24-Feb-20

ASB Std 113

Standard for Identification Criteria in Forensic Toxicology

Note: a specific Proposed Resolution must accompany each comment or it cannot be considered.

#	Section	Type of Comment (E-Editorial, T-Technical)	Comments	Proposed Resolution	Final Resolution
9	Throughout	E	Throughout the document, there are references to spectral libraries. If a drug is absent from a library, is the use of a reference material acceptable?	Add language that allows spectral library matching or comparison to a reference material, using the laboratory's standard operating procedures.	Reject: This is more relevant and already allowed in Std 098; however Section 4.2.2 (Chromatography) was modified to read: "At least one chromatographic or electrophoretic separation technique, including a concurrently analyzed reference standard/positive control of the analyte of interest, shall be performed to achieve identification. "
80	General	T	It is not clear how class based screens or targeted screens count toward points if more than one compund being confirmed. E.g. Cannab ELISA screen is targeted for CTHC and has little activity for THC, but the confirmation is for THC, OHTHC and CTHC. Does the ELISA + screen give points toward the confirmation of all 3 conpounds? OR a chromatographic screen looks for just BE, but the confirmation method confirms cocaine, CE, and BE. Does the BE screen give points to the cocaine and CE confirmations?	Better articulate how screening points can be counted.	Accept: This concept is explained in section 4.1.3 "The combination of the data obtained from all techniques contribute to the identification of an analyte." This means that each compound that crossreacts with the immunoassay can use those points towards their identification. Section 4.3.1.4 was also added to help clarify some of the situations the commenter has mentioned.
3	Scope	T	What about GHB? Would this be considered low mlecular weight? Is there a molecular weight where this document could give a number for compounds considered low molecular weight	just clarification in the document	Accept: The scope was modified to exclude only alcohols, carbon monoxide, cyanide, and metals from this document.
17	1	T	Examples are appreciated here, but it would be much more useful to define the mass range for low molecular weight analytes.	Define mass range for "low molecular weight analytes"	Accept with Modification: The scope was modified to exclude only alcohols, carbon monoxide, cyanide, and metals and removed the phrase "low molecular weight analytes".
31	1	T	"This document sets minimum criteria, based on a point system, for the identification of an analyte…" This would indicate that for each analyte the minimum number of points must be obtained. It is unclear how this might be applied when using metabolites/target analytes to make an identification of a metabolite/target analyte. For example, a urine specimen is analyzed by scan GC-MS and a quetiapine metabolite (norquetiapine) is identified by spectral library match. An LC-MSMS is performed using MRM with two product ions for each compound and quetiapine, norquetiapine, and hydroxy-quetiapine are identified. Can the scan GC-MS be used to count points for the identification of quetiapine and hydroxy-quetiapine? Or if an ELISA screen targeted to benzoylecgonine (with low cross for cocaine) is positive, can the ELISA be used for identification of cocaine?	Add clarifying language to address the permissability of using related parent and/or metabolite compounds as a screening test. Consider "A related parent and/or metabolite compound may serve as a screening test, given that the drug or metabolite is confirmed by GC or LC with MS with concurrent analysis of a standard."	Accept with Modification: While the recommended modification to the scope was not made, section 4.3.1 was modified to provide clarity.
4	3 and 4	T	I feel like if you are using a spectral library match for identifcation there should be some guidelines on where the library entry came from. Can you use the ones supplied by vendors, do you have to create your own? Making sure it was made from a valid standard and not from a standard that has been ina closet ofr 20 years.	Either clarification in this document orASB 098 Standard for Mass Spectral Data Acceptance in Forensic Toxicology	Reject: This comment is best addressed under the scope of ASB 098 Standard for Mass Spectral Data Acceptance in Forensic Toxicology.
33	3	E	Suggest including definition of tandem MS.	Insert definition of tandem MS (consistent with 098).	Reject: The term "tandem MS" is not used in this document. MS^n is used and is defined in Section 3.12
42	3	T	Definitions have been previously ratified by the international community to engender common language in the science of mass spectrometry and related techniques. These definitions do not match those. Additionally, some definitions are incorrect; i.e. ionization can also occur in the liquid phase and is not restricted to gas phase ionizaiton to produce pseudo-molecule ions	Reconcile the definitions with the IUPAC gold book or other similar accepted standard definition.	Reject: The terms used in this document are approved for use through the OSAC Lexicon. See https://www.nist.gov/topics/organization-scientific-area-committees-forensic-science/osac-lexicon
34	3.3	T	Incorporate information from definition in 098 to match the definition in 113.	Add "or compositional" relevance and include that water losses are not structurally significant.	Reject:The definition was modified but not as suggested. The appropriateness of water losses as diagnostic ions is found in ASB 098.
20	3.3	T	the definition of diagnostic ion in 113 is different than 098	consider using the definition 098, as it does not restrict diagnostic ions to fragments	Accept: The definition was updated and confirmed to be consistent with ASB 098. The current definition includes the molecular ion as a diagnostic ion.

