| Name of organization or individual* | Line from* (line Nr or 0 for general comment) | Line to* (line Nr or 0 for general comment) | Section number | Comment and rationale (to go to next line within the same cell use Alt + Enter) | Proposed changes / recommendation (if applicable - to be used if you want to propose specific text changes) |
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| IPAC-RS | 0 | 0 | | General comment on "reference procedure": it seems that a multivariate development is possible only using a pre-existent validated procedure (reference procedure), so that a multivariate approach is possible only where prior knowledge is available (i.e. as part of control strategy lifecycle management) | Please clarify |
| IPAC-RS | 0 | 0 | | Guidelines refers to many statistical concepts that require a certain expertise | References and a bibliography, that can be used to support statistical concepts will be helpful both in the guidance and in training materials. |
| IPAC-RS | 1 | 659 | | General comment: glossary is too extensive - some principles could be included in the core documents (Q2 or Q14) | |
| IPAC-RS | 32 | 32 | 1 | Its not 'the' SST | change 'the' to 'a' |
| IPAC-RS | 59 | 72 | 3 | Table 1: "Suitability of calibration model" should be tested. However, looking to section 4.2.1.3 / line 256 the term “Calibration model” is solely used for multivariate procedures. In the whole remaining document only "response" in terms of linearity (4.2.1.1 line 226) is used. In Table 1 below "working range" only "suitability of calibration model" is listed, which is not connected to linearity over the whole document (often needed e.g., for ordinary impurities NCE). | implement “response” instead of "Suitability of Calibration model" in table 1 in line “working range” to cover the general approach; Implement "response" instead of "Validation of Calibration model" in Figure 2 (line 657) |
| IPAC-RS | 59 | 72 | 3 | Last row “Precision”: the “-“ and “+” entries are repeated for repeatability and intermediate testing, although there is no difference. | No repetition necessary. |
| IPAC-RS | 67 | 67 | 3 | Reference to Inherent justification: mainly appropriate for specificity. However, the footnote, table 9 (line 679) and table 6(line 670) point out that such justification might be also appropriate for other characteristics, such as range (linearity for 1H-NMR) and/or accuracy (for particle size distribution). It would be helpful to add the term inherent justification also in the respective sections response (range) and accuracy to allow this possibility (as in line 171 for specificity) | Add section 4.2.1.4. Inherent justification might be appropriate (e.g. NMR and e.g. titrations); Add section 4.3.1.4 Inherent justification might be appropriate (e.g. instrument qualification e.g. particle size) -> new 4.3.1.5. recommended data; Add definition in the glossary |
| IPAC-RS | 69 | 70 | 3 | Footnotes 3 and 4 appear to have the text transposed - i.e. the text against footnote 3 should be against footnote 4 and vice versa (as footnote 3 is supposed to relate to specificity and footnote 4 to accuracy and precision). | (3) lack of specificity of one analytical procedure could be compensated by one or more other supporting analytical procedures. (4) a combined approach can be used alternatively to evaluating |
| IPAC-RS | 74 | 76 | 2 | Mentions documenting and justifying objective, performance characteristics and criteria of procedure - is this a good place to introduce ATP? | Could introduce ATP in Section 3 |
| IPAC-RS | 92 | 93 | 3.1 | "Co-validation can be used to demonstrate that the analytical procedure meets predefined performance criteria by using data from multiple sites." -> Co-validation might also be used in the context of analytical procedure transfer" | Co-validation can be used to demonstrate that the analytical procedure meets predefined performance criteria by using data from multiple sites **and can also be used for the transfer of analytical procedure**". |
| IPAC-RS | 95 | 95 | 3.1 | No reference to the term bridging studies | Referencing bridging studies further in the main guideline and providing examples of these studies in training materials will be helpful |
| IPAC-RS | 96 | 97 | 3.1 | cross validation is not exemplified. Can we use it for concomitant validation of online and offline methods ? | The cross validation could be used in the context of simultaneous validation of an on/it/atline and an offline method. |
| IPAC-RS | 99 | 101 | 3.2 | The text says "The reportable range is confirmed by demonstrating that the analytical procedure provides results with acceptable accuracy, precision and specificity." "specificity was probably placed in leu of "linearity" Please adapt text | Proposed adaptation: "The reportable range is confirmed by demonstrating that the analytical procedure provides results with acceptable accuracy, precision and **linearity**" |

