Deadline of Submission of Comments: 27-Mar-23
Document Number: ANSI/ASB Std 039
Document Title: Standard for Internal Validation of Short Tandem Repeat Profiling by Capillary Electrophoresis

#	Section	Updated Section	Type of Comment (E-Editorial, T-Technical)	Comments	Proposed Resolution	Final Resolution
18	General		T	It seems this document only applies to established labs with a previous STR typing system on line and seems to not apply to a new lab validating STR testing methods for the first time. Shouldn't that be added to the Scope to provide a limitation of this document? It's unclear why this document was written with that limitation.	Address limitations of this requirement in the Scope and/or Foreword. This document does not apply for a first time internal validation study for an STR amplification kit with CE.	Reject: This standard does apply to a new laboratory. Nowhere does the document say that is it only for established laboratories.
8	Foreword - added sentence (and the Scope)		E/T?	This document seems to include the amplification step as well as data analysis for STR kits but that is not included in this sentence; only mentions validation of the CE	Clarify what steps of the DNA testing process this document is intended to cover and modify the sentence as needed	Accept: The validation of STR profiling kits is one part of the process of generating a DNA result. There are steps prior to and after this amplification step and their impact on the STR profiling kit validation studies should be considered.
9	Foreword - added sentence		E/T?	suggest breaking sentence up and adding more contextual information	The validation of CE is one part of the process…a DNA result. There are additional steps in the DNA testing process prior to and after the use of a capillary electrophoresis platform that should be considered and included as necessary in the internal validation study	Accept with Modification: The validation of STR profiling kits is one part of the process of generating a DNA result. There are steps prior to and after this amplification step and their impact on the STR profiling kit validation studies should be considered.
10	Foreword or Scope		E	need to reference other document	Add: It is the intent that this document be used in conjuction with BPR 129 (or other appropriate wording as used in the Scope of BPR 129).	Reject: This reference is described in Section 4.1.
19	3		E	If 039 and 129 are connected, only 039 has interpretation defined	No change needed in 039, Add in definition from 129 into 039: interpretation The process of evaluating DNA data for purposes including, but not limited to, defining assumptions related to mixtures and single source profiles, distinguishing between alleles and artifacts, assessing the possibility of degradation, inhibition, and stochastic effects, and determining whether the data are suitable for comparison.	Reject: This comment is not related to Std 039. The same comment is made for BPR 129 and will be addressed there.
24	3		E	If 039 and 129 are connected, only 129 has a definition of probablistic genotyping	3.8 probabilistic genotyping The use of biological modeling (i.e., statistical modeling informed by biological data), statistical theory, computer algorithms, and/or probability distributions to infer genotypes and/or calculate likelihood ratios	Accept: Added the definition used in BPR 129
20	3.8		E	If 039 and 129 are connected, only 129 has precision study(s) vs 039 just listed as precision	Either stick with only precision or modify to precision study(s) to be consistent, modify 039 to precision studies	Reject: The term precision study is not used in Std 039 as it doesn't make sense in the context of the sentence.

21	3.14	Now 3.15	E	If 039 and 129 are connected, minor wording changes in definition of validaiton b/t documents	Select one or the other for both documents: The process of performing and evaluating a set of experiments that **establish/establishes** the efficacy, reliability, and limitations of a method, procedure or modification thereof; establishing recorded documentation that provides a high degree of assurance that a specific process will consistently produce an outcome meeting its predetermined specifications and quality attributes. May include developmental and/or internal validation.	Reject: No change in Std 039, establishes is correct
1	3.12	Now 3.13	T	The current language for this section defines stochastic threshold as the peak height above which "it is reasonable to assume" that drop-out has not occurred. The proposed revision adds the important clarification that such an assumption does not apply to DNA mixtures.	The OSAC HFTG supports this clarification.	No Action
2	3.12	Now 3.13	T	While the proposed revision is important, further clarification is needed. The term "stochastic threshold" only applies when the assumption that dropout has not occurred is based on a statistical analysis of data from appropriate validation studies. From a human factors perspective, it is important to clarify that analytical and stochastic thresholds can only be derived from statistical analysis of data, not from subjective judgments of what is reasonable.	Add language to state explicitly that the term applies only to thresholds based on statistical analysis of validation data, e.g., "The peak height value in a DNA profile above which the results of validation studies show that it is statistically justified to assume..."	Accept
11	4.1		E	missing word? Awkward statement	maybe add "be" - "...038 and **be** supported by..."	Accept with modification: "...in conjunction with ANSI/ASB Standard 038, and should be supported by relevant developmental validation studies."
12	4.1		E/T?	clarification needed - not sure what "this work shall also be supplemented with published scientific literature..." means; unclear how "work" is supplemented by literature; seems the purpose is probably to ensure there are published developmental validation studies and that those studies are used to assist with planning and carrying out the internal studies.	Need to make this clearer regarding what is actually required for the lab to understand how to fulfil this and for an auditor to know what is needed. Clarify what "work" means and the purpose of the literature. Design of the internal validations studies and evaluation of data perhaps?	Accept with modification: Removed the "shall". Reworded for clarity. "The validation results may also be supplemented with published scientific literature or other appropriate scientific resources that support or add to the validation findings, where available."
25	4.1.3-4.1.7, 4.1.9, 4.1.9.1		T	Just concerned these requirements are really best amp kit practice, rather than a CE validation, should the title be more aimed at amp kit validation vs. CE validation?		Reject: No resolution provided. The title describes the validation of an amp kit using the technique of capillary elelctrophoresis. It is NOT a validation of the CE instrument.
13	4.1.7 Note		E	add Standard 40 (Interpretation Protocol Standard); equally relevant as Standard 20	add Standard 40 to the note	Accept
3	4.1.7		T	The proposed revisions to this section substantially strengthen this standard by specifying that protocols for the interpretation of DNA mixtures must be based on empirical results from validation studies in compliance with ASB Standard 020. These revisions significantly reduce the scope of subjective judgments and the risk of cognitive bias in the interpretation of DNA mixtures.	The OSAC HFTG supports the revisions.	No action to be taken.
14	4.1.9.1 & 4.1.9.2		T	Unclear why this is under 4.1.9 re: contamination studies; seems it should have been left as is under 4.1.10	Don't believe this should stay under contamination & drop in studies	Accept: Added Ballot 01 Document 4.1.10 with revisions and 4.1.9.1 and 4.1.9.2 are now under 4.1.10
5	4.1.9.1	4.1.10.1	T	The proposed revision replaces "shall" with "should," eliminating any requirement that the laboratory verifies that all extraction procedures and chemistries used by the laboratory are compatible with the STR test kit being evaluated.	If there are circumstances in which it would be valid to use extraction procedures and chemistries that have not been evaluated for compatibility, these should be clearly specified and the reasons documented in all reports based on the use of procedures that were not included in the validation studies.	Accept

