PROPOSED 7th edition of Standards for Molecular Testing for Red Cell, Platelet, and Neutrophil Antigens

Effective January 1, 2025

A Note to Readers

Individuals not familiar with the standards-setting practices of AABB should be aware of the following:

- Requirements, once stated, are not repeated. For example, standard 5.0 requires that all processes and procedures be validated. Therefore, it is not necessary to require in other areas that a specific process or procedure be validated.
- Words or phrases used in a way different from their usual meaning are defined in the glossary.
- The term "specified requirements" is defined broadly to include accreditation requirements, national, state, or local laws, and any other applicable requirement.
- Please note, that the Summary of Significant Changes to the proposed 7th edition begins on page 2 and runs through page 10. The proposed 7th edition begins on page 11 and runs through page 84.

Updated Quality System Essentials

The proposed 7th edition of Standards for Molecular Testing for Red Cell, Platelet, and Neutrophil Antigens has incorporated the updated quality system essentials (QSE) template for this edition. This includes a number of updates to the chapters and the tone and flow of the edition.

Highlights of the updated QSEs include:

- All standards written in the active voice.
- Once a requirement has been stated, it is not repeated.
- Each chapter begins with a description of what the standards therein cover.
- Each chapter contains a list of examples of key terms that mirror the content of the chapter and that should be kept in mind when reviewing the standards.
- Each chapter contains a list of examples of key objectives that an assessor could look for during an onsite assessment, however, this list is not comprehensive, nor will it be assessed against by an assessor. It is merely for guidance purposes only.
- Each chapter now concludes with the record retention table for that chapter. Note a comprehensive record retention table still exists at the end of chapter 6**.**

Driving factors behind the revisions to the updated QSEs:

- Deliver a streamlined template that mirrors current quality concepts.
- Make it user-friendly to shorten learning curves.
- A top-to-bottom reworking of tone, formatting, language, and style.
- Preserve chapter headings and overall structure, to make it easier for users to follow and understand the core quality concepts.
- Maintain the exact same standards numerology for all core quality standards across all sets of AABB Standards.
    - Incorporate activity-based standards into that structure
- Responding to member needs and requests.
- Beneficial to facilities with multiple accreditations (uniformity of language and numbering).

Significant Changes to the Proposed Standards for Molecular Testing for Red Cell, Platelet, and Neutrophil Antigens

1.9 Staffing Changes

The laboratory shall communicate to AABB **in electronic or written format** all initial appointments and changes for the laboratory director within 30 days of appointment.

1.10Laboratory Status Changes

The laboratory shall communicate to AABB **in electronic or written format** within 30 days of the date the laboratory ceases or resumes all on-site testing.

The committee added the clause "in electronic or written format" for clarity. The committee notes that questions could arise from members about the need to submit information in a particular format.

2.1.3.1 Training shall include:

1) Orientation.

2) Initial job specific training.

3) Quality-systems-related training.

4) Ongoing job-specific training.

2.1.3.2 The organization shall approve subject matter experts who provide training.

Standards 2.1.3.1 and 2.1.3.2 are new to this proposed edition and was pulled from the 11th edition of Standards for Cellular Therapy Services. The committee felt that the content fit their scope and would provide context for the training standard.

2.1.6.1 Employees performing and/or reviewing specific testing methods as defined by Standards 5.3 and 5.4 shall participate in a minimum of 24 hours of relevant continuing education ~~biennially~~ **every two years**.

The committee replaced the term "biennially" with "every two years" for clarity. The committee felt that the term "biennially" may not be as easily understood as the direct clause added.

2.2.1 Previously characterized samples shall have been tested by available serologic and/or molecular methods and be concordant **with the known phenotype**.

The committee added the clause "with the known phenotype" to the end of the standard for clarity, understanding that phenotypes are the actual characteristics of the samples.

Reference Standard 2.2A–Minimum DNA Resources – Red Blood Cells[1]
Reference Standard 2.2B–Minimum DNA Resources – Platelets*
Reference Standard 2.2C–Minimum DNA Resources – Neutrophils*

The committee edited the Reference Standards for completeness. The representation of the tables have been updated to include an additional column for "rs numbers" while also creating a differentiation of variant description as an overarching header.

5.1.1.1 This process shall include identification of specifications and verification that **they** ~~specifications~~ have been met. Standard 2.1.3 applies.

The committee removed the clause in strikethrough as it was deemed redundant to the first inclusion of "specifications" in the sentence.

5.1.6.2 Positive and negative controls shall be ~~performed~~ **tested** at defined intervals.

The committee edited this standard for accuracy, the intent of the standard has not changed.

5.1.6.3 When deviating from the manufacturer's written instructions **including the use of FDA cleared or approved tests** ~~or using unlicensed~~ tests, materials shall be qualified for use and shall meet specified requirements and appropriate controls shall be used to ensure reliability of the test results ~~when deviating from manufacturers' instructions of FDA licensed tests~~.*

*42 CFR 493.1253(b)(2).

The committee edited this standard for clarity. The intent of the standard has not changed.

5.1.8.3 A laboratory responsible for labeling blood components shall have documented procedures for the labeling of those blood components, **if applicable**. *

*21 CFR 606.121.

FDA Guidance for Industry: Labeling of Red Blood Cell Units with Historical Antigen Typing Results, December 2018.

The committee updated this standard for clarity. The inclusion of "if applicable" recognizes that there are instances where a molecular testing laboratory does not have the responsibility for labelling blood components.

5.1.10.1 Laboratories shall ensure that no interlaboratory communications pertaining to proficiency test events occur until after the submission deadline.*

***42 CFR 493.801(b)(4).**

The committee added new standard 5.1.10.1 to address requirements set forth by CMS in July 2022 with an effective date of 2024. This mostly focuses on waived testing, however the new requirement also addresses proficiency testing referrals and what is and is not allowed until the results of proficiency testing are complete and submitted. The CLIA memo detailing this CFR can be found here. This addition is consistent with additions to the BBTS and IRL Standards.

5.1.10.2 The laboratory shall ensure that no portion of a proficiency testing sample is sent to another laboratory for analysis.†

†42 CFR 493.801 (b)(4)

The committee added new standard 5.1.10.1.2 in conjunction with the addition of the CFR cited, which requires that laboratories perform proficiency testing to show that they can successfully perform the tests. Laboratories outsource their proficiency testing would not meet the requirements in the CFR. The CLIA memo detailing this CFR can be found here. This addition is consistent with additions to the BBTS and IRL Standards.

5.1.10.3 Any laboratory that receives a proficiency testing sample from another laboratory for testing shall notify CMS of the receipt of the sample.†

†42 CFR 493.801(b)(4).

The committee added new standard 5.1.10.1.3 in conjunction with the addition of the CFR cited, which requires that if a laboratory receives samples for proficiency testing from an outside source that they immediately contact CMS who will instruct them on how to move forward. The CLIA memo detailing this CFR can be found here. This addition is consistent with additions to the BBTS and IRL Standards.

5.2.3.2 Test methods shall be validated for each specimen type (e.g., buccal swab, peripheral blood).

5.2.3.2.1 If the laboratory performs the same test method on more than one specimen type, equivalency shall be demonstrated.

Standards 5.2.3.2 and 5.2.3.2.1 have been added to the proposed edition of Standards in recognition that there are molecular testing laboratories that perform testing in the biotherapies area and the sample collection methods described would allow for that expanded scope for the Standards and users.

5.3 Test Validation

The laboratory shall use validated methods for molecular testing. *****

***42 CFR 493.1253(b)(2)**

The committee added a crossrefernce to the CFR for completeness.

5.3.1 The laboratory shall validate FDA cleared or approved test kits in accordance specified requirements.

The committee elected to add new standard 5.3.1 for completeness. The focus on FDA cleared or approved tests kits is being put in place for facilities that follow FDA regulations. This standard supplements standard 5.3 focused on testing validation.

5.3.2 Laboratory developed tests (LDT) or research use only (RUO) kits shall comply with the following standards.

With the understanding that more and more laboratories are using LDTs and RUO, the committee felt it important to create a standard around the need to follow the pertinent standards that populate this edition.

5.3.2.1 To implement a **genotyping** ~~tests~~ system ~~or a test for variant(s)~~, the validation protocol shall require the analysis of:

1) Homozygous wild-type sample(s)
2) Heterozygous sample(s)
3) Homozygous variant sample(s) when available
4) Hemizygous sample(s), when applicable.

~~Test results shall show consistency within the laboratory (precision) and concordance with results from another method or another laboratory (accuracy). The validation protocol shall define acceptable results.~~

The committee edited former standard 5.3.1 for readability and accuracy. The element in strikethrough has been removed and made its own standard as 5.3.4.

5.3.2.2 To implement a sequence-based typing system, the validation protocol shall demonstrate:

1) Gene specific alignment
2) Ability to detect and annotate previously characterized variant(s)
3) For next generation sequencing (NGS), the bioinformatics pipeline functions as intended.

Based on the updates to standard 5.3.2.1, the committee created new standard 5.3.2.2 focused around sequence based typing.

5.3.2.3 Results for analytes for which a second method has been used to confirm the minor allele shall be reported with a disclaimer that they are for investigational use only. Reference Standards 2.2B, Minimum DNA Resources - Platelets and 2.2C, Minimum Resources - Neutrophils apply.

The committee included new standard 5.3.2.3 in the proposed edition for clarity, ensuring that products for investigational use are labeled accordingly.

5.3.3 To implement a novel test method, the validation protocol shall require the analysis of at least 20 biological test samples ~~with consistency of test results within the laboratory~~:

1) Homozygous wild-type sample(s)
2) Heterozygous sample(s)
3) Homozygous variant sample(s) when available
4) Hemizygous sample(s), when applicable.

The committee edited standard 5.3.3, previously standard 5.3.2 for readability and clarity. The structure of the standard was made to mimic the other standards in this section.

5.3.4 Test results shall show consistency within the laboratory (precision) and concordance with results from another method or another laboratory (accuracy). The validation protocol shall define acceptable results.

Standard 5.3.4 is new to this edition in the sense of an existing standard, however the content previously appeared as a part of standard 5.3.1.

5.4.1 General Test Criteria

Test criteria shall be incorporated into the testing processes to ensure accurate results.

1) The assay shall interrogate the region(s) interest.

2) For systems dependent on accurate measurement of alleles by fragment sizes, a size standard shall be tested with each analysis.3) A control without DNA shall be run to monitor contamination, when required by protocol.

4) The laboratory shall evaluate **sample** contamination ~~for each sample~~.

5) Postamplification products shall be prevented from contaminating preamplification materials.

Subnumber 1 is new to the proposed edition and was included to ensure that testing done through next generation sequencing and serologic testing which is being performed currently by AABB accredited molecular testing laboratories.
The replacement of where the term "sample" appears in subnumber 4 was edited for clarity.

5.4.2 The laboratory shall ensure version control of **analytic** algorithms ~~in genotype prediction are maintained~~.

The committee edited this standard for clarity and accuracy.

5.6.1 Interpretations of investigations shall contain the following information*:

9) For laboratories operating in the United States (US) using test method(s) and/or reagent(s) that are not FDA cleared or approved, a statement, "This test was developed, and its characteristics determined by [Insert Laboratory Name]. It has not been cleared or approved by the US FDA." shall be included in the report.

The committee created new subnumber 9 for completeness. The new subnumber was included to ensure facilities under US FDA regulations are labeling finalized test reports using investigational methods appropriately.

5.6.2 ISBT Nomenclature

The laboratory shall have a plan for the implementation of ISBT nomenclature for antigens and alleles.

The committee created new standard 5.6.2 as a first step towards full ISBT nomenclature implementation in accredited laboratories. This style of standard is written in a similar fashion to how standards first appeared in the BBTS and CT Standards when they began the process for implementation of IBST nomenclature and ISBT 128 labeling implementation.

6.2.5.2 If an amended report is issued, the original report shall be maintained. Standard 6.2.1 applies.

The committee added new standard 6.2.5.2 has been added to the proposed edition for completeness. This standard also appears in the Standards for Relationship Testing Laboratories as well.

6.2.13 The record system shall make it possible to trace **and review** any sample, report, or service from its source to final disposition ~~and to review the interpretation of test records applying to the specific sample, report, or service~~.

The committee elected to edit standard 6.2.13 for clarity. The committee felt that adding the clause "and review" to the beginning of the standard made the elements in strikethrough redundant.

Glossary

Alarm: Audible, visual, or central monitoring system signaling the need for immediate or timely action.

The committee created this new definition for completeness.

Analyte: Substance or chemical constituent ~~that is assayed~~ **for which the laboratory performs testing**.

The committee edited the definition for clarity.

~~**Genetic Screening:** Testing performed on a donor, groups of donors, or a population subset or on patients for the purpose of transfusion or transplantation.~~

~~**Genetic Testing:** Testing performed on patients for the purpose of diagnosis or reproductive decisions (ie, hemolytic disease of the fetus and newborn).~~

The committee deleted these definitions as the terms are no longer included in the proposed edition.

Hemizygous: Having only one allele rather than the usual two alleles.

Heterozygous: Having two different alleles on both chromosomes.

The committee added these definitions recognizing that the terms appear in chapter 5 of the edition.

Homozygous: ~~Two copies of~~ **Having** the same allele on ~~different~~ **both** chromosomes.

The committee edited the definition of homozygous to mirror the style of the new definitions above.

Laboratory Developed Test (LDT): A type of in vitro diagnostic test that is developed, manufactured, and used within a single laboratory.

The committee created this new definition for completeness.

Oligonucleotide: ~~See probe and primer~~ **A single-stranded nucleic acid molecule that is chemically synthesized and is typically comprised of 25 or less nucleotides of known sequence.**

The committee edited the definition for oligonucleotide to provide more substantive content.