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| IPAC-RS | 107 | 107 | 3.2 | Table 2: Low end of reportable result changed from -20 % (ICH Q2 R1) to "Q-45 % (immediate release) of the dosage form strength first measurement time point or QL (modified release)". Is that harmonized with other guidelines (e.g., USP)? The wording Q-45% (immediate release) of the dosage form strength first measurement timepoint or QL (modified release) is ambiguous. It is unclear whether the words "first measurement timepoint" belongs to immediate release formulation or to modified release formulations. | Proposed change: For Column "Low end reportable range":<br>1. Dissolution Immediate release (IR) -- One point specification: Q-45% of the dosage form strength -- Multiple point specification and/or dissolution profiles: Q% value of the first measurement timepoint must be included in the reportable range. 2. Modified release (MR): Multipoint specification: Q% value of the first measurement timepoint must be included in the reportable range (extended release (ER)) Quantification limit (QL) (delayed release (DR)). 3. Dissolution profiles: Q% value of the first measurement timepoint must be included in the reportable range |
| IPAC-RS | 107 | 107 | 3.2 | Table 2: Purity testing (as area %): 80 % of specification limit to 100 % of specification limit. Please define what kind of procedures are meant. Applicable for limit tests? Could be mixed up with 100 % peak area normalization (area %) for purity testing (range RTh-120 % of sample weight). | Clarify objective of the Purity testing (as area %)-> for NBE charge variants? Clarify difference working range vs. Reportable range!<br>Include an example to Annex 2 for a dedicated assay method |
| IPAC-RS | 107 | 107 | 3.2 | Table 2: "Assay of a drug substance or a finished (drug) product": not clear which analytical procedures fall into this category. | Include an example to Annex 2 for a dedicated assay method |
| IPAC-RS | 108 | 116 | 3.3 | Stability indicating properties as shown in table 5 (line 669), demonstration of stability indicating properties through appropriate forced degradation samples, is not necessary for dissolution testing (i.e., performance tests). It would be helpful to state this in the general section 3.3. (line 108) | Add clarification: Demonstration of stability indicating properties through appropriate forced degradation samples, is not necessary for performance test. |
| IPAC-RS | 108 | 116 | 3.3 | Demonstration of stability indicating properties, mentions use of physical and chemical stress conditions but does no mention ICH Q1A or B. | Add reference to ICH Q1A and B. Would also need to add to line 654 if mentioned as references. |
| IPAC-RS | 109 | 116 | 3.3 | Some procedures are stability indicating per design ex: the quantitative measurement of a degradation product. In that case performing challenges (degradation,…) does not add value as long as the procedure has been demonstrated to be accurate. | Proposal to add after the section:<br>"In some cases, and depending on proper justification as well as validation of other parameters, the demonstration of the stability indicating capacity of a procedure is not necessary. For instance the demonstration of specificity, accuracy, precision, and linearity of a procedure used for the quantitative determination of an impurity can be sufficient to ensure tat the procedure is stability indicating. |
| IPAC-RS | 118 | 510 | | There are many areas that are written using highly specialized language, without much clarification or any other help for the average target reader of these guidelines. | Recommend text simplification and/or clarification, especially in the following lines.<br>118-134<br>238-240<br>251-255<br>293-297<br>359-368<br>407-410<br>451-456<br>506-510 |
| IPAC-RS | 121 | 122 | 3.4 | A model is also possible with several inputs and more than one attribute | The multivariate calibration model relate the input data to one or more values for the property of interest (i.e., the model output). |
| IPAC-RS | 136 | 137 | 3.4.1 | Double "require" and "should have" | either "require" or "should have" |

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| IPAC-RS | 157 | 159 | 4.1 | test can not minimize interference but show if there is interference or not --> you cannot minimize the interference, you can only show if interference is present --> sentence is not clear | Proposed rewording:<br>However, during the development of the procedure, the potential interference should be minimized in order to obtain a procedure tat is fit for purpose. |
| IPAC-RS | 187 | 213 | 4.1.4.2 | The topics at Lines 200 and 209 would benefit from having information presented earlier in the document at lines 111-116 repeated here to ensure that the reader is aware that this aspect from earlier in the document is applicable here. The suggested place to repeat the test is between lines 198 and 199 (repeated text from earlier in the document indicated in red in the next cell in the context of the preceding and following sentences) | 195 In case a single procedure is not considered sufficiently selective, an additional procedure should be used to ensure adequate specificity. For example, where a titration is used to assay a drug substance for release, the combination of the assay and a suitable test for impurities can be used.be used.<br>To demonstrate specificity/selectivity of a stability indicating test, a combination of challenges should be performed with appropriate justification from development studies. These can include: the use of samples spiked with target analytes and all known interferences; samples that have been exposed to various physical and chemical stress conditions; and actual product samples that are either aged or have been stored at higher temperature and/or humidity.<br>199 The approach is similar for both assay and impurity tests: |
