	Feedback for changes to Part II - Education and Training	Response
1	Given the requirement that drug analysts must be trained properly, SWGDRUG should help make its members aware of quality, relevant training opportunities. I am a faculty member of California Criminalistics Institute (CCI) , , a state agency which arranges training courses for the forensic scientists of the state. CCI offers many courses relevant to controlled substance analysis, and these courses are open to the public. SWGDRUG should make its members aware of these opportunities.	Given the changing nature of conferences, training courses, and workshops, it is not appropriate to include such a listing within the document. However, efforts will be made to maintain accurate listings of such offerings on the SWGDRUG website.
2	Understandable change in light of COVID graduates	No response needed
3	I love the inclusion of the note regarding virtual labs not being a replacement for in-person labs. We have seen this problem and think it definitely needs included.	No response needed
4	1. Section II.2 “The individual shall have: theoretical knowledge in foundational chemistry concepts, organic chemistry, and analytical chemistry, including quantitative analysis and instrumental analysis; and...” Recommendation: Analytical chemistry covers quantitative analysis and instrumental analysis. Hence it is not necessary to specify what constitutes analytical chemistry. Suggest to remove "quantitative analysis and instrumental analysis" from the paragraph. 2. Section II.4 “All forensic scientists have an ongoing responsibility to remain current in their field.” Recommendation: To use "analysts" instead of "forensic scientists" for consistency in terminologies throughout the whole document.	Response to 1: It is important to specify what constitutes analytical chemistry as not all "Analytical Chemistry" Courses cover the same concepts. For example, some universities do not offer an "Analytical Chemistry" course but instead offer separate "Quantitative Analysis" and "Instrumental Analysis" courses. Response to 2: Agree that language within the document should be consistent.

	Feedback for changes to Part IIIA - Sampling Seized Drugs for Qualitative Analysis (including Figure 2)	SWGDRUG Response
1	Nice job!	Thank you!
2	For the section regarding statistical sampling, can this be interpreted in the context of the legal guidance in the state. For example, if the state verbiage for charging requires statistical analysis to identify a "Fentanyl Mixture" and that's reported. The consistency would be the identification of fentanyl in all representatively sampled items.	Correct. Inferences are often based on legal guidance. See Part IIIA.3.2.2.1a) verbiage "…contains the drug of interest or is positive for a given characteristic" (characteristic in this example would be a "fentanyl mixture").

	Feedback for changes to Part IVB - Validation of Analytical Methods	SWGDRUG Response
1		N/A
2	Excellently done!	Feedback on future guidance, including an upcoming supplemental document for validation, will be appreciated
3	IVB.1.4: Remove requirement for written validation report and address requirement in IVB.2.1 as "An analytical method validation report shall be required and include the following elements:" IVB.2.1.1.2 should reference 2.1.1.1 not 2.1.1 IVB.4.1.3: remove comma after precision.	IVB.1.4 removed written report requirement from this section and moved to IVB.2.1 IVB.2.1.1.2 corrected to reference 2.1.1.1 IVB.4.1.3: removed comma after precision.
4	Section IVB.1.1: Consider removing "conclusions" from this clause. Method validation provides objective evidence that a method performs at a level predefined as being ""adequate for use". Conclusions (or more appropriately, "interpretations") are made from the data and are outside of what is "fit-for-purpose". Proper interpretation has to do with an individual's training and understanding of the limitations of a validated method.	Agreed: "and conclusions" has been removed from IVB.1.1.
5	Section IVB 1.2.1.1: As written, this implies that if a laboratory uses a method published in a journal that was previously validated (to some unknown standard) that the lab must only verify the performance and not conduct a full validation. Is that the intent? Generally, verification is only allowed when following a standard test method. See Section 4.2 of the reference EURACHEM document for support of this concept.	No change. Section IVB 1.2.1.1: It is not the intent to allow any published method to simply be verified in the end-user laboratory. As written, IVB.1.2.1.1 requires the analytical method to have been validated and the results are available for reference.
6	Section IVB.1.2.1.2: The use of the term "significant" is subjective. I recommend that full validation must be done if the laboratory modifies the previously published method.	Section IVB.1.2.1.2: Agreed that the use of the term "significant" is subjective. This was intentional to allow for expected and reasonable changes to a method that would not require a full method validation. For example, if the column stationary phase is changed from an HP-5 to a DB-5, the change to the method is insignificant and method verification would be justified. IVB.1.2.2. has been edited to include a requirement to perform a method validation should the method verification testing demonstrate the change to the method resulted in the method not performing as expected.
