

EUROPEAN FEDERATION OF  
PHARMACEUTICAL INDUSTRIES  
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**Ref.: JR.IC 52.509**

Dockets management branch (HFA-305)  
**FOOD AND DRUG ADMINISTRATION**  
5630 Fishers Lane, rm 1061  
Rockville,  
MD 20852

November 28, 2000

Dear Sir,

**EFPIA Comments on FDA Guidance for Industry "Analytical procedures and Methods validation"**

Please find enclosed the EFPIA comments with respect to the above-mentioned document.

Yours sincerely,

PP. 

**Dr Jürgen Reden**  
Manager  
Scientific & Regulatory Affairs

Encl.

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*EFPIA Comments*  
*on*  
*CDER Guidance for Industry: Analytical Procedures and Methods Validation; Chemistry, Manufacturing and Controls Documentation.*

*Draft Guidance; August 2000*

*Executive Summary*

- We object to this draft guidance, on principle, since guidelines that address this subject area have already been developed and agreed within ICH (i.e. Q2A and Q2B).
- We consider that these guidelines, in conjunction with others within the ICH matrix – principally Q3A & B; Q6A and Q7A - provide a more than adequate framework within which to develop regulatory submissions.
- Should the Agency, an ICH signatory, consider it necessary to revise these guidelines, then a proposal should be submitted via the appropriate ICH channels.
- Developing local, and in this case divergent, regulatory guidance documents compromises the ultimate goal of ICH – i.e. a harmonised regulatory framework.
- **Thus, we recommend that this guideline be withdrawn, not implemented, or refocussed on areas not covered by ICH.**

An illustrative selection of points of concern is presented below. **NB:** This list is not comprehensive, and is intended to illustrate some major points of divergence between the draft guidance and existing ICH texts.

<i>Line Number</i>	<i>Comment</i>
36	The principles in this guidance are not applicable for some pharmacopoeial procedures, (e.g. disintegration test).
113	We recommend the use of the text in <b>Q6A; Section2.7</b> .
139	<b>Q6A</b> states that a reference standard should “have a quality appropriate to its use”. The same wording should be employed here. <b>Q7A</b> contains definitions of both primary and secondary reference standards; these ICH definitions should be used.
164	Reference standards can be required to enable determination of impurities. Where a new reference standard is set up to replace one that has become depleted, acquiring all the physico-chemical data again is irrelevant.
323	<b>Q3A and B</b> describe adequately the treatment of impurities. Reporting limits are defined by ICH.
402	A polymorph is not considered as an impurity and is excluded by <b>Q3A</b> ; moreover <b>Q6A</b> addresses the need to control polymorphs.
436	<b>Q2B</b> only suggests that robustness data should be considered but not submitted.
439	The recommendations on stress studies in the recently approved <b>Q1AR</b> are appropriate. There is confusion here also about what is relevant to validate a method and what should be in the stability section. Stability should be only defined as in <b>Q1AR</b> .

1091	There could be significant differences in validation parameters (accuracy and precision) between an automated and manual method. <b>Q6A</b> discusses alternative procedures and evolving technologies; this guidance may lead to confusion as to what is the official regulatory procedure.
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It is accepted that the information included within Section X B/C of the draft guidance (i.e. selection and shipment of samples) provides additional information which is pertinent to local operational requirements. It is on this type of guidance that this document should focus.

There are many other concerns at the detail level which are not articulated here. Their omission does not mean they are not of concern also. However, we choose not to list them in order that the Agency may focus at the strategic level.