6	4.1.9.2	4.1.10.2	T	The proposed revisions partially address the comment above regarding 4.1.10 by requiring that validation study results "shall be used to evaluate the thresholds and other parameters that have been established during previous studies"; but then says, "where possible" address the limitations of the protocols to be used. Under what circumstances would it not be possible to at least evaluate the limitations of a protocol using results from a properly designed validation study?	Either delete the phrase "where possible" or provide some other, separate statement about the importance of addressing the limitations of a protocol when the relevant validation studies have not addressed those limitations.	Accept
16	4.1.9.2	4.1.10.2	T	This requirement is too nebulous and lacks clarity. It does not provide a clear requirement to the lab or to an auditor for what is actually needed here.	Need to further clarify what is actually needed for this requirement and what it is addressing. This seems to fit better with earlier requirements in the list (e.g., 4.1.3, 4.1.6, 4.1.7); it's unclear why this was added in this manner.	Accept: Added clarity to section 4.1.10, including 4.1.10.2.
4	4.1.10		T	The proposed revisions delete any explicit requirement that SOPs must be based on validation study results. This is only partially addressed by revisions to 4.1.7 and 4.1.9.2. The value of validation studies rests on the expectation that the laboratory will use the results as the basis for their SOPs. Removing this as an explicit requirement opens the door to greater reliance on subjective judgment in the development of SOPs.	There should be an explicit statement that SOPs must be based on results of the validation studies and consistent with the peer-reviewed scientific literature.	Accept: Added 4.1.10.
15	removed 4.1.10		T	Is this a formating typo? Keep 4.1.10 as is?	fix formating and/or better rearrange/organize requirements	Accept: Sections of 4.1.10 were added back into the document with additional clarity.
17	4.1.10		T	The entire original focus of this requirement seems to have been altered in this modification. The requirement to conduct a verification step of the protocol has been completely removed. What was the purpose of making such a substantial change to the original intent of the requirement?	Return the requirement to its original form. These concepts are clearly in agreement with Standard 020; a NOTE referencing Standard 020 could be added.	Accept with modification: Section 4.1.10 added to document with the exception of Verification Statement as it is too specific.
22	4.10.1		E	If 039 and 129 are connected, minor change to capilatization in 129 for known and casework	No change is really needed for 039, recommend updating 129, The laboratory shall conduct studies utilizing **k**nown and **c**asework-like samples with a range of sample types representative of those regularly analyzedexpected to be encountered by the testing laboratory."	Reject: Relates to BPR 129
23	4.10.1		E	If 039 and 129 are connected, 129 appear to refer to 4.1.10 in 39, but in 39, that number appears crossed off	Either replace 4.1.10 in 39 or further clarify in 129 standard it is referencing	Accept: Section 4.1.10 returned to the document.
7	5		T	The proposed revisions to this section are very valuable, especially the requirements for documentation and for making the documentation readily available to users of reports generated from DNA mixture test protocols and parameters. However, the language in section 5(c) is confusing. It is not clear what the technical leader (or other person) must approve or what must be documented. The statement should be re-written for clarity.	Potential modification: 5 (c) documentation indicating that the documents listed in 5(a) and 5(b) were approved by the DNA Technical Leader or other appropriate personnel and that the approved documents were communicated to all analysts prior to implementation in the laboratory.	Accept