Document Number: ANSI/ASB Standard 038

Document Title: Standard for Internal Validation of Forensic DNA Analysis Methods

#	Section	Type of Comment (E-Editorial, T-Technical)	Comments	Proposed Resolution	Final Resolution
23	General	T/E	The purpose of this overarching standard is not clear. While the purpose of the document may be organizational in nature, there is nothing written here that makes it obvious that this would be the first place individuals performing internal validation should come, rather than immediately referencing a standard that addresses a specific topic at hand.	Reference should be made to all the relevant standards that fall under the umbrella of this standard. The relevant standards can be added to the foreword with a statement that the document will continue to be updated as more standards are created or an annex with the relevant standards could be added as well. Lastly, there should be something inserted to explicitly let readers know that this standard is the precursor to any standard affiliated with internal validation. Since the document is meant to be an overarching document, the basic tenants of conducting a validation should be included in the document, which would be supported in any subsequent standards documents.	Reject. The subsequent relevant standards are not published yet and therefore cannot be referenced. The basic tenants of a validation are addressed in Section 4 Requirements.
24	General	E	The first sentence of the foreword can be easily misinterpreted to mean that internal validation can come before developmental validation although the defined terms specify the order in which they come. The use of the word “development” and its placement is where the potential for confusion exists.	The sentence can be restructured to read: Internal validation in an integral step in the implementation of DNA methodologies and the development of standard operating procedures used in forensic testing.	Accepted.
10	Foreword	E	Stronger statement needed to replace the second line of the first paragraph ("Internal validation provides opportunity to characterize….")	Substitute stronger language, e.g., "Internal validation establishes the uses and limitations of a methodology prior to laboratory implementation."	Accepted.
14	Definitions	T	Add definition of database sample	Use FBI QAS definition of database sample: "Database sample is a sample obtained from an individual who is legally required to provide a DNA sample for databasing purposes and whose identity is established at the time of collection of the sample." available at https://docs.wixstatic.com/ugd/4344b0_db3f4f16aab6495a8558e3d79bd90d5d.pdf	Accept with modification. The sentence was modified to improve clarity and the term "database sample" was removed.
2	3.1	E	3.1 second sentence uses the term 'worked out' colloquialism	replace 'worked out' with 'optimised'	Reject. The definition was taken from the OSAC Lexicon.
11	3.1	E/T	Second sentence of the developmental validation definition is confusing.	I am unsure of the meaning sought to be conveyed, but maybe instead of "This generally occurs while the conditions and parameters are being worked out prior to the estabilishment of a defined assay procedure or product." say, "This process occurs prior to the establishment of a defined assay, procedure or product..."	Reject. The definition was taken from the OSAC Lexicon.
3	3.3	E	Delete 'the laboratory'	Delete 'the laboratory' after 'developing'	Accept with modification. The definition was reworded. Note: CB - see Standard 77 - the definitions for internal validation are now the same.
4	3.3		Delete 'the laboratory' after 'as expected'	Delete 'the laboratory' and put full stop after 'expected'	Accept with modification. The definition was reworded. Note: CB - see Standard 77 - the definitions for internal validation are now the same.
12	3.3	T	It should be made clearer that limitations for the use of a methodology in the lab is established during internal validation.	Add "determination of the limitations of the methodology in the laboratory" to the definition	Accept with modification. The definition was reworded. Note: CB - see Standard 77 - the definitions for internal validation are now the same.
32	3.5	E	the definition needs some refinement. A typing kit is not a process or procedure; NGS is not a platform. The word being defined should not be in the definition.	Delete first 5 words; start with "The analytical processes..." Suggest further work on this definition to more clearly define processes and procedures and what is appropriately included under this term.	Accepted with modification. The definition was updated to reflect the new definition in the FBI's QAS.
13	3.5	T	The examples of methodology don't include interpretation. Add to clarify that methodology includes intepretational methodologies	Add after the colon for the definition of methodology--"and intepretation methods."	Accepted with modification. The definition was updated to reflect the new definition in the FBI's QAS. Note: Subgroup member Bicka Barlow agrees with commenter that intrepretation methods should be included in the definition.
21	Requirements	T	It is critical that any non-conformities, adverse events, e.g. contamination events which occur during validation be investigated, documented and included as part of the validation study. To ensure transparency, these events should be listed in a separate section (in addition to any particular substudy in the validation as appropriate).	Add a requirement: "The laboratory shall investigate, document, and include as part of the validation study all non-conformities and/or unusual occurrences (e.g., contamination events) which occur during the validation study."	Accepted with modifications. The following sentence was added: "The documentation shall include any unexpected results (e.g., contamination events) which occur during the internal validation study."

