PROPOSED Standards for Molecular Testing for Red Cell, Platelet, and Neutrophil Antigens, 6th edition

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 4th edition begins on page 3 and runs through page 15.

The proposed 6th edition begins on page 16 and runs through page 69.

Quick Reference

Abbreviations Used

✎	Record required
CNV	Copy Number Variation
CFR	Code of Federal Regulations
DNA	Deoxyribonucleic acid
FDA	Food and Drug Administration
HGVS	Human Genome Variation Society
ISBT	International Society for Blood Transfusion
PCR	Polymerase Chain Reaction
SNV	Single Nucleotide Variant

1.1.2.1 The supervisor shall have at least 2 years of relevant experience in molecular testing and one of the following qualifications:
2) Certification as a Specialist in Blood Banking (SBB) from the American Society for Clinical Pathology (ASCP), as a Certified Histocompatibility Specialist (CHS) from the American **College** ~~Board~~ of Histocompatibility and Immunogenetics (ACHI), certified in Molecular Biology (MB) by ASCP, or certification from an organization or agency issuing an equivalent credential.
3) Advanced science degree in a **relevant** ~~related~~ field.

The committee edited subnumber 2 to match the current terminology.
The committee replaced the term "related" with "relevant" as it strengthened the intent of the standard.

1.9 Assessment of Risk
The laboratory shall have a process in place to perform risk assessments for critical activities at defined intervals.

This standard is new to the edition and is a part of the Quality Systems Framework. Other sets of Standards (CT, RT, and Periop) have begun implementing this requirement into their editions as well.

2.1.3 Competence
Evaluation of ~~continued~~ competence shall **be performed before independent performance of assigned activities and** at specified intervals.*

The committee updated this standard to mirror the language included in all other sets of standards for which AABB provides accreditation.

2.1.4 Continuing Education

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. The laboratory director shall define the continuing education needs of these personnel.

The committee added a record retention requirement to standard 2.1.4 to ensure that personnel records contains documentation that continuing education evidence is maintained.

Reference Standard 2.2A–Minimum DNA Resources – Red Blood Cells*

ISBT Name (System Number)	Gene/Transcript†	HGVS	**Chromosome Position (GRCh38)**	Nucleotide	Antigen(s)

Reference Standard 2.2B–Minimum DNA Resources – Platelets*

ISBT Name	Gene/ Transcript	HGVS	**Chromosome Position (GRCh38)**	Nucleotide	Antigen(s)

Reference Standard 2.2C–Minimum DNA Resources – Neutrophils*

ISBT Name	Gene/ Transcript	HGVS	**Chromosome Position (GRCh38)**	Nucleotide	Antigen(s)

The committee added a third column to reference standards 2.2A, 2.2B and 2.2C concerning "Chromosome Position" which relates to chromosome position from the current human reference genome assembly. This provides completeness for the tables.

3.6.6 The laboratory shall have a process in place to minimize the risk and impact of an internal and external data breach.

The committee added new standard 3.6.6 for completeness. This standard has been incorporated into all sets of AABB Standards to date.

4. SUPPLIERS AND CUSTOMERS ~~ISSUES~~

4.0 Suppliers and Customers ~~Issues~~

The laboratory shall have policies, processes, and procedures to evaluate the ability of suppliers of critical materials and services to consistently meet agreed-upon requirements.

The committee has replaced the title of chapter 4 and standard 4.0 to reflect similar changes made in every other set of Standards.

5.0 Process Control

The laboratory shall have policies and validated processes and procedures that ensure the quality of the **reports** ~~products~~ and services. The laboratory shall ensure that these policies, processes, and procedures are carried out under controlled conditions.

The committee replaced the term "products" with "reports" as the product that the molecular testing standards focus on are the reports.

5.1.1 Change Control

The laboratory shall have a process to develop new processes and procedures and to change existing ones. This process shall include identification of specifications and verification that specifications have been met. Before implementation, the new or changed processes and procedures shall be validated. **Standard 2.1.2 applies.**

The committee added a crossreference to standard 2.1.2 (focused on training) to ensure that employees are trained on new or updated processes and procedures.

5.1.2 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 federal, state, ~~or~~ **and** laws **and regulations**. Results shall be reviewed and corrective action taken, where appropriate, when expected results are not achieved. Standard 7.3 applies.

The committee, edited this standard to include regulations from regulatory bodies for completeness.

5.1.2.1 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.

The committee included new standard 5.1.2.1 to include laboratories that operate outside the United States (of which AABB currently accredits a facility in Kuwait), to allow for compliance with the Standards without having to request a variance. This language exists in all other sets of AABB Standards that require proficiency testing.

5.1.3 DNA Contamination ~~Operational~~ 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.~~

3) Staff attire, gowning, and use of personal protective equipment.

4) Movement and storage of materials (including waste), equipment, and workflow within workspaces.

5) Physical and/or temporal segregation of equipment or materials.

6) Use and storage of reagents and amplified products.

7) Cleaning and setup of workspaces or equipment.

The committee edited the title to be more specific to the requirements that exist in the list below and in the Standards on the whole.
Subnumber 3 has been removed as the committee felt it was redundant to requirements in chapter 2.

5.1.4.1 The validity of test results and methods and the acceptability of **reports and** ~~products or~~ services ~~provided~~ shall be **investigated** ~~evaluated~~ when quality control

failures occur.

The committee edited this standard for clarity. The wording is written in an active fashion about what the laboratory in this case must do when quality control failures occur.

5.1.4.1.1 <u>The laboratory shall have policies for repeating any testing runs that have failed.</u>

Standard 5.1.4.1.1 is new to the proposed edition and was built off of the second sentence of standard 5.1.5.2.1 which has been deleted. See below for more information.

