

Comment Number	Section	Comment	Response
1	IIIB.1	<p>How is the analyst coming up with question that needs to be answered? Is the question being asked determined by the needs of law enforcement, the limitations of instrumentation being used by the laboratory, or both? We would assume that a laboratory would always strive for the highest level of identification possible at all times, but there are levels to identification. Both documents could be improved by adding more detail to the example given in the introduction of the <i>Methods for Analysis</i> and adding more information to the purpose of the supplemental document on the different levels of identification and the intended value of this information.</p>	<p>No changes made. The source of the question is based on the customer's request, the observations of the materials submitted, and jurisdictional requirements.</p>
2	IIIB.2.1	<p>One suggestion is to add the definition of selectivity to both documents. Although this term may be familiar to the forensic drug chemistry community, many other disciplines use the term "specificity" for this concept. Making people aware of the interchangeability of these terms would be extremely helpful.</p>	<p>The two terms are not interchangeable. Selectivity is defined in the SWGDRUG glossary.</p>

<p>3</p>	<p>IIIB.2.2</p>	<p>Need to define "sufficient level" Discussion: For example, I have heard from lab analysts in court, that a visual comparison of MS Unknown with a copy of a standard mass spectrum under different conditions is sufficient for a positive result. There are general chemistry protocols in Analytical chemistry and Instrumental analysis that apply to ALL laboratory analyses. Since Drug Identification is an application of Chemical Analyses, the minimum protocols for "sufficient level" are already in place. I have noticed many analyses do not comport to these minimum requirements, such as fragment ratios not within ranges accepted in published mass spectral protocols and in GC retention times based upon the use of packed columns much wider than the accepted ranges for capillary columns.</p>	<p>Acceptance criteria for individual techniques is beyond the scope of this document. Refer to the IIIB.3.3.1 for relevant information.</p>
<p>4</p>	<p>Figure 1</p>	<p>I would either make the colors of the techniques correspond with the colors in figure one, or make a clear line between the categories</p>	<p>The figures were re-designed and clarified.</p>

<p>5</p>	<p>Figure 1</p>	<p>Add a fourth category Category D (Non-specific indicators of class characteristics) Discussion: Basically, color tests and immunoassay tests are well accepted as testing positive for class and not for molecular characteristics, such as functional groups. The other techniques listed in the current Category C can be related to molecular characteristics but are still considered non-specific tests. I suggest that a full UV spectrum be debated as belonging to Category C as it is still non-specific and based mainly upon class characteristics. I also suggest that a Macroscopic examination be moved from Category B to Category C as there are known very close and sometimes easily confused visual characteristics when the plant material is viewed on NOT WHOLE leaf material. Finally, I would limit the use of the new Category D for use for screening only, not for substantiating identification, for forensic identifications. (In medical use, the presence of a drug class is more determines the treatment more so than the presence of a specific drug.) See below for additions comments.</p>	<p>The current categories are sufficient to address current analytical needs of different laboratories and jurisdictional requirements. Techniques providing class information are considered in Category C. Macroscopic examination has sufficient selectivity for a category B when the sample has appropriate botanical features.</p>
<p>6</p>	<p>Table 1</p>	<p>the testing category chart does not do a good job of distinguishing a/b/c. There is no border between them. It isn't much different from the previous</p>	
<p>7</p>	<p>Table 1</p>	<p>Based on the examples with varying types of mass spectrometry not meeting the selectivity requirements for Category A, I would suggest breaking this into two techniques: MS with and without fragmentation. Or at least including a footnote similar to the note for X-Ray crystallography and diffraction data. I think many more labs have MS instruments and the clear guidance in this document as opposed to the supplemental would be helpful.</p>	<p>The footnote for X-ray Diffractometry was removed and an expanded statement was added to IIIB.2.3. SD7 contains more clarification and examples.</p>