~~**New Test Method:** As opposed to a novel test method, a new test method is a change to or addition of a peer-reviewed existing technology already applied in molecular testing.~~

The committee deleted this definition as the term is no longer included in the proposed edition.

~~**Organizational Structure:** The responsibilities, authorities, and relationships, through which an organization performs its functions~~.

The committee deleted this definition as the term is no longer included in the proposed edition.

Primer: An ~~known single-stranded nucleic acid sequence,~~ **oligonucleotide** complementary to the target of interest, used to initiate PCR.

Probe: An **oligonucleotide** ~~known single-stranded nucleic acid sequence~~ used to identify specific DNA or RNA molecules bearing the complementary sequence. The probe may carry a chemical label to facilitate detection of the target sequence.

The definitions above were edited based on the edit made to the definition of "oligonucleotide".

Repeatability: The expectation that the same results will be obtained if all testing parameters are unchanged ~~within the same run~~.

The committee removed the clause in strikethrough as it was deemed redundant.

Research Use Only (RUO): Tests intended for scientific research only. They are not cleared or approved by the Competent Authority and are not intended for clinical diagnosis or as the sole means for patient management decisions.

The committee created this new definition based on its inclusion in the proposed edition of Standards in chapter 5.

Restriction Enzyme: A~~n endonuclease; any of a large number of~~ bacterial enzyme, **such as an endonuclease,** that cleaves double-stranded DNA at specific nucleotide sequences.

The committee updated the definition above for clarity. The intent of the definition has not changed.

~~**Sensitivity:** The proportion of actual positives that are correctly identified.~~

The committee elected to remove this term from the glossary as the term no longer appears in the proposed Standards.

Sequence Based Typing (SBT): Determination of the order of nucleotides in gene(s) or gene region(s).

The committee added this definition based on its inclusion in chapter5.

Single Nucleotide Variant (SNV): A sequence variation of a single nucleotide, **without any frequency limitations**.

The committee updated the definition of this term for clarity.

~~**Specificity:** The proportion of negatives that are correctly identified.~~

The committee elected to remove this term from the glossary as the term no longer appears in the proposed Standards.

Single Nucleotide Polymorphism (SNP): A sequence variation of a single nucleotide, seen in more than one percent of the members of a population.

The committee added the term to the Glossary for completeness as a complement to the newly updated definition of Single Nucleotide Variant.

Specimen: A human biologic sample, **such as** ~~of~~ peripheral blood, buccal tissue **swab**, amniotic fluid, urine or other samples containing human tissue, cells, or bodily fluid obtained by invasive or noninvasive means. For these standards, a specimen is submitted to a laboratory for the purposes of obtaining DNA or RNA for molecular ~~nucleic acid based~~ testing.

The committee edited this standard for clarity.

~~**Stringency:** Testing parameters that ensure optimal identification of alleles.~~

The committee elected to remove this term from the glossary as the term no longer appears in the proposed Standards.

QSE 1 – Organization

Key Concepts:
This quality system essential (QSE) describes the responsibilities of executive management, the nature of the quality system, and the need for ongoing attention to operational and quality issues through demonstrated management commitment.

Key Terms:
Customer: The recipient of a product or service. A customer may be internal (eg, another organizational unit within the same organization) or external (eg, a patient, client, donor, or another organization).

Emergency Management: Strategies and specific activities designed to manage situations in which there is a significant disruption to organization operations or a significantly increased demand for the organization's products or services.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Organization: An institution, or a location or operational area within that organization; the entity assessed by the AABB and receiving AABB accreditation for specific activities.

Policy: A set of basic principles or guidelines that direct or restrict the organization's plans, actions, and decisions.

Procedure: A defined series of tasks and instructions that specify how an activity is to be performed.

Process: A set of related activities that transform inputs into outputs.

Quality Management System: The organizational structure, responsibilities, policies, processes, procedures, and resources established by executive management to achieve quality.

Examples of Objective Evidence:
- Policies, processes, and procedures related to this chapter.
- Organizational charts or documents describing roles, responsibilities, and decision-making authority.
- Evidence of executive management review of a quality system.
- Applicable federal, national, state, and local laws and regulations, as well as copies of any required certificates.
- Defined quality system.
- Process for approving exceptions to policies, processes, and procedures, as well as documented examples, if applicable.
- Risk assessments and mitigation strategies.
- Emergency operation and disaster continuity plan(s).
- Executive management review of customer feedback.

1.0 Organization

The organization shall define the parties responsible for the provision of products or services.

1.1 Executive Management

The organization shall have a defined executive management. Executive management shall have:

1) Responsibility and authority for the quality system and operations.
2) Responsibility for compliance with these *MT Standards* and applicable laws and regulations, including all applicable current good manufacturing practice (cGMP) requirements.
3) Authority to establish or make changes to the quality system.

1.1.1 Laboratory Director Responsibilities

The laboratory shall have a director who has a doctoral degree in medical, biological, clinical laboratory sciences, or genetics and has at least 2 years of relevant training or experience in molecular testing. The laboratory director shall have responsibility and authority for all policies, processes, and procedures. The laboratory director may delegate these responsibilities to another qualified individual; however, the laboratory director shall retain ultimate responsibility for laboratory director duties.*

* 42 CFR 493.1443 and 42 CFR 493.1445

1.1.2 Laboratory Supervisor Responsibilities

The laboratory shall have a supervisor who is qualified by training or experience. The supervisor shall have responsibility for technical aspects of molecular testing.

1.1.2.1 The supervisor shall have at least 2 years of relevant experience in molecular testing and one of the following qualifications*:

1) Medical license and certification in blood banking/transfusion medicine or Molecular Genetic Pathology by the American Board of Pathology or non-US equivalent organization or agency.
2) Certification as Technologist in Molecular Biology (MB) by the American Society for Clinical Pathology (ASCP), Certification as a Technologist in Blood Banking (BB) from ASCP, Certificate as Specialist in Blood Banking (SBB) from ASCP, Certified Histocompatibility Specialist (CHS) from the American College of Histocompatibility and Immunogenetics (ACHI), or certification from an organization or agency issuing an equivalent credential.
3) Advanced science degree in a relevant field.

*42 CFR 493.1411

1.1.2.1.1 When the individual does not meet the requirements stated in Standard 1.1.2.1, exceptions shall be considered on a case-by-case basis by the Molecular Testing Accreditation Committee.

1.2 Quality System

The organization shall have a quality system. The organization's executive management shall ensure that this quality system is implemented and followed at all levels of the organization.

1.2.1 Quality Representative

The quality system shall be under the supervision of a designated person who reports to executive management.

1.2.2 Management Reviews

Management shall assess the effectiveness of the quality system at defined intervals.

1.3 Policies, Processes, and Procedures

Policies, processes, and procedures shall be implemented and maintained to satisfy the applicable requirements of these *Standards*. All such policies, processes, and procedures shall be in writing or captured electronically and shall be followed.

1.3.1 The medical director and/or laboratory director (as applicable) shall approve all medical and technical policies, processes, and procedures.

1.3.2 Any exceptions to medical and technical policies, processes, and procedures shall require justification and preapproval by the medical director and/or laboratory director, as applicable.

1.4 Risk Assessment

The facility shall have a process in place to perform risk assessments for activities at defined intervals.

1.4.1 Mitigation strategies shall identify, assess, and address the level of risk associated with quality and safety.

1.5 Operational Continuity

The organization shall address continuity in the event that operations are at risk.

1.6 Emergency Preparedness

The organization shall have an emergency operation plan(s) to respond to the effects of internal and external disasters.

1.6.1 The emergency management plan, including emergency communication systems, shall be tested at defined intervals.

1.7 Communication of Concerns

The organization shall have a process for personnel to anonymously communicate concerns about quality or safety. Personnel shall be given the option to communicate such concerns either to their organization's executive management, AABB, or both. AABB's contact information shall be readily available to all personnel.

1.8 Customer Focus

Executive management shall identify the organization's customers and their needs and expectations for products or services.

1.9 Staffing Changes

The laboratory shall communicate to AABB in electronic or written format all initial appointments and changes for the laboratory director within 30 days of appointment.

1.10Laboratory Status Changes

The laboratory shall communicate to AABB in electronic or written format within 30 days of the date the laboratory ceases or resumes all on-site testing.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
1.2.2	Management review of effectiveness of the quality system	5
1.3	Policies, processes, and procedures	10
1.3.2	Exceptions to policies, processes, and procedures	10
1.4	Risk assessment	5
1.6.1	Emergency operation plan tested at defined intervals	2 years, or two organizational testing intervals (whichever is longer)
1.9	Laboratory director representative change notification within 30 days	5
1.10	Interruption of on-site testing notification within 30 days	5

[1]Applicable state or local law may exceed this period.

QSE 2 – Resources

Key Concepts: This QSE describes the need for resources—human, financial, and otherwise—to support the work performed. It also describes personnel issues such as the qualification of staff, assessments of competence [including those performed under Clinical Laboratory Improvement Amendment (CLIA) regulations], and continuing education requirements.

Key Terms:
Competence: An individual's demonstrated ability to apply knowledge and skills needed to perform the job tasks and responsibilities.

Qualification (individuals): The aspects of an individual's education, training, and experience that are necessary for the individual to successfully meet the requirements of a position.

Examples of Objective Evidence:

- Policies, processes, and procedures related to this chapter.
- Current job descriptions.
- Evaluation of staffing levels and workload, if performed.
- Process for recruiting and hiring.
- Personnel records (eg, certifications, qualifications, competence assessments, diplomas, transcripts).
- Training records.
- Evaluations of competence records.
- Evidence that job qualifications are met.
- Continuing education records.

2.0 Resources

The organization shall have adequate resources to perform, verify, and manage all the activities described in these *Standards*.

2.1 Human Resources

The organization shall employ an adequate number of individuals qualified by education, training, and/or experience.

2.1.1 Job Descriptions

The organization shall establish and maintain job descriptions defining the roles and responsibilities for each job position related to the requirements of these *Standards*.

2.1.2 Qualification

Personnel performing critical tasks shall be qualified to perform assigned activities on the basis of appropriate education, training, and/or experience.

2.1.3 Training

The organization shall provide training for personnel performing critical tasks.

2.1.3.1 Training shall include:

1) Orientation.
2) Initial job specific training.
3) Quality-systems-related training.
4) Ongoing job-specific training.

2.1.3.2 The organization shall approve subject matter experts who provide training.

2.1.4 Competence

Evaluations of competence shall be performed before independent performance of assigned activities and at specified intervals.*

*42 CFR 493.1235 and 42 CFR 493.1451(b)(8)(9).

2.1.4.1 Action shall be taken when competence has not been demonstrated.

2.1.5 Personnel Records

Personnel records for each employee shall be maintained.

2.1.5.1 For those authorized to perform or review critical tasks, records of names, signatures, initials or identification codes, and inclusive dates of employment shall be maintained.

2.1.6 Continuing Education

The organization shall ensure that continuing education requirements applicable to these *MT Standards* are met when applicable.

2.1.6.1 Employees performing and/or reviewing specific testing methods as defined by Standards 5.3 and 5.4 shall participate in a minimum of 24 hours of relevant continuing education every two years.

2.2 DNA Resources

The laboratory shall use previously characterized DNA samples to validate the reported test. Previously characterized samples containing variants that the laboratory reports shall be available for use as detailed in Reference Standard 2.2A, Minimum DNA Resources – Red Blood Cells; Reference Standard 2.2B, Minimum DNA Resources – Platelets; and Reference Standard 2.2C, Minimum DNA Resources – Neutrophils.

2.2.1 Previously characterized samples shall have been tested by available serologic and/or molecular methods and be concordant with the known phenotype.

Reference Standard 2.2A–Minimum DNA Resources – Red Blood Cells[1]

Blood Group System		Variant Description[2]				
ISBT name ISBT number	Gene[3] Transcript RefSeq Gene Chromosome	Transcript (NM_)	RefSeq Gene (NG_)	Chromosome[4] (NC_)	rs number	Comment Antigen(s)
ABO 001	*ABO* NM_020469.3 NG_006669.2 NC_000009.12	ABO:c.261delG[5] ABO:c.526C>G ABO:c.703G>A ABO:c.796C>A ABO:c.802G>A ABO:c.803G>C ABO:c.930G>A ABO:c.1061delC	ABO:g.22694delG[6] ABO:g.24011C>G ABO:g.24188G>A ABO:g.24281C>A ABO:g.24287G>A ABO:g.24288G>C ABO:g.24415G>A ABO:g.24546delC	9:g.133257521delG[7] 9:g.133256205G>C 9:g.133256028C>T 9:g.133255935G>T 9:g.133255929C>T 9:g.133255928C>G 9:g.133255801C>T 9:g.133255672delC	rs15560582 84 rs7853989 rs8176743 rs8176746 rs41302905 rs8176747 rs8176749 rs56392308	Phenotype O (O_1) B B B Phenotype O (O_2) B B Phenotype A_2
MNS 002	*GYPA* NM_002099.5 NG_007470.3 NC_000004.12	GYPA:c.59C>T GYPA:c.71G>A GYPA:c.72T>G	GYPA:g.25185C>T GYPA:g.25197G>A GYPA:g.25198T>G	4:g.144120567G>A 4:g.144120555C>T 4:g.144120554A>C	rs7682260 rs7687256 rs7658293	M/N M/N M/N
	GYPB NM_002100.6 NG_007483.3 NC_000004.12	GYPB:c.143C>T GYPB:c.230C>T GYPB:c.270+5g>t	GYPB:g.27419C>T GYPB:g.29282C>T GYPB:g.29327g>t	4:g.143999443G>A 4:g.143997580G>A 4:g.143997535c>a	rs7683365 rs56172553 rs13951187 6	S/s Mt(a+) U^{var}
P1Pk	*A4GALT4* NM_017436.7	A4GALT4:c.-188+3010G>T	A4GALT:g.8515G>T	22:g.42717787C>A	rs5751348	P1+/P1-