24	3.3	T	Definition of diagnostic ion "It is not appropriate to use fragment ions with little structural relevance such as the loss of derivatizing agent-derived fragments, isotopomers, or certain adducts (including, for example, dimers)." In general I agree with this statement. However, this language seems too restrictive. There should be permissable exceptions. Some compounds don't play well and isotopomers may be the best option for that compound. While for the majority of compounds these ions would not be the best selection, method validation may demonstrate the suitability for using isotopes.	Allow for the use of water loss or isotopes when suitable alternatives are not available and method validation demonstrates suitable selectivity. Consider removing requirements from definitions as it would seem more appropriate to address requirements in other sections of the document.	Partial Accept: The definition was updated. The appropriateness of use of water loss or isotopes as diagnostic ions is found in ASB 098.
57	3.3	E	Definition of "diagnostic ion" is not the same as in ASB 098.	Uniformize definitions.	Accept: The definitions were synchronized.
58	3.3	T	The exclusion of loss of water or derivatizing agent as diagnostic ions across the board seems excessive. In some cases this is well and truly the only option to monitor a compound. If a successful and through validation is performed, why wouldn't it be an option?	Add a provision that loss of water or derivatizing agent may be acceptable if no other option is possible.	Reject: The appropriateness of use of water loss or isotopes as diagnostic ions is found in ASB 098.
71	3.3	T	The language of "It is not appropriate to use fragment ions with little structural relevance such as the loss of derivatizing agent-derived fragments, isotopomers, or certain adducts" seems very restrictive. There may be compounds whose MS breakdowns only show these specific types of breakdowns. There should be language added to allow for exceptions, given that all other method validation parameters are met. Also, these restrictions should be delineated in the document itself and not in the definitions section.	Consider allowing for the use of derivatizing agent-derived fragments, isotopomers, or certain adducts when other alternatives are not available, and/or if all other method validation parameters are met. Consider removing from definitions section to a more appropriate section in the standard.	Partial Accept: The definition was updated. The appropriateness of use of the use of derivatizng agent derived fragments as diagnostic ions is found in ASB 098.
73	3.3	E	definition does not match Std 098	have consistent definition (recommend using the one in Std 098). Remove requirements from the definition.	Accept: The definitions were synchronized and the requirements were removed from the definition.
35	3.4	T	Question words "nominal mass" in the definition, inconsistent with cited reference.	Remove the words nominal mass from the definition.	Reject: The definition is direct from the OSAC Lexicon and appropriate for this document.
74	3.4	E	this is separated into a definition for HR and MS in Std 098	have consistent definitions	Accept: The definition for HRMS between the two documents has been synchronized.
21	3.6	T	the definition of diagnostic ions as described in 3.3 is problematic in this section, unless the authors are considering the molecular ion to be a fragment	adjust the definition of diagnostic ions to eliminate fragment	Accept: This comment is related to 3.3. The current definition includes the molecular ion as a diagnostic ion.
75	3.7	E	very slight difference in definition in Std 098 ("...chemical ionization and electron ionization.")	have consistent definition	Accept: The definitions were sychronized
76	3.10.	E	Std 098 uses the term isotopomers	suggest consistency in terminology between the 2 standards	Reject: The term isotopomer was removed from this document
18	3.10	T	The definition of isotopomeric isomer is incomplete and, as a result, is very confusing especially since it appears to be a rewording of the definition of isomer above	Redefine isotopomeric isomers, specifically referencing the role of isotopes to provide clarity	Reject: The term isotopomer was removed from this document
43	3.11	T	Low resolution is generally not defined as a being capable of measuring an aggregate of masses within 1 m/z. m/z values are identified by the middle of the normal distribution of a recorded spectra - at a resoluition at full-width-half-mass of say, 5 m/z, the identified mass could still be within 1 m/z.	Low resolution should be defined with limits if the authors believe such resolution would be utilized in analysis. It is not equivalent to nominal mass analysis.	Accept with Modification: The definition for LRMS was updated and a definition of nominal mass added. Both are the same as those in the ASB 098 document.
77	3.11	E	referred to as a nominal mass analyzer in Std 098	suggest consistency in terminology between the 2 standards	Accept: The definitions were synchronized
25	3.12	E	Definition of mass spectrometry - "Study of matter through the formation of gas phase ions that are characterized using mass spectrometers..."	Consider changing "mass spectrometers" to "mass analyzers"? Seems somewhat strange to use almost the same word in the definition when a mass spectrometer is not defined.	Reject: This is the verbatim definition from the listed source.
44	3.13	T	MS to the N may not record spectra at each sequential step of the fragmentation process. Furthermore, the generation of product ions can occur prior to any mass analysis stage (as seen during in-source dissociation).	Correct to IUPAC language	Reject: The definition is the same as in the IUPAC document and as in 098. It is now referenced to that document.
36	3.16	E	Definition inconsistent with 098.	Remove the word "particular."	Reject: The word "particular" is included in the cited reference. The definition is now synchronized with ASB 098.
78	3.16	E	very slight difference in definition in Std 098	have consistent definition	Accept: The definitions have been synchronized between the two documents.
59	3.18	E	In the context of this standard, "measured" and "other substances" not uniform with previous vocabulary.	Replace "measured" with "identified and/or measured" and "other substances" with "non-targeted analytes" (as written in Section 3.5).	Partial Accept: The definition was modified: "Ability of a method to distinguish between the targeted analyte being measured and other non-targeted substances."
45	3.19	T	This definitions seems to indicate collisional cross-section or transmission efficiency. It is not a measured abundance of a precursor relative to the measured abundance of a product ion. Did the authors mean the relationship of the abundance of at least 2 differnent product ions from a shared precursor?	Correct to indicate transition ratio as measured between various product ions rather than a precursor/product ion relationship	Reject: The term "transition ratio" was removed from Section 3 as it is not used in this document.

