PDA
Parenteral Drug Association
Connecting People, Science and Regulation®

PDA Europe gGmbH
Georg Roessling, PhD
Sr. Vice President
Adalbertstr. 9
16548 Glienicke/ Berlin
Germany
Tel: +49 (0) 33056 2377-0
Fax: +49 (0)33056 2377-77
Email: roessling@pda.org
www.pda.org

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Martin VanTrieste
Amgen

31 May 2010

European Medicines Agency
Compliance and Inspection, London
ADM-GMP@ema.europa.eu

European Commission
Pharmaceuticals Unit, Brussels
entr-gmp@ec.europa.eu

Ref: EU Guidelines to Good Manufacturing Practice, Part 1
Medicinal Products for Human and Veterinary Use
**Chapter 1 Quality Management System**
Brussels, 18 November 2009
ENTR/F2/MT/AM/jr D (2009) 37658, 18 Nov 2009
Deadline for comments: 31 May 2010

To: Resp. Person: European Medicines Agency, Inspections Sector
Resp. Person: European Commission, Pharmaceuticals Unit

PDA is pleased to provide comments on the revised *Chapter 1 of the EU GMP,* dated 18 November 2009. Our comments were prepared by an international group of volunteer experts with experience in GMP and regulatory affairs. They consist of one general comment, mentioned below, and a series specific technical comments found in the attached EMA matrix format.

General comment:
While PDA understands the importance of incorporating ICH Q10 principles into Chapter 1, we believe it should be done with a balance in understanding ICH Q8, Q9 and Q10 are optional guidances. As such, it is desirable their incorporation into Chapter 1 should not result in heightening the legal requirements for the European GMPs.

The language used for mandatory GMP standards should be clear, concise and objective. However, some revisions of the Chapter have the tone and language found in guidance documents, thus being subjective and open to interpretation. In such cases it is unclear if GMP expectations can be consistently interpreted and followed by users (for example, section 1.1.i).

**Recommendation:** We have made appropriate recommendations related to the above comment in our specific comments below. We also recommend the Agency review the revised chapter and remove wording that is not a legal expectation but rather guidance, and rely on ICH Q10 as the source detailed guidance information.

If you have any questions please contact me, or James Lyda of the PDA staff (lyda@pda.org) who coordinated this project.

With very best regards,

Georg Roessling, Ph.D.
Senior VP, PDA Europe
Roessling@pda.org

cc: S. Mendivil, S. Rönninger, S. Schmitt, J. Lyda, R. Levy, R. Dana

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 May 2010

# Submission of comments on

## EU GMP Guide, Part 1, “Chapter 1 Quality Management System”

## ENTR/F2/MT/AM/jr D (2009) 37658

## 18 November 2009

## Comments from:

Parenteral Drug Association (PDA), Berlin Contact: James C. Lyda, lyda@pda.org

*Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.*

*When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).*

# 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)* |
|---|---|---|
| | **Comment 1.**<br>While PDA understands the importance of incorporating ICH Q10 principles into Chapter 1, we believe it should be done with a balance in understanding ICH Q8, Q9 and Q10 are optional guidances. As such, it is desirable their incorporation into Chapter 1 should not result in heightening the legal requirements for the European GMPs.<br><br>The language used for mandatory GMP standards should be clear, concise and objective. However, some revisions of the Chapter have the tone and language found in guidance documents, thus being subjective and open to interpretation. In such cases it is unclear if GMP expectations can be consistently interpreted and followed by users (for example, section 1.1.i).<br><br>**Recommendation:** We have made appropriate recommendations related to the above comment in our specific comments below. We also recommend the Agency review the revised chapter and remove wording that is not a legal expectation but rather guidance, and rely on ICH Q10 as the source detailed guidance information. | |

## 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)* |
|---|---|---|---|
| Principle,<br>3rd paragraph | | **Comment 2:**<br>The opening sentence states, "The scope of the guidance in this chapter applies to the technology transfer, manufacture and control and discontinuation of a product." The opening phrase includes the term "guidance" which is sometimes understood to be non binding. As this phrase is unnecessary, it can be deleted.<br><br>Proposed change (if any):<br>Revise opening sentence to read, ~~The scope of the guidance in~~ **T**his chapter applies to the technology transfer, manufacture and control and discontinuation of a product." | |
| Principle<br>4. paragraph | | **Comment 3:**<br>This section should be aligned with wording in ICH Q10 and in the ICH Q-IWG Q&A document.<br><br>Proposed change (if any):<br>…ICH Q10 as transposed in full into EU GMP as Annex 21 of the guide provides an example of **elements of** a pharmaceutical quality system designed for the entire product lifecycle and therefore goes beyond the expectations of this chapter… | |