5.1.4.2 Quality control failure **<u>investigations</u>** shall be **<u>concluded</u>** ~~investigated~~ before release of test results, ~~products~~ or services.

The committee updated the standard for clarity. The new language ensures that all investigations are finalized before any test results are released.

5.1.4.3 Laboratories that use different methods, ~~instruments~~ **<u>critical equipment</u>**, or testing sites shall have a process that evaluates the comparability of test results obtained. This evaluation shall be performed twice annually.

The committee replaced the term "instruments" with "critical equipment" as that term better represents what is covered in the standard and would be included as a part of the definition of "critical equipment."

5.1.5 Use of Materials

All materials that are used by the laboratory shall be **<u>stored and</u>** used in accordance with manufacturer's written

instructions or shall be qualified for use and shall meet specified requirements.*

*21 CFR 606.65(e).

The committee added the term "…stored and…" to the standard for completeness.

5.1.5.2 Positive and negative controls shall be performed at defined intervals.

5.1.5.3 When deviating from manufacturer's written instructions 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 manufacturer's instructions or unlicensed tests~~.

~~**5.1.5.2.1** Positive and negative controls shall be performed at a frequency defined by laboratory policy. The laboratory shall have policies for repeating any testing run with failed positive and/or negative controls.~~

The committee elected to delete standard 5.1.2.1 and create new standard 5.1.5.2 with the first sentence of the standard. Standard 5.1.5.3 has been edited for clarity. Note that the second sentence of standard 5.1.5.2.1 now appears as stand-alone standard 5.1.4.1.1.

5.1.6.1 The laboratory shall ensure the identification and traceability of **specimens**, samples, critical materials, and critical equipment.

The committee added the term "specimens" to the standard for completeness.

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

The committee added this sentence to ensure that patient orders were complete and to provide needed information to the laboratory.

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

Standard 5.1.6.3 is new to the proposed standard however it previously appeared as the second sentence of standard 5.1.6.2. The committee felt this concept should stand alone as a standard.

5.1.9 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 national and local~~ law**s and regulations**.

The committee, in an effort to ensure that the standards read as internationally as possible, removing "federal and state" and replacing the terms with "applicable laws and regulations" ensures that the standard maintains the level of stringency with broader language.

5.2.3 Sample Collection

The laboratory shall define collection methods **that** ~~shall~~ maintain **the** integrity of the sample and **minimize the potential for** ~~and preclude~~ contamination. **Standard 4.2 applies**.

The committee edited standard 5.2.3 for clarity. The intent of the standard has not changed.

5.3.1 To implement a test system or a test for ~~an allele or~~ variant**(s)**, the validation protocol shall require the analysis of heterozygous and homozygous wild-type samples and, when available, a homozygous variant test sample and a hemizygous test sample, 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 standard 5.3.1 for clarity. Alleles would be incorporated into variants as written in the standard.

5.4.1 General Test Criteria

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

1) For systems dependent on accurate measurement of alleles by fragment sizes, **a size standard** ~~DNA control~~ shall be tested with each analysis.
2) A control without DNA shall be run to monitor contamination, when required by protocol.
3) The laboratory shall have policies and procedures to evaluate contamination ~~and preferential amplification~~ for each sample.
4) Postamplification products shall be prevented from contaminating preamplification materials.

The committee edited sub numbers 1 and 3 for clarity.

6.2.1.2 Copies

Before the destruction of the original records, the laboratory shall have a process to ensure that copies of records are:
1) Verified as containing the original content;
2) Legible, complete and accessible; and
3) Identified as a copy.

The committee edited this standard for legibility and to mirror the changes included in other sets of standards, the content of the standard has not changed.

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

The committee edited the standard replacing the term "product" with "report" as the report is the product that these MT Standards are focused on.

6.2.8 Storage of Records
Records shall be ~~stored to~~:
1) **Stored in a manner that** preserve record integrity for the entire retention period.
2) Protect**ed** from accidental or unauthorized:
a) access;
b) destruction;
c) modification.
3) **Able to be retrieved** ~~Allow retrieval~~.

The committee edited the structure of this standard for clarity, the content has not changed.

6.2.9 Destruction of Records
Confidential content shall be protected during the ~~D~~ destruction of records ~~shall be conducted in a manner that protects the confidential content of the records~~.

The committee edited this standard to mirror other changes being put forth in other sets of AABB Standards. The intent of the standard has not changed.

7.1.1 **For nonconforming test results,** the laboratory shall have a process for:

1) The identification and management of ~~nonconforming~~ test reports and services.

2) The identification and notification for quarantine, retrieval, and/**or** recall **of associated products, if applicable** ~~with nonconforming tests results~~.

3) Notification of customers and outside agencies as required.

The committee edited standard 7.1.1 for clarity. The intent of the change is to clarify that products need to be recalled and quarantined as necessary. In subnumber 1 the term "nonconforming" was removed as it was deemed redundant per the new clause that begins the standard.

8.0 Assessments: Internal and External

The laboratory shall have **policies**, processes, **and procedures** to ensure that internal **and external** assessments of operations and the quality system are scheduled and conducted ~~and that external assessments (inspections, surveys) are obtained at appropriately defined intervals~~.

The committee edited standard 8.0 for clarity, the intent of the standard has not changed.

9.1 Corrective Action

The laboratory shall have a process for corrective action of deviations, nonconformances, and complaints relating to test reports and test services, which includes the following elements:

3) **Evaluation of the need for** ~~Determination of~~ ~~the~~ corrective action.

4) Evaluation to ensure that corrective action is taken **as necessary** and that it is effective.

The committee edited subnumber 3 for clarity, noting that corrective action might not be necessary in all occasions.
The committee also added the clause "as necessary" to subnumber 4 in conjunction with the edit made to subnumber 3 recognizing corrective action is not always needed.