22	3.19	T	Is this definition correct? As stated in 113, one would divide the product ion response by the precursor ion response; however, there is no measured precursor response in MRM in LC/MS/MS, for instance, as there is only one detector post-Q2. Typically, transition ratios are calculated as the response of one precursor->product ion transition divided by the response of a second precursor->product ion transition.	Update the definition of transition ratio to be consistent with actual practice	Reject: The term "transition ratio" was removed from Section 3 as it is not used in this document.
26	4.1.1	E	"Screening techniques have limits of detection for analytes of interest." This statement does not seem applicable to this document as it is already covered in the method validation document.	If this statement will be maintained consider adding limit of detection to the definitions section.	Accept: A definition for limit of detection was added to section 3
72	4.1.1	E	"The purpose is to rule out the presence of analytes..." - this language is vague as another purpose is to initially identify which analytes might be present, thus indicating when further testing may be warranted.	Consider expanding language to include the reason for when further testing may be warranted, such as when an analyte is detected and not just ruled out.	Reject: 4.1.1The section now reads: "Toxicological examinations typically begin with screening techniques that rule out the presence of analytes or indicate if further testing is warranted. Screening techniques shall have limits of detection for analytes of interest."
90	4.1.2	T	"...based upon a different chemical principle." is not necessary with today's analytical power. Two LCMS techniques that identify the exact compound is superior to an immunoassay and LCMS technique that identify a class of drug and then the exact drug.	Remove “and based upon a different chemical principle."	Partial Accept: Section 4.1.2 was modified to clarify that this was an historical approach
60	4.1.3	E	"(...) drug, metabolite, or other analyte" could be simplified to "analyte".	Replace "(...) drug, metabolite, or other analyte" to "analyte".	Accept: Removed "drug, metabolite"
1	4.1.5	Question	I am not sure if it is acceptable to repeat the same method using two independent aliquots of the same specimen.... using the same UPLCMSMS (5 points).	To clarity the statement in 4.1.5, 4.3.2.3.	Accept: Section 4.1.5 states "Two aliquots of the same specimen should be analyzed" and section 4.3.1.3 states that the same technique may be used, but no additonal points are awarded.
14	4.1.5	T	Clarification needed regarding what analyzing two aliquots or matrices mean. There are several scenarios that needs clarification with regard to immunoscreening and LC-MSMS screening especially since a confirmation assay can sometimes confirm analytes not identified in the screening.. Which of the following are ok: 1. Immunoassay showing BE followed by LC-MSMS showing cocaine and BE, 2. LC-MSMS screen showing BE in urine followed by LC-MSMS showing cocaine in blood. 3. Immunoassay showing benozdiazepines followed by LC-MSMS showing diazepam and flualprazolam. 4. LC-MSMS screen showing diazepam followed by LC-MSMS showing diazepam and flualprazolam.	4.1.5. be amended to identify in which cases a confirmation can be said to identify a specific analyte.	Accept: Section 4.1.3 was modified to address scenarios such as this. Further, 4.1.5 was clarified and 4.3.1.4. now contains examples to help clairify.
23	4.1.5	T	How would the committee suggest handling low volume samples (i.e. hospital samples in delayed death cases) where there is not enough sample to test two aliquots and there are no other suitable matrices?	Address situations where 4.1.5 is not possible or practical	Reject: Section 4.1.5. already indicates that a laboratory "should" do the second sample, but does not mandate it with a "shall"
46	4.1.5	T	Analysis of duplicate specimens may not be appropriate. Additionally, the requirements for duplicate analysis is not clear - for example, if two samples assayed against a single calibration curve does not mean that the calibration curve couldn't be sufficiently biased to provide a reproducible but inaccurate result.	Remove the recommendation for duplicate testing or elaborate on rationale	Reject: Section 4.1.5 already states the rationale in that duplicate analysis helps ensure "reliability, reproducibility, quality, and integrity of results." Nonetheless, it also indicates that a laboratory "should" do the second sample, but does not mandate it with a "shall"
61	4.1.5	E	Does "one analytical technique" refer to one line of the 4.3.1 table, e.g. LC-MS/MS = two analytical techniques? Or does it refer to a whole validated method, e.g. LC-MS/MS = one analytical technique? Unclear as currently written.	Replace "Although one analytical technique (...)" with "Although one specific technique (see Section 4.3.1) (...)" or with "Although one validated analytical method (including one or more specific techniques, see Section 4.3.1) (...)" depending on the indented meaning.	Partial Accept: Section 4.1.5 was modified and now includes an example
82	4.1.5	E	There is no language in this document concerning results from cases where sample volume is insufficient for a second analysis/confirmation.	Add a sentence on whether or not it is appropriate to report results from a single analysis if there is insufficient sample volume for confirmation. If it is acceptable to report results from a single analysis, how should the result be reported? (Presumptive positive, Detected by a single analysis but not confirmed, etc.)	Reject: Section 4.1.5. already indicates that a laboratory "should" do the second sample, but does not mandate it with a "shall". Reporting is outside the scope of this document. See ASB/ANSI 053.
