Response to Comments Received to the 3rd edition of Standards for Molecular Testing for Red Cell, Platelet, and Neutrophil Antigens

Please note that public comments that were submitted address the proposed 3rd edition of MT Standards, and not the final version. The changes are best understood when the proposed Standards are compared to the final published version. The program unit has elected to make the substance of public comments that were submitted a part of this document. This document does not represent a full summary of significant changes to the 3rd edition of MT Standards. Guidance that appears with the 3rd edition of MT Standards in the Standards Portal provides a more in-depth look at the additions, deletions and changes and the rationales behind those decisions that what appears below.

Standard	SC/RTC	Comment	Change made?	Outcome
1.1.2.1 #3	RTC	We suggest adding the clause "in a related field" to subnumber 3 to specify that the laboratory supervisor have a degree in a field related to molecular testing as there are several advanced science degrees that may not relate to job requirements.	Yes	The committee agreed with this comment and the change was made to include the clause, "in a related field" to subnumber 3.
2.2.1.1	RTC	We recommend changing the wording of the standard to read as follows: "When serologic testing is not possible, molecular results shall be confirmed by another method." Our rationale is that many times validation of a genotyping assay requires controls carrying rare single nucleotide polymorphisms (SNPs). In some cases the variant is a marker of an altered antigen while not solely responsible for antigen gain or loss (ex. RHCE c.48G>C). In such cases, DNA standards confirmed by Sanger sequencing can serve this purpose without requiring phenotype information.	Yes	The committee agreed with the comment and replaced the term "serological" with "serologic."
2.2.1.1	RTC	Some laboratories may not have a second molecular	Yes	The committee agreed with the

		technique available to them to confirm a sample as a Standard DNA. The option to send it for sequencing or serological testing by another laboratory should remain. Would suggest the following to make the standard clearer: "When a serological reagent is not available, molecular results shall be confirmed by either another molecular method or by an external lab".		comment and added the clause, "…or by an external laboratory." to the end of the standard to ensure that laboratories that do not have second molecular techniques would be able to meet the standard.
Reference Standards 2.2A – 2.2C	RTC	I suggest that the common names column should be removed from these three reference standards.	Yes	The committee agreed with the comment and has removed the "Common Names" column from the aforementioned reference standards.
Reference Standard 2.2A, Target Nucleotide Column	RTC	Please make the following changes: - 1061delC in place of 1069G>A (?). 1061 is important to detect A2 and 1096 is for the rare B(A). - However, If it is 1069G>A, then use 3'UTR+31g>a in place of 1069G>A - IVS5+5g>t in place of intron +5g>t - Absence of exons 4 & 7 in place of Exon 4 & 7 - 505ins37 in place of 37 bp insert in exon 4 - IVS2+3045ins109 in place of intron 2 109bp insertion	Yes	The committee reviewed the linked edits and the changes were made accordingly.
Reference Standard 2.2A, Predicted Phenotype Column	RTC	Please make the following changes: - Remove U-. The publication by Storry J et al. Transfusion 2003:43,1738 indicates that thethat the intro +%g.t results in a Uvar phenotype not U-.	Yes	The committee reviewed the edits and made changes accordingly.
Reference	RTC	- Remove 'homozygote for	Yes	The committee

Standard 2.2A, Comments Column		rare not required'. Indicate that the standards required for each polymorphism are those needed to demonstrate assay performance. Minimum standards should not be specified since they vary across assays and populations. - The requirement for both heterozygote and homozygote was based on RFLP technology which is rarely in use today for blood group genotyping. Also, what is rare in one country may not be rare in another so how is the decision made as to what is rare?		agreed with the intent of the comment, however the wording we added was adjusted to read: "homozygote for rare when available." This change allows for the requirement to be written as a positive statement, which is the intent of all standards.
4.2.2	RTC	We suggest the following alternative wording to standard 4.2.2, "The laboratory shall have a process to inform the customer of instances when testing is performed by **off label use** of reagents, methods, techniques or equipment not approved for the **applied purpose** by the corresponding regulatory authority The addition of the bolded wording would maintain the broad scope of the standard while providing specific clarification as to the intent of the standard.	No	The committee noted this comment but did not feel that the change suggested would strengthen the standard. The term "off label use" was deemed to be too FDA centric and that the inclusion of "competent authority" language ensures that this standard remains relevant to facilities both inside and outside of the United States.
5.2.1, 5.2.2	RTC	While we understand the move to merge these two standards because of redundancy we disagree with the removal of a physician's order in lieu of patient consent. The justification appears to be due to some states requiring specific consent	No	The committee reviewed the comment and believes the standard is consistent with the intent of the comment. The

		for molecular testing. The inaugural MTSPU spent much time discussing and defining molecular testing vs. molecular screening (see definitions in glossary). They concluded that molecular typing (screening) is just an alternative method to determine blood group type which can be done by serology and serological testing does not require specific patient consent. Since most of the blood group genotyping is done in blood centers, while the patients are in the hospitals, it will be very difficult to get individual patient consent which could delay testing and optimal treatment for the patients. Do the MTSPU or the MTAPU have a suggestion as to how patient consent should be documented?		committee noted that the clause, "…in accordance with applicable law" ensures that specific consent is obtained if required, and allows for the physician order to serve as consent where permitted.
9.1, #5	RTC	We suggest altering the wording of new subnumber 5 in standard 9.1 to read as follows: Alternative Wording: 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: 5) **Customer** notification ~~to the customer~~ **and issuing of** ~~that~~ a corrected/amended report ~~is forthcoming~~.	Yes	After reviewing this comment and the one beneath the committee elected to remove proposed subnumber 5 as it was deemed unnecessary as it is already occurring in all laboratories.

		We suggest this change in verbiage to allow for a clearer structure and parallel construction of the standard.		
9.1, #5	RTC	We request additional clarification regarding when notification to customer is required (based on severity of change/error). It is unclear whether notification must be sent for all errors including minor clerical errors that do not change interpretation vs. misreported test results.	Yes	The committee noted this comment and as stated above, elected to remove proposed subnumber 5.