10.0 Facilities and Safety

The laboratory shall have policies, processes, and procedures to ensure the provision of safe and adequate environmental conditions in the workplace. Programs shall meet **applicable laws and** ~~local, state and federal~~ regulations ~~where applicable~~.

The committee, in an effort to ensure that the standards read as internationally as possible, removing "federal and state" and replacing the terms with "applicable laws and regulations" ensures that the standard maintains the level of stringency with broader language.

10.1 Safe Environment

The laboratory shall have a process to minimize environment-related risks to the health and safety of employees, donors, volunteers, **patients**, and visitors, **as applicable**. Suitable quarters, environment, and equipment shall be available to maintain safe operations.

The committee added the term "patients" for clarity, understanding there are cases where the patient can be in the laboratory. The "as applicable" is included in instances where not all laboratories would have all of the listed individuals in their laboratory.

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.

The committee added subnumbers 1 and 2 to the proposed edition for completeness. The committee pulled this language from the 10th edition of Standards for Cellular Therapy Services.

10.2.1 Environmental Controls

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

The committee replaced the term "barriers" with "measures to" for clarity, not all measures include the use of a barrier.

1. ORGANIZATION

1.0 Organization

The laboratory performing molecular testing (herein after referred to as the laboratory) shall have a structure that clearly defines and documents the parties responsible for the provision of reports containing molecular test results and services, and the relationship of individuals responsible for key quality functions.

1.1 Executive Management

The laboratory shall have a defined executive management team. Executive management shall have:

1) Responsibility and authority for the laboratory's operations.

2) Authority to establish or make changes to the laboratory's quality system.

3) Responsibility for compliance with these *MT Standards* and applicable laws and regulations.

4) Involvement in review of the quality system.

5) A process to identify the laboratory's customers and their needs and expectations for tests and services.

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.

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 a Specialist in Blood Banking (SBB) from the American Society for Clinical Pathology (ASCP), as a Certified Histocompatibility Specialist (CHS) from the American College of Histocompatibility and Immunogenetics (ACHI), certified in Molecular Biology (MB) by ASCP, or certification from an organization or agency issuing an equivalent credential.

3) Advanced science degree in a relevant field.

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

A quality system shall be defined, documented, implemented, and maintained. All personnel shall be trained in its application.

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 through scheduled management reviews.

1.3 Policies, Processes, and Procedures

Quality and operational policies, processes, and procedures shall be developed and implemented to ensure that the requirements of these *MT Standards* are satisfied. All such policies, processes, and procedures shall be in writing or captured electronically and shall be followed.

1.3.1 Any exceptions to policies, processes, and procedures warranted by clinical situations shall require justification and preapproval by the laboratory director. Chapter 7, Deviations and Nonconformances, applies.

1.4 Operational Continuity

Executive management shall ensure that the facility has policies, processes, and procedures that address continuity of operations for potential events that put operations at risk.

1.5 Staffing Changes

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

1.6 Laboratory Status Changes

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

1.7 Emergency Preparedness

The laboratory shall have emergency operation policies, processes, and procedures to respond to the effects of internal and external disasters.

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

1.8 Communication of Concerns

The laboratory 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 facility's executive management, AABB, or both. AABB's contact information shall be readily available to all personnel. Standards 6.1.5 and 9.1 apply.

✎1.9 Assessment of Risk

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

2. RESOURCES

2.0 Resources

The laboratory shall have policies, processes, and procedures to ensure the provision of adequate resources to perform, verify, and manage all activities in the laboratory.

2.1 Human Resources

The laboratory shall have a process to ensure the employment of an adequate number of qualified (by education, training, and/or experience) individuals. Current job descriptions shall be maintained and shall define appropriate qualifications for each job position.

2.1.1 Qualification

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

2.1.2 Training

The laboratory shall have a process for identifying training needs and shall provide for the training of all personnel performing critical tasks.

2.1.3 Competence

Evaluation 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).

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

2.1.4 Continuing Education

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. The laboratory director shall define the continuing education needs of these personnel.

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 processing steps, records of names, signatures, initials or identification codes, and inclusive dates of employment shall be maintained.

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.

Reference Standard 2.2A–Minimum DNA Resources – Red Blood Cells*

ISBT Name (System Number)	Gene/Transcript†	HGVS	Chromosome Position (GRCh38)	Nucleotide	Antigen (s)
ABO 001	*ABO* NM_020469.2	ABO:c.261delG ABO:c.526C>G ABO:c.703G>A ABO:c.796C>A ABO:c.802G>A ABO:c.803G>C ABO:c.930G>A	9:133257521 9:133256205 9:133256028 9:133255935 9:133255929 9:133255928 9:133255801	261 delG 526C/G 703G/A 796C/A 802G/A 803G/C 930G/A	A/B
MNS 002	*GYPA* NM_002099.5	GYPA:c.59C>T GYPA:c.71G>A GYPA:c.72T>G	4:144120567 4:144120555 4:144120554	59C/T 71G/A 72T/G	M/N
	GYPB NM_002100.5	GYPB:c.143T>C GYPB:c.230C>T GYPB:c.270+5G>T	4:143999443 4:143997580	143T/C 230C/T intron 5+5g/t	S/s

			4:143997535		
					U^{var}
RH 004	*RHD* NM_016124.4	1:25272555 1:25303329 1:25321899		Exon 4± and 7±	D (present)
				8 C/G 809 T/G 1154 G/C	D weak Variant
				CNV 0/1/2	D (zygosity)
RH 004	*RHD* Ψ	RHD:c.487-20_504dup or RHD:c.807T>G		37 bp insert in exon 4 or RHD c.807T/G	
	RHCE NM_020485.5	RHCE:307T>C	1:25408709	intron 2 109 bp insertion 307T/C	C/c^
		RHCE:c.676C>G	1:25390874	676C/G	E/e
		RHCE:c.122A>G	1:25420665	122A/G	C^{W}
		RHCE:c.106G>A	1:25420681	106G/A	C^{X}