| IPAC-RS | 214 | 218 | | ~~c.~~ It is ~~would be~~ important to clarify the range categories (especially working range) and how they link to development & validation. Positioning in ICH Q2(R2) would be the best option. | Propose addition to 4.2 line 218.<br>"In most cases the reportable range is identical or corresponds directly (when considering the effect of dilution) to the validated working range. However in some cases the reportable range can be wider than the corresponding validated working range. This is the case when additional alternative samples dilutions are planned to be used in a procedure and in order to accommodate the fact that some samples may fall outside of the validated working range when applying the initial sample dilution. This means that the validated working range of the procedure is too narrow when compared to the amplitude of product specification. In that case the alternative samples dilutions proposed must be validated by demonstrating that method performances are acceptable whatever the planned dilutions applied to the samples. Another case is encountered when validating purity assays and when a sample at 100% purity is not available in order to cover experimentally the higher part of the product specification range. The validated working range will cover (at least) the lower product specification but will be limited to the % purity of the sample presenting the highest purity % and which is available at the moment of the validation. In that case, and upon appropriate justification, the reportable range will be extended to 100% of purity while the validated working range will be limited to the highest % purity for which the analytical procedure has been experimentally demonstrated to have a suitable level of precision, accuracy and linearity." |

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| IPAC-RS | 219 | 265 | 4.2.1 | Why replacing "Linearity" with "Response". The idea to add a text on non-linear model is good and the proposed approach to validated the linearity of results is good but it could be extended to linear quantification models as well. This would proved a very simplified and unified approach for both linear and non-linear model. Regarding the fitness of the quantification model, this should be addressed in ICH Q14 as part of method development. | Proposal to structure the section like this:<br>4.2.1 Linearity.<br>Then do not discriminate between 4.2.1.1/2/3<br>In the text explain that several quantification models can exist and must be developed to be fit for purpose (see ICH Q14) and the explain that in any case linearity evaluation must be performed at the level of the results (linearity of results) by comparing average measured results and theoretical results. |
| IPAC-RS | 238 | 240 | 4.2.1.1 | It is not clear in which cases scedasticity should be evaluated. In many cases (especially with non-complex matrices for small molecules analytics), scedasticity evaluation is not needed. The validation model is appropriately evaluated by accuracy testing. In cases of accuracy testing fails, scedasticity evaluation might be beneficial. | Clarify in which cases scedasticity evaluation might be beneficial (e.g., with complex matrices and not being able to test for accuracy by spiking). However, this should be decided upon by companies during development (whether evaluated or not). |
| IPAC-RS | 238 | 242 | 4.2.1.1 | Not clear what is meant by 'Other approaches should be justified' on line 238, also duplication with line 242 | remove 'Other approaches should be justified' from line 238 and maybe also on line 242 |
| IPAC-RS | 262 | 264 | 4.2.1 | “Linearity assessment, apart from comparison of reference and predicted results, should include information on how the analytical procedure error (residuals) changes across the calibration range “ --> the use of the word "Linearity" can be confusing and restrictive | Look at the homoscedasticity of normalized residuals |
| IPAC-RS | 272 | 273 | 4.2.2.4 | The text here 'Signals in an appropriate baseline region can be used instead of blank samples.' would benefit form having reference to regional guidance added as there is a pending release of USP<621> which requires the use of blank samples, whereas other regional guidance have alternate wording. Recommend to add the text in the adjacent cell to ensure that users also refer to relevant regional guidance in addition to ICH (as regional guidance is referenced elsewhere in ICH guidelines this would not be atypical) | Signals in an appropriate baseline region can be used instead of blank samples. Refer to regional pharmacopoeias for regional expectations. |