| 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)* |
|---|---|---|---|
| 1.1. i)<br>p4 | | **Comment 4:**<br>The wording in this section is open to interpretation. The needs of patients and health care professionals, while valid concerns, are best not addressed through GMP standards. The section can be revised as below.<br><br>Proposed change (if any):<br>Reword this section as follows, "To establish, implement and maintain a system that allows the delivery of products with the **appropriate** quality attributes.<br><br>Delete the text, ~~appropriate to meet the needs of patients, health care professionals, regulatory authorities (including compliance with approved regulatory filings) and other internal and external customers~~. | |
| 1.1. ii) | | **Comment 5:**<br>This section should reference the wording in ICH Q9.<br><br>Proposed change (if any):<br>Revise the text as follows, "To develop and use effective monitoring and control systems for process performance and product quality, thereby providing assurance of continued suitability and capability of processes. Quality risk management **principles** can be useful in **assessment** ~~identifying the monitoring and~~, control and the **review and monitoring** of systems…" | |

| Line number(s) of the relevant text<br><br>*(e.g. Lines 20-23)* | Stakeholder number<br><br>*(To be completed by the Agency)* | Comment and rationale; proposed changes<br><br>*(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome<br><br>*(To be completed by the Agency)* |
|---|---|---|---|
| 1.2 | | **Comment 6:**<br>See General Comment 1. The wording, "...ensure confidence that…" is subjective.<br><br>Proposed change (if any):<br>Reword the section to delete the word confidence, "...as well as activities necessary to ensure ~~confidence~~ that the product..." | |
| 1.3 | | **Comment 7:**<br>This wording can be made more clear and concise.<br><br>Proposed change (if any):<br>Delete original text:<br>~~Senior management of the manufacturer should ensure that all parts of the Quality Management System are adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities.~~<br><br>Add replacement text:<br>**Senior management should ensure that all relevant departments contributing to quality management are adequately resourced** | |

| 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)* |
|---|---|---|---|
| 1.8 | | **Comment 8:**<br>There are two different sections marked "1.8", appearing on pages 4 & 5.<br><br>Proposed change (if any):<br>Correct the numbering system | |
| 1.8 (viii)<br>p4 | | **Comment 9:**<br>There should be notification of responsible management of deficiencies from regulatory commitments.<br><br>Proposed change (if any):<br>Modify text to read, "(viii) there are procedures for notifying responsible management in a timely manner of regulatory inspections, serious GMP deficiencies**, deviations regarding regulatory commitments (e.g. in submissions),** deviations, product defects and related actions (e.g. quality related complaints, recalls, regulatory actions, etc.)" | |
| 1.9 (iii) | | **Comment 10:**<br>GMP also suggests appropriate security of the manufacturing and storage areas.<br><br>Proposed Change (if any):<br>Add final bullet point to this list,<br>"**Appropriate security**" | |

| 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)* |
|---|---|---|---|
| 1.11 (viii) | | **Comment 11:**<br>The term 'exceptionally large' is not measurable, and will result in different interpretations. Final pack is the desirable sample packaging.<br><br>Proposed change (if any):<br>We suggest the following changes to the text in this section,<br>"(viii) sufficient reference samples of starting materials and products are retained to permit future examination of the product if necessary and that the product is retained in the final pack unless **otherwise justified.** ~~exceptionally large packs are produced~~. | |
| 1.14 | | **Comment 12:**<br>There is a potential conflict between this section and the requirements in the redraft of Chapter 7 of the EU GMP guide.<br><br>Proposed change (if any):<br>Revise the last sentence of opening paragraph of 1.14, as follows:<br>"These processes should incorporate the **principles** of quality risk management. **Refer to Chapter 7 of the GMP Guide for more information**."<br><br>Delete the balance of the text, items (a) thru (d). | |

| Line number(s) of the relevant text<br><br>*(e.g. Lines 20-23)* | Stakeholder number<br><br>*(To be completed by the Agency)* | Comment and rationale; proposed changes<br><br>*(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome<br><br>*(To be completed by the Agency)* |
|---|---|---|---|
| 1.19 | | **Comment 13:**<br>The phrase "experience with the process" is not included in ICH Q9. We recommend conformance with the wording in the Q9 text.<br><br>Proposed change (if any):<br>Revise the section to read, "...the evaluation of the risk to quality is based on scientific knowledge, ~~experience with the process~~ and ultimately links to the protection of the patient..." | |
| | | END | |

Please add more rows if needed.