		RHCE:c.733C>G	1:25390817	733C/G	V/VS
		RHCE:c.1006G>T	1:25385778	1006G/T	V
LU 005	*LU* NM_005581.4	BCAM:c.230A>G	19:44812188	230A/G	Lu^a/Lu^b
KEL 006	*KEL* NM_000420.2	KEL:c.578T>C	7:142957921	578T/C	K/k
		KEL:c.841T>C	7:142954267	841T/C	Kp^a/Kp^b
		KEL:c.1790C>T	7:142943026	1790C/T	Js^a/Js^b
FY 008	*FY* NM_002036.4	ACKR1:c.125G>A	1:159205564	125G/A -67t/c (GATA)	Fy^a/Fy^b
		ACKR1:c.-67T>C	1:159204893		
		ACKR1:c.265C>T	1:159205704		
JK 009	*JK* NM_015865.7	SLC14A1:c.838G>A	18:45739554	838G/A	Jk^a/Jk^b
DI 010	*DI* NM_000342.3	SLC4A1:c.2561T>C	18:44251253	2561T/C	Di^a/Di^b

YT 011	*YT* NM_001302621.1	ACHE:c.1057C>A	7:100893176	1057C/A	Yt^a/Yt^b
SC 013	*SC* NM_001017922.1	ER-MAP:c.169G>A	1:42830850	169G/A	Sc1/Sc2
DO 014	*DO* NM_021071.2	ART4:c.793A>G	12:14840505	793A/G	Do^a/Do^b
		ART4:c.323G>T	12:14840975	323G/T	Hy
		ART4:c.350C>T	12:14840948	350C/T	Jo^a)
CO 015	*CO* NM_198098.2	AQP1:c.134C>T	7:30912043	134C/T	Co^a/Co^b
LW 016	*LW* NM_001544.4	ICAM4:c.299A>G	19:10287311	299A/G	LW^a/LW^b
CROM 021	*CR* NM_000574.3	CD55:c.679G>C	1:207331122	679G/C	Cr^a
KN 022	*KN* NM_000573.3	CR1:c.4681G>A CR1:c.4768A>G CR1:c.4801A>G CR1:c.4843A>G CR1:c.4223C>T	1:207609424 1:207609511 1:207609544 1:207609586 1:207587428	4681G/A 4768A/G 4801A/G 4843A/G 4223C/T	Kn^a/Kn^b McC^a/McC^b Sl: 1, 2, 3 KCAM Yk^a

IN 023	*IN* NM_001001391.1	CD44:c.137C>G	1:35176644	137C/G	In[a]/In[b]
OK 024	*OK* NM_198589.2	BSG:c.274G>A	19:580428	274G/A	Ok[a]
VEL 034	*VEL* NM_001163724.2	SMIM1:c.64_80delAGCCTAGGGGCTGTGTC	1:3775437	17 bp del in exon 3	Vel–

* 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.

+ ISBT name

Reference Standard 2.2B–Minimum DNA Resources – Platelets*

ISBT Name	Gene/ Transcript	HGVS	Chromosome Position (GRCh38)	Nucleotide	Antigen (s)
HPA-1	*ITGB3* NM_000212	ITGB3:c.176 T>C	17:47283364	176T/C	HPA-1a/1b
HPA-2	*GP1BA* NM_000173	GP1BA:c.482 C>T	17:4933086	482C/T	HPA-2a/2b
HPA-3	*ITGA2B* NM_000419	ITGA2B:c.26 21T>G	17:44375697	2621T/ G	HPA-3a/3b
HPA-4	*ITGB3* NM_000212	ITGB3:c.506 G>A	17:47284587	506G/A	HPA-4a/4b
HPA-5	*ITGA2* NM_002203	ITGA2:c.160 0G>A	5:53062927	1600G/ A	HPA-5a/5b
HPA-15	*CD109* NM_133493	CD109:c.210 8C>A	6:73783709	2108C/ A	HPA-15a/15 b

*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.
ISBT = International Society of Blood transfusion; HGVS = Human Genome Variation Society.

Reference Standard 2.2C–Minimum DNA Resources – Neutrophils*

ISBT Name	Gene/Transcript	HGVS	Chromosome Position (GRCh38)	Nucleotide	Antigen(s)
HNA-1	*FCGR3B* NM_000570.4	FCGR3B:c.108G>C FCGR3B:c.114C>T FCGR3B:c.194A>G FCGR3B:c.233C>A FCGR3B:c.244G>A FCGR3B:c.316G>A	1:161629989 1:161629983 1:161629903 1:161629864 1:161629853 1:161629781	108G/C 114C/T 194A/G 233C/A 244G/A 316G/A	HNA-1a/1b/1c
HNA-2	*CD177* NM_020406	CD177:c.787A>T CD177:c.1291G>A	19:43361169 19:43362297	787A/T 1291G/A	HNA-2
HNA-3	*SLC44A2* NM_001145056	SLC44A2:c.455G>A	19:10631494	455G/A	HNA-3a/3b
HNA-4	*ITGAM* NM_000632	ITGAM:c.230G>A	16:31265490	230G/A	HNA-4a/4b
HNA-5	*ITGAL* NM_002209	ITGAL:c.2372G>C	16:30506720	2372G/C	HNA-5a/5b

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

3. EQUIPMENT

3.0 Equipment

The laboratory shall identify equipment that is critical to the provision of products and services. The laboratory shall have policies, processes, and procedures to ensure that calibration, maintenance, and monitoring of equipment conform to these *MT Standards* and other specified requirements.