	NG_007495.2 NC_000022.11					
RH 004	*RHD* NM_016124.6 NG_007494.1 NC_000001.11	None[8] RHD:c.8C>G RHD:c.809T>G RHD:c.1154G>C	None[8] RHD:g.5066C>G RHD:g.35840T>G RHD:g.54400G>C	1:g.25264585_25335813del 1:g.25272555C>G 1:g.25303329T>G 1:g.25321889G>C	Not available rs144969459 rs121912763 rs71652374	*RHD* deletion Weak D type 3 Weak D type 1 Weak D type 2
		RHD:c.1227G>A	RHD:g.54473G>A	1:g.25321962G>A	rs549616139	Asian-type DEL (DEL1)
		RHD:c.487-19_504dup or RHD:c.807T>G	RHD:g.33438_33474dup or RHD:g.35838T>G	1:g.25300927_25300963dup or 1:g.25303327T>G	rs748783394 rs141833592	RHDΨ
	RHCE NM_020485.8 NG_009208.3 NC_000001.11	RHCE:c.336-2846_336-2845ins109 RHCE:307T>C	RHCE:g.29601_29602ins109 RHCE:g.26482C>T	1:g.25405592_25405593ins109 1:g.25408711G>A	Not available rs676785	C/c C/c
		RHCE:c.676G>C	RHCE:g.44319G>C	1:g.25390874C>G	rs609320	e/E
		RHCE:c.122A>G	RHCE:g.14528A>G	1:g.25420665T>C	rs138268848	CW
		RHCE:c.106G>A	RHCE:g.14512G>T	1:g.25420681C>T	rs145034271	CX
		RHCE:c.733C>G	RHCE:g.44376C>G	1:g.25390817G>C	rs1053361	V/VS
		RHCE:c.1006G>T	RHCE:g.49415G>T	1:g.25385778C>A	rs116261244	V
LU 005	*LU* NM_005581.5 NG_007480.1	BCAM:c.230A>G	BCAM:g.8108A>G	19:g.44812188A>G	rs28399653	Lu^a/Lu^b

	NC_000019.10					
KEL 006	*KEL* NM_000420.3 NG_007492.3 NC_000007.14	KEL:c.578T>C KEL:c.841T>C KEL:c.1790C>T	KEL:g.9496T>C KEL:g.13150T>C KEL:g.24391C>T	7:g.142957921T>C 7:g.142954267T>C 7:g.142943026C>T	rs8176058 rs8176059 rs8176038	K/k Kp^a/Kp^b Js^a/Js^b
LE 007	*FUT3* NM_000149.4 NG_007482.2 NC_000019.10	FUT3:c.202T>C	FUT3:g.17485T>C	19:g.5844638=	rs812936	Le(a-b-) [9]
FY 008	*FY* NM_002036.4 NG_011626.3 NC_000001.11	ACKR1:c.125G>A ACKR1:c.-67T>C ACKR1:c.265C>T	FY:g.6552G>A FY:g.5881T>C FY:g.6692C>T	1:g.159205564G>A 1:g.159204893T>C 1:g.159205704C>T	rs12075 rs2814778 rs34599082	Fy^a/Fy^b $Fy(b-)^{ES}$, $Fy(a-)^{ES}$ $Fy(b+^w)$, Fy^x $Fy(b+^w)$, Fy^x
JK 009	*JK* NM_015865.7 NG_011775.4 NC_000018.10	SLC14A1:c.838G>A	SLC14A1:g.57530G>A	18:g.45739554G>A	rs1058396	Jk^a/Jk^b
DI 010	*DI* NM_000342.4 NG_007498.1 NC_000018.10	SLC4A1:c.2561T>C	SLC4A1:g.21882T>C	18:g.44251253T>C	rs2285644	Di^a/Di^b
YT 011	*YT* NM_001302621.3 NG_007474.2 NC_000007.14	ACHE:c.1057C>A	ACHE:g.7958C>A	7:g.100893176C>A	rs1799805	Yt^a/Yt^b

XG 012	*XG* NM_175569.3 NG_011627.1 NC_000023.11	None[8]	XG:g.1292G>C	X:g.2748343G>C	rs311103	Xg(a-) [9]
SC 013	*SC* NM_001017922.2 NG_008749.1 NC_000001.11	ERMAP:c.169G>A	ERMAP:g.18747G>A	1:g.42830851G>A	rs56025238	Sc1/Sc2
DO 014	*DO* NM_021071.4 NG_007477.2 NC_000012.12	ART4:c.793A>G ART4:c.323G>T ART4:c.350C>T	ART4:g.7975A>G ART4:g.7505G>T ART4:g.7532C>T	12:g.14840505A>G 12:g.14840975G>T 12:g.14840948C>T	rs11276 rs28362797 rs28362798	Do^a/Do^b Hy Jo^a
CO 015	*CO* NM_198098.4 NG_007475.2 NC_000007.14	AQP1:c.134C>T	AQP1:g.63650C>T	7:g.30912043C>T	rs28362692	Co^a/Co^b
LW 016	*LW* NM_001544.5 NG_007728.1 NC_000019.10	ICAM4:c.299A>G	ICAM4:g.5338A>G	19:g.10287311A>G	rs77493670	LW^a/LW^b
CH/RG 017	*CH(C4B)* NM_001002029.4 NG_011639.1 NC_000006.12	C4B:c.3694_3695dupTC	C4B:g.19790_19791dupTC	6:g.32029583_32029584dupTC	rs367709216	Ch-[9]

	RG(C4A) NM_007293.3 NG_011638.1 NC_000006.12	C4A:c.3694_3695dupTC	C4A:g.19790_19791dupTC	6:g.31996846_31996847dupTC	rs760602547	Rg-[9]
H 018	*FUT1* NM_000148.4 NG_007510.2 NC_000019.10	FUT1:c.948C>G	FUT1:g.10057C>G	19:g.48750334G>C	rs104894686	H negative [9]
XK 019	*XK* NM_021083.4 NG_007473.3 NC_000023.11	XK:c.397C>T	XK:g.13558C>T	X:g.37694437C>T	rs1556442175	kx negative [9]
GE 020	*GE* NM_002101.5 NG_007479.1 NC_000002.12	GYPC:c.60_116del	GYPC:g.39158_42766del	2:g.126690265_126693873del	Not available	Ge:–2,3,4 or Yus type [9]
CROM 021	*CROM* NM_000574.5 NG_007465.1 NC_000001.11	CD55:c.679G>C	CD55:g.14651G>C	1:g.207331122G>C	rs60822373	Cr(a-) [9]
KN 022	*KN* NM_000573.4 NG_007481.1 NC_000001.11	CR1:c.3623A>G CR1:c.4223C>T CR1:c.4681G>A CR1:c.4768A>G CR1:c.4801A>G CR1:c.4843A>G	CR1:g.89149A>G CR1:g.96301C>T CR1:g.118297G>A CR1:g.118384A>G CR1:g.118417A>G CR1:g.118459A>G	1:g.207580276A>G 1:g.207587428C>T 1:g.207609424G>A 1:g.207609511A>G 1:g.207609544A>G 1:g.207609586A>G	rs2274567 rs3737002 rs41274768 rs17047660 rs17047661 rs6691117	DACY/YCAD Yk(a-) Kn^a/Kn^b McC^a/McC^b Sl:1,2,3 KCAM/KDAS
IN 023	*IN* NM_000610.4	CD44:c.137C>G	CD44:g.42775C>G	11:g.35176644C>G	rs369473842	In^a/In^b

	NG_008937.1 NC_000011.10					
OK 024	*OK* NM_001728.4 NG_007468.1 NC_000019.10	BSG:c.274G>A	BSG:g.14104G>A	19:g.580428G>A	rs104894669	Ok[a][9]
RAPH 025	*RAPH* NM_004357.5 NG_007478.1 NC_000011.10	RAPH:c.511C>T and RAPH:c.579G>A	RAPH:g.9563C>T and RAPH:g.9631G>A	11:g.837514C>T and 11:g.837582G>A	rs139042921 and rs1130663	MER2 negative[9]
JMH 026	*SEMA7A* NM_003612.5 NG_011733.1 NC_000015.10	SEMA7A:c.1040G>T	SEMA7A:g.24066G>T	15:g.74414893C>A	rs387907241	JMH1 negative [9]
I 027	*GCNT2* NM_145655.4 NG_007469.3 NC_000006.12	GCNT2:c.1049G>A	GCNT2:g.139225G>A	6:g.10626447G>A	rs56141211	I negative [9]
GLOB 028	*B3GALNT1* NM_033169.3 NG_007854.1 NC_000003.12	B3GALNT1:c.202C>T	B3GALNT1:g.23820C>T	3:g.161086553G>A	rs200235398	P negative [9]
GIL 029	*AQP3* NM_004925.4 NG_007476.1 NC_000009.12	AQP3:c.710+1G>A	AQP3:g.10293G>A	9:g.33442300C>T	rs1347380973	GIL negative [9]

RHAG 030	*RHAG* NM_000324.3 NG_011704.1 NC_000006.12	RHAG:c.316C>G	RHAG:g.22671C>G	6:g.49619204G>C	rs1180686517	Duclos negative [9]
FORS 031	*GBGT1* NM_021996.6 NG_033868.1 NC_000009.12	GBGT1:c.887G>A	GBGT1:g.15212G>A	9:g.133153734C>T	rs375748588	FORS positive [9]
JR 032	*ABCG2* NM_004827.3 NG_032067.2 NC_000004.12	ABCG2:c.376C>T	ABCG2:g.104518C>T	4:g.88131805G>A	rs72552713	Jr(a-) [9]
LAN 033	*ABCB6* NM_005689.4 NG_032110.1 NC_000002.12	ABCB6:c.196dupG	ABCB6:g.5513dupG	2:g.219218483dupG	rs781146478	LAN negative [9]
VEL 034	*SMIM1* NM_001163724.3 NG_033869.1 NC_000001.11	SMIM1:c.64_80delAGCCTAGGGGCTGTGTC	SMIM1:g.7677_7693delAGCCTAGGGGCTGTGTC	1:g.3775437_3775453delAGCCTAGGGGCTGTGTC	rs566629828	Vel negative [9]
CD59 035	*CD59* NM_203330.2 NG_008057.1 NC_000011.10	CD59:c.146delA	CD59:g.24086delA	11:g.33717393delT	rs587777149	CD59 negative [9]
AUG 036	*SLC29A1* NM_001304463	SLC29A1:c.1171G>A	SLC29A1:g.18414G>A	6:g.44232918G>A	rs45458701	At[a] negative [9]

	NG_042893.1 NC_000006.12					
KANNO 037	*PRNP* NM_000311.5 NG_009087.1 NC_000020.11	PRNP:c.655G>A	PRNP:g.18725G>A	20:g.4699875G>A	rs1800014	KANNO1 negative [9]
SID 038	*B4GALNT2* NM_153446.3 RefSeq Gene[10] NC_000017.11	B4GALNT2:c.1396T>C	Not applicable	17:g.49168801T>C	rs7224888	Sd(a-) [9]
CTL2 039	*SLC44A2* NM_001145056.2 RefSeq Gene[10] NC_000019.10	SLC44A2:c.455A>G	Not applicable	19:g.10631494A>G	rs2288904	Cs(b-) [9]
PEL 040	*ABCC4* NM_005845.5 NG_050651.2 NC_000013.11	None[8]	None[8]	13:g.95018454_95085982del	Not available	PEL negative [9]
MAM 041	*EMP3* NM_001425.3 RefSeq Gene[10] NC_000019.10	EMP3:c.123C>G and c.373A>G	Not applicable	19:g.48327565C>G and g.48330351A>G	rs201392469 and rs4893	MAM negative [9]
EMM 042	*PIGG* *NM_001127178.3* NG_051621.1 NC_000004.12	PIGG:c.2624_2625delTA	PIGG:g.39671_39672delTA	4:g.533870_533871delTA	rs771819481	Emm negative [9]

ABCC1 043	*ABCC1* NM_004996.4 NG_028268.2 NC_000016.10	ABCC1: intron 21_26del 21249 bp	Not available	Not available	Not available	WLF negative [9]
Er 044	*PIEZO1* NM_001142864.4 NG_042229.1 NC_000016.10	PIEZO1:c.5289C>G	PIEZO1:g.68569C>G	16:g.88721652G>C	rs72811487	Er null [9]
CD36 045	*CD36* NM_001001548.3 NG_008192.1 NC_000007.14	CD36:c.1133G>T	CD36:g.75590G>T	7:g.80672777G>T	rs146027667	CD36 null [9]
GATA1	*GATA1* NM_002049.4 NG_008846.2 NC_000023.11	GATA1:c.1240T>C	GATA1:g.12589T>C	X:g.48794162T>C	rs587776456	XS2 Lu-mod [9]
KLF1	*KLF1* NM_006563.4 NG_013087.1 NC_000019.10	KLF1:c.874A>T	KLF1:g.6848A>T	19:g.12885356T>A	rs137852687	In(Lu) [9]

[1] Note that this list is not exhaustive and is the minimum required for a molecular testing laboratory to be accredited if testing for that specific system.

[2] VariantValidator.org was used for mapping and formatting of sequence variant descriptions.

[3] ISBT name

[4] Genome Reference Consortium Human Build 38 patch release 14 (GRCh38.p14)

[5] The variant in HGVS format will be NM_020469.3:c.261del

[6] The variant in HGVS format will be NG_006669.2:g.22694del

[7] The variant in HGVS format will be NC_000009.12:g.133257521del

[8] As per the HGVS nomenclature guidelines, it is not informative to describe a promoter or intergenic variant in relation to a transcript (NM_) reference sequence or to a genomic (NG_) reference sequence.