7	Section IVB.1.4: Consider adding a requirement that the written validation report shall compare the results of the validation study to the pre-defined criteria documented in the validation plan (Section IVB.2.1.3).	Section IVB.1.4: No change as the requirement to evaluate each performance characteristic identified in the validation plan (Section IVB.2.1.3) to determine if the method is fit for purpose is already present in Section IVB.2.1.6.
8	Section IVB.1.4.3.3: Again, the use of a subjective term - "regularly". Why not define that if the same deviation or modification is made more than 3 times, the modification must be validated? Otherwise, this becomes an argument as to how it should be interpreted.	Section IVB.1.4.3.3: Agreed that "regularly" is subjective. For this recommendation, SWGDRUG prefers to not set a prescriptive requirement to allow for flexibility and for each laboratory to establish a risk-based approach to these scenarios.
9	Section IVB.2.1.3: Consider requiring the validation plan to pre-define what acceptable performance looks like for the method. It needs to document what is going to be considered as "acceptable" performance vs "unacceptable" performance for each of the validation parameters that will be evaluated.	Section IVB.2.1.3: Added the sentence "If specific method performance is required, consider defining acceptance criteria for the applicable performance characteristics."
10	Section IVB.2.1.10: Consider including a requirement to compile this information together in one location for easy retrieval and review. If scattered around on different instrument systems, there is a significant risk of losing data when instruments are replaced and validation data needs to be retained even after a method is retired from service.	Not persuasive. IV.2.1.10 is the minimum requirement for retention of data, the document is not intended to be prescriptive on how laboratories maintain their data.
11	Section IVB.3: Performance Characteristics: I again suggest that not only do the performance characteristics to be evaluated need to be identified, but predefined criteria as to what is considered as "acceptable" for each parameter must also be declared to know how to evaluate the validation data that is generated.	Not persuasive. However, a sentence was added to section IVB.2.1.3 stating that "If specific method performance is required, consider defining acceptance criteria for the applicable performance characteristic." In addition, IVB.3, the introduction was modified to clarify that acceptance criteria are dependent on the method, the intended use of the method, and the samples it is expected to handle.

12	Section IVB.3.1.2: Precision is typically a quantitative evaluation (see EURACHEM reference Table 3). It is odd to include this requirement under qualitative methods.	Not persuasive. Section IVB.3.1.2: Table 3 in the EURACHEM reference requires only selectivity testing for validation of a qualitative method. SWGDRUG has determined that testing of additional performance characteristics, including testing of the reliablity of the method, is warranted to validate a qualitative method. The glossary section of the SWGDRUG guidelines defines precision and adds the terms for short term precision, intermediate precision, and long term precision. Although a numerical value may not be assessed for all qualitative methods, the reliability over varied conditions is appropriate testing to conduct during method validation.
13	Section IVB.3.1.2.3, 3.1.2.4, and 3.1.2.5: These parameters seem to address "robustness" and not "precision".	Not persuasive. Section IVB.3.1.2.3, 3.1.2.4, and 3.1.2.5: The variables discussed in these sections are included within the terms short term (repeatability), intermediate (ruggedness) and long term (reproducibility) precision, defined in the glossary section under "precision". Robustness, as defined in the glossary, refers to variations in the internal method parameters, not factors external to the method.
14	Section IVB.3.1.3: Consider retitling this to Limit of Detection.	Not persuasive. Section IVB.3.1.3: This section is intended to establish the range over which the method may be used. The limit of detection (LOD) is one component of the operating range, but not the only factor to consider in this section.
15	Section IVB.3.1.4.1: As written, this is vague as to the expectation. How many different sample matrices are the minimum to analyze to assess the impact of matrix effects?	Not persuasive. SWGDRUG's practice in the minimum recommendations is to not set arbitrary numerical values, such as the suggested minimum number of matrices to test. The vague nature of the requirement was selected intentionally to allow for flexibility and to allow those matrices included in the method scope and encountered in casework to be evaluated.
16	Section IVB.3.2: Shouldn't a statement be made about establishing metrological traceability in this section?	Section IVB.3.2: In response to the comment about traceability, a sentence was added to section IVB.2.1.5 stating "Metrological traceability shall be considered where applicable."
17	Section IVB.3.2.4: Consider removing the term "sensitivity" and use "LOD" for this section.	Not persuasive. Section IVB.3.2.4: Sensitivity, as a measure of instrument response for a given amount of material, is a useful performance characteristic to measure in quantitative method validation and is in alignment with the objective of Section IVB.3.2.4. The limit of detection (LOD) is one component of the operating range, but not the only factor to consider in this section.
18	Section IVB.3.2.4.3: I am not sure that reporting "estimated numbers" under the LLOQ is appropriate. Why not indicate that you can report something as "less than" the lowest calibrator?	Section IVB.3.2.4.3: Reworded section to state "The limit of detection shall be established if the laboratory permits threshold reporting below the lower limit of quantitation (e.g., THC present at less than 0.001 mg/mL)."