83	4.1.5	T	The standard says that two independent aliquots of the sample specimen or two matrices from the same cas should be analyzed. In some cases, this may not be possible (e.g. infant blood sample in a post-mortem case, hospital sample in a drug impaired driving case). In cases with limited sample volume, one may go straight to a quantitative analysis without first doing a screening analysis. The current recommendations would mean that a positive finding could not be reported.	Consider allowing identification/reporting from a single quantitative measurement from a method that has been thoroughly validated, with the appropriate limitations imposed on those results. For example, a laboratory could report the concentration with a notation that the detection and concentration was determined by a single analysis. The lab acknowledges that scientific condifence in the accuracy and reliability of the result is increased when duplicate analysis is undertaken.	Reject: Section 4.1.5. already indicates that a laboratory "should" do the second sample, but does not mandate it with a "shall". Reporting is outside the scope of this document. See ASB/ANSI 053.
85	4.1.5	E	It is concerning to use the words "reliability, reproducibility, quality, and integrity" to question the use of methods for analysis that are fully accepted by the scientific community. More careful wording could be used to convey the same message. Addressing sample volume may also be appropriate.	Although one anlaytical technique may be sufficient to achieve identification, it is suggested that two independent aliquots of the same specimen or two matrices from the same case be analyzed. Maintaining adequate sample volume for independent analysis may be considered when accessing sample analysis.	Reject: The Consensus Body supports analysis of a second aliquot to ensure "reliability, reproducibility, quality, and integrity of results." See ASB/ANSI 053 for reporting requirements related to limitations of testing, such as inadequate specimen volume.
47	4.1.6	T	There are alternative methodologies for positively identifying compounds of interest. These should be included in a scoring of acceptability	Include UV, ECD, NMR, FID, and other techniques with scores appropriate for each. Each has their own pros and cons, especially when taking the molecule into context.	Reject: Table 4.3.2 includes points for the most commonly used techniques in forensic toxicology laboratories and already includes some of the mentioned examples. NMR is not typically used in forensic toxicology laboratories.

10	4.1.6	T	…This document does not mandate the use of mass spectrometry. (I like the last sentence that they afford more specificity).	Since ethanol and carbon monoxide are excluded from this document, I think mass spectrometry should always be required for confirmation for the reason stated at the end of this clause.	Reject: The Consensus Body supports setting a "minimum criteria...for the identification of an analyte..." At this time, the group does not support the requirement of mass spectrometry techniques to identify an analyte provided properly validated methods are used in the identification process.
11	4.2.2	E	There are no specified criteria for the chromatographic requirements (retention time, peak shape, resolution, signal to noise, etc.) and no references to another document. Many labs have very different criteria for these, it would be helpful to have an idea of the minimum requirements.	Add minimum criteria to provide consistency between labs, such as (examples only): 3:1 S/N for screening, 10:1 for confirmations, ±2% retention time, library matching criteria, required sampling rate or points across a peak for identification.	Reject: The document already requires laboratories to define their own chromatographic criteria for these parameters and to then demonstrate through validation that they are appropriate in order to count these points toward the identification. The ASB 098 document on Mass Spectrometry defines requirements for that instrumental approach.
27	4.2.2	E	"At least one chromatographic or electrophoretic separation technique shall be performed to achieve identification. Chromatographic acceptability criteria…" If electrophorectic separation will also be allowed acceptability criteria for this technique should also be specified.	Consider modifying to "Chromatographic or electrophoretic acceptability criteria…"	Accept: Modified as suggested.
48	4.2.2	T	Requirements for mass resolution and peak width are set forth in the document. Given the author's requirement for a chromatographic or electrophoretic separation motif to be used in identification, defined expectations for such performance seems appropriate	Provide distinct performance expectations for chemical separation parameters to include peak shape characteristics, minimum resolution requirements, signal to noise, etc, as well as the mechanisms to determine earch measure	Reject: The document already requires laboratories to define their own chromatographic criteria for these parameters and to then demonstrate through validation that they are appropriate in order to count these points toward the identification.
68	4.2.2	T	There are MS technologies (e.g., Direct Analysis in Real Time) that allow for specific identification without the need for chromatography. Such technology should be permissible if all validation requirements are met.	Remove this section entirely. Incorporate chromatography into the point system.	Reject: At this time, the Consensus Body supports the requirement for chromatographic separations in order to identify a compound. This is consistent with reference #4 in the bibiliography: The Official Journal of the European Communities, 2002, L221/8.
79	4.2.2	E	Are the things listed in parentheses requirements or examples?	Add "e.g." if just examples; remove "etc" if each is required	Accept: Removed the "etc."
86	4.3.1	T	It seems reasonable to obtain 3 points from low-resolution full scan library matches when multiple libraries are searched. Especially if quality of the match (i.e. 80 or 800) and quality of Forensic Mass Spectral library (i.e. SWGTOX, NIST) are taken into consideration.	Low Resolution Full Scan = 3 points	Reject: The Consensus Body does not support the identification of an analyte with only chromatography (1 point) and low resolution full scan library matches (2 points).
5	4.3.1	T	Examples are given of selective and non-selective detectors but no definitions.	Add a list as an Annex of selective and non-selective detectors, or a definition of each in section 3	Reject: The listed detectors are examples of the most common in the field of forensic toxicology. Other detectors may be utilized if selectivity is properly documented.