[9] Minimum of at least two alleles, preferably the wild type allele and the designated variant allele or one of several various alleles listed by the ISBT, or a novel allele that is relevant to the laboratory.

[10] RefSeq Gene (:g.) ID not assigned.

HGVS ⊢ Human Genome Variation Society; ISBT ⊢ International Society of Blood Transfusion.

Reference Standard 2.2B–Minimum DNA Resources – Platelets[1]

		Variant Description[2]				
ISBT name	**Gene[3] Transcript RefSeq Gene Chromosome**	**Transcript (NM_)**	**RefSeq Gene (NG_)**	**Chromosome[4] (NC_)**	**rs number**	**Comment Antigen(s)**
HPA-1	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.176T>C[5]	ITGB3:g.34523T>C[6]	17:g.47283364T>C[7]	rs5918	HPA-1a/1b
HPA-2	*GP1BA* NM_000173.7 NG_008767.2 NC_000017.11	GP1BA:c.482C>T	GP1BA:g.5792C>T	17:g.4933086C>T	rs6065	HPA-2a/2b
HPA-3	*ITGA2B* NM_000419.5 NG_008331.1 NC_000017.11	ITGA2B:c.2621T>G	ITGA2B:g.18809T>G	17:g.44375697A>C	rs5911	HPA-3a/3b
HPA-4	*ITGB3* NM_000212.3 NG_008332.2	ITGB3:c.506G>A	ITGB3:g.35746G>A	17:g.47284587G>A	rs5917	HPA-4a/4b

	NC_000017.11					
HPA-5	*ITGA2* NM_002203.4 NG_008330.2 NC_000005.10	ITGA2:c.1600G>A	ITGA2:g.78602G>A	5:g.53062927G>A	rs1801106	HPA-5a/5b
HPA-6	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.506G>A	ITGB3:g.35746G>A	17:g.47284587G>A	rs13306487	HPA-6a/6b
HPA-7	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1297C>G	ITGB3:g..43334C>G	17:g.47292175C>G	rs121918448	HPA-7a/7b
HPA-8	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1984C>T	ITGB3:g.51707C>T	17:g.47300548C>T	rs151219882	HPA-8a/8b
HPA-9	*ITGA2B* NM_000419.5 NG_008331.1	ITGA2B:c.2602G>A	ITGA2B:g.18790G>A	17:g.44375716C>T	rs74988902	HPA-9a/9b

	NC_000017.11					
HPA-10	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.263G>A	ITGB3:g.34610G>A	17:g.47283451G>A	rs200358667	HPA-10a/10b
HPA-11	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1976G>A	ITGB3:g.51699G>A	17:g.47300540G>A	rs377302275	HPA-11a/11b
HPA-12	*GP1BB* NM_000407.5 NG_007974.1 NC_000017.11	GP1BB:c.119G>A	GP1BB:g.5420G>A	22:g.19723962G>A	rs375285857	HPA-12a/12b
HPA-13	*ITGA2* NM_002203.4 NG_008330.2 NC_000022.11	ITGA2:c.2483C>T	ITGA2:g.88846C>T	5:g.53073171C>T	rs79932422	HPA-13a/13b
HPA-14	*ITGB3* NM_000212.3 NG_008332.2	ITGB3: c.1912_1913+1del	ITGB3:g.50688_50690del	17:g.47299529_47299531del	n/a	HPA-14a/14b

	NC_000017.11					
HPA-15	*CD109* NM_133493.5 NG_033971.1 NC_000017.11	CD109:c.2108A>C	CD109:g.92925A>C	6:g.73783709A>C	rs10455097	HPA-15a/15b
HPA-16	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.497C>T	ITGB3:g.35737C>T	17:g.47284578C>T	rs74708909	HPA-16a/16b
HPA-17	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.662C>T	ITGB3:g.37466C>T	17:g.47286307C>T	rs770992614	HPA-17a/17b
HPA-18	*ITGA2* NM_002203.4 NG_008330.2 NC_000005.10	ITGA2:c.2235G>T	ITGA2:g.85935G>T	5:g.53070260G>T	rs267606593	HPA-18a/18b
HPA-19	*ITGB3* NM_000212.3	ITGB3:c.487A>C	ITGB3:g.35727A>C	17:g.47284568A>C	rs80115510	HPA-19a/19b

	NG_008332.2 NC_000017.11					
HPA-20	*ITGA2B* NM_000419.5 NG_008331.1 NC_000017.11	ITGA2B:c.1949C>T	ITGA2B:g.15999C>T	17:g.44378507G>A	rs78299130	HPA-20a/20b
HPA-21	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1960G>A	ITGB3:g.51683G>A	17:g.47300524G>A	rs70940817	HPA-21a/21b
HPA-22	*ITGA2B* NM_000419.5 NG_008331.1 NC_000017.11	ITGA2B:c.584A>C	ITGA2B:g.9180A>C	17:g.44385326T>G	rs142811900	HPA-22a/22b
HPA-23	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1942C>T	ITGB3:g.51665C>T	17:g.47300506C>T	rs139166528	HPA-23a/23b
HPA-24	*ITGA2B*	ITGA2B:c.1508G>A	ITGA2B:g.14084G>A	17:g.44380422C>T	rs281864910	HPA-24a/24b

	NM_000419.5 NG_008331.1 NC_000017.11					
HPA-25	*ITGA2* NM_002203.4 NG_008330.2 NC_000005.10	ITGA2:c.3347C>T	ITGA2:g.102715C>T	5:g.53087040C>T	rs771035051	HPA-25a/25b
HPA-26	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1818G>T	ITGB3:g.50594G>T	17:g.47299435G>T	rs1156382155	HPA-26a/26b
HPA-27	*ITGA2B* NM_000419.5 NG_008331.1 NC_000017.11	ITGA2B:c.2614C>A	ITGA2B:g.18802C>A	17:g.44375704G>T	rs149468422	HPA-27a/27b
HPA-28	*ITGA2B* NM_000419.5 NG_008331.1 NC_000017.11	ITGA2B:c.2311G>T	ITGA2B:g.18161G>T	17:g.44376345C>A	rs368953599	HPA-28a/28b

HPA-29	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.98C>T	ITGB3:g.25596C>T	17:g.47274437C>T	rs544276300	HPA-29a/29b
HPA-30	*ITGA2B* NM_000419.5 NG_008331.1 NC_000017.11	ITGA2B:c.2511G>C	ITGA2B:g.18583G>C	17:g.44375923C>G	rs377753373	HPA-30a/30b
HPA-31	*GP9* NM_000174.5 NG_008715.1 NC_000017.11	GP9:368C>T	GP9:g.6306C>T	3:g.129062107C>T	rs202229101	HPA-31a/31b
HPA-32	*ITGB3* NM_000212.3 NG_008332.2 NC_000003.12	ITGB3:c.521A>G	ITGB3:g.35761A>G	17:g.47284602A>G	rs879083862	HPA-32a/32b
HPA-33	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1373A>G	ITGB3:g.43410A>G	17:g.47292251A>G	rs1555572829	HPA-33a/33b

HPA-34	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.349C>T	ITGB3:g.34696C>T	17:g.47283537C>T	rs777748046	HPA-34a/34b
HPA-35	*ITGB3* NM_000212.3 NG_008332.2 NC_000017.11	ITGB3:c.1514G>A	ITGB3:g.43551G>A	17:g.47292392G>A	rs779974422	HPA-35a/35b

[1]Note that this list is not exhaustive and is the minimum required for a molecular testing laboratory to be accredited if testing for that specific system.
[2]VariantValidator.org was used for mapping and formatting of sequence variant descriptions.
[3]ISBT name
[4]Genome Reference Consortium Human Build 38 patch release 14 (GRCh38.p14)
[5]The variant in HGVS format will be NM_000212.3:c.176T>C
[6]The variant in HGVS format will be NG_008332.2:g.34523T>C
[7]The variant in HGVS format will be NC_000017.11:g.47283364T>C

HGVS ⊢ Human Genome Variation Society; ISBT ⊢ International Society of Blood Transfusion.

Reference Standard 2.2C–Minimum DNA Resources – Neutrophils[1]

		Variant Description[2]				
ISBT name	Gene[3] Transcript RefSeq Gene Chromosome	Transcript (NM_)	RefSeq Gene (NG_)	Chromosome[4] (NC_)	rs number	Comment Antigen(s)
HNA-1	*FCGR3B* NM_000570.5 NG_032926.2 NC_000001.11	FCGR3B:c.108C>G[5] FCGR3B:c.194A>G FCGR3B:c.233C>A	FCGR3B:g.6975C>G[6] FCGR3B:g.7061A>G FCGR3B:g.7100C>A	1:g.161629989G>C[7] 1:g.161629903T>C 1:g.161629864G>T	rs200688856 rs448740 rs5030738	HNA-1a/1b/1c
HNA-2	*CD177* NM_020406.4 RefSeq Gene[8] NC_000019.10	CD177:c.787A>T CD177:c.1291G>A	Not applicable	19:g.43361169A>T 19:g.43362297G>A	rs201821720 rs78718189	HNA-2/ HNA-2 null
HNA-3	*SLC44A2* NM_001145056.2 RefSeq Gene[8] NC_000019.10	SLC44A2:455G>A	Not applicable	19:g.10631494A>G	rs2288904	HNA-3a/3b
HNA-4	*ITGAM* NM_000632.3 NG_011719.1	ITGAM:c.230G>A	ITGAM:g.10524G>A	16:g.31265490G>A	rs1143679	HNA-4a/4b

	NC_000016.10					
HNA-5	*ITGAL* NM_002209.3 RefSeq Gene[8] NC_000016.10	ITGAL:c.2372G>C	Not applicable	16:g.30506720G>C	rs52230433	HNA-5a/5b

[1]Note that this list is not exhaustive and is the minimum required for a molecular testing laboratory to be accredited if testing for that specific system.
[2]VariantValidator.org was used for mapping and formatting of sequence variant descriptions.
[3]ISBT name
[4]Genome Reference Consortium Human Build 38 patch release 14 (GRCh38.p14)
[5]The variant in HGVS format will be NM_000570.5:c.108C>G
[6]The variant in HGVS format will be NG_032926.2:g.6975C>G
[7]The variant in HGVS format will be NC_000001.11:g.161629989G>C
[8]RefSeq Gene (:g.) ID not assigned.

HGVS ⊢ Human Genome Variation Society; ISBT ⊢ International Society of Blood Transfusion.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
2.1.1	Job descriptions	5
2.1.2	Qualification of personnel performing critical tasks	5
2.1.3	Training records of personnel	5
2.1.4	Evaluations of competence	5
2.1.5	Personnel records of each employee	5 years following conclusion of employment period
2.1.6	Continuing education requirements	5

[1]Applicable state or local law may exceed this period.

QSE 3 – Equipment

Key Concepts: This QSE describes the selection, use, maintenance, and monitoring of equipment, including information systems. It also describes the use and testing of alternative systems when primary systems fail.

Key Terms:
Backup: Digital data and/or physical storage containing copies of relevant data.

Calibrate: To set or align measurement equipment against a known standard.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Critical Equipment/Materials: A piece of equipment or material that can affect the quality of the organization's products.

Data Integrity: The accuracy, completeness, and consistency of information resources.

Equipment: A durable item, instrument, or device used in a process or procedure.

Installation Qualification: Verification that the correct equipment is received and that it is installed according to specifications and the manufacturer's recommendations in an environment suitable for its operation and use.

Operational Qualification: Verification that equipment will function according to the operational specifications provided by the manufacturer.

Performance Qualification: Verification that equipment performs consistently as expected for its intended use in the organization's environment, using the organization's procedures and supplies.

Validation: Establishing evidence that a process, executed by users in their environment, will consistently meet predetermined specifications.

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been met.

Examples of Objective Evidence:

- Policies, processes, and procedures related to this chapter.
- Processes for equipment selection, qualification, and maintenance.
- List or tool used for critical equipment identification.
- Equipment calibration and maintenance records, if applicable.
- Equipment qualification records.
- Manufacturer's written instructions.
- Records of investigation of equipment malfunction, failure, repair, and requalification, if applicable.

- Alarm system testing and records of alarm management, if appropriate.
- Evidence of information system backup and records of testing.

3.0 Equipment

The organization shall define and control critical equipment.

3.1 Equipment Specifications

Equipment specifications shall be defined before purchase.

✎**3.2 Qualification of Equipment**

All critical equipment shall be qualified for its intended use. Equipment shall be requalified, as needed, after repairs and upgrades.

3.2.1 Installation Qualification

Equipment shall be installed per manufacturer specifications.

3.2.2 Operational Qualification

Each piece of equipment and component of an information system shall be verified before actual use.

3.2.3 Performance Qualification

Equipment shall perform as expected for its intended use.

3.2.3.1 Performance specifications established by the manufacturer shall be met.

3.3 Use of Equipment

Equipment shall be used in accordance with the manufacturer's written instructions.

✎**3.4 Unique Identification of Equipment**

Equipment shall have unique identification.

3.5 Equipment Monitoring and Maintenance

Equipment shall be monitored and maintained in accordance with the manufacturer's written instructions.

✎ **3.5.1 Calibration and Accuracy of Equipment**

Calibrations and/or adjustments shall be performed using equipment and materials that have adequate accuracy and precision. At a minimum, calibrations and/or adjustments shall be confirmed as described below unless otherwise indicated by the manufacturer:

1) Before use.
2) After activities that may affect the calibration.
3) At prescribed intervals.

3.5.1.1 Calibration of equipment shall include details of equipment type, unique identification, location, frequency of checks, check method, acceptance criteria, and specified limitations.