19	IVB.3.1.3: "...that can be analyzed used the method." Change to "...that can be analyzed using the method."	IVB.3.1.3: grammatically corrected by changing "used" to "using"
20		N/A
21	IVB.2.1.1.2 should reference the previous section IVB2.1.1.1. (The final 1, is missing from the reference.)	IVB.2.1.1.2 corrected to reference 2.1.1.1
22		N/A
23	I strongly recommend a complete revision of the chapter IVB.3 . The use of some terms is incorrect, or at least very unusual. There should also be an orientation towards general validation guidelines (e.g.the EURACHEM Guide, which is listed here under References) for the ISO-regulated area. Below I have listed some of the points that particularly caught my attention: IVB.3.1 It does not make sense to list the "precision" parameter in IVB.3.1 (Qualitative). Precision is generally associated with quantitative values. It should therefore be dealt with exclusively in IVB.3.2. E.g. definition in "International vocabulary of metrology – Basic and general concepts and associated terms (VIM) :"precision: closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions"	Not persuasive. IV.B.3.1 The SWGDRUG glossary cites a precision definition from ISO 3534-2:2006 similar in scope to the reviewer's definition. The SWGDRUG glossary entry continues with a discussion of other aspects of precision, specifically short term, intermediate and long term precision, which are valuable to explore for qualitative methods. Part IV.B.3.1 reflects this value by requiring a study of these aspects of precision during a qualitative method validation study.

24	IVB.3.2.3 Accuracy: Accuracy should not be used here. Use "Trueness" instead, according to the usage in the ISO and IUPAC environment. Accuracy is only used in this meaning in the GxP regulated area.	Persuasive. IVB.3.2.3 The reviewer is correct that use of the word "Accuracy" in this section by stating "agreement of experimentally measured results with the true concentrations of reference solutions" is better described as "Trueness" instead. IVB.3.2.3 term "accuracy" changed to "trueness". In addition, trueness was substituted for accuracy in IVB.4.1.2
25	IVB.3.2.4 Sensitivity is not a validation parameter described in other guidelines. This makes no sense and should be deleted here.	Not persuasive. IVB.3.2.4 Sensitivity is defined in the SWGDRUG glossary citing a UNODC document. It characterizes this measure as the gradient of the instrument response to the amount of measurand. For a quantitative method there is value in establishing how responsive the method is to an analyte and it is recommended to include a sensitivity study in a quantitative method validation along with determining the shape of the response curve and establishing the operating range of the instrumental method.
26	IVB.3.2.5 Matrix Effects It also does not make sense to define matrix effects as individual parameters. It would be better to validate the robustness as usual. This would also include the matrix effects, but also other parameter, such as pH and temperature change..	Not persuasive. IVB.3.2.5 Matrix Effects are important in seized drug submissions and should be explored separately, where appropriate, to mimic the expected matrices submitted to the laboratory. Robustness studies deliberately change internal method parameters and would not assess matrix effects. Ruggedness may be broadened in scope to include matrix effects, but they are not specifically required by the definition. Attention is drawn to ensuring matrix effects are considered during method validation by listing it as a separate performance characteristic.
27	1. Section IVB.1.1.1 “Method validation occurs after a method is developed and documented, but before it is put into use analyzing casework.” Recommendation: Suggest to rephrase the sentence to "Method validation occurs after an analytical method is developed and documented prior to using the validated method for casework."	Perusasive. 1. Section IVB.1.1.1 incorporating part of the suggestion, changed to "Method validation occurs after a method is developed and documented, but before being used in casework"
28	2. Section IVB.1.2.1.2 “the validated analytical method is being used without significant modification.” Recommendation: Suggest to include some examples of significant modification such as modification to oven temperature or flow rate for LC methods. To also include a statement to remind laboratories to assess the significance of modification.	2. Section IVB.1.2.1.2 the suggestion to incorporate examples of a significant modification has merit. However, in the SWGDRUG recommendations, the number, type and scope of possibilities is too numerous and is a better fit to be explored in a Supplemental Document in which examples can be fleshed out. Regarding the suggestion to assess the significance of the modification, IVB.1.2.2 discussing method verification was modified to state "If these conditions are not met, *or the method is not found to perform as expected when compared to the method validation results,* method verification is not appropriate and a method validation shall be performed." This clause is intended to direct the laboratory to do a method validation if the change were too significant.