7	4.3.1	E	"Chromatographic or Electrophoretic Separation" is listed twice	Clarify or reduce redundancy	Reject: While this is listed 3 times in the table, it is to clarify that the 1 point granted for chromatography or electrophoresis is added to the points for the detector.
16	4.3.1	T	Sometimes other evidence in the case can support the identification to such a degree that reasonable certainty is achieved even without sufficient points according to this document. This could include identification in paraphernalia, medical records or when a specific drug was indicated from investigators. This could be relevant in cases with low sample volume, when a confirmatory assay was specifically ordered, when two assays are not available for a novel NPS or when confirming prescription drugs of limited importance in the case.	Suggest adding a section or line item identifying that extra points can be awarded for "case evidence" - the value of this should be discussed and decided by the committee.	Reject: Analyte identifications in biological samples need to stand on their own and not be biased by other evidence in the case.
29	4.3.1	T	For chromatographic separation with spectral library matching it would seem to make sense to obtain an additional point if a standard is run concurrently with the unknown. This would then allow enough points for identification using GC-MS scan and be more in line with what is currently required in seized drug analysis (See SWGDRUG recommendations) for identificaiton of the same compounds. In many cases this may be more specific than LR LC-MS with product ion spectral library match which is given a higher point value.	Consider adding a line item for Chromatographic Mass Spectrometric techniques with spectral library matching when a standard is analyzed concurrently with the unknown for an additional point. If accepted, also add an example in Annex B.	Reject: The document was clarified that to receive 1 point for chromatographic or electrophorectic separations, a concurrently analyzed reference standard/positive control must be analyzed. An example was included in Annex B for clarification.
37	4.3.1	T	Points awarded for HR product ion spectrum (4) seems low compared to points awarded for a single HR transition (3) or for low resolution product ion spectral matching (3).	Increase the points awarded for HR product ion spectral matching.	Reject: The Consensus Body supports the assignment of 4 points for HR product ion spectral matching.
40	4.3.1	T	EMIT + HR LC-MS with library matching scores 5.5 yet HR-LC-MS with 2 ions scores 6 points.	The less powerful technique is scored higher than the similar, but more complex technique. Please reconcile.	Reject: The Consensus Body disagrees with the commenters assessment that library matching is always the more complex technique. This will depend on the number of ions available in a given spectrum. The HR LC-MS with 2 ions requires an ion ratio that meets the acceptability criteria defined in the 098 Mass Spec Criteria document.
41	4.3.1	T	An example of LR LC-MS/MS with two transitions is lacking	Insert example of scoring for this technique.	Reject: The document cannot have examples (Annex B) of every possible combination of techniques a laboratory may use. Instead, an attempt was made to demonstrate how values from different techniques are combined to achieve the minimum of four points required for identification.
49	4.3.1	T	Low resolution is inappropriate here.	Consider the use of "unit resolution" or similar. Unit resolution is commonly defined as FWHM at 0.5-0.8 or more stringent (0.6-0.7).	Reject: For the purposed of this document, the use of "low resolution" mass spectrometry aligns with the 098 Mass Spectrometry Criteria document.

50	4.3.1	T	Would DART or LDT preceded by a chromatographic preparation technique (such as solid phase extraction, which is chromatogtraphy) be in the chromatographic mass spec scoring or in the non-chromatographic scoring?	Identify whether preparative chromatography prior to surface/ambient ionization techniques is sufficient to meet the scoring criteria for different models	Reject: Section 4.2.2. already specifies that the chromatographic (or electrophoretic) techniques must have defined acceptability criteria that must be validated and met for identification. No points are assigned for preparative techniques, such as SPE.
51	4.3.1	T	The rationale for high resolution at 2.5 points versus unit resolution at 1 point is unclear. In some cases, scoring structures in high resolution is weighted towards unique atomic consitituents (such as a chlorine atom in the structure affords a very distinct isotopic distribution, thus increasing the confidence interval substantially). However, this is not universally true. HIgh resolution for C/H/N/O molecules has liabilities not identified in the document and does not deserve the a 2.5 -fold higher score than a quadrupole.	Reduce high res MS to 2 points	Reject: The Consensus Body supports the assignment of 2.5 points for for high resolution. This is already set lower than the points assigned in the fourth reference of the bibliography.
52	4.3.1	T	Spectral library matching is not sufficeint in certain atmospheric ionization protocols as the ion(s) generated trend towards only the mono-isotopica molecular ion.	Indicate that the low resolution full scan approach is indicated for ionization protocols which induce a spectra with more than 2 identifiying constituents.	Reject: Spectral library matching is covered in 098 Mass Spectral Criteria and outside the scope of this document.
53	4.3.1	T	Number of points across a chromatographic peak becomes a significant issue in scanning during product ion spectra. Cycle time determinations in either unit or high resolution MS is a critical feature in appropriate data acquisition. Requirements for this mode shoiuld be clearly defined	Add section for recommendations regarding data acquisition/ion sampling rates for product ion spectra analysis.	Reject: This is outside the scope of this document. Instrumental parameters are established during method development and verified during method validation. Section 4.2.1 specifies that points are only awarded when validated methods are followed.
62	4.3.1	T	Two (2) points for a low resolution full scan seems very low, especially considering the fact that each MS/MS transition offers 2 points. A GC-MS (EI) full scan would yield only three points?	Increase to 3 points, at least for EI-MS scans which have several ions.	Reject: The Consensus Body supports the assignment of 2 points for low resolution full scan mass spectral library matches. The power of the full scan library match will depend on the number of ions available in a given spectrum.