3.5.1.2 Equipment used for calibration, inspection, measuring, and testing shall be certified to meet nationally recognized measurement standards. Certification shall occur before initial use, after repair, and at prescribed intervals. Where no such measurement standards exist, the basis for calibration shall be described and recorded.

3.5.1.3 Equipment shall be safeguarded from adjustments that would invalidate the calibration setting.

3.5.2 When equipment is found to be out of calibration or specification, the validity of previous inspection and test results and the conformance of potential affected products or services (including those that have already been released or delivered) shall be verified.

3.5.3 The organization shall:

1) Define cleaning and sanitization methods and intervals for equipment.
2) Ensure that environmental conditions are suitable for the operations, calibrations, inspections, measurements, and tests carried out.
3) Remove equipment from service that is malfunctioning/out of service and communicate to appropriate personnel.
4) Monitor equipment to ensure that defined parameters are maintained.
5) Ensure that the handling, maintenance, and storage of equipment are such that the equipment remains fit for use.
6) Ensure that all equipment maintenance and repairs are performed by qualified individuals and in accordance with the manufacturer's recommendations.

3.5.4 Investigation and Follow-up

Investigation and follow-up of equipment malfunctions, failures, or adverse events shall include:

1) Assessment of products or services provided since the equipment was last known to be functioning per the manufacturer's written instructions or organization-defined specifications.
2) Assessment of the effect on the safety of individuals affected.
3) Removal of equipment from service, if indicated.
4) Investigation of the malfunction, failure, or adverse event, and a determination if other equipment is similarly affected, as applicable.
5) Requalification of the equipment.
6) Reporting the nature of the malfunction, failure, or adverse event to the manufacturer, when indicated. *

*21 CFR 803.30.

3.6 Equipment Traceability

The organization shall maintain records of equipment use in a manner that permits:

1) Equipment to be uniquely identified and traceable.
2) Tracing of any given product or service to all equipment associated with the procurement, processing, storage, distribution, and administration of the product or service.

3.7 Information Systems

The organization shall have controls in place for the implementation, use, ongoing support, and modifications of information system software, hardware, and databases. Elements of planning and ongoing control shall include:

1) Numeric designation of system versions with inclusive dates of use.
2) Validation/verification/qualification of system software, hardware, databases, and user-defined tables before implementation.
3) Fulfillment of life-cycle requirements for internally developed software.
4) Defined processes for system operation and maintenance.
5) Defined process for authorizing and documenting modifications to the system.
6) System security to prevent unauthorized access.
7) Policies, processes, and procedures and other instructional documents developed using terminology that is understandable to the user.
8) Functionality that allows for display and verification of data before final acceptance of the additions or alterations.
9) Defined process for monitoring of data integrity for critical data elements.
10) System design that establishes and maintains unique identity of the donor, the product, or service, and the recipient (as applicable).
11) Training and competency of personnel who use information systems.
12) Procedures to ensure confidentiality of protected information.

3.7.1 Alternative Systems

An alternative system shall be maintained to ensure continuous operation in the event that computerized data and computer-assisted functions are unavailable. The alternate system shall be tested at defined intervals. Processes and procedures shall address mitigation of the effects of disasters and include recovery plans.

3.7.2 Personnel responsible for management of information systems shall be responsible for compliance with the regulations that affect the use of the system.

3.7.3 The organization shall support the management of information systems.

3.7.4 A system designed to prevent unauthorized access to computers and electronic records

shall be in place.

3.7.5 The organization shall have measures in place to minimize the risk of internal and external data breaches.

3.8 Alarm Systems

Storage devices for specimens and/or reagents shall have alarms and shall conform to the following standards (Standard 5.1.2 applies):

3.8.1 The alarm shall be set to activate under conditions that will allow enough time for proper action to be taken before specimens and/or reagents reach unacceptable conditions.

3.8.2 Activation of an alarm shall initiate a process for immediate action, investigation, and appropriate corrective action.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
3.2	Equipment qualification	10 years after retirement of the equipment
3.4	Unique identification of equipment	10
3.5.1	Equipment calibration activities	10 years after retirement of the equipment
3.5.2	Equipment found to be out of calibration	10
3.5.3	Equipment monitoring, maintenance, calibration, and repair	10 years after retirement of the equipment
3.6	Equipment traceability	10
3.7	Implementation and modification of software, hardware, or databases	2 years after retirement of system

[1]Applicable state or local law may exceed this period.

QSE 4 – Suppliers and Customers

Key Concepts: This QSE describes the need for agreements between the organization and its suppliers and customers. The agreements define expectations between both parties and measures taken when one entity fails to meet the expectations of an agreement.

Key Terms:
Agreement: A contract, order, or understanding between two or more parties, such as between an organization and one of its customers.

Agreement Review: Systematic activities carried out before finalizing the agreement to ensure that requirements are adequately defined, free from ambiguity, documented, and achievable.

Customer: The receiver of a product or service. A customer may be internal (eg, another organizational unit within the same organization) or external (eg, a patient, client, donor, or another organization).

Quality: Characteristics of a product or service that bear on its ability to fulfill customer expectations. The measurable or verifiable aspects of a product or service that can be used to determine if requirements have been met.

Quality Control: Testing routinely performed on materials and equipment to ensure their proper function.

Supplier: An entity that provides a material, product, or service.

Supplier Qualification: Evaluation of a supplier to assess its ability to consistently deliver products or services that meet specified requirements.

Examples of Objective Evidence:
- Policies, processes, and procedures related to this chapter.
- Processes for defining and updating or changing agreements.
- Process for recording verbal agreements, if practiced.
- Agreement records.
- Agreement review records.
- Supplier qualification records.
- Supplier evaluation records.
- Supplier selection process.
- Evidence of action taken when a supplier fails to meet expectations, if applicable.
- Evidence of receipt of product(s) as stipulated in agreements.
- Records of inspection and testing.

4.0 Suppliers and Customers

The organization shall ensure that agreements to provide or receive products or services are reviewed, approved, and meet supplier and customer expectations.

✎4.1 Supplier Qualification

The organization shall evaluate the ability of suppliers of critical materials, equipment, and services to meet specified requirements.

4.1.1 The organization shall evaluate and participate in the selection of suppliers. If executive management is not included in the selection process, there shall be a mechanism to provide feedback to management with contracting authority.

4.1.2 When a supplier fails to meet specified requirements, it shall be reported to the management with contracting authority.

✎4.2 Agreements

Agreements and any incorporated changes shall be reviewed and communicated.

✎ **4.2.1** Agreements shall be reviewed at defined intervals to ensure that the terms of the agreement continue to meet requirements.

4.2.2 Changes to agreements shall be communicated to affected parties.

✎ **4.2.3** The responsibilities for activities covered by these *MT Standards* when more than one organization is involved shall be specified by agreement.

4.2.4 The laboratory shall inform the customer of instances when testing is performed using reagents, methods, techniques, or equipment not approved for the purpose by the Competent Authority.

✎4.3 Incoming Receipt, Inspection, and Testing

Incoming products or services, equipment, and materials shall be received, inspected, and tested, as necessary, before approval for use.

4.3.1 Critical materials shall meet specified requirements.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
4.1	Evaluation and participation in selection of suppliers	5
4.2	Agreements	5
4.2.1	Agreement review	5
4.2.3	Agreements concerning activities involving more than one organization	5
4.3	Inspection of incoming critical materials	10

[1]Applicable state or local law may exceed this period.

QSE 5 – Process Control

Key Concepts: This QSE covers the organization's operations and production functions. It describes the need to ensure that this work is controlled, that processes function as expected, and that expected outcomes are met. This QSE encapsulates what occurs in each organization and forms the basis of its accreditation.

Key Terms:
Change Control: A structured method of revising a policy, process, or procedure, including hardware or software design, transition planning, and revisions to all related documents.

Critical Equipment/Materials/Tasks: A piece of equipment, material, service, or task that can affect the quality of the organization's products.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Process Control: Activities designed to ensure that processes are stable and consistently operate within acceptable limits of variation in order to produce predictable output that meets specifications.

Product: A tangible output from a process.

Reference Standard: Specified requirements defined by the AABB. Reference standards define how or within what parameters an activity shall be performed and are more detailed than quality system requirements.

Service: An intangible output of a process.

Standard: A set of specified requirements upon which an organization may base its criteria for the products, components, and/or services provided.

Validation: Establishing evidence that a process, executed by users in their environment, will consistently meet predetermined specifications.

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been met.

Examples of Objective Evidence:

- Policies, processes, and procedures related to this chapter.
- Implementation records.
- Records enabling traceability.
- Storage records.
- Quality control records.
- Process planning, process validation, and change control records.
- Records of material storage, handling, and use.

- Records of inspection of materials.
- Product inspection records.
- Testing records.

5.0 Process Control

The organization shall ensure the quality of products or services.

5.1 General Elements

The organization shall ensure that processes are carried out under controlled conditions.

5.1.1 Change Control

When the organization develops new processes or procedures or changes existing ones, they shall be validated before implementation.

5.1.1.1 This process shall include identification of specifications and verification that they have been met. Standard 2.1.3 applies.

5.1.1.2 The laboratory shall ensure that the implementation of new or changed processes is controlled.

5.1.2 Quality Control

A program of quality control shall be established that is sufficiently comprehensive to ensure that products, equipment, materials, and analytical functions perform as intended.

5.1.2.1 Quality control results shall be reviewed and evaluated against acceptance criteria.

5.1.2.2 Quality control failures shall be investigated before release of test results, products, or services.

5.1.2.3 The validity of test results and methods and the acceptability of products or services provided shall be evaluated when quality control failures occur.

5.1.2.3.1 The laboratory shall have policies for repeating any testing runs that have failed.

5.1.2.4 Laboratories that use different methods, critical equipment, or testing sites shall have a process that evaluates the comparability of test results obtained. This evaluation shall be performed twice annually.

5.1.3 Process Planning

Quality requirements shall be incorporated into new or changed processes, products, services, and novel methods. Planning and implementation activities shall include the following:

1) Evaluation of accreditation, regulatory, and legal requirements related to the new or changed process, product, or service.
2) Review of current available knowledge (eg, review of medical practice and/or literature).
3) Evaluation of risk.
4) Identification of affected internal and external parties and mechanism to communicate relevant information.
5) Identification of performance measures applicable to the new or changed process, product, or service.
6) Evaluation of resource requirements.
7) Evaluation of the impact of the new or changed process, product, or service on other organization (or program) processes.
8) Evaluation of the need to create or revise documents for the new or changed process, product, or service.
9) Review and approval of the output of process development and design activities (eg, pilot or scale-up study results, process flow charts, procedures, data forms).
10) Evaluation of the extent and scope of process validation or revalidation depending on the level of risk and impact of the new or changed products or services.

5.1.4 Process Validation

Before implementation, the new or changed processes and procedures shall be validated.

5.1.4.1 Validation activities shall include the following:

1) Identification of objectives, individual(s) responsible, expected outcomes, and/or performance measures.
2) Criteria for review of outcomes.
3) Approval of validation plan.
4) Review and approval of actual results.
5) Actions to be taken if objectives are not met.

5.1.5 Process Implementation

The implementation of new or changed processes and procedures shall be planned and controlled.

5.1.5.1 Postimplementation evaluations of new or changed processes and procedures shall be performed.

5.1.6 Use of Materials

All materials shall be stored and used in accordance with the manufacturer's written instructions* and shall meet specified requirements.

*21 CFR 606.65(e).

5.1.6.1 Reagents that are prepared by the organization shall meet or exceed applicable criteria.

5.1.6.2 Positive and negative controls shall be tested at defined intervals.

5.1.6.3 When deviating from the manufacturer's written instructions including the use of FDA cleared or approved tests, materials shall be qualified for use and shall meet specified requirements and appropriate controls shall be used to ensure reliability of the test results.*

*42 CFR 493.1253(b)(2).

5.1.7 Inspection

The organization shall ensure that products or services are inspected at organization-defined stages.

5.1.7.1 Final Inspection

The laboratory shall have a process to ensure that finished test reports and services are acceptable before distribution, issue, or delivery. Standard 5.5 applies.

5.1.8 Identification and Traceability

The organization shall ensure that all products or services are identified and traceable.

5.1.8.1 The laboratory shall ensure that testing has been requested either internally or externally. Patient orders shall include the health-care provider's identifying information.

5.1.8.2 Requests shall contain sufficient information to uniquely identify the individual for whom the test was requested.*

*42 CFR 493.1241.

5.1.8.3 A laboratory responsible for labeling blood components shall have documented procedures for the labeling of those blood components, if applicable. *

*21 CFR 606.121.

FDA Guidance for Industry: Labeling of Red Blood Cell Units with Historical Antigen Typing Results, December 2018.

5.1.9 Handling, Storage, and Transportation

The organization shall ensure that products or services are handled, stored, and transported in a manner that prevents damage, limits deterioration, and provides traceability.

5.1.10 Proficiency Testing Program

The laboratory shall participate in a proficiency testing program or verify the accuracy and reliability of test results twice annually or as required by applicable federal, state, and local laws and regulations. Results shall be reviewed, and corrective action taken, where appropriate, when expected results are not achieved. Standard 7.5 applies.*

*42 CFR 493.1236.

5.1.10.1 Laboratories shall ensure that no interlaboratory communications pertaining to proficiency test events occur until after the submission deadline.*

*42 CFR 493.801(b)(4).

5.1.10.2 The laboratory shall ensure that no portion of a proficiency testing sample is sent to another laboratory for analysis.*

*42 CFR 493.801 (b)(4)

5.1.10.3 Any laboratory that receives a proficiency testing sample from another laboratory for testing shall notify CMS of the receipt of the sample.*

*42 CFR 493.801(b)(4).

5.1.10.4 Proficiency Testing for Facilities not Subject to US Regulation

Laboratories not subject to US regulation shall participate in an external proficiency testing or external quality assessment program, if available, for each analyte.