29	3. Section IVB.1.4.1 to IVB.1.4.3 contains information about what should be included in a validation report. Recommendation: It is more appropriate to mention the information present in IVB.1.4.1 to IVB.1.4.3 in Section IVB.2 Documentation.	3. Section IVB.1.5 to IVB.1.7 (formerly IVB.1.4.1 to IVB.1.4.3 in public comment draft) contains information about additional testing, case documentation, data, and appendices to validation documentation if changes are made to the method. Each section has the requirement to keep and append additional documentation to the original validation report.
30	4. Section IVB.1.4.3.1 “Case documentation shall include sufficient quality control samples and practices...” Recommendation: To specify "quality assurance practices" instead of "practices"	Persuasive. 4. Section IVB.1.7.1 (formerly labelled IVB.1.4.3.1 in public comment draft) "quality assurance" added to "practices".

31	5. Section IVB.2.1 “An analytical method validation report...” Recommendation: This section talks about validation and verification of methods. Suggest to change to "method validation/verification".	5. Section IVB.2.1 The section describes method validation documentation requirements. Section IVB.1.4 has been edited to add method verfication to the requirement to document and retain the results and conclusions. Because all of the requirements listed in IVB.2.1 are not applicable to method verifications, the modification was not made in the section the public commenter suggested, but in a previous section to clarify that method verifications do have a documentation requirement.
32	6. IVB.3.1.2.3 “Evaluate the effect of different operators, if the method will be routinely operated by more than one analyst.” Recommendation: To rephrase to "If the method will be routinely used by several operators, evaluate the effect of different operators." to be consistent with the sentences in IVB.3.1.2.4 and IVB.3.1.2.5.	Persuasive. 6. IVB.3.1.2.3 Harmonized style of wording with sentences in IVB.3.1.2.4 and IVB.3.1.2.5.
33	7. IVB.3.1.3 “Operating range – Evaluate a range of sample concentrations or amounts that can be analyzed used the method.” Recommendation: Grammar- To amend “used” to “using”	Persuasive. 7. IVB.3.1.3 Corrected Grammar: “used” to “using”
34	8. IVB.3.1.5 “Additional performance characteristics…” Recommendation: Suggest to provide examples of additional performance characteristics such as robustness, carryover, stability of target analyte.	Persuasive. 8. IVB.3.1.5 Added examples of carryover or stability of analyte.
35	9. IVB.3.2.6 Additional performance criteria… Recommendation: Suggest to amend “criteria” to “characteristics” and give examples of additional performance characteristics such as robustness, carryover, stability of target analyte.	Persuasive. 9. IVB.3.2.6 Changed “criteria” to “characteristics" Examples reiterated from IVB.3.1.5
36	10. IVB.5.4 “Quality Control and Uncertainty.” Recommendation: To specify “Uncertainty (Measurement)”	Not persuasive. 10. IVB.5.4 Uncertainty of measurement not added to this term. Qualitative uncertainty could include method limitations such as a positional isomer limitation and would be precluded by the term uncertainty of measurement.
37	11. IVB.5.5.2.2 “To the method validation report(s).” Recommendation: To consider amending to “method validation/verification”	Persuasive. 11. IVB.5.5.2.2 added "or verification” to the types of reports analyst needs to be responsive to in court.
38		IVB.3.1.2.1 and IVB.3.1.2.2. the term "standard" was changed to "reference material". Editorial change, no change to the intent of either clause.
39		Added references for method validation
40		N/A

	Feedback for changes to Annex A - SWGDRUG Glossary of Terms and Definitions	SWGDRUG Response
1		None
2	None	N/A
3	Using definitions from the upcoming ASTM E2549 is a valuable addition. This ASTM document was extremely valuable in recent method validations performed by my laboratory and harmonized many of the varying definitions found across publications.	SWGDRUG strives to provide guidance in line with published standards, when appropriate. This year, ASTM E2549 is not currently available, so references to that standard have been removed
4		None
5		None
6		None
7		None
8		None
9		None
10	1. General comment- “Discussion” used in the glossary section can be revised to “Note” as the word “Discussion” seems to imply that the information is meant for an exchange of ideas and is not confirmed. 2. General comment- To include the definitions of equipment and instrument. Suggest to make reference to ISO documents. 3. A.2.46 “range the analyte concentration or sample amount limits for which the method is applicable; this is also referred to as the working range.” Recommendation: To revise to operating range instead of working range as the term operating range was also used in IVB.3.1.3	1.There are six (6) instances of the use of DISCUSSION in the glossary section and numerous NOTES. To address what these are intended to convey, the introductory paragraph of Annex A now includes what is meant by these terms. 2. section IVA.7 Instrument/Equipment performance listed, but no definitions are given for either term. Added 2 definitions to Annex A from ASTM E3255 for each EQUIPMENT and INSTRUMENT 3. Throughout Part IV B "QA/Validation..." Operating range is the preferred term. The glossary definition was updated to reflect operating range instead of working range.
11		None