EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO- OPERATION SCHEME

2 February 2015
EMA/INS/GMP/735037/2014
GMP/GDP Inspectors Working Group (GMP/GDP IWG)

8 January 2015
PS/W 1/2015

Concept paper on the revision of annex 1 of the guidelines on good manufacturing practice – manufacture of sterile medicinal products

Agreed by GMP/GDP IWG and PIC/S	January 2015
Start of public consultation	5 February 2015
End of consultation (deadline for comments)	31 March 2015

The proposed guideline will replace:

- 'Eudralex Volume 4: annex 1 manufacture of sterile medicinal products'
- for PIC/S participating authorities: PE 009-11: annex 1 - manufacture of sterile medicinal products

Comments should be provided using this template. The completed comments form should be sent to ADM-GMDP@ema.europa.eu

Keywords	GMP, sterile, annex 1

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1. Introduction

This concept paper addresses the need to update annex 1 (manufacture of sterile medicinal products) of the good manufacturing practice (GMP) guide. Annex 1 is common to the member states of the European Union/European Economic Area as well as to the participating authorities of the Pharmaceutical Inspection Co-operation Scheme (PIC/S)[1].The original version was partially revised in 1996, 2003 and 2007; however, there has not been a complete review of the document since it was originally issued. Since this time there have been changes in technologies and significant changes in GMP following the adoption of the ICH Q9 and Q10 guidelines.

The current annex 1 is therefore being reviewed in order to facilitate implementation of the principles in these ICH guidelines, to extend the underlying concepts to include new areas of technology and processing not previously covered and also to clarify areas that have been highlighted as ambiguous due to the age of the document.

The current guideline, including its title, is focused on the manufacture of sterile medicinal products. However, this annex is the only source of guidance in EU-PIC/S GMP for the conditions of manufacture of some non-sterile finished products and for the early stages in the manufacture of a range of products.

2. Discussion

Since annex 1 was published, introduction of the relevant ICH concepts and consequential regulatory changes and technological advancements are not reflected in the current GMP guideline. In addition, and in keeping with greater international convergence, opportunities will be taken where appropriate to align this guideline with international requirements. The opportunity will also be taken to ensure maintenance of coherence with other EU or PIC/S pharmaceutical guideline documents.

The current GMP guideline on the manufacture of sterile medicinal products was developed before the development of the ICH Q9 risk management concepts that offer a systematic approach to quality risk management, Q10 describes a modern quality system in order to establish and maintain a state of control, the realisation of product quality and to facilitate continual improvement over the entire life cycle.

The revised guideline will clarify to what extent Q9 and Q10 should be followed in the design and implementation of facilities, equipment and processes for the manufacture of sterile medicinal products. Other changes that may require new GMP guidance include those for the revision to the Ph.Eur. monograph on methods other than distillation for the production of water for injection.

Since the current guideline is used to provide guidance on the conditions of the manufacture of some non-sterile finished products and the early stages in the manufacture of a range of products, the revised guideline will also clarify these areas of applicability utilising quality risk management principles. The scope and title of the guideline should therefore be broadened to encompass these references. It is stressed that this is a clarification of current practices and that no new expectations will be created.

The current guideline does not reflect the advances in the manufacture of sterile medicinal products; the revised guideline will embrace the use of new technologies to prevent detrimental impact on product and also to encourage the introduction of new technologies that are not currently covered.

The current guideline contains historical inaccuracies and areas of ambiguity, the revised guideline will correct the inaccuracies and offer more detail to remove ambiguity and to give clearer interpretation of GMP expectations.

[1] For the complete list of the 46 PIC/S Participating Authorities, see http://www.picscheme.org/members.php

3. Recommendation

The GMP/GDP Inspectors Working Group and the PIC/S Committee jointly recommend that the current version of annex 1, on the manufacture of sterile medicinal products, is revised to reflect changes in regulatory and manufacturing environments. The new guideline should clarify how manufacturers can take advantage of new possibilities deriving from the application of an enhanced process understanding by using innovative tools as described in the ICH Q9 and Q10 guidelines.

The revision of annex 1 should also take into account related changes in other GMP chapters and annexes as well as in other regulatory documents. The revised guideline will seek to remove ambiguity and inconsistencies and will take account of advances in technologies.

4. Proposed timetable

Preparation of draft concept paper - September 2014
Approval of draft concept paper - October 2014
Released for consultation – February 2015
Deadline for comments – March 2015
Discussion in PIC/S Committee – May 2015
Discussion in GMDP IWG - June 2015
Discussion with other Working Parties - June 2015 – September 2015
Proposed date for release of draft guideline - October 2015
Deadline for comments - April 2016
Re-discussion in GMDP IWG - June 2016
Re-discussion in PIC/S Committee – July 2016

5. Resource requirements for preparation

A drafting group will be established by GMP/GDP Inspectors Working Group and the PIC/S Committee with a rapporteur from the UK and supporting experts from other EU member regulatory authorities and from non-EU PIC/S participating authorities.

The guideline will be discussed at GMP/GDP IWG and the PIC/S Committee as necessary and at other involved working parties and groups. Further discussions are expected with interested parties.

6. Impact assessment (anticipated)

No adverse impact on industry with respect to either resources or costs is foreseen, although clarification of the use of new systems may lead to the requirement for some facilities, equipment and processes to be modified over a period of time.

Revision of the guideline will facilitate a better understanding of expectations which will lead to more consistent and improved manufacture of sterile medicinal products and thereby enhancing the continuity of supply.

7. Interested parties

EMA (GMP/GDP Inspectors Working Group, Quality Working Party, Biologics Working party), PIC/S (Committee, Sub-committee on GMDP Harmonisation, WG on annex 1), national competent authorities of EU/EEA member states and PIC/S participating authorities, EDQM, the pharmaceutical industry.

8. References to literature, guidelines, etc.

1. ICH Q9 Quality Risk Management
   http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002873.pdf
2. ICH Q10 Pharmaceutical Quality System
   http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002871.pdf
3. GMP guide to good manufacturing practice for medicinal products annex 1
   http://ec.europa.eu/health/files/eudralex/vol-4/2008_11_25_gmp-an1_en.pdf
4. FDA guidance for industry sterile drug products produced by aseptic processing - current good manufacturing practice
   http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070342.pdf
5. WHO annex 6 good manufacturing practices for sterile pharmaceutical products
   http://apps.who.int/prequal/info_general/documents/TRS961/TRS961_Annex6.pdf