3.1 Selection of Equipment

The laboratory shall have a process to define the selection criteria for equipment.

3.2 Qualification of Equipment

All equipment shall be qualified for its intended use.

3.2.1 Installation Qualification

Equipment shall be installed per the manufacturer's specifications.

3.2.2 Operational Qualification

The functionality of each piece of equipment and each component of an information system shall be verified before actual use and shall meet the manufacturer's operational specifications.

3.2.3 Performance Qualification

The laboratory shall demonstrate that equipment performs as expected for its intended use.

3.2.3.1 Performance specifications established by the manufacturer shall be met.

3.3 Unique Identification of Equipment

The laboratory shall identify critical equipment.

3.3.1 Critical equipment shall have unique identification.

3.4 Equipment Monitoring and Maintenance

The laboratory shall have a process for scheduled monitoring and maintenance of equipment. The process shall include: frequency of checks, check methods, acceptance criteria, and actions to be taken for unsatisfactory results.

3.4.1 Calibration of Equipment

Calibrations and/or adjustments shall be performed using equipment and materials that have adequate accuracy and precision. Calibrations and/or adjustments shall be performed:

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

3.4.1.1 There shall be safeguards to prevent equipment from adjustments that would invalidate the calibrated setting. Standard 5.1.3 applies.

3.4.1.2 Calibration procedures shall follow manufacturer's written instructions, and shall include:

1) Instructions for performing calibrations.
2) Acceptance criteria.
3) Actions to be taken when unsatisfactory results are obtained.

3.4.2 Investigation and Follow-up

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

1) Assessment of products and services provided since the equipment was last known to be functioning per the manufacturer's written instructions or laboratory-defined specifications.
2) Assessment of the impact on test results and donor and patient safety.
3) Steps to ensure that the equipment is removed from service.
4) Investigation of the malfunction, or failure.
5) Steps for requalification of the equipment.
6) Reporting the nature of the malfunction or failure to the manufacturer, when indicated.*

*21 CFR 803.30.

Chapter 7, Deviations and Nonconformances, applies.

3.5 Alarm Systems

Storage devices for specimens and/or reagents shall have alarms and shall conform to the following standards (Standard 5.1.4 applies):

3.5.1 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.

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

3.6 Information Systems

The laboratory shall have processes to support the implementation and modification of software, hardware, and databases relating to the requirements of these *MT Standards*. Standard 5.1.1 applies. These processes shall include:
1) Risk analysis, training, validation, implementation, and evaluation of post implementation performance.

2) Description of system maintenance and operation.
3) Documentation written in language that is understandable to the user.
4) A system for display and verification of added or amended data before final acceptance.
5) Description of how modifications to the system are authorized and documented.

3.6.1 Information System Records

Records of the following shall be maintained:

1)Validation of:

a) system software.
b) hardware.
c) databases.
d) user-defined tables.
e) electronic data transfer.
f) electronic data receipt.

2) Fulfillment of life-cycle requirements for internally developed software.
3) Numerical designation of system versions, if applicable, with inclusive dates of use.
4) Monitoring of data integrity for critical data elements.

3.6.2 The laboratory shall have a backup system that allows continuous access to clinically relevant molecular testing data in the event that information system assisted functions are unavailable. The alternative system shall be tested periodically.

3.6.3 Personnel responsible for management of information systems shall be responsible for compliance with specified requirements.

3.6.4 There shall be processes and procedures to support the management of information systems.

3.6.5 A system designed to prevent unauthorized access to information systems and electronic records shall be established and followed.

3.6.6 The laboratory shall have a process in place to minimize the risk and impact of an internal and external data breach.

4. SUPPLIERS AND CUSTOMERS

4.0 Suppliers and Customers

The laboratory shall have policies, processes, and procedures to evaluate the ability of suppliers of critical materials and services to consistently meet agreed-upon requirements.

4.1 Supplier Qualification

The laboratory shall evaluate and participate in the selection of suppliers before acceptance of an agreement.

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

4.2 Agreements

Agreements, or changes to those agreements, to obtain or provide products and services shall define supplier and customer expectations and shall reflect agreement.

4.2.1 Agreement Review

Agreements shall be reviewed and changes shall be incorporated as needed.

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

4.3 Inspection of Materials

Incoming materials shall be received, inspected, and tested, as necessary, before acceptance or use.

4.3.1 Critical materials shall meet specified requirements.

5. PROCESS CONTROL

5.0 Process Control

The laboratory shall have policies and validated processes and procedures that ensure the quality of the reports and services. The laboratory shall ensure that these policies, processes, and procedures are carried out under controlled conditions.

5.1 General Elements

5.1.1 Change Control

The laboratory shall have a process to develop new processes and procedures and to change existing ones. This process shall include identification of specifications and verification that specifications have been met. Before implementation, the new or changed processes and procedures shall be validated. Standard 2.1.2 applies.

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

5.1.2 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 7.3 applies.

5.1.2.1 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.

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

5.1.3 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 attire, gowning, and use of personal protective equipment.
4) Movement and storage of materials (including waste), equipment, and workflow within workspaces.
5) Physical and/or temporal segregation of equipment or materials.
6) Use and storage of reagents and amplified products.
7) Cleaning and setup of workspaces or equipment.

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

5.1.4 Quality Control

A program of quality control shall be established that is sufficiently comprehensive to ensure that reagents, equipment, and methods function as expected. Results shall be reviewed and corrective action taken, where appropriate.

5.1.4.1 The validity of test results and methods and the acceptability of reports and services shall be

investigated when quality control failures occur.

