

Draft



Final



Submission of EFPIA comments on Commission Implementing Act on Principles and guidelines on good manufacturing practices for medicinal products for human use, pursuant to the first paragraph of Article 47 of Directive 2001/83/EC

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1. General comments

EFPIA would like to express its strong concerns with regard to the potential duplication of GMP requirements in different sections or outside of EudraLex - Volume IV Good manufacturing practice (GMP) Guidelines. There is the need to maintain consistency across different parts of the guidance, which if not managed appropriately has the high potential to lead to divergences.

EFPIA recommends that all GMP requirements for different kinds of products - IMPs, ATMPs and commercial medicinal products will be posted in Eudralex Volume 4. A core set of common GMP principles is proposed to be referred to in Part I. Rather than duplicating these core requirements in separate sections (e.g. in part III or Annexes) addressing, for example, IMPs or ATMPs, EFPIA recommends that only the differences in the GMP requirements for these kinds of products and their development phase should be described. Emphasising these core principles will facilitate the common application within the company's pharmaceutical quality system, and consistency in inspections across these different kinds of products by the different agencies of the member states.

We agree that so far, the Directive 2003/94 has been well functioning. This update may benefit from aligning the terminology to the recent updates in EUDRALEX Vol. 4 (EU-GMPs) and by adding a glossary.

2. Specific comments on text

<p>Line number(s) of the relevant text</p> <p>(e.g. Lines 20-23)</p>	<p>Comment and rationale; proposed changes</p> <p><i>(If changes to the wording are suggested, they are highlighted using 'track changes')</i></p>
<p>67</p>	<p><u>Comment:</u> This requirement, if placed in the community code, could be misinterpreted that each time there is a new technique the manufacturer should change the process and consequently file variations. Therefore we suggest adding a sentence for clarification.</p> <p><u>Proposed change:</u> Manufacturer shall regularly review his manufacturing methods in light of scientific and technical progress. Risk benefit considerations shall drive the potential need for a change in the process.</p>
<p>132</p>	<p><u>Comment:</u> Allow implementation of ICH Q8(R2) / Q11</p> <p><u>Proposed change:</u> Ongoing process verification should be added as alternative to re-validation Proposed change: shall be regularly re-validated or subjected to ongoing process verification</p>
<p>188-198</p>	<p><u>Comment:</u> <i>As of the scope the ATMPs should not be covered by this document because of their specific characteristics and the different legal base. The reference here would produce problems.</i></p> <p><u>Proposed change:</u> <i>To delete point 2.13</i></p>
<p>41/42</p>	<p><u>Editorial Comment:</u> The full details of the reference are missing.</p> <p><u>Proposed change:</u> "By means of the repeated inspections referred to in Article 111(1a) of Directive 2001/83/EC, the Member States shall ..."</p>
<p>46</p>	<p><u>Editorial comment:</u> Minor typographical error.</p>

<p>Line number(s) of the relevant text (e.g. Lines 20-23)</p>	<p>Comment and rationale; proposed changes (If changes to the wording are suggested, they are highlighted using 'track changes')</p>
	<p><u>Proposed change:</u> "procedures on inspections"</p>
<p>71</p>	<p><u>Editorial comment:</u> We suggest adding a definition for a pharmaceutical quality system <u>Proposed change:</u> Management system to direct and control a pharmaceutical company with regard to quality (EUDRALEX Vol 4 (EU-GMP, Part III, ICH Q10) or <i>A pharmaceutical quality system means the total sum of the organised arrangements made with the objective of ensuring that medicinal products are of the quality required for their intended use. (Commission Delegated Act on Principles and guidelines on good manufacturing practice for investigational medicinal products for human use and inspection procedures, pursuant to the first subparagraph of Article 63(1) of Regulation (EU) No 536/2014")</i></p>
<p>109</p>	<p><u>Editorial comment:</u> Minor wording addition suggested <u>Proposed change:</u> "shall enable the history of the manufacture of each batch to be traced."</p>
<p>161</p>	<p><u>Editorial comment:</u> As updated terminology should apply throughout the new document, the title "Work contracted out" should also change. <u>Proposed change:</u> The title should change from "Work contracted out" to "Outsourced activities" to conform with the recently revised Chapter 7 of the GMPs</p>
<p>177-179</p>	<p><u>Comment:</u> The text should reflect other recent revisions in the GMPs. In the point 2.11 "Complaints and product recall", in line 177 to 179, it is written: "The manufacturer shall inform the competent authority of any defect that could result in a recall or an abnormal restriction on supply and, in so far as possible, indicate the countries of destination." In a recent revision of Chapter 8 (para. 8.15), it was introduced that in this case, the manufacturer should also inform the Marketing</p>

<p>Line number(s) of the relevant text (e.g. Lines 20-23)</p>	<p>Comment and rationale; proposed changes (If changes to the wording are suggested, they are highlighted using 'track changes')</p>
	<p>authorisation holder (MAH). The IA should coordinate with this requirement as well. <u>Proposed change</u> "The manufacturer shall inform the competent authority and the Marketing Authorisation Holder of any defect that could result in a recall or an abnormal restriction on supply and, in so far as possible, indicate the countries of destination."</p>
<p>183-184</p>	<p><u>Editorial comment:</u> In the point 2.13 "Self-Inspections" title, it is written: "The manufacturer shall conduct repeated self-inspections as part of the quality assurance system in order to monitor the implementation and respect of good manufacturing practice.....". Because of terminology update, the "quality assurance" should change. <u>Proposed change:</u> The manufacturer shall conduct repeated self-inspections as part of the quality assurance system Pharmaceutical Quality System in order to monitor the implementation and respect of good manufacturing practice....."</p>