69	4.3.1	T	There are MS technologies (e.g., Direct Analysis in Real Time) that allow for specific identification without the need for chromatography. Such technology should be permissible if all validation requirements are met.	Delete footnote a	Reject: At this time, the Consensus Body supports the requirement for chromatographic separations in order to identify a compound. This is consistent with reference #4 in the bibliography: The Official Journal of the European Communities, 2002, L221/8.
38	4.3.1, Annex B	T	"HR LC-MS with 2 ions" doesn't clearly convey what is meant. Does this mean precursor-product ion transitions, or would isotopes count as separate ions?	Clarify what "ion" means in single stage HRMS.	Reject: The example specifies LC-MS (not LC-MS/MS) which makes it clear this is a single stage mass spectrometer.
28	4.3.1c	E	"c Mass spectrometry library matches shall meet pre-defined library match criteria as specified in the validated analytical method." This is redundant as it is already covered in ASB 098.	Remove redundant information so that when updated it does not need to be changed in multiple documents.	Reject: The footnote helps tie the two documents together and emphasizes this very important point.
13	4.3.1, 4.3.2	E	Instead of the point system, would the group consider two lists: A and B, where A is all of the non-chromatographic or immunoassay tests and B includes all mass spectral tests.	A proposed resolution would be: "a minimum of two tests are required for confirmation, at least one test of those tests will be from the B list."	Reject: The SWGDRUG approach was considered early in the drafting of this document, but the screening and confirmatory analyses of biological samples was determined to require a more complex approach.
6	4.3.2	T	Explanation needed in regard to ethanol and other volatile compound identification requirements.	Additional point under 4.3.2 allowing less total points required for ethanol and other volatile identifcation and quantitation, allowing for the use of identifcation via running separate aliquots on two different columns via HS-GC w/FID (a commonly used method in the field). Not requiring the use of an additional technique such as MS. (Otherwise, clarification at the beginning of the document that these guidelines are not intended for ethanol and other volatile identification.)	Reject: As noted in the scope, "This document does not address identification of alcohols, carbon monoxide, cyanide, or metals."
8	4.3.2	E	The requirements are listed after the table so you have to read all the way through the table until you know how many points are required	Switch 4.3.1 and 4.3.2	Accept: These two sections were reordered as suggested.
89	4.3.2.	T	The standard should also recognize the value of associated evidence (e.g., analyte was identified in paraphernalia or screened positive in hospital records; or prescription medication), particularly in cases of low specimen volume [insufficient for secondary analysis] or non-forensically significant compounds.	Please add a 4.3.2.5. to indicate that in cases of low specimen volume/poor specimen quality or where secondary analysis is otherwise infeasible, when identification has been made based on one technique it can be listed with the appropriate caveats ["unconfirmed" or "based on one analysis"], but [as appropriate] acknowledging the consistency with case history.	Reject: The analytical identification needs to stand on its own and not be biased by other evidence in the case. Section 4.1.5. already indicates that a laboratory "should" do the second sample for quality purposes, but does not mandate it with a "shall". See ASB/ANSI 053 for reporting requirements related to limitations of testing, such as inadequate specimen volume.
87	4.3.2. (1,2,3)	T	The standard does not address the additional value added to the identification by a) analyzing multiple matrices or b) compounds related by metabolism (e.g., sertraline & norsertraline).	If identified separately, even within the same method or technique, related compounds should lend "points" to one another. Moreover, analysis of two different matrices with the same method, both resulting in detection of a certain drug(s) and/or its metabolite(s), *should* earn additional points toward the total needed for identification [revision of 4.3.2.3 to include this exception--say, 1 point per additional matrix]. For example, ID of a parent in blood and metabolite in urine, even if the technique only added up to 3 points, should be sufficient.	Reject: Section 4.3.1.2 provides further clarification that each identified analyte (whether parent or metabolite) in each matrix type must meet the minimum point criteria. Section 4.1.3 was modified to address scenarios such as this. Further, 4.1.5 was clarified.
2	4.3.2.1	Question	A hyphenated technique can also be an UPLCMSMS, so this technique will count as one technique.	To include more examples	Reject: The document cannot have examples (Annex B) of every possible combination of techniques a laboratory may use. Instead, an attempt was made to demonstrate how values from different techniques are combined to achieve the minimum of four points required for identification. UPLCMSMS is a hyphenated technique in which the chromatography would earn 1 point and the MSMS would earn additional points as described in the table of section 4.3.2.

12	4.3.2.3	E	Define "repetition of same method." Is this defined as the use of the same sample preparation method or the use of the same type of instrument? As an example, we confirm some drugs in urine with two LC-QTOF tests, but we use two different sample preparations (one dilute and filter, the other SLE). Would this only count as 1 test, but 4 points so we would meet the criteria?	Clarify what is meant by repetition of the same method.	Reject: The Consensus Body feels the language is already clear in this section. The example provided shows that the commenter understands this clause, provided the method is validated and the QTOF achieves at least 3 points, the required minimum of 4 points was met. The second aliquot analyzed using the same method will not add any additional points towards the identification, as described in this example, even if a different sample prepartion technique is used. No points are awarded for sample preparation techniques.