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

5.1.4.2 Quality control failure investigations shall be concluded before release of test results, or services.

5.1.4.3 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.

5.1.5 Use of Materials

All materials that are used by the laboratory shall be stored and used in accordance with manufacturer's written instructions * or shall be qualified for use and shall meet specified requirements.

*21 CFR 606.65(e).

5.1.5.1 Reagents that are prepared by the facility shall meet or exceed applicable criteria.

5.1.5.2 Positive and negative controls shall be performed at a defined intervals.

5.1.5.3 When deviating from manufacturer's written instructions 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.

5.1.6 Identification and Traceability

5.1.6.1 The laboratory shall ensure the identification and traceability of specimens, samples, critical materials, and critical equipment.

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

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

5.1.6.4 A laboratory responsible for labeling blood components shall have documented procedures for the labeling of those blood components.*

*21 CFR 606.121.
FDA Guidance for Industry: Labeling of Red Blood Cell Units with Historical Antigen Typing Results, December 2018.

5.1.7 Inspection

The laboratory shall have a process to ensure that samples are inspected at facility-defined stages to verify that specified requirements are met.

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 Handling, Storage, Distribution, and Transportation

The laboratory shall have a process to ensure that samples are handled, stored, distributed, and transported in a manner that prevents damage and limits deterioration.

5.1.9 Privacy and Confidentiality

The laboratory shall have a policy to ensure that the molecular testing results are private and confidential as required by applicable 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. Standard 4.2 applies.

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

5.3 Test Validation

The laboratory shall use validated methods for molecular testing.

5.3.1 To implement a test system or a test for variant(s), the validation protocol shall require the analysis of heterozygous and homozygous wild-type samples and, when available, a homozygous variant test sample and a hemizygous test sample, 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.

5.3.2 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. Heterozygous and homozygous wild-type samples and, when available, a homozygous variant test sample and a hemizygous test sample, when applicable, shall be included. 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) For systems dependent on accurate measurement of alleles by fragment sizes, a size standard shall be tested with each analysis.

2) A control without DNA shall be run to monitor contamination, when required by protocol.

3) The laboratory shall have policies and procedures to evaluate contamination for each sample.

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

5.4.2 The laboratory shall have a method to ensure that version control of algorithms in genotype prediction are maintained.

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 have a process for the investigation and resolution of discordance 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.

*42 CFR 493.1291(c).

6. DOCUMENTS AND RECORDS

6.0 Documents and Records

The laboratory shall have policies, processes, and procedures to ensure that documents are identified, reviewed, approved, and retained and that records are created, stored, and archived in accordance with record retention policies.

6.1 Documents

The laboratory shall have a process for document control that includes the following elements:

6.1.1 A master list of documents, including policies, processes, procedures, labels, and forms that relate to the requirements of these *MT Standards*.

6.1.2 Use of approved formats for all policies, processes, and procedures. Additional procedures (such as those in an operator's manual) may be incorporated by reference.

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

6.1.4 Biennial review of each policy, process, and procedure by an authorized individual.

6.1.5 Use of only current and valid documents. Relevant documents shall be available at all locations where activities

essential to meeting the requirements of these *MT Standards* are performed.

6.1.6 Identification and archival of obsolete documents.

6.1.7 Storage and transmission in a manner that preserves data integrity, and protects from accidental or unauthorized access, destruction, or modification.

6.2 Records

The laboratory shall ensure identification, collection, indexing, access, filing, storage, and disposition of records.

6.2.1 Facility Records

Records shall be complete, retrievable in a period appropriate to the circumstances, and protected from accidental or unauthorized disclosure, destruction, or modification. Reference Standard 6.2.1A, Retention of Records, applies.

6.2.1.1 Records shall be legible and indelible.

6.2.1.2 Copies

Before the destruction of the original records, the laboratory shall have a process to ensure that copies of records are:

1) Verified as containing the original content;
2) Legible, complete and accessible; and
3) Identified as a copy.

6.2.2 A system designed to prevent unauthorized access and ensure confidentiality of records shall be established and followed.

6.2.3 The record system shall make it possible to trace 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.

6.2.4 The records system shall ensure the traceability of all of the following:

1) Critical activities performed.
2) The individual who performed the activity.
3) When the activity was performed.
4) Results obtained.
5) Method(s) used.
6) Equipment used.
7) Critical materials used.
8) The facility where the activity was performed.

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

6.2.6 Changes to Records

Changes to records shall be controlled.

6.2.6.1 The date of changes and the identity of the individual who changed the record shall be documented and this information shall be maintained for the retention period of the original record.

6.2.6.2 Record changes shall not obscure previously recorded information.

6.2.6.3 Changes to records (including electronic records and amended reports) shall beverified for accuracy and completeness.

6.2.7 Electronic Records

There shall be processes and procedures to support the management of electronic records.

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

6.2.7.1.1 Backup data shall be stored in an off-site location.

6.2.7.1.2 Procedures shall be in place to ensure that data are retrievable and usable.

6.2.8 Storage of Records

Records shall be:

1) Stored in a manner that preserves record integrity for the entire retention period.
2) Protected from accidental or unauthorized:
   a) access;
   b) destruction;
   c) modification.
3) Able to be retrieved.

6.2.9 Destruction of Records

Confidential content shall be protected during the destruction of records.