22	Requirements	T	The full validation studies must be made publicly available for review in a commonly used digital format. It promotes reproducibility, encourages scientific exchange, the discovery and resolution of errors or methodological reviews, and is important to the peer review process. It is critical that the defense have access to the internal validation studies in order to understand, assess, and, if necessary, challenge the empirical foundations on which the lab's protocols and methods are built.	Add a requirement: "The laboratory shall make the complete set of internal validation studies publicly available in a commonly used digital format."	Reject. The public disclosure of internal validation studies is out of the scope of this document.
17	Requirements	T	Add requirement making full validation studies, including all additional validation studies made due to alterations, publicly available.	Add Requirement 4.10: "The laboratory shall make the complete set of internal validation studies publicly available."	Reject. The public disclosure of internal validation studies is out of the scope of this document.
25	4	T	The quality of the samples used for an internal validation will undoubtedly impact the implementation and quality control measures that are derived for that method. The use of samples/scenarios that will best mimic casework situations encountered in the laboratory is something that is applicable to any and all internal validations.	A statement on the use of samples/scenarios that the lab intends to report on should be added to the requirements section.	Reject. This recommendation is too specific for this umbrella document. The sample types required will be detailed in each of the subsequent validation standards.
26	4	T	Individuals performing an internal validation should create a validation plan to define the scope and goals of the internal validation prior to conducting the validation. A validation plan is helpful in following the scientific method where the hypothesis is stated in the plan and the validation write-up explains the results.	Use of a validation plan should be added to the requirements section as an overarching quality of performing an internal validation.	Accepted with modifications. The use of a validation plan will be detailed in each of the subsequent validation studies. Section 4.3 was edited to include documentation of the validation plan.
27	4	T	Reproducibility is a fundamental belief in conducting good science. There is no mention of experiments being run multiple times to get the most accurate and reliable results.	A statement should be added to the requirements that stress the importance of running experiments multiple times.	Reject. This recommendation is too specific for this umbrella document. The sample types required will be detailed in each of the subsequent validation standards.
28	4.2	T	Additional clarity is needed on the types of alterations that rise to the level of requiring an internal validation.	Examples of alterations like changes in reagents, the repositioning of instruments, and changes in operational conditions could be given to clarify what is meant by alterations. This standard needs to define what a performance check is and when it is proper to conduct an internal validation instead of a performance check.	Accepted with modifications. 4.2 was reworded to include several examples of alterations. Defining a performance check is out of scope of this document.
18	4.2	T	The additional internal validation studies performed because an alteration that had the potential to influence results was made should be clearly documented (similar to a version control history) and included as part of the internal validation study.	Add requirement to 4.2 that " any additional internal validation studies performed because an alteration that had the potential to influence results was made should be clearly documented (similar to a version control history) and included as part of a larger internal validation for a a forensic DNA analysis method."	Reject. This recommendation is too specific for this umbrella document. Documentation requirements are covered under Standard 4.3.
29	4.3	E	The results of internal validations should be made available to the public.	A statement should be added to the standard that states upon the approval of the DNA Technical Leader the aforementioned documents should be made available to the public.	Reject. The public disclosure of internal validation studies is out of the scope of this document.
15	4.3	E or T	All data in a validation study should be documented. This may in fact be the intention of requirement 4.3, but the word "summary" at the start of the list may be confusing (i.e. does it mean the executive summary marshalling the conclusions of the study or does it mean a summary of the raw data and statistical calculations as well...)	Delete " a summary of" ***OR*** insert after conclusions, : "and **all** raw data and statistical calculations (if applicable) used to support conclusions; ***OR*** simply state "Internal validation studies shall be documented to include all testig results....."	Accepted with modifications based on comments from other reviewers.
33	4.3	T	Expand documentation requirements for more clarity and for preservation of information.	Revise to read "...at a minimum, specific details of the samples used, including how produced; the experimental protocol used in each study to generate the data; the data collected for analysis; and the steps taken to analyze the data; as well as a summary of all testing results..."	Reject. This recommendation is too specific for this umbrella document.
16	4.3	E or T	Raw data should include computer files (e.g., .hid, .fsa of the runs). This may be obvious to the authors, but term raw data has occassionally been (mis)interpreted in court proceedings to apply only to printed out electroperograms. Both the printed out epgs and the unedited computer files of the electronic raw data should be preserved as part of the validation study.	Either add definition of raw data under definitions to include the computer files or any other unedited data that is produced by instrumentation before intepretation or manipulation or filtering or editing ***OR*** clarify it in a paranthetical in 4.3	Accepted with modification. A parenthetical was added to include unedited electronic files.
19	4.3	T	All data in a validation study should be documented.	Substitute for 4.3 "Internal validation studies shall be documented to include all testing results and conclusions, raw data, and statistical calcuations (if applicable) used to support conclusions."	Accepted with modifications based on comments from other reviewers.