32	4.3.2.3	T	The second independent analysis of a separate aliquot, injected and analyzed in a different run from the original set of data, should be awarded points for the testing matrix. If they are analyzed separately and not in the same run, they can both considered valid tests for the identification of an analyte.	clarify the scenario in the requirement by using the following verbiage: Repetition of the same method does not earn additional points toward the total needed for identification, unless a second extracted/sampled aliquot is analyzed in a separate run.	Reject: The Consensus Body does not support the suggested modification to meet the identification criteria (see 4.3.1.3).
63	4.3.2.3	T	Clarify whether this comment means repetition of the same technique on a second aliquot, or the same technique but on a different matrix (e.g., analyze femoral and cardiac blood by LC-MS/MS), or both.	Repetition of the same technique on a different matrix could grant a limited number of points, say 0.5 or 1.	Reject: Identification of an analyte must meet the minimum 4 point criteria for each matrix. Repetition of the same technique on a *different* matrix is awarded all of the points for the identification of analytes in that matrix only. For clarification, see section 4.3.1.2 and 4.3.1.3.
64	4.3.2.4	T	Although the citalopram/escitalopram case is a clear-cut one where both names need to be on the report, is "Amphetamine" on the report reputed to refer to both isomers? A lot of analytes relevant to toxicological analyses have isomers, this is going to put a lot of details (confusing for the client) on the report. And does "reporting" refer to the final report handed out to the client, or the instrumental report kept in the file?	Unless otherwise specified, the name of the compound with no further detail should refer to both enantiomers, e.g. amphetamine refers to d/l-amphetamine. Replace "reporting" by "final reporting to the client" or "instrumental reporting".	Partial Accept: Section 4.3.1.5 was modified: "Specific identification of an isomeric compound shall meet the minimum point requirements of this document (e.g., escitalopram, d-amphetamine). Unless differentiation is achieved, it is only acceptable to identify the mixed isomeric compound (e.g., amphetamine or d/l-amphetamine, methorphan or dextro/levomethorphan)."
15	4.3.2.4	T	Separating isobaric and isotopic compounds is not always relevant and should be at the discretion of the laboratory.	Change wording to "When known isobaric and isotopomeric compounds exist and chromatographic separation and/or spectrometric differentiation is was not attained for the isobaric or isotopomeric compounds during method validation, reporting shall reflect this limitation (e.g., citalopram/escitalopram or d/l amphetamine)."	Partial Accept: Section 4.3.1.5 was modified: "Specific identification of an isomeric compound shall meet the minimum point requirements of this document (e.g., escitalopram, d-amphetamine). Unless differentiation is achieved, it is only acceptable to identify the mixed isomeric compound (e.g., amphetamine or d/l-amphetamine, methorphan or dextro/levomethorphan)."
54	4.3.2.4	T	Do the authors intend to require identification or clarity in reporting of every chrial/stereo center for all compounds intended to be measured? Would this also be applied to those molecules which, by virtue of samples preparation (i.e. derivitization for GC separation) be identified in a report? This seems unnecessary unless there is a meaningful implication to the interpretation of the data	Remove the requirement for identification of isomers unless there is a clear, scientifically established reason for doing so.	Partial Accept: Section 4.3.1.5 was modified: "Specific identification of an isomeric compound shall meet the minimum point requirements of this document (e.g., escitalopram, d-amphetamine). Unless differentiation is achieved, it is only acceptable to identify the mixed isomeric compound (e.g., amphetamine or d/l-amphetamine, methorphan or dextro/levomethorphan)."
88	4.3.2.4.	T	The wording should be changed to allow for laboratory discretion. It may not be relevant to the scope of the laboratory or worth the necessary time and resources to attempt to separate all possible isotopomers/isobaric compounds during validation.	Change wording to indicate that "Laboratories that did not address isobaric and isotopomeric compounds during validation shall ensure reporting reflects this limitation (e.g., citalopram/escitalopram or d/l amphetamine)."	Partial Accept: Section 4.3.1.5 was modified: "Specific identification of an isomeric compound shall meet the minimum point requirements of this document (e.g., escitalopram, d-amphetamine). Unless differentiation is achieved, it is only acceptable to identify the mixed isomeric compound (e.g., amphetamine or d/l-amphetamine, methorphan or dextro/levomethorphan)."
84	4.5.1	T	Consider differentiating requirements between screening methods and confirmation methods. In some cases on an LC-MS instrument (e.g. cocaine, benzoylecgonine), the detector may become saturated, which may affect the ion ratio. In their current format, the standard does not allow for tentative identification by a screening method with further confirmation by a quantitative method. This means that a positive benzoylecgonine ELISA and an LC-MS/MS cocaine, benzoylecgonine, and egconing methyl ester quantitative result would be acceptable, but that an LC-qTOF with saturated cocaine, benzoylecgonine, and ecgonine methyl ester followed by a quantitation on LC-MS/MS would not be sufficient. The standard also imply that identifying a class of drugs by ELISA and confirming each drug is sufficient, but that each drug individually needs to be identified by other, more specfic screening methods (e.g. opioids, d/l-amphetamine). Therefore, if you have a positive oxycodone and inconclusive oxymorphone on an LC-qTOF screen but quant both, you would need to repeat the LC-qTOF screen in order to meet the identification requirements.	Consider revising standard to allow the tentative identification of analytes on screening methods with confirmation on quantitative methods.	Reject: This standard does not allow for a "tentative" identification. The Consensus Body believes the commenter means "presumptive positive". Nonetheless, to identify an analyte, a minimum of 4 points is required. The ion ratio criteria requirement of section 4.5.1 is mandated for points to be be included from the method towards the analyte identification.