Reference Standard 6.2.1A–Retention of Records

Item No.	Standard	Record to Be Maintained	Minimum Retention Time (in years)*,†
1	1.2.2	Management review of effectiveness of the quality system.	5
2	1.3.1	Exceptions to policies, processes, and procedures.	5
3	1.5	Laboratory director representative change notification within 30 days.	5
4	1.6	Interruption of on-site testing notification within 30 days.	5
5	1.9	Level of risk associated with laboratory activities	5
6	2.1	Current job descriptions.	5
7	2.1.1	Qualification of personnel performing critical tasks.	5
8	2.1.2	Training for personnel performing activities affecting quality.	5
9	2.1.3	Regular competency evaluation of staff.	5
10	2.1.4	Continuing education	5
11	2.1.5	Personnel records of all staff.	5
12	2.1.5.1	For those authorized to perform or review critical significant processing steps, maintain records of signatures, initials, or identification codes.	10

13	3.3	Unique identification of critical equipment.	5
14	3.4	Monitoring of critical equipment.	5
15	3.6	Implementation of new or modified software, hardware, or databases and modifications of existing software, hardware, or databases.	2 years after retirement of the system
16	3.6.1	Validation of information system software, hardware, databases, and user-defined tables; fulfillment of life-cycle requirements for internally developed software; numeric designation of system versions, if applicable, with inclusive dates of use; monitoring of data integrity for critical data elements.	2 years after retirement of the system
17	4.1	Evaluation and participation in selection of suppliers.	5
18	4.2.1	Review of agreements.	5
19	4.3 4.3.1	Inspection of incoming materials.	5
20	5.1.1	Validation of new or changed processes.	5
21	5.1.2	Participation in proficiency testing program.	5
22	5.1.4	Review of quality control results for reagents, equipment, and methods.	5

23	5.1.4.3	Twice annual review of comparability of test results obtained.	5
24	5.1.5.1	Reagents prepared by facility meet or exceed applicable criteria.	5
25	5.1.7.1	Final inspection of test reports before distribution, issue, or delivery.	10
26	5.3.1	Validation studies for test systems.	10
27	5.3.2	Validation of novel test methods	10
28	5.4.2	Version control of algorithms in genotype prediction.	10
29	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
30	5.5.1	Investigation and resolution of discordant results.	10
31	5.6	Interpretations of investigations reported.	10
32	6.1.3	Review and approval of new and revised documents before use.	5
33	6.1.4	Biennial review of policies, processes, and procedures.	5
34	6.1.6	Archival of obsolete documents.	5
35	6.2.4	The record system ensures traceability of:	5

		1) Critical activities performed. 2) The individual who performed the activity. 3) When the activity was performed. 4) Results obtained. 5) Method(s) used. 6) Equipment used. 7) Critical materials used. 8) The facility where the activity was performed.	
36	7.1	Evaluation of nonconforming products and services.	5
37	7.3.1	Evaluation of, and corrective action taken in response to, nonconforming proficiency testing results.	5
38	7.3.2	Investigation and resolution of discrepant test results among laboratories participating in a sample exchange program.	5
39	7.4	Retraining of laboratory personnel who fail to meet expected performance criteria for competency testing.	5
40	8.1	Management of assessment results.	5
41	9.1, #4 9.2.3	Results of follow-up action to corrective and preventive actions.	5
42	10.1.1.1.1	Alarm investigation.	5

43	10.1.2	Monitoring of biological, chemical, and radiation safety.	5
44	10.2	Monitoring of environmental conditions	5

*Applicable state or local law may exceed this period.
†21 CFR 606.160(d).

7. DEVIATIONS AND NONCONFORMANCES

7.0 Deviations and Nonconformances

The laboratory shall have policies, processes, and procedures to ensure the identification, assessment, investigation, and monitoring of deviations from, or of failures to meet, specified requirements. The responsibility for review and authority for the disposition of nonconforming products, services, and release of test results shall be defined. Deviations and nonconformances 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 Nonconformances

Upon discovery, nonconforming products, services, test results, and test reports shall be evaluated and their disposition determined. Standard 3.4.2 applies.

7.1.1 For nonconforming test results, the laboratory shall have a process for:

1) The identification and management of test reports and services.

2) The identification and notification for quarantine, retrieval, and/or recall of associated products, if applicable.

3) Notification of customers and outside agencies as required.

7.1.2 Products and services that do not conform to specified requirements shall be prevented from unintended distribution for that specific nonconforming test result.

7.2 Released Nonconforming Test Results and Reports

Test results or reports that are determined after release not to conform to specified requirements shall be evaluated to determine the effect of the nonconformance on the quality of the test result. In cases where quality may have been affected, the nonconformance shall be reported to the customer. Records of the nature of nonconformances and subsequent actions taken, including acceptance for use, shall be maintained in conformance with Chapter 6, Documents and Records.

7.3 Nonconforming Proficiency Test Results

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

7.3.1 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.

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

7.4 Nonconforming Competency Assessments

When expected performance criteria for competency testing are not met, the laboratory shall have a process to ensure the competency of personnel before they are permitted to resume testing. Standard 2.1.3.1 applies.

8. ASSESSMENTS: INTERNAL AND EXTERNAL

8.0 Assessments: Internal and External

The laboratory shall have policies, processes, and procedures to ensure that internal and external assessments of operations and the quality system are scheduled and conducted.

8.1 Management of Assessment Results

8.1.1 The results of internal and external assessments shall be reviewed by personnel having responsibility for the area being assessed.

8.1.2 Corrective and/or preventive action shall be implemented to address deviations and nonconformances discovered through internal and external assessments.

8.1.3 Follow-up action shall verify the implementation and effectiveness of corrective and preventive action.

8.1.4 The results of internal and external assessments and associated corrective and preventive action shall be reviewed by executive management.

8.2 Quality Monitoring

The laboratory shall have a process to collect and evaluate quality indicator data on a scheduled basis.

9. PROCESS IMPROVEMENT THROUGH CORRECTIVE AND PREVENTIVE ACTION

9.0 Process Improvement Through Corrective and Preventive Action

The laboratory shall have policies, processes, and procedures for data collection, analysis, and follow-up of issues requiring corrective and preventive action.