| IPAC-RS | 276 | 285 | 4.2.2.1 and 4.2.2.2 | "For quantitation limit, a ratio of at least 10:1 is considered acceptable" & "QL=10sigma/S", ~~I know that it is commonly used but it doesn't make sense to me.~~ Using DL=3.3sigma/S is a preferred option ~~make sense~~ (sigma being obtained considering a normal distribution) because ~~has it means that~~ statistically it is highly probable that a signal beyond 3 sigma can't be attributed to the noise of the method.~~.. but Why 10sigma means that you Quantify correctly?~~ | The proposed QL strategy is~~ remove this strategy for QL,~~ only applicable for DL. QL is addressed by the accuracy and precision that must be demonstrated across the reportable range (line 327) |
| IPAC-RS | 308 | 308 | 4.2.2.4 | inconsistent notation: the text 'signal to noise' is not hyphenated - update as per the adjacent cell to be consistent with the rest of the document | 308 determined based on visual evaluation or based on signal-to-noise ratio, |
| IPAC-RS | 320 | 415 | 4.3 | There is no reference to replication strategy / assay format and the link with procedure performance (specifically with precision).<br>This section should express the requirement to evaluate precision data in the assay format corresponding to the replication strategy selected for the procedure.<br>It should also explain that it is acceptable to perform the validation studies using an assay format that is different from the final replication strategy but, in that case, the results of the validation - and specifically of the precision - must be expressed (after calculation) in the final assay format corresponding to the selected final replication strategy. | Proposal to add the following text:<br>"4.3.4 Replication strategy<br>The results of Precision must be representative of the replication strategy / assay format selected for the procedure as the final result of a procedure can be calculated as an average of several intermediate results. It is acceptable to perform the validation using a replication |
| IPAC-RS | 324 | 324 | 4.3 | ICH wording for analytical method characteristics not aligned with USP (i.e., accuracy as trueness) | ~~It may be too ambitious, but as it is a major review of the ICH document, could it be considered to take this opportunity to A~~lignment of wording with other international guidances, on ~~such as USP ? For instance,~~ trueness vs accuracy, for example with USP, is recommended. |
| IPAC-RS | 324 | 347 | 4.3.1 | There is no mention in the Accuracy paragraph of Relative Accuracy to be used for example in Potency assay or assay where accuracy cannot be established via an orthogonal method (as an absolute value).<br>This case is however illustrated in an example provided in Annex 2 - Table 3 (right column), line 661. | Proposal to add the following text:<br>"4.3.1.4 Relative accuracy<br>In some cases it is not possible to determine an absolute expected value to compare measured results. Examples are potency assays |
| IPAC-RS | 341 | 347 | 4.3.1.3 | General comment: it could be useful to detail some requirements that could define an independent method to set the boundaries of orthogonality principle. (e.g. Different analytical technique or just different detector, etc..) | Please clarify the use of orthogonal procedures. Inclusion of examples in training materials will be helpful. |
| IPAC-RS | 344 | 344 | 4.3.1.3 | Wrong reference to independent procedure. | Please change reference to part 1.2 with part 4.1.2 |

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| IPAC-RS | 355 | 360 | 4.3.1.4 | Ambiguous language for Accuracy could be interpreted to mean that a 95% confidence on mean percent recovery or 95% confidence interval on difference is recommended/expected. | Split the first sentence into two sentences, which would allow either (1) difference between observed/expected and/or confidence interval on the %recovery |
| IPAC-RS | 356 | 358 | 4.3.1.4 | This represents a new requirement compared to ICHQ2(R1). Suggest changing 'should be' to 'can be' | change 'should be' to 'can be' |
| IPAC-RS | 370 | 375 | 4.3.2 | As a method validation is a **demonstration** that a method is fit for purpose, replace the word "investigation" by "demonstration" or something similar to it. Before method validation, we already know what kind of precision the method can provide. Otherwise, the activity would be a qualification of feasibility study. | Replace investigation by demonstration or a word of a similar meaning as demonstration. |
| IPAC-RS | 388 | 389 | 4.3.2.2 | Clarification proposed for "The use of design of experiments studies is encouraged." | Proposed adaptation:<br>"The use of design of experiments studies **to combine the examination of several effects** is encouraged. |
| IPAC-RS | 396 | 398 | 4.3.2.4 | Ambiguous reference to a confidence interval under recommended data for Precision | Add clarity to what level of confidence is requested, or remove confidence interval as a recommended result/data requirement |