8	Table 1	<p>I would remove the footnote for the description of X-ray diffractometry. First, single crystal x-ray diffraction when performed properly has more than "the potential" for identification. The data is able to provide the three dimensional structure of the compound in question. The technique's limitation is on sample prep, not analysis. One could argue that there is no better instrument for providing complete structural elucidation than having a three dimensional model of the compound in question.</p>	Footnote was removed.
9	Table 1	<p>Add footnote 3 placed upon Thin Layer Chromatography, Microscopic Examination, and Color Tests that would allow for the traditional identification of Cannabis plant material using either a combination of Microscopic Analysis and Duquenois-type or Fast Blue B type color test with or without the Thin-layer test showing the presence of TLC.</p> <p>Add footnote 4 placed upon Category A which would require that the data collected from an unknown MUST be compared with the same data from a standard (when available) sample obtained under the same conditions AND, if that is not done, that technique used be considered to be under Category B.</p>	Footnotes are not required. Comments relate to jurisdictional requirements and laboratory procedures. This is a guidance document.
10	Table 1	<p>Clarification on how UV/Vis is defined, and if only UV is used, is it a Category C?</p>	The table was clarified.

<p>11</p>	<p>Table 1</p>	<p>Our lab has specific experience with vacuum UV (VUV) detectors for gas chromatography. Although implied, we would recommend that a full VUV spectrum (e.g., 120 - 240 nm or 125 - 430 nm) would be a category B technique. The use of GC/VUV in drug analysis has been published in peer-reviewed literature: 1. Leghissa, A.; Hildenbrand, Z. L.; Schug, K. A., A review of methods for the chemical characterization of cannabis natural products. J Sep Sci 2018, 41 (1), 398-415. 2. Lurie, I.; Szewczak, A.; Vaught, C.; Smuts, J., THE ULTITLITY OF GC COUPLED TO VACUUM UV SPECTROSCOPY FOR THE ANALYSIS OF EMERGING DRUGS. Forensic Sci.Int. 2017, 277, 129-130. 3. Lurie, I. S.; Tremeau-Cayel, L.; Rowe, W. F., Recent Advances in Comprehensive Chromatographic Analysis of Emerging Drugs. Lc Gc N. Am. 2017, 35 (12), 878-883. 4. Schug, K. A.; Sawicki, I.; Carlton, D. D., Jr.; Fan, H.; McNair, H. M.; Nimmo, J. P.; Kroll, P.; Smuts, J.; Walsh, P.; Harrison, D., Vacuum ultraviolet detector for gas chromatography. Anal Chem 2014, 86 (16), 8329-35. 5. Skultety, L.; Frycak, P.; Qiu, C.; Smuts, J.; Shear-Laude, L.; Lemr, K.; Mao, J. X.; Kroll, P.; Schug, K. A.; Szewczak, A.; Vaught, C.; Lurie, I.; Havlicek, V., Resolution of isomeric new designer stimulants using gas chromatography - Vacuum ultraviolet spectroscopy and theoretical computations. Anal Chim Acta 2017, 971, 55-67.</p>	<p>Clarification has been added to the table to use a defined wavelength range and remains a category B.</p>
<p>12</p>	<p>Table 1</p>	<p>Is macro exam of marijuana defined? How is this used for ground leafy material when macroscopic features aren't visible?</p>	<p>The material must be suitable for the technique selected. Ground material would be suitable for a chemical analysis, rather than macroscopic botanical examination. Refer to IIIB.4.3 for guidance on cannabis analysis.</p>
<p>13</p>	<p>Table 1</p>	<p>Could Duquenois-Levine be considered a Category B test? Numerous research articles give this color test much more weight than any other in its specificity for cannabinoids.</p>	<p>Although this test may have a higher degree of selective than other color tests, collectively color tests remain in category C until there are published literature to the contrary.</p>