9.1 Corrective Action

The laboratory shall have a process for corrective action of deviations, nonconformances, and complaints relating to test reports and test services, which includes the following elements:

1) Documentation.
2) Investigation of the cause.
3) Evaluation of the need for corrective action.
4) Evaluation to ensure that corrective action is taken as necessary and that it is effective.

9.2 Preventive Action

The laboratory shall have a process for preventive action that includes the following elements:

9.2.1 The review of appropriate sources of information, including assessment results, proficiency testing results, quality control records, complaints, and aggregate data to detect and analyze potential causes of nonconformances.

9.2.2 Determination of steps needed to deal with any potential problems requiring preventive action.

9.2.3 Initiation of preventive action and application of controls to ensure that it is effective.

10. FACILITIES AND SAFETY

10.0 Facilities and Safety

The laboratory shall have policies, processes, and procedures to ensure the provision of safe and adequate environmental conditions in the workplace. Programs shall meet applicable laws and regulations.

10.1 Safe Environment

The laboratory shall have a process to minimize environment-related risks to the health and safety of employees, donors, volunteers, patients, and visitors, as applicable. 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.

10.1.2 Biological, Chemical, and Radiation Safety

The laboratory shall have a process for monitoring adherence to biological, chemical, and radiation safety standards and regulations, where applicable. Standard 2.1.1 applies.

10.2 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 3.4 applies.

10.2.1 Environmental Controls

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

GLOSSARY

Adverse Event: A complication in a donor or patient. Adverse events may occur in relation to a donation, a transfusion, or a diagnostic or therapeutic procedure.

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

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

Allele: An alternative form of a gene or sequence of nucleic 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 PCR product.

Amplification: The enzymatic replication in vitro of a target nucleic acid commonly performed using the polymerase chain reaction (PCR) method.

Analyte: Substance or chemical constituent that is assayed.

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. Assessments usually include a comparison of actual results to expected results. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Audit: Assessment.

Backup: Digital data storage media (magnetic tape, disc, CD, cloud based software, etc) containing copies of computer data.

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

Calibration: 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, organization, and transition planning, including revisions to all related documents.

Copy Number Variation (CNV): When the number of copies of a particular gene or genomic region varies from one individual to the next. **Competence:** Ability of an individual to perform a specific task according to procedures.

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

Compliance: Conformance.

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.

Contract Review: Agreement review.

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

Corrective Action: An activity performed to eliminate the cause of an existing nonconformance or other undesirable situation in order to prevent reoccurrence.

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

Customer: The receiver of a product or service. A customer may be internal, ie, another department within the same organization, or external, ie, another organization.

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

Document (noun): Written or electronic information used as the basis for organizational function and work instruction. Documents include quality manuals, policies, processes, procedures, labels, and forms. Documents are not the same as records.

Equipment: A durable item used in a process or procedure such as laboratory instruments, analyzers, computer systems, and devices.

Executive Management: The highest level personnel within a facility, including employees and independent contractors, who have responsibility for the operations of the facility and who have the authority to establish or change the quality management system. Facility or program leadership may be an individual or a group of individuals.

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

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).

Genotype: The genetic makeup 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.

Homozygous: Two copies of the same allele on different 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 such as a microtiter plate or glass beads.

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

Label: An inscription affixed to a unit of blood, blood component, tissue, or sample 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.

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.

Material: A good or supply item used in a process or procedure to prepare the final product or service. Note Reagents are a type of material.

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.

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

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.

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: See probe and primer.

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

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

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

Policy: A documented general principle that guides present and future decisions.

Polymerase Chain Reaction (PCR): A method of enzymatic DNA amplification, utilizing pairs of oligonucleotide primers to form short 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 activity performed to reduce the potential for nonconformances or other undesirable situations.

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

Probe: A known single-stranded nucleic acid sequence used to identify specific DNA or RNA molecules bearing the complementary sequence. The probe often carries a chemical label to facilitate detection of the target sequence.

Procedure: A series of tasks usually performed by one person according to instructions.

Process: A set of related tasks and activities that accomplish a work goal.

Process Control: Efforts made to standardize and direct processes in order to produce predictable output.

Product: A tangible result of a process or procedure.

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

Qualification: With respect to individuals, the aspects of an individual's education, training, and experience that are necessary to successfully meet

the requirements of a position. With respect to equipment, verification that specified attributes required to accomplish the desired task have been met.

Quality: Characteristics of a product or service that bear on its ability to meet requirements, including those defined during agreement review.

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 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.

Quality Management: The activities of an organization's management that establish quality policy, objectives, and responsibilities, and implement the functions involved in determining and achieving quality.

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

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. A substance used (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 Standards: Specified requirements defined by AABB (see Specified Requirements). Reference standards are more detailed than quality system requirements.

Regulation: Rules promulgated by local authorities to implement laws enacted by legislative bodies.

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

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

Restriction Enzyme: An endonuclease; any of a large number of bacterial enzymes that cleave 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.

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

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

Service (noun): An action that leads to the creation of a product or a result.

Shall: A term used to indicate a requirement.

Single Nucleotide Variant (SNV): A sequence variation of a single nucleotide.

Specificity: The proportion of negatives that are correctly identified.

Specified Requirements: The expectations for products or services. Specified requirements may be defined by customers, regulatory agencies (such as the FDA), practice standards, or accrediting organizations (such as the AABB).

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

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

Stringency: Testing parameters that ensure optimal identification of alleles.

Supplier: An entity that provides an input material or service.

Supplier Qualification: An evaluation method designed to ensure that materials, products, and services obtained from a supplier 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 by means of recorded identification.

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.

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