| IPAC-RS | 398 | 400 | 4.3.2.4 | Remove confidence interval as this is a new requirement compared to ICHQ2(R1) | Remove confidence interval |
| IPAC-RS | 396 | 398 | 4.3.2.4 | Recommended data for Precision requires the upper CI for the CV. There is an impact on the n° of replicates to be performed in order to obtain a reasonable upper CI. | Better clarify the use of Confidence Intervals |
| IPAC-RS | 399 | 400 | 4.3.2.4 | "Additionally, for multivariate analytical procedures, the routine metrics of RMSEP encompass accuracy and precision". RMSEP = standard error of prediction.<br>More details needed to understand what it is and also more details or examples of multivariate procedures. | Further clarification of RMSEP and its use in multivariate procedures is required |
| IPAC-RS | 401 | 404 | 4.3.3 | Combined approach for accuracy and precision: "The approach should be reflective of the individual criteria that would have been established for accuracy and precision", not clear. The approach should be driven by consideration on the process and specifications. In some cases, we may not have precise individual requirements on accuracy and precision, but a requirement on total error | Refine the wording so as to allow a criteria on the total error not directly linked to individual criteria on accuracy and precision |
| IPAC-RS | 401 | 415 | 4.3.3 | No mention to Total Error concept, although it is defined in Section 5 (lines 590-593) | Add wording to Total Error in 4.3.3 |
| IPAC-RS | 425 | 599 | 5 | Glossary should include a definition of replication strategy. | Add replication strategy concepts and examples to the guideline and training materials as this is a key element of analytical procedures. |
| IPAC-RS | 430 | 433 | 5 | include that the sample prep is part of the analytical procedure + explain the impact of sample prep should be also evaluated during method validation | |

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|---|---|---|---|---|---|
| IPAC-RS | 434 | 650 | 5 | There is no requirement to include in a glossary the explanation of terms that are not used anywhere else in this guideline - superfluous and makes the document longer than it needs to be and more challenging to find terms that are actually included. If they are important definitions for terms used in other guidances then they should be included in the glossary of those. | Remove definitions of the following:<br>ANALYTICAL PROCEDURE ATTRIBUTE<br>ANALYTICAL PROCEDURE CONTROL STRATEGY<br>ANALYTICAL PROCEDURE PARAMETER<br>ANALYTICAL PROCEDURE VALIDATION STRATEGY<br>ANALYTICAL TARGET PROFILE (ATP)<br>CRITICAL QUALITY ATTRIBUTE (CQA)<br>ESTABLISHED CONDITIONS (ECs)<br>KNOWLEDGE MANAGEMENT<br>METHOD OPERABLE DESIGN REGION (MODR)<br>ONGOING MONITORING<br>PROVEN ACCEPTABLE RANGE FOR ANALYTICAL PROCEDURES (PAR)<br>QUALITY RISK MANAGEMENT<br>REAL TIME RELEASE TESTING<br>SAMPLE SUITABILITY ASSESSMENT<br>TOTAL ANALYTICAL ERROR<br>DATA TRANSFORMATION<br>INTERNAL TEST SET<br>MODEL MAINTENANCE<br>OUTLIER DIAGNOSTIC<br>REFERENCE SAMPLE<br>VALIDATION SET |
| IPAC-RS | 463 | 467 | 5 | co-validation should also include the notion of "initial" validation, not only a "re-validation" | |
| IPAC-RS | 516 | 517 | 5 | Recommendations on Precision expression in Section 5 are not fully aligned with those in 4.3.2.4 (line 396): variance, SD or CV vs SD, RSD(CV) and Confidence interval | Align recommendations in the two sections |
| IPAC-RS | 535 | 543 | 5 | Distinction between working range and reportable range is not very precise, where working range produces "meaningful" results. The examples often include "linearity" in working range. Examples for reportable range include detailing results that exceed specs but are accurate and precise at those levels. | Add distinguishing qualities to working range (as opposed to) reportable range and/or define "meaningful" results. |
| IPAC-RS | 600 | 600 | 5 | no definition of the term "multivariate" in the glossary | please add multivariate definition into the glossary |
| IPAC-RS | 642 | 644 | 5 | Reference procedure definition in the glossary section is not exhaustive (refer to the general comment on reference procedure) | Please clarify the role of a reference procedure during development |
| IPAC-RS | 657 | 657 | 7 | Figure 2: Please indicate which validation tests are mandatory to proof performance characteristics (e.g., by and/or). E.g., it is understood that for precision testing Repeatability AND Intermediate Precision AND (if >1 laboratory Reproducibility is needed. However, for specificity testing Absence of Reference OR Orthogonal Procedure OR Technology Inherent Justification should be needed. There is no difference for decision on quantification of impurities (red) and content/potency (yellow) determination. Could be depicted in one field instead of two. | Clearly define which validation tests are a "must" and which ones are "instead" testing. |