14	Table 1	<p>Why move pharmaceutical ID to Category C? If the analysis shows that the ingredients agree with the logo, the info from the logo is very selective. If the analysis does not agree with the logo (counterfeit), then that is an inconclusive test anyway and would not be a Category B or C. We do not see the benefit in moving it to a Cat C.</p>	<p>Visual observation is still only indicative making high quality counterfeit preparations difficult to assess. Therefore, this test has a high risk of resulting in false positives.</p>
15	IIIB.3.1.1	<p>Section IIIB.3.1.1: I would add the number of constituents in the mixture. If this is Raman spectroscopy for example, excipients may have a stronger Raman activity than the analyte of interest, the quality and content of the library, and the matching algorithm will play important roles in assessing the quality of the result obtained.</p>	<p>Refer to IIIB.3.1.2.2 and IIIB.3.1.2.3.</p>
16	IIIB.3.1	<p>Thank you for the opportunity to provide feedback. Part III B . 3. 1 & IIIB.3.1.1 - Category A (highest selectivity) - remove "other" from "one other technique". ---> "at least one technique (from Category A, B, or C)..." If Category A is best/highest selectivity, it should outweigh Category C. Therefore, two (2) Category A tests (even if same test) on two (2) separate, distinct aliquots should be acceptable for the analytical scheme. This eliminates contamination issues and assumes the good working condition of the instrument. If one Category A test is positive and working, then another consecutive (same) Category A test (on another portion that supports it) is CONSISTENT - no reason to suddenly assume that instrument is not working or failed. This second test should outweigh the quality of any another Category B, or C test, even if it is the same repeat Category A test. The quality practices in Part IIIB.5 would and should be followed (especially IIIB.5.2).</p>	<p>Clarification has been added to say that a second test must exploit different chemical or physical properties, which is not the same as repeating a technique in duplicate samplings.</p>
17	IIIB.3.1	<p>Make a distinction between the A and B tests for minimum ID requirements and other tests that are used for basic screening. There is not a clear distinction between B and C testing</p>	<p>Refer to IIIB.2.3.</p>

<p>18</p>	<p>IIIB.3.1.1</p>	<p>Change to A technique is considered Category A when the spectral data obtained provide structural information, a high level of selectivity, a high level of match when compared to standard data, and are reviewable. Technically, I would not consider X-ray diffractometry to give spectral data. I think a high level of match (not quality of match, but generically a high level of match) complements the high level of selectivity).</p>	<p>The word “spectral” was removed. TO DO - put a new footnote</p>
<p>19</p>	<p>IIIB.3.1.2.3</p>	<p>Add: IIIB.3.1.2.4 The quality of match between the data obtained from an unknown sample with that data from a standard sample does not meet acceptable chemical or instrumental analytical protocols.</p>	<p>Value of the results is discussed in section IIIB.3.3.1.</p>

<p>20</p>	<p>IIIB.3.1.3</p>	<p>I think would be helpful if it were spelled out here how the data with limitations fits into the scheme – is it still a category A, or is it now a category B or C? If it is no longer an A that will impact how much additional testing is needed.</p> <p>If selectivity is such that the data is able to narrow it down to 2-3 compounds, then perhaps it is still an A and only one additional test that alleviates this limitation is needed (B or C). (Example – pseudo/eph MS + LC retention time).</p> <p>If selectivity is such that it truly is only a B or C category test, then another A or two additional tests are needed. (Example – DART-TOFMS; Another A or two tests are needed).</p> <p>Also – can data from compounds that degrade in the inlet be used as cat B or C for ID of parent? Example – psilocybin GC-MS. Can the MS (which is of psilocin after dephosphorylation) be used as a cat B or C presumptive ID of psilocybin provided another test alleviates the limitation of it possibly being psilocin?</p>	<p>The details are outside the scope of this guidance document. Refer to SD-7 for more relevant examples.</p>
<p>21</p>	<p>IIIB.3.1.3</p>	<p>IIIB.3.1.3 and IIIB.3.3.3 are still not clear. If there are limitations, these descriptions indicate that they can be used in the scheme, but IIIB.3.2 contradicts that. It says that two B's and a C must be used (no mention of how a limited A would fit in the scheme). Also, a limited A result would not necessarily be a "positive" result (as required for use in IIIB.3.3). These results are typically referred to as indicating, but not confirmed due to (fill in the reason such as qualitative uncertainty, lack of sample, lack of reference standard, etc.). A true positive result would meet the requirements in IIIB.3.3 but a limited value result from a cat. A technique would not meet the requirements. Exactly how the limited value results can be used should be spelled out.</p>	<p>Additional clarification added to the respective sections.</p>