55	4.5.1 and 4.5.2	E	The 2 documents are intrinsically linked; reviewing one without the context/support of the other is challenging.	Combine the related MS documents into a single document.	Reject: The Consensus Body agrees the two documents are linked, but they stand on their own.
39	4.5.2 d, 4.4.2.c	T	Question the appropriateness of 5 ppm as required mass accuracy. This seems potentially too restrictive or too permissive depending on the resolving power of the analyzer and the m/z of the analyte of interest.	Reconsider cutoff, or cite resource demonstrating the appropriateness.	Reject: This comment is outside the scope of this document and is a requirement of the 098 Standard for Mass Spectral Data Acceptance in Forensic Toxicology document.

30	4.5.2	E	"Spectral library searches may be conducted and results shall meet or exceed a predefined match factor that is documented in the laboratory's standard operating procedures and meet the criteria specified in the current ASB Standard 098..." Some language here is redunadant to that which is already specified in ASB 098.	Revise to remove redundant information that is already covered in ASB 098. Consider revising to "Spectral library searches may be conducted and results shall meet the criteria specified in the current ASB Standard 098..."	Partial Accept: Section was slightly modified. The Consensus Body views the redundant information with 098 as minor and retained for clarity.
56	4.5.4	T	Non-chromatographic high resolution MS should not be considered. Of note, the change in determined m/z can be heavily affected by the phenomena of space-charge effects. The risk of performing such a scan while maintining a 5 ppm window is exceedinly high in many samples.	Redact 4.5.4 and note that space-charge effects are a limitation of high resolution MS that must be addressed during the course of analysis.	Reject: The purpose of this section is to make it understood that laboratories cannot accrue sufficient points to achieve identification without chromatographic or electrophoretic separation. The concern with space-charge effects should be addressed in method validation (ASB Standard 036).
70	4.5.4	T	There are MS technologies (e.g., Direct Analysis in Real Time) that allow for specific identification without the need for chromatography. Such technology should be permissible if all validation requirements are met.	End last sentence after "...library match."	Reject: At this time, the Consensus Body supports the requirment of chromatographic or electrophoretic separation to achieve identification.
19	6.2.4	T	Not specifying stereochemistry is most appropriate when you don't know what stereoisomers are present. When you require amphetamine (which may have one or both stereoisomers present) to be repoted as d/l amphetamine, the reader assumes that the reporter knows that both stereoisomers are in fact present.	Don't require "d/l" labeling when reporting things like amphetamine when it is not known which stereoisomers are present.	Accept: This is actually referring to section 4.3.2.4. (now section 4.3.1.5). This was modified: "Specific identification of an isomeric compound shall meet the minimum point requirements of this document (e.g., escitalopram, d-amphetamine). Unless differentiation is achieved, it is only acceptable to identify the mixed isomeric compound (e.g., amphetamine or d/l-amphetamine, methorphan or dextro/levomethorphan)."
65	Annex B	E	This section would greatly benefit from laying out some of the more traditional combinations of forensic toxicology by themselves, to clarify the point system. With the table as it is, we are reduced to performing a series of deductions to clarify the point system laid out in the document.	Add a section at the begining of the table, "Common toxicology methods" (or something along those lines), which could list points for e.g., GC-FID, GC-FID (2 columns), GC-MS, LC-MS/MS, LC-QToF (DIA).	Partial Accept: The table within section 4.3.2 of the document provides individual points for common toxicology methods. One additional example was included (dual column GC-NPD). The title of Annex B was modified.
66	Annex B	T	"LR GC-MS/MS with 2 precursor product ion transitions" can be read as "You need two different precursor ions that each generate a fragment" or "You need two transitions" (i.e., the same parent but two different fragments can be used).	The second one (two transitions, which can use the same parent) is probably the intended one, but clarify, maybe using a table footnote?	Accept: This was clarified by the addition of a new section 4.5.2.
67	Annex B	T	Say GC-(EI)-MS is used in full scan with a library match (already, 1 + 2 points). In adition, 3 specific ions from this scan are isolated and monitored. Does this add 3 points to the total, or since these are part of the full scan and not SIM/SRM/MRM monitored, they are not counted towards the total?	Specify, either in an example in Annex B or earlier, whether ions from the full scan can be used towards the total number of points or whether only specifically monitored ions (not scanned) can be counted as "ions" that gather points.	Accept: Section 4.5.4 was added to clarify that "When ions are acquired in the full scan mode, points may only be awarded for either the library match or extracted ion ratios. If the instrument is capable of simultaneously acquiring ions in both full scan mode and selected ion monitoring, then points may be awarded for both library matches and ion ratios."
81	Annex B	T	3rd from bottom of table - CEDIA + HR GC-MS with product ion spectral match does not equal 6	Change HR GC-MS with product ion spectral match to GC-MS/MS or HR GC-MS full scan spectral library match and math to 1+1+3.5=5.5	Accept: Changed to HR GC-MS/MS for correct point assignment