30	4.4	E	The word “limitations” only appears once in the document and that is in the foreword. It is important that anyone performing an internal validation knows that they are looking to establish the limits of the methodology being tested.	A statement should be added to the requirements section that clearly states that the purpose of internal validation is to establish the limitations of the method. Standard 4.4 could be edited to read: The limits of quality assurance parameters, interpretation guidelines, and analytical procedures shall be derived from internal validation studies.	Accept in part. 4.4 was edited to state "including any applicable limitations"

20	4.5	T	If a laboratory relies on validation studies to satisfy certain elements of its internal validation, the lab should make the developmental validation publicly available (see comment below on making internal validations publicly available)	Add a requirement, "If a laboratory relies on validation studies to satisfy elements of its internal validation, the laboratory should document this, include those portions of the developmental validation within the internal validation study, and make the developmental validation publicly available."	Reject. The public disclosure of developmental validation studies is out of the scope of this document.
34	4.5, 4.9	E	Should the hanging sentence be introduced as a Note?	Add "Note:" if appropriate.	Reject. It is allowable to have a non-numbered sentece.
35	4.4, 5.3	E	Guidelines may not provide sufficient specificity, whereas "protocols" should.	change "guidelines" to "protocols"	Accepted. Guideline was changed to "protocols" in section 4.4. Section 5 was deleted.
36	4.4	E	The requirement for "review" is too general as stated. It would be difficult for an auditor to know if this requirement has been met.	Specify for whom the studies should be available for review.	Accept in part. The sentence was edited in section 4.4.
37	4.5	T	This is not a requirement but a statement. Change to a requirement and require document of the involvement.	The laboratory shall document comprehensively any portion of developmental validation studies in which it participated and how those studies satisfy any elements of the internal validation requirements, as applicable.	Accepted with modifications. Standard 4.5 was edited to clarify and require the lab maintains documentation of their participation
38	4.7	T	It seems appropriate that *all* validation studies conducted should be retained as they may have significance at a later time, particularly those that are beyond the limited scope of developmental validation. It is unclear why any study or data would be deleted as even "failed" studies have meaning and may provide information regarding limitations. A new techical leader should have access to all studies previously conducted in order to "accept" the prior validation studies and protocols. A comment in the summary could state why certain studies were not evaluated or summarized.	Delete this requirement as stated. Substitute with a requirement that documentation for all validation studies conducted shall be maintained even if not a direct basis for a portion of the protocol. A "Note:" could be added to specify that the summary may include a list of any studies that were not included in the validation summary with a justifiable reason.	Accepted in part. Sections 4.6, 4.7, and 4.8 were moved under 4.3 because they are related to documentation. Those requirements are now covered in 4.3.1, 4.3.2, and 4.3.3.
31	4.6	T	The two statements in standard 4.9 seem contradictory. The standard is not clear in stating if satellite laboratories within a laboratory system are performance checking to meet a preexisting validation outcome or if it is truly evaluating differences in the testing outcome of their facility versus another. Although the term is not used in this standard, the forensic DNA community is familiar with and has utilized performance checks. Is it possible for a performance check to be subsituted for an internal validation?	The definition of a performance check should be added to the standard. The distinction between when a performance check and an internal validation are done should be clearly stated.	Accept with modifications. Section 4.6 was reworded to clarify the approval process to share internal validations (or portions thereof) with labs within a multi-lab system
5	5	E	5.1' incorrectly placed	delete 5.1	Section 5 was deleted.
6	5	E	no colon after following	place colon after 'following'	Section 5 was deleted.
7	5	E	First point after colon should read 5.1	replace 5.2 with 5.1	Section 5 was deleted.
8	5	E	Second point after colon should read 5.2	replace 5.3 with 5.2	Section 5 was deleted.
9	5	E	Third point after colon should read 5.3	replace 5.4 with 5.3	Section 5 was deleted.
39	5	E	Sections 5.2, 5.3 and 5.4 seem to be subsections for 5.1 so the formatting may be inappropriate.	Delete section numbers and combine into one list with ":" after "following" and perhaps list as a), b) and c) for clarity if the sentence is too long.	Section 5 was deleted.
1	7.1	T	Many lab systems use secure electronic equivalents for initials and/or signatures.	Reword last sentence as follows: "Approval shall be documented…. with initials (or secure elctronic equivalent) and the date of review."	This comment is not applicable to Std 38. There is no section 7.1
40			I agree with Ryan's comment below otherwise the Conformance section does appear to be formatted incorrectly.		Section 5 was deleted.
41			Nice catch Ryan! Agreed w/r/t conformance section to conform with the rest of the document.		Section 5 was deleted.
42			Editorial comment: In Section 5 Conformance, it appears that 5.2-5.4 need to be numbered under 5.1 to be 5.1.1, 5.1.2 and 5.1.3.		Section 5 was deleted.
43			I think the conformance section needs to be reformatted before it goes out so that the last three requirements are under 5.1.		Section 5 was deleted.