<p>22</p>	<p>IIIB.3.4</p>	<p>Also, in IIIB.3.4 it indicates that the hyphenated technique counts as 2 tests, but ignores the fact that the tests are performed on the same sample. Best practices state that testing should be performed on 2 separate samples - a single GCMS run may use 2 techniques, but only one sample is tested. I suggest pointing out that the scheme should still have a test (of any category) on a separate sample as well (such as a color test or a second GCMS aliquot).</p>	<p>Refer to section IIIB.5.2.</p>
<p>23</p>	<p>IIIB.4</p>	<p>We would also like to raise concerns and questions regarding the analytical schemes proposed for the identification of cannabis. Greater detail should be added to explain why two visual methods are permissible for the identification of cannabis. The Methods for Analysis document explains how two category B techniques can be used to obtain high selectivity, by targeting different chemical and physical properties of the analytes being tested. How does this principle apply to cannabis? Macroscopic and microscopic examinations for cannabis are not orthogonal and rely on the same visual method, but with different levels of sensitivity/resolution. If all of the characteristics of a macroscopic examination can be seen with a microscopic examination, what purpose does the macroscopic examination actually serve and are these tests truly independent of each other? In addition, moving from two objective instrumental analyses to subjective human interpretation raises quality control concerns that are not adequately addressed in the document. Lastly, the Methods for Analysis document does not provide adequate information on what is sufficient macroscopic and microscopic botanical detail on trace amounts of cannabis that may be damaged by consumption, like fire from being smoked.</p>	<p>Macroscopic and microscopic examination characterize different morphological features of a plant. Such examinations are based on objective identification of specific plant features.</p>

24	IIIB.4.1	<p>Finally, although I know I'll never win this argument, I'd like to speak out against the continued exception to the cat. A requirement for cannabis. Cat. A techniques provide reviewable data that are not dependent on the analyst's experience or eyesight. Detailed descriptions are not nearly as reliable as a GCMS printout. If the observations were recorded photographically, I might be willing to say that it is acceptable based on the lab's risk analysis, but written descriptions or drawings are just too subjective. Cannabis has a simple extraction with a relatively short retention time. I just don't buy the idea that labs cannot do a GCMS test on it. It should be held to the same scientific standards as all other identifications made in the laboratory.</p>	<p>There is no requirement for a category A technique for any scheme. Laboratories may choose to use two category B and one category C techniques for all types of analyses, if validated. In order to certify a plant from the genus cannabis, microscopic and macroscopic examinations need to be conducted. Identification of the botanical, requires morphological plant identification and cannot be based solely on the chemical identification of a single component.</p>
25	IIIB.4.2	<p>There are no recommendations for states that have changed the legal definition of cannabis vs hemp vs CBD only. Additionally, some of the techniques are antiquated and not used in most labs</p>	<p>Section IIIB.4 was updated to include differentiation of cannabis varieties based on THC concentration.</p>
26	IIIB.5.1	<p>If contemporaneous documented peer-reviewed notes are considered reviewable data, why not require it for category C techniques as well?</p>	<p>These are minimum guidelines and category C techniques are generally indicative or to guide the analysis. A laboratory may choose to, but is not required, to provide reviewable data for category C techniques.</p>
27	IIIB.5.1	<p>When provided as examples, these are not requirements. If you want to see actual data for instrumental techniques, this should be a clause and not an example.</p>	<p>The first sentence already requires reviewable data. The second sentence has been modified to add clarity to this section.</p>
28	IIIB.5.1	<p>Having to make copies of TLC or verify is that only if that is your only other test? We run MS, GC for RT , TLC and color tests. Since we have MS and GC, would we still have to copy them? They are just extra tests. PLease clarifiy that in the document</p>	<p>If its part of your analytical scheme, then it must meet the requirements of the category.</p>
29	IIIB.5.1	<p>Part IIIB.5.1 - is this a strict requirement for reviewable data for Category A & B techniques? Is a "QC or QA program" an acceptable substitute for reviewable data, for example for microcrystalline tests or other tests?</p>	<p>Categories A and B require reviewable data. QC and QA data is not an acceptable substitute for reviewable data.</p>

30	IIIB.5.1	Add to IIIB.5.1 another bullet "a copy of the standard results used for the comparison and the conditions under which that data was obtained"	It is outside the scope of this section. The comment is being addressed in section IVA.6.1.6.
31	IIIB.5.2	Add to IIIB.5.2 another bullet "running a standard sample, if available, under the same conditions under which the unknown data was collected close in time to the collection of the unknown data OR stating that library standard data was used and providing that data and the date that data was collected"	It is outside the scope of this section. The comment is being addressed in section IVA.6.1.6.