bioinformatic analysis, and reporting. Laboratories that refer any part of the NGS process to a referral laboratory are responsible for ensuring the referral laboratory is accredited to perform the relevant steps of testing in accordance with the following criteria.

**D.5.2.11.10** Have a protocol for tracking specimens and data when any part of NGS testing is referred to another laboratory. This protocol must include methods and records for confirming sample and data identity.

**D.5.2.11.11** Participate in PT relevant to components of NGS testing performed in the laboratory.

**D.6.2.2.12.2** Results reported may exclude non-common, intermediate, or well-documented (CIWD 3.0.0) ~~do not need to list non-CWD~~ alleles if stated in the report, transplant agreement, or client written request.