| IPAC-RS | 657 | 657 | 7 | In Table 1 (Line 58-59), for assay content/potency, no lower range limit verification is required. In Figure 2, the yellow path for content/potency goes to range without note/footnote that validation of range limits is not required. This could be explained by a footnote in the same way as the footnote for calibration model "* may not be needed for limit test" | Add footnote ** to "Validation of range limits": "** may not be needed for assay/content/potency testing. |
| IPAC-RS | 657 | 657 | 7 | Consistent wording in Table 1 (Line 58-59) would be helpful. Table 1: Working range – Figure 2: Range. Table 1: Suitability of calibration model – Figure 2: Validation of Calibration Model. Table 1: Lower range limit verification – Figure 2: Validation of Range Limits | Check for consistency in the entire document |
| IPAC-RS | 657 | 657 | 7 | Consistent wording in Chapter 4 would be helpful. Line 152 / 4.1 Specificity / Selectivity. Figure 2: Specificity (w/o selectivity). Line 167 / 4.1.2 Orthogonal procedure comparison. Figure 2: Orthogonal procedure verification | Check for consistency in the entire document |

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| IPAC-RS | 660 | 660 | 7 | Figure suggests that Orthogonal Procedures for accuracy and specificity are always required - they are not | Insert footnote to explain that orthogonal procedures are not always required |
| IPAC-RS | 664 | 664 | Table 3 | In the right column, for reportable range the text says "Validation of calibration model across the range". In this case it is not a calibration model (because result is a ratio without the use of a calibration standard). Proposal to adapt the text | Proposed adaptation: "Validation of **quantification** model across the range" |
| IPAC-RS | 660 | 687 | 8 | None of the examples is using the combined approach for accuracy and precision / total analytical error | Add at least one example using combined approaches for accuracy and precision / Total analytical error |
| IPAC-RS | 668 | 670 | 8 | In the final row of Table 5, the right hand cell would benefit from the addition of a reference to Table 3 to provide clarification of the reference. | Deliberate variation of parameters of the quantitative procedure, see separation technique (Table 3) |
| IPAC-RS | 672 | 672 | Table 5 | Accuracy, Spiking Study: This is better conducted using volumetric glassware rather than directly into a vessel | Change section Accuracy, Spiking Study: This is better conducted using volumetric glassware rather than directly into a vessel |
| IPAC-RS | 662 | 662 | | Reportable range: Validation of the reportable range | The wording "validation of calibration model across range" is confusing. Indeed the purpose of the method validation is not only to validate the calibration model. As example, the precision is not directly related to the calibration model. |
| IPAC-RS | 676 | 677 | 8 | "Intermediate precision<br>Comparison of measurements using the same procedure performed by another analyst on a different day." The word COMPARISON is not appropriate. What is assessed is variability | Adapt vocabulary to ICH Q2 definition |
| IPAC-RS | 686 | 687 | 8 | The content of the example from table 11 in Annex 2 is not clear/not aligned to the concept of ICH Q2 R2: what is described as intermediate precision in the example is reproducibility | adapt example |
| IPAC-RS | 686 | 687 | 8 | "Measurements of the same samples performed in the same laboratory but under varying conditions (e.g., different LC/MS systems, different analysts, different days). ' instead of 'Comparison of measurements of the same samples performed in the same laboratory but under varying conditions (e.g., different LC/MS systems, different analysts, different days). " The word COMPARISON is not appropriate. What is assessed is variability | Adapt vocabulary to ICH Q2 definition |
| IPAC-RS | 686 | 687 | 8 | The items in row 1 of Table 11 relating to specificity/selectivity would benefit from the inclusion of 'OR' between the items listed (in line with the other points in the table) as the list is for options, not required to do all of them. Refer to adjacent text for suggestion in Red text | Technology inherent justification:<br>Inferred through use of specific and selective MS detection (e.g., MRM transition with specified quantitative to qualitative ion ratio, accurate m/z value) in combination with retention time, consider potential for isotopes<br>Or:<br>Absence of interference:<br>from other components in sample matrix.<br>Or:<br>Orthogonal procedure comparison:<br>By comparison of impurity profiles determined by an alternative validated method |
| IPAC-RS | 686 | 687 | 8 | Table 11 last row - the details provided are examples as they are not always included (the current way it is written is prescriptive rather than a suggestion/recommendation). In addition, as this covers LC in addition to MS, a reference to Table 3 which contains all the LC aspects would be beneficial. | Deliberate variation of parameters and stability of test conditions:<br>The following factors should be considered during assessment of analytical procedure performance: e.g. LC flow rate, LC injection volume, MS drying/ desolvation temperature, MS gas flow, mass accuracy and MS collision energy. (also note Table 3) |
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