5.1.10.5 When an external proficiency testing program is not available, there shall be a system for determining the accuracy and reliability of test results.

5.1.11 DNA Contamination Controls

The laboratory shall establish and maintain policies, processes, and procedures for controls that address the following:

1) Environmental controls and monitoring commensurate with the risk of contamination.
2) Process controls.
3) Staff training in contamination prevention.
4) Staff attire, gowning, and use of personal protective equipment.
5) Movement and storage of materials (including waste), equipment, and workflow within workspaces.
6) Physical and/or temporal segregation of equipment or materials.
7) Use and storage of reagents and amplified products.
8) Cleaning and setup of workspaces or equipment.

5.1.11.1 The effectiveness of such measures shall be monitored and reviewed on a defined basis.

5.1.12 Privacy and Confidentiality
The laboratory shall have a policy to ensure that the molecular testing results are private and confidential as required by applicable federal, state, and local laws and regulations.

5.2 Consent and Sample Collection
The laboratory shall have policies, processes, and procedures for consent, collection, verification of sample collection, and acquisition and maintenance of identification records.

5.2.1 Donor Consent
Testing shall be performed consistent with consent obtained from the donor at the time of donation and applicable law.

5.2.2 Patient Orders
A health-care provider order for testing shall be obtained in accordance with applicable law.

5.2.3 Sample Collection
The laboratory shall define collection methods that maintain the integrity of the sample and minimize the potential for contamination.

5.2.3.1 Samples shall be identified with an affixed label bearing information for unique identification.

5.2.3.2 Test methods shall be validated for each specimen type (e.g., buccal swab, peripheral blood).

5.2.3.2.1 If the laboratory performs the same test method on more than one specimen type, equivalency shall be demonstrated.

5.3 Test Validation
The laboratory shall use validated methods for molecular testing. *

*42 CFR 493.1253(b)(2)

5.3.1 The laboratory shall validate FDA cleared or approved test kits in accordance with specified requirements.

5.3.2 Laboratory developed tests (LDT) or research use only (RUO) kits shall comply with the following standards.

5.3.2.1 To implement a genotyping system, the validation protocol shall require the analysis of:
1) Homozygous wild-type sample(s)
2) Heterozygous sample(s)

3) Homozygous variant sample(s) when available
4) Hemizygous sample(s), when applicable.

5.3.2.2 To implement a sequence-based typing system, the validation protocol shall demonstrate:
1) Gene specific alignment
2) Ability to detect and annotate previously characterized variant(s)
3) For next generation sequencing (NGS), the bioinformatics pipeline functions as intended.

5.3.2.3 Results for analytes for which a second method has been used to confirm the minor allele shall be reported with a disclaimer that they are for investigational use only. Reference Standards 2.2B, Minimum DNA Resources - Platelets and 2.2C, Minimum Resources - Neutrophils apply.

5.3.3 To implement a novel test method, the validation protocol shall require the analysis of: at least 20 biological test samples:.
1) Homozygous wild-type sample(s)
2) Heterozygous sample(s)
3) Homozygous variant sample(s) when available
4) Hemizygous sample(s), when applicable.

5.3.4 Test results shall show consistency within the laboratory (precision) and concordance with results from another method or another laboratory (accuracy). The validation protocol shall define acceptable results.

5.4 Specific Testing Methods

Specific testing methods shall ensure that accurate results are produced. The laboratory shall use validated processes and procedures for DNA extraction, amplification, and testing methods. The laboratory shall have a process that demonstrates reproducibility of test results.

5.4.1 General Test Criteria

Test criteria shall be incorporated into the testing processes to ensure accurate results.
1) The assay shall interrogate the region(s) interest.
2) For systems dependent on accurate measurement of alleles by fragment sizes, a size standard shall be tested with each analysis.3) A control without DNA shall be run to monitor contamination, when required by protocol.
4) The laboratory shall evaluate sample contamination for each sample.
5) Postamplification products shall be prevented from contaminating preamplification materials.

5.4.2 The laboratory shall ensure version control of analytic algorithms.

5.5 Review of Results

All results shall be reviewed by two people, one of whom shall be the laboratory director or designee, before the release of results. Standard 1.1.1 applies. At a minimum, the review shall

include critical test results, and the worksheets that record interpretations and conclusions, including computer-generated interpretations and reports.

5.5.1 The laboratory shall investigate and resolve discordance(s) discovered in the course of testing.

5.6 Reports

The laboratory shall have policies, processes, and procedures to ensure that interpretations of investigations are reported in a timely manner following completion of testing.

5.6.1 Interpretations of investigations shall contain the following information*:

1) Patient name and/or unique identifier.
2) Sample identification or accession number.
3) Name of referring laboratory or health-care provider.
4) Sample source and date drawn, when indicated.
5) Final interpretation of results to include phenotype (molecular) and/or genotype for red cells, platelets, and/or neutrophils.
6) Date of final written report.
7) Laboratory identification.
   a) laboratory name and address.
   b) name of person responsible for report.
8) A disclaimer when testing samples that would have been rejected by laboratory-defined requirements.
9) For laboratories operating in the United States (US) using test method(s) and/or reagent(s) that are not FDA cleared or approved, a statement, "This test was developed, and its characteristics determined by [Insert Laboratory Name]. It has not been cleared or approved by the US FDA." shall be included in the report.

*42 CFR 493.1291(c).

5.6.2 ISBT Nomenclature

The laboratory shall have a plan for the implementation of ISBT nomenclature for antigens and alleles.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
5.1.1	Validation of new or changed processes and procedures	5
5.1.2	Quality control records and review of quality control results	10
5.1.2.4	Twice annual review of comparability of test results obtained	5
5.1.6.1	Reagents prepared by facility meet or exceed applicable criteria	5
5.1.7.1	Final inspection of test reports before distribution, issue, or delivery	10
5.1.8	Identification and traceability of products	5
5.3.1	Validation studies for test systems	10
5.3.2	Validation studies for laboratory developed tests and research use only kits	10
5.3.3	Validation of novel test methods	10
5.4.2	Version control of algorithms in genotype prediction	10
5.5	Review of case by two people, including the laboratory director or designee; review of critical test results, worksheets that record interpretations, conclusions, critical calculations, and case reports	10
5.5.1	Investigation and resolution of discordant results	10
5.6	Interpretations of investigations reported	10

[1]Applicable state or local law may exceed this period

QSE 6 – Documents and Records

Key Concepts: This QSE focuses on the need to maintain all documents and records in a manner that ensures their confidentiality, traceability, completeness, uniformity, and ability to be retrieved and located in a time deemed adequate. This QSE also includes the need to ensure data integrity and that all data can be backed up and retrieved.

Key Terms:
Backup: Digital data and/or physical storage containing copies of relevant data.

Confidentiality: The protection of private, sensitive, or trusted information resources from unauthorized access or disclosure.

Data Integrity: The accuracy, completeness, and consistency of information resources.

Document (noun): Written or electronically generated information and work instructions. Examples of documents include quality manuals, procedures, or forms.

Document (verb): To capture information through writing or electronic media.

Label: An inscription affixed or attached to a product for identification.

Labeling: Information that is required or selected to accompany a product, which may include content, identification, description of processes, storage requirements, expiration date, cautionary statements, or indications for use.

Master List of Documents: A reference list, record, or repository of an organization's policies, processes, procedures, forms, and labels related to the *Standards,* including information for document control.

Record (noun): Information captured in writing or through electronically generated media that provides objective evidence of activities that have been performed or results that have been achieved, such as test records or audit results. Records do not exist until the activity has been performed and documented.

Record (verb): To capture information for use in records through writing or electronic media.

Examples of Objective Evidence:

- Policies, processes, and procedures related to this chapter.
- Records of activities performed.
- Record system.
- Master list of documents.
- An electronic record system, if applicable.
- Uniform storage media and ability to track newer technologies to older ones as needed.
- Evidence of document and record review.
- Evidence of standardized formats for all documents and records.
- Record retention periods.
- Record traceability.

- Data backup plans.
- Record change process.
- Obsolescence of records and disposition.
- Record destruction.

6.0 Documents and Records

The organization shall ensure that documents and records are created, stored, and archived in accordance with record retention policies.

6.1 Document Control

The organization shall control all documents that relate to the requirements of these *Standards*. Documents shall be protected from unauthorized access and accidental or unauthorized modification, deletion, or destruction.

6.1.1 Format

Documents shall be in standardized formats. Additional policies, processes, and procedures (such as those in an operator's manual or published in the AABB *Technical Manual*) may be incorporated by reference.

6.1.2 Document Review, Approval, and Distribution

The document control process shall ensure that documents:

1) Are reviewed by personnel trained and/or qualified in the subject area.
2) Are approved by an authorized individual.
3) Are identified with the current version and effective date.
4) Are available at all locations where operations covered by these *MT Standards* are performed.
5) Are not used when deemed invalid or obsolete.
6) Are identified as archived or obsolete when appropriate.

6.1.3 Document Changes

Changes to documents shall be reviewed and approved by an authorized individual.

6.1.3.1 The organization shall track changes to documents.

6.1.4 Master List of Documents

The organization shall maintain complete lists of all active policies, processes, procedures, labels, forms, and other documents that relate to the requirements of these *MT Standards*.

6.1.5 Review of Policies, Processes, and Procedures

Review of each policy, process, and procedure shall be performed by an authorized individual at a minimum of every 2 years.

6.1.5.1 Review and approval by the laboratory director of new and revised documents before their use.

6.1.6 Document Retention

The organization shall determine which documents shall be archived, destroyed, or made obsolete.

6.1.7 Document Storage

Documents shall be stored in a manner that preserves integrity and legibility; protects from accidental or unauthorized access, loss, destruction, or modification; and ensures accessibility and retrievability.

6.1.8 Document Retrieval

The organization shall ensure that documents are retrievable in a timely manner.

6.1.9 The organization shall use only current and valid documents. Applicable documents shall be available at all locations where activities essential to meeting the requirements of these *MT Standards* are performed.

6.2 Record Control

The organization shall maintain a system for identification, collection, indexing, accessing, filing, storage, maintenance, and disposition of original records.

6.2.1 Records

Records shall be complete, retrievable in a period appropriate to the circumstances, and protected from accidental or unauthorized destruction or modification.

6.2.2 Record Traceability

The records system shall ensure traceability of:

1) Critical activities performed.
2) The individual who performed the activity.
3) Date the activity was performed.
4) Time the activity was performed, if applicable.
5) Results obtained.
6) Method(s) used.
7) Equipment used.
8) Critical materials used.
9) The organization where the activity was performed.

6.2.3 Information to Be Retained

Records shall demonstrate that a material, product, or service conforms to specified requirements and that the quality system is operating effectively.

6.2.4 Legibility
All records shall be legible and indelible.

6.2.5 Record Change
The organization shall establish processes for changing records. The date and identity of the person making the change shall be recorded. Record changes shall not obscure previously recorded information.

6.2.5.1 Changes to records (including electronic records) shall be verified for accuracy and completeness.

6.2.5.2 If an amended report is issued, the original report shall be maintained. Standard 6.2.1 applies.

6.2.6 Records shall be created concurrently with the performance of each critical activity.

6.2.7 Copies
Before destruction of original records, copies of records shall be verified as containing the original content and shall be legible, complete, and accessible.

6.2.8 Confidentiality
The organization shall ensure the confidentiality of records.

6.2.9 Retention
Records required by these *MT Standards* shall be retained for a period indicated in the record retention table at the end of each chapter.

6.2.10 Record Review
Records shall be reviewed for accuracy, completeness, and compliance with applicable standards, laws, and regulations.

6.2.11 Storage of Records
Records shall be stored to:
1) Preserve record legibility and integrity for the entire retention period.
2) Protect from accidental or unauthorized access, loss, deterioration, damage, destruction, mix-up, or modification.
3) Permit ready identification.
4) Allow retrieval in a defined time frame.

6.2.12 Destruction of Records
Destruction of records shall be conducted in a manner that protects the confidential content of the records.

6.2.13 The record system shall make it possible to trace and review any sample, report, or service from its source to final disposition.

6.3 Electronic Records

The organization shall support the management of information systems.

6.3.1 Access to Data and Information

Access to data and information shall be controlled.

6.3.1.1 The authorization to access and release data and information shall be defined, and individuals authorized to enter, change, and release results shall be identified.

6.3.1.1.1 Electronic records shall include the date and identity of the person making a change.

6.3.2 Data Integrity

Data integrity shall ensure that data are retrievable and usable.

6.3.2.1 Data shall be accurately, reliably, and securely sent from the point of entry to final destination.

6.3.2.2 Data shall be retrievable for the entire retention period.

6.3.2.2.1 The organization shall archive records or data from media and platforms no longer in use.

6.3.2.3 There shall be a process in place for routine backup of all critical data.

6.3.3 Storage Media

Data storage media shall be protected from damage or unintended access and destruction.

6.3.4 Backup Data

The organization shall back up all critical data.

6.3.4.1 Backup data shall be stored in a secure off-site location.

6.3.4.2 Backup data shall be protected from unauthorized access, loss, or modification.

6.3.4.3 The ability to retrieve data from the backup system shall be tested at defined intervals.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
6.1.2	Document control, including review and approval of all documents before use	5
6.1.3	Review and approval of changes to documents	5
6.1.4	List of all active policies, processes, procedures, labels, and forms	5
6.1.5	Biennial review of each policy, process, or procedure	5
6.1.6	Documents that are archived, destroyed, or made obsolete	5
6.2.5	Record change	5
6.2.7	Verification that copies of records contain the original content and are legible, complete, and accessible before the original records are destroyed	5
6.2.10	Review of records for accuracy, completeness, and compliance with applicable standards, laws, and regulations	5
6.3	Electronic records	5
6.3.1.1.1	Date and identity of person making change(s) to electronic records	5

[1]Applicable state or local law may exceed this period.

