# Regulatory Commenting Guidelines for Subject Matter Experts

1. If the guidance is a revision to a current guidance, focus comments on the new items in the regulation/ guidance rather than on the existing sections that remain unchanged (applies to documents which have been previously released by the agency). This is generally most relevant for EMA publications.
2. Comments need to be meaningful and specific. For example, a comment of "This is stupid" does not meet the criteria and will generally be eliminated from consideration.
3. Meaningful comments need to include sound justification for the proposed change as well as specific language that could be substituted for what the regulators propose. Comments that do not include a valid justification and proposed change will likely be omitted.
4. If the incorrect grammar in a document could result in a misinterpretation of the requirements, then please correct it. If not, and if there are many grammatical errors, a single suggestion that the "…grammar should be reviewed and edited as necessary prior to issuance of the final document" is an appropriate comment to be made one time.
5. Identify the line, section, or page number on which you are commenting, per the commenting form.
6. Write clearly and simply.
7. When making reference to other regulations/guidance, be specific and provide the official title and publication date where relevant either within the text or as a footnote.
8. Avoid comparing the document under consideration to a similar one published by another regulatory authority. While this is important to do internally within a company, it's generally not met with any favor by the regulatory authorities.
9. Check and correct grammar, punctuation and spelling before submitting for review. Your comments should be publication-ready when you are done.

Last updated January 2013

## 1. General comments

| Stakeholder number<br>*(To be completed by the Agency)* | General comment (if any) | Outcome (if applicable)<br>*(To be completed by the Agency)* |
|---|---|---|
| | It is suggested that the title of the document be adjusted to more closely reflect its purpose. It is suggested that the "Guideline on Process Validation" be changed to "Guideline on Process Validation Information to be Included in Regulatory Submission" or similar. | |
| | It would be desirable to have additional information about statistical expectations in PV (if any) included in Annex 15 when revised. | |
| | When Annex 15 is revised, it would be desirable to have terminology harmonized with ICH and FDA PV Guidance, where possible. Explanation of any intended differences would also be helpful. | |
| | It is suggested that the use of "continued" and "continuous" be clarified throughout the document: ISPE members are voicing concerns over mis-interpretation and recommend emphasising the differences. It may be helpful to create a separate section discussing implementation of advanced technologies for products already commercialized. It seems some of these are intermingled in other sections at present, which can be confusing. Using "advanced technology/PAT rather than "continuous verification" where appropriate may also improve clarity. | |
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## 2. Specific comments on text

| Line number(s) of the relevant text<br>*(e.g. Lines 20-23)* | Stakeholder number<br>*(To be completed by the Agency)* | Comment and rationale; proposed changes<br>*(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome<br>*(To be completed by the Agency)* |
|---|---|---|---|
| 112 -113 | | A control strategy contains elements more than critical process parameters (definition ICH Q10) and therefore suggest “which primarily includes critical process parameters” is redundant and should be deleted | |
| 133 | | Suggest change from “if a design space is implemented” to “if a design space is to be proposed in the dossier”. This is more consistent with purpose of the document – validation related information to be included in submission. Additionally, suggest a change from “should provide the validation strategy at production scale” to “should provide verification strategy to show the model is representative of full scale.” We consider models to be subject to verification not validation. The guide does not indicate validation expectations when a proposed design space does not use a model (in the chemometric sense) or where a design space is based on dimensionless attributes. We suggest “Similarly, where a design space is proposed that does not use a statistical model, the applicant should provide a verification strategy to show that the design space is representative of full scale.” | |
| 135 | | "Validation at production scale may be conducted step-wise..." We recommend to delete or revise this sentence. The extent of validation activity, if any, associated with movement within a design space should be commensurate with the science, risk and any control strategy modifications. Additionally, most design space movements would likely occur post-approval, which this guideline does not address. | |