Reference Standard 6.2.9A – Retention of Records

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
1.2.2	Management review of effectiveness of the quality system	5
1.3	Policies, processes, and procedures	10
1.3.2	Exceptions to policies, processes, and procedures	10
1.4	Risk assessment	5
1.6.1	Emergency operation plan tested at defined intervals	2 years, or two organizational testing intervals (whichever is longer)
1.9	Laboratory director representative change notification within 30 days	5
1.10	Interruption of on-site testing notification within 30 days	5
2.1.1	Job descriptions	5
2.1.2	Qualification of personnel performing critical tasks	5
2.1.3	Training records of personnel	5
2.1.4	Evaluations of competence	5
2.1.5	Personnel records of each employee	5 years following conclusion of employment period
2.1.6	Continuing education requirements	5

3.2	Equipment qualification	10 years after retirement of the equipment
3.4	Unique identification of equipment	10
3.5.1	Equipment calibration activities	10 years after retirement of the equipment
3.5.2	Equipment found to be out of calibration	10
3.5.3	Equipment monitoring, maintenance, calibration, and repair	10 years after retirement of the equipment
3.6	Equipment traceability	10
3.7	Implementation and modification of software, hardware, or databases	2 years after retirement of system
4.1	Evaluation and participation in selection of suppliers	5
4.2	Agreements	5
4.2.1	Agreement review	5
4.2.3	Agreements concerning activities involving more than one organization	5
4.3	Inspection of incoming critical materials	10
5.1.1	Validation of new or changed processes and procedures	5
5.1.2	Quality control records and review of quality control results	10
5.1.2.4	Twice annual review of comparability of test results obtained	5
5.1.6.1	Reagents prepared by facility meet or exceed applicable criteria	5
5.1.7.1	Final inspection of test reports before distribution, issue, or delivery	10
5.1.8	Identification and traceability of products	5
5.3.1	Validation studies for test systems	10
5.3.2	Validation studies for laboratory developed tests and research use only kits	10
5.3.3	Validation of novel test methods	10
5.4.2	Version control of algorithms in genotype prediction	10
5.5	Review of case by two people, including the laboratory director or designee; review of critical test results, worksheets that record interpretations, conclusions, critical calculations, and case reports	10
5.5.1	Investigation and resolution of discordant results	10
5.6	Interpretations of investigations reported	10
6.1.2	Document control, including review and approval of all documents before use	5
6.1.3	Review and approval of changes to documents	5
6.1.4	List of all active policies, processes, procedures, labels, and forms	5
6.1.5	Biennial review of each policy, process, or procedure	5

6.1.6	Documents that are archived, destroyed, or made obsolete	5
6.2.5	Record change	5
6.2.7	Verification that copies of records contain the original content and are legible, complete, and accessible before the original records are destroyed	5
6.2.10	Review of records for accuracy, completeness, and compliance with applicable standards, laws, and regulations	5
6.3	Electronic records	5
6.3.1.1.1	Date and identity of person making change(s) to electronic records	5
7.1	Deviations	10 years after any impacted product is used or discarded
7.2	Nonconforming products or services	10 years after any impacted product is used or discarded
7.2.4	Nature of nonconformances discovered after release and subsequent actions taken, including acceptance for use	10
7.2.4.1	Disposition of the nonconforming product or service	10
7.4.1	Evaluation of, and corrective action taken in response to, nonconforming proficiency testing results	5
7.4.2	Investigation and resolution of discrepant test results among laboratories participating in a sample exchange program	5
7.5	Retraining of laboratory personnel who fail to meet expected performance criteria for competency testing	5
8.1	Internal assessments	5
8.2	External assessments	5
8.3	Management of assessment results	5
9.0	Implementation of changes to policies, processes, and procedures resulting from corrective and preventive action	5
9.1	Corrective action	5
9.2	Preventive action	5
10.1.1.1.1	Alarm investigation	5
10.2	Monitoring of biological, chemical, and radiation safety	5
10.3	Appropriate discard of products	10
10.4	Monitoring of environmental conditions	5

[1]Applicable state or local law may exceed this period.

QSE 7 – Deviations, Nonconformances, and Adverse Events

Key Concepts: This QSE focuses on the need to ensure capture of, management of, and response to deviations, nonconformances, or adverse events. This also includes the need to maintain records of resolution.

Key Terms:
Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Disaster: An event (internal, local, or national) that can affect the safety and availability of the organization's products or the safety of individuals.

Near-Miss Event: An unexpected occurrence that did not adversely affect the outcome but could have resulted in a serious adverse event.

Nonconformance: Failure to meet requirements.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Traceability: The ability to follow the history of a product or service from source to final distribution or disposition using records.

Examples of Objective Evidence:
- Policies, processes, and procedures related to this chapter.
- Records and evaluation of deviations, nonconformances, and adverse events.
- Notification to customer(s) following investigation, if appropriate.
- Records of evidence that measures were taken to ensure deviations, nonconformances, and adverse events do not recur.
- Planned deviation records, if any.
- Records of deviation reporting to appropriate parties [eg, Food and Drug Administration (FDA)].

7.0 Deviations, Nonconformances, and Adverse Events

The organization shall capture, assess, investigate, and monitor failures to meet specified requirements. The responsibility for review and authority for the disposition of nonconformances shall be defined. These events shall be reported in accordance with specified requirements and to outside agencies as required.*

*21 CFR 606.171 and 21 CFR 1271.350.

7.1 Deviations

The organization shall capture, assess, investigate, and report events that deviate from accepted policies, processes, or procedures. The assessment shall ensure timely and appropriate clinical management of the recipient, if applicable.

7.2 Nonconformances

Upon discovery, nonconforming products or services shall be evaluated and their disposition determined.

7.2.1 Nonconforming products or services shall be quarantined and/or destroyed.

7.2.1.1 For nonconforming test results, the laboratory shall:

1) Identify and manage test reports and services.
2) Identification and notify for quarantine, retrieval, and/or recall of associated products, if applicable.
3) Notify customers and outside agencies as required.

7.2.2 The unintended distribution or use of products or services that do not conform to specified requirements shall be prevented.

7.2.3 The organization shall:

1) Identify, quarantine, retrieve, recall, and determine the disposition of nonconforming products or services.
2) Identify and manage nonconforming products or services.

7.2.4 Released Nonconforming Products or Services

Products or services that are determined after release not to conform to specified requirements shall be evaluated to determine the effect of the nonconformance on the quality and/or safety of the product or service.

7.2.4.1 Records shall include the disposition of the nonconforming product or service, the rationale, and the name(s) of the individual(s) responsible for the decision.

7.2.4.2 In cases where quality may have been affected, the nonconformance shall be reported to the customer.

7.3 Adverse Events

The organization shall detect, monitor, evaluate, manage, and report adverse events related to safety and quality.

7.3.1 Records of adverse events and the related investigations, evaluations, and notifications shall be maintained.

7.3.2 Investigation results and analysis shall be communicated among all facilities involved, if applicable.

7.4 Nonconforming Proficiency Test Results

When nonconforming proficiency test results are obtained, the laboratory shall evaluate and take appropriate action.

7.4.1 Nonconforming results in a graded proficiency testing program shall be investigated in accordance with Standard 9.1 and a corrective or preventive action plan shall be developed and implemented.

7.4.2 Discrepant test results among laboratories participating in a sample exchange program shall be investigated in accordance with Standard 9.1.

7.5 Nonconforming Competency Assessments

When expected performance criteria for competency testing are not met, the laboratory shall ensure the competency of personnel before they are permitted to resume testing. Standard 2.1.4.1 applies.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
7.1	Deviations	10 years after any impacted product is used or discarded
7.2	Nonconforming products or services	10 years after any impacted product is used or discarded
7.2.4	Nature of nonconformances discovered after release and subsequent actions taken, including acceptance for use	10
7.2.4.1	Disposition of the nonconforming product or service	10
7.4.1	Evaluation of, and corrective action taken in response to, nonconforming proficiency testing results	5
7.4.2	Investigation and resolution of discrepant test results among laboratories participating in a sample exchange program	5
7.5	Retraining of laboratory personnel who fail to meet expected performance criteria for competency testing	5

[1]Applicable state or local law may exceed this period.

QSE 8 – Internal and External Assessments

Key Concepts: This QSE addresses the organization's internal quality assessment functions as well as processes to support external assessments by accreditors, health authorities, and regulators This chapter also describes the need for the organization to engage in ongoing quality monitoring and utilization review.

Key Terms:
Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Assessment: A systematic examination to determine whether actual activities comply with planned activities, are implemented effectively, and achieve objectives. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Competent Authority: The agency responsible under its national law for regulations applicable to the organization.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Nonconformance: Failure to meet requirements.

Preventive Action: An action taken to reduce or eliminate the potential for unexpected deviations, nonconformances, or other undesirable situations.

Quality Indicator Data: Information that may be collected and used to determine whether an organization is meeting its quality objectives as defined by top management in its quality policy. Indicators are measured by data for movement or regression with regard to those quality intentions. The data used for monitoring a quality indicator may consist of single-source data or multiple-source data, as long as it is clear how the data will come together to define the indicator.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Examples of Objective Evidence:

- Policies, processes, and procedures related to this chapter.
- Records of internal assessments scheduled and conducted.
- Records of evidence that deficiencies discovered during assessments and inspections have been addressed, including changes to quality or operational functions.
- Records of external assessments being conducted.
- Quality indicator data collection and review.

8.0 Internal and External Assessments

The organization shall conduct assessments of operations and quality systems.

8.1 Internal Assessments

The organization shall conduct internal assessments. Internal assessments shall be performed by personnel independent of those having direct responsibility for the activity being assessed.

8.2 External Assessments

The organization shall participate in an external assessment program applicable to the activities performed in the organization.

8.3 Management of Assessment Results

The results of assessments shall be:

1) Reviewed by the personnel having responsibility for the area assessed.
2) Evaluated to determine the need for corrective and preventive action.
3) Communicated to the appropriate staff.
4) Reported to executive management.

8.3.1 When corrective action is taken, it shall be developed, implemented, and evaluated in accordance with Chapter 9, Process Improvement.

8.4 Quality Monitoring

The organization shall collect and evaluate quality indicator data on a scheduled basis, including adverse events.

8.4.1 The organization shall provide data generated to the personnel who have responsibility for the quality indicator data collected.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
8.1	Internal assessments	5
8.2	External assessments	5
8.3	Management of assessment results	5

[1]Applicable state or local law may exceed this period.

QSE 9 – Process Improvement

Key Concepts: This QSE focuses on the use of corrective and preventive actions to drive process improvement. It describes measures to ensure that the root causes of nonconformances are effectively addressed.

Key Terms:
Adverse Event: A complication. Adverse events may occur in relation to organization defined activities.

Assessment: A systematic examination to determine whether actual activities comply with planned activities, are implemented effectively, and achieve objectives. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Near-Miss Event: An unexpected occurrence that did not adversely affect the outcome but could have resulted in a serious adverse event.

Nonconformance: Failure to meet requirements.

Preventive Action: An action taken to reduce or eliminate the potential for unexpected deviations, nonconformances, or other undesirable situations.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Examples of Objective Evidence:

- Policies, processes, and procedures related to this chapter.
- Records of collected data analysis and corrective action taken when near-misses, deviations, or adverse events are discovered.
- Tracking of relevant data that affect the organization's current and future operations.
- Records indicating that corrective and preventive action was taken.
- Records indicating that corrective and preventive action taken was effective and is being monitored.
- Documentation that process improvement data are included in executive management review.

9.0 Process Improvement

The organization shall collect data, perform analysis, and follow up on issues requiring corrective and preventive action, including near-miss events.

9.1 Corrective Action

The organization shall have a process for corrective action that includes:

1) Description of the event.
2) Investigation of the root cause(s) of nonconformances relating to the product or service, the process, and the quality system.
3) Determination of the corrective action needed to eliminate the cause of nonconformances, as applicable.
4) Ensuring that corrective action is reviewed and found to be effective.

9.1.1 Investigation and corrective action shall include consideration of deviations, nonconformances, and complaints.

9.2 Preventive Action

The organization shall have a process for preventive action that includes:

1) Analysis of appropriate sources of information to detect, analyze, and eliminate potential causes of nonconformances.
2) Determination of steps needed to address any problems requiring preventive action.
3) Initiation of preventive action and application of controls to ensure that it is effective.

9.3 Performance Improvement

The organization shall track and identify trends in information related to its operational and quality system performance to identify opportunities for improvement.

Standard	Record to Be Maintained	Minimum Retention Time (Years)[1]
9.0	Implementation of changes to policies, processes, and procedures resulting from corrective and preventive action	5
9.1	Corrective action	5
9.2	Preventive action	5

[1]Applicable state or local law may exceed this period.

QSE 10 – Facilities and Safety

Key Concepts: This QSE addresses the safety and adequacy of areas where the work required by these *MT Standards* is performed. This includes occupational safety, biohazardous material disposal, environmental monitoring, and compliance with applicable local and national regulations.

Key Terms:
Environmental Monitoring: Policies, processes, and procedures used for monitoring any or all of the following: temperature, humidity, particulates, and microbial contamination in a specific area. Where appropriate, the program shall include sampling sites, frequency of sampling, and investigative and corrective actions that should be followed when specified limits are exceeded.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Organization: An institution, or part thereof, that has its own functions and executive management.

Examples of Objective Evidence:
- Policies, processes, and procedures related to this chapter.
- Safe environmental conditions for all individuals in the organization.
- Local, state, and national regulations being followed.
- Proper discard of hazardous and potentially hazardous materials.
- Personal protective equipment (PPE) is available and in use.

10.0 Facilities and Safety

The organization shall ensure safe environmental conditions. The work area shall be suitable for the activities performed. Safety programs shall meet local, state, and national regulations.

10.1 Safe Environment

The organization shall minimize and respond to environmentally related risks to the health and safety of all individuals and products or services. Suitable quarters, environment, and equipment shall be available to maintain safe operations.

10.1.1 Where liquid nitrogen is stored, specific hazards shall be addressed including:

1) Visible signage posted both inside and outside the storage space.
2) Ventilation and airflow adequate to the space where the liquid nitrogen is stored.

10.1.1.1 Facilities with liquid nitrogen tanks shall have a system in place to monitor oxygen levels and an alarm system set to activate under conditions that will allow action to be taken.

✎ **10.1.1.1.1** Oxygen alarm activation shall require personnel to investigate and document the condition activating the alarm and to take immediate corrective action as necessary.

✎**10.2 Biological, Chemical, and Radiation Safety**

The organization shall monitor adherence to biological, chemical, and radiation safety standards and regulations.

10.3 Handling and Discarding of Biological Materials

Biological materials shall be handled and discarded in a manner that minimizes the potential for human exposure to infectious agents.

10.4 Environmental Monitoring

The laboratory shall monitor, control, and record environmental conditions, as required by relevant specifications or where they may influence the quality of the results. Standard 3.8 applies.

10.4.1 Environmental Controls

The laboratory shall perform preamplification (upstream) and postamplification (downstream) procedures in areas separated by physical barrier(s) and/or biochemical measure(s) to prevent nucleic acid contamination.*

*42 CFR 493.1101(a)(3).

Standard	Record to Be Maintained	Minimum Retention Time[1]
10.1.1.1.1	Alarm investigation	5
10.2	Monitoring of biological, chemical, and radiation safety	5
10.3	Appropriate discard of products	10
10.4	Monitoring of environmental conditions	5

[1]Applicable state or local law may exceed this period.

Glossary

Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Agreement: A contract, order, or understanding between two or more parties, such as between an organization and one of its customers.

Agreement Review: Systematic activities carried out before finalizing the agreement to ensure that requirements are adequately defined, free from ambiguity, documented, and achievable.

Alarm: Audible, visual, or central monitoring system signaling the need for immediate or timely action.

Allele: An alternative form of a gene or sequence of DNA at a genetic locus.

Allele-specific oligonucleotide (ASO): A nucleic acid primer or probe of short length, complementary to one or more alleles, most often used for the detection or amplification of nucleotide variants.

Amplicon: Fragment of DNA produced by polymerase enzyme amplification of a genetic target sequence. Also referred to as polymerase chain reaction (PCR) product.

Amplification: The enzymatic replication in vitro of a target nucleic acid commonly performed using the PCR method.

Analyte: Substance or chemical constituent for which the laboratory performs testing.

Annealing: The hybridization of two complementary strands of nucleic acid, as in the hybridization of a probe with the target DNA.

Array: A test system using a panel of markers placed at defined positions on a solid substrate to determine the alleles present.

Assessment: A systematic examination to determine whether actual activities comply with planned activities, are implemented effectively, and achieve objectives. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Audit: Assessment.

Backup: Digital data and/or physical storage containing copies of relevant data.

Blood Groups: Antigenic determinants present on red cells. For the purposes of these MT Standards, blood groups include platelet and neutrophil antigens.

Calibrate: To set or align measurement equipment against a known standard.

Change Control: A structured method of revising a policy, process, or procedure, including hardware or software design, transition planning, and revisions to all related documents.

Competence: An individual's demonstrated ability to apply knowledge and skills needed to perform their job tasks and responsibilities.

Competency Testing: Evaluation of the ability to perform a specific task according to procedures and to obtain expected results.

Competent Authority: The agency responsible under its national law for regulations applicable to the organization.

Compliance: See Conformance.

Confidentiality: The protection of private, sensitive, or trusted information resources from unauthorized access or disclosure.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Contamination Control: A method to detect contamination.

Contract: Agreement.

Control: A material intended for use in the quality control process.

Copy Number Variation (CNV): When the number of copies of a particular gene or genomic region varies from one individual to the next.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Critical Equipment/Materials/Tasks: A piece of equipment, material, service, or task that can affect the quality of the organization's products or services.

Customer: The recipient of a product or service. A customer may be internal (eg, another organizational unit within the same organization) or external (eg, a patient, client, donor, or another organization).

Data Integrity: The accuracy, completeness, and consistency of information.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Disaster: An event (internal, local, or national) that can affect the safety and availability of the organization's products or the safety of individuals.

Document (noun): Written or electronically generated information and work instructions. Examples of documents include quality manuals, procedures, or forms.

Document (verb): To capture information through writing or electronic media.

Equipment: A durable item, instrument, or device used in a process or procedure.

Emergency Management: Strategies and specific activities designed to manage situations in which there is a significant disruption to organization operations or a significantly increased demand for the organization's products or services.

Environmental Monitoring: Policies, processes, and procedures used for monitoring any or all of the following: temperature, humidity, particulates, and microbial contamination in a specific area. Where appropriate, the program shall include sampling sites, frequency of sampling, and investigative and corrective actions that should be followed when specified limits are exceeded.

Establish: To perform all of the activities required to plan, validate, and implement a system or process.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Facility: A location or operational area within an organization. The part of the organization that is assessed by the AABB and receives AABB accreditation for its specific activities.

Genotype: The genetic composition of an organism, or group of organisms, with reference to a single trait, set of traits, or an entire complex of traits; the specific allelic composition of a gene, or set of genes, established at the DNA level.

Guidelines: Documented recommendations.

Hemizygous: Having only one allele rather than the usual two alleles.

Heterozygous: Having two different alleles on both chromosomes.

Homozygous: Having the same allele on both chromosomes.

Hybridization: Base pairing of complementary strands of nucleic acid by hydrogen bond formation; the binding of probe to specific nucleic acid sequences, or amplification products.
Note: Hybridization can be performed with both nucleic acid target and probe in solution, or with either one bound to a solid support.

Inspect: To measure, examine, or test one or more characteristics of a product or service and compare results with specific requirements.

Installation Qualification: Verification that the correct equipment is received and that it is installed according to specifications and the manufacturer's recommendations in an environment suitable for its operation and use.

Key Quality Functions: Essential job functions that affect the services provided by the organization.

Label: An inscription affixed or attached to a product for identification.

Labeling: Information that is required or selected to accompany the product, which may include content, identification, description of processes, storage requirements, expiration date, cautionary statements, or indications for use.

Laboratory Developed Test (LDT): A type of in vitro diagnostic test that is developed, manufactured, and used within a single laboratory.

Locus (loci): A specific region(s) of a chromosome.

Maintain: To keep in the current state; to preserve or retain; to keep in a state of validity.

Master List of Documents: A reference list, record, or repository of an organization's policies, processes, procedures, forms, and labels related to the Standards, including information for document control.

Material: A supply item used in a process or procedure.

Molecular Testing: For the purpose of these MT Standards, molecular testing is defined as the analysis of nucleic acid to determine blood group alleles and phenotypes.

Near-Miss Event: An unexpected occurrence that did not adversely affect the outcome but could have resulted in a serious adverse event.

Negative Control: A sample that does not have the targeted allele.

Nonconformance: Failure to meet requirements.

Novel Test Method: A method that has not been peer reviewed for the purposes of molecular testing. It may include a procedure that has been peer reviewed for other purposes or a method that has not been peer reviewed for any purpose.

Oligonucleotide: A single-stranded nucleic acid molecule that is chemically synthesized and is typically comprised of 25 or less nucleotides of known sequence.

Operational Qualification: Verification that equipment will function according to the operational specifications provided by the manufacturer.

Operational Systems: Processes, resources, and activities that work together to result in a product or service.

Organization: An institution, or a location or operational area within that organization; the entity assessed by the AABB and receiving AABB accreditation for specific activities.

Phenotype: The expression or absence of blood group antigens determined by molecular and/or serologic methods.

Performance Qualification: Verification that equipment performs consistently as expected for its intended use in the organization's environment, using the organization's procedures and supplies.

Policy: A set of basic principles or guidelines that direct or restrict the organization's plans, actions, and decisions.

Polymerase Chain Reaction (PCR): A method of enzymatic DNA amplification, utilizing pairs of oligonucleotide primers to form double-stranded DNA regions to serve as initiation sites for DNA polymerase-catalyzed replication. This involves successive, repetitive rounds of heating-cooling cycles to achieve denaturation, annealing, and extension of the target sequence.

Positive Control: A sample that contains the targeted allele.

Preventive Action: An action taken to reduce or eliminate the potential for unexpected deviations, nonconformances, or other undesirable situations.

Primer: An oligonucleotide complementary to the target of interest, used to initiate PCR.

Probe: An oligonucleotide used to identify specific DNA or RNA molecules bearing the complementary sequence. The probe may carry a chemical label to facilitate detection of the target sequence.

Procedure: A defined series of tasks and instructions that specify how an activity is to be performed.

Process: A set of related activities that transform inputs into outputs.

Process Control: Activities designed to ensure that processes are stable and consistently operate within acceptable limits of variation in order to produce predictable output that meets specifications.

Product: A tangible output from a process.

Proficiency Testing: The structured evaluation of laboratory test results that encompasses the suitability of processes, procedures, equipment, materials, and personnel.

Qualification (individuals): The aspects of an individual's education, training, and experience that are necessary for the individual to successfully meet the requirements of a position.

Qualification (materials): For materials that come into contact with the product, verification that the materials are sterile, the appropriate grade and suitability for the intended use, and, whenever possible, approved for human use by the US Food and Drug Administration (FDA) or relevant Competent Authority.

Quality: Characteristics of a product or service that bear on its ability to fulfill customer expectations. The measurable or verifiable aspects of a product or service that can be used to determine if requirements have been met.

Quality Control: Testing routinely performed on materials and equipment to ensure their proper function.

Quality Function: Activities of persons designated by the organization to administer the approved quality system.

Quality Indicator Data: Information that may be collected and used to determine whether an organization is meeting its quality objectives as defined by executive management in its quality policy. Indicators are measured by data for movement or regression with regard to those quality intentions. The data used for monitoring a quality indicator may consist of single-source data or multiple-source data, as long as it is clear how the data will come together to define the indicator.

Quality Management System: The organizational structure, responsibilities, policies, processes,

procedures, and resources established by executive management to achieve quality.

Quarantine (verb): To isolate unqualified or nonconforming materials or products in a clearly marked area so that they cannot accidentally be used in a downstream process.

Reagent: A substance used to perform an analytical procedure as in detecting or measuring a component or preparing a product, because of its biological or chemical activity.

Record (noun): Information captured in writing or through electronically generated media that provides objective evidence of activities that have been performed or results that have been achieved, such as test records or audit results. Records do not exist until the activity has been performed and documented.

Record (verb): To capture information for use in records through writing or electronic media.

Reference Standard: Specified requirements defined by the AABB. Reference standards define how or within what parameters an activity shall be performed and are more detailed than quality system requirements.

Regulation: Rules promulgated by federal, national, state, or local authorities to implement laws enacted by legislative bodies.

Release: Removal of a product from quarantine or in-process status for the purpose of distribution.

Repeatability: The expectation that the same results will be obtained if all testing parameters are unchanged.

Reproducibility: The consistency of test results when operating conditions or operators are varied.

Research Use Only (RUO): Tests intended for scientific research only. They are not cleared or approved by the Competent Authority and are not intended for clinical diagnosis or as the sole means for patient management decisions.

Restriction Enzyme: A bacterial enzyme, such as an endonuclease, that cleaves double-stranded DNA at specific nucleotide sequences.

Restriction Fragment Length Polymorphism (RFLP): A DNA variant (previously polymorphism) associated with the presence or absence of a specific restriction endonuclease cleavage site.

Risk: The threat of quantifiable damage or any other negative occurrence that is caused by external or internal vulnerabilities and that may be avoided through preemptive action.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Sample (noun): The biological substance from which DNA or RNA can be extracted.

Sequence Based Typing (SBT): Determination of the order of nucleotides in gene(s) or gene region(s).

Service (noun): An intangible output of a process.

Service (verb): An action that leads to the creation of a product or a result that can affect donors, patients, and/or recipients.

Shall: A term used to indicate a requirement.

Single Nucleotide Variant (SNV): A sequence variation of a single nucleotide, without any frequency limitations.

Single Nucleotide Polymorphism (SNP): A sequence variation of a single nucleotide, seen in more than one percent of the members of a population.

Specimen: A human biologic sample, such as peripheral blood, buccal tissue swab, amniotic fluid, urine or other samples containing human tissue, cells, or bodily fluid obtained by invasive or noninvasive means. For these standards, a specimen is submitted to a laboratory for the purposes of obtaining DNA or RNA for molecular testing.

Specified Requirements: Any requirements in these Standards, including, but not limited to, FDA requirements; requirements of a facility's internal policies, processes, and procedures; manufacturers' instructions; customer agreements; practice standards; and requirements of accrediting organizations such as the AABB.

Standard: A set of specified requirements upon which an organization may base its criteria for the products, components, and/or services provided.

Standard Operating Procedures (SOP): Approved and current documented instructions for performing techniques, methods, or tasks.

Supplier: An entity that provides a material, product, or service.

Supplier Qualification: Evaluation of a potential supplier to assess its ability to consistently deliver products or services that meet specified requirements.

Thermal Cycler: A programmable laboratory instrument used to amplify segments of DNA via the polymerase chain reaction.

Traceability: The ability to follow the history of a product or service from source to final distribution or disposition using records.

Tracking: To follow all steps of a process or procedure from the beginning to end.

Validation: Establishing evidence that a process, executed by users in their environment, will consistently meet predetermined specifications.

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been met.

Wild-type allele: The most prevalent allele that occurs in the population, in general the reference allele.