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Committee for Medicinal Products for Veterinary Use (CVMP)
Committee for Medicinal Products for Human Use (CHMP)

Concept paper on the establishment of a guideline on the selection of sterilisation processes for drug products

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

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7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

1. Introduction

This concept paper addresses the need for a revision of the guidance on the selection of sterilisation methods currently provided for in the annexes to the (separate) human and veterinary development pharmaceutics guidelines, that is, CPMP/QWP/054/98 “Annex to development pharmaceutics: Decision trees for selection of sterilisation methods” adopted in 1999 (1), and EMEA/CVMP/065/99-FINAL “Annex to note for guidance: Development pharmaceutics for veterinary medicinal products: Decision trees for the selection of sterilisation methods” (2) adopted in 2000.

The (parent) development pharmaceutics guideline for human medicinal products, CPMP/QWP/155/96 “Note for Guidance on Development Pharmaceutics” (3) was originally adopted in January 1998. Since then new guidance has been developed, e.g. ICH Q8 (4), comprising most of the content in this note for guidance and rendering it superfluous. The development pharmaceutics guideline for human products should therefore be withdrawn. As a consequence of the withdrawal, it is proposed to develop both decision trees for the selection of sterilisation methods (human and veterinary) into one stand-alone note for guidance.

As the ICH guidance does not include veterinary medicinal products within its scope, there are no proposals to withdraw the (parent) veterinary development pharmaceutics guideline (EMEA/CVMP/315/98 - FINAL) at this time.

2. Problem statement

The information on the selection of the sterilisation methods included in the annexes to the human and veterinary Notes for Guidance on Development Pharmaceutics needs to be revised to include the current view of the choice of sterilisation methods in terms of terminal sterilisation and aseptic processing.

3. Discussion

The Development pharmaceutics guideline for human medicinal products was developed before ICH Q8 and much of its content is now provided in the ICH document. Other sections of the Development pharmaceutics guideline have been further elaborated in specific guidelines such as “Excipients in the Dossier for Application for Marketing Authorisation of a Medicinal Product”, CHMP/QWP/396951/06 (5); “Investigation of bioequivalence”, CPMP/EWP/QWP/1401/98 Rev. 1 (6); “Quality of Modified Release Products A) Oral Solid Dosage Forms B) Transdermal Dosage Forms Section I (Quality)”, CPMP/QWP/604/96, “Pharmaceutical Quality of Inhalation and Nasal Products”, CHMP/QWP/49313/2005 (7). As the contents of the guideline on Development pharmaceutics (human) guideline have already been updated and replaced by other documents it is proposed to withdraw the outdated (human) guideline.

The corresponding veterinary Note for Guidance: Development pharmaceutics for veterinary medicinal products, EMEA/CVMP/315/98 (8) should remain since ICH Q8 is not applicable for veterinary products.

The only currently available guidance on the choice and development of sterilisation processes for sterile products is that included in the annexes to the human and veterinary development pharmaceutics guidelines and the information provided in Ph. Eur. 5.1.1, “Methods of preparation of sterile products” (9). It is proposed to revise the EU guidance in line with the current view on sterilisation methods. As a consequence of the proposed withdrawal of the human parent document, the new guidance should be developed into a separate guidance document.

The objective of this Guideline on the selection of sterilisation process for drug products is to underline aspects of the method of sterilisation (terminal sterilisation and aseptic processing) that are important both for applicants and regulators. The following issues will be taken into account during the revision:

- Specifying conditions when aseptic processing could be accepted for medicinal products.
- Requirements for justification of the choice of sterilisation method.
- The possibility to combine aseptic processing with a terminal process to provide a limited sterilisation assurance level (such as limited moist heat treatment).
- Gas sterilisation processes.
- Sterilisation of medicinal products with a very short shelf-life, for example, radiopharmaceutical products.
- Revision of the decision trees.
- The need for biological validation of a terminal sterilisation process.
- Reference to the (human) Guideline on Real Time Release Testing (formerly Guideline on Parametric Release) (10).
- Transfer and revision of the text on sterilisation provided in the (human) Note for Guidance on the manufacture of the finished dosage form (11).

4. Recommendation

The Quality Working Party recommends the revision of the information in CPMP/QWP/054/98 “Annex to development pharmaceutics: Decision trees for selection of sterilisation methods” and EMEA/CVMP/065/99-FINAL “Annex to note for guidance: development pharmaceutics for veterinary medicinal products: Decision trees for the selection of sterilisation methods” in line with current expectations, and then publication of the revised guidance in the form of a new guideline (which would apply equally for both human and veterinary medicinal products). Consequently, and in addition to the reasons detailed above, the CPMP/QWP/155/96 “Note for Guidance on Development Pharmaceutics” for human medicinal products should be withdrawn. The Annex (only) to the veterinary guideline would be withdrawn; the veterinary guideline would not be withdrawn or revised at this time.

5. Proposed timetable

The concept paper will be published for a three month consultation phase.

QWP will take into account all comments received during the public consultation of the concept paper, and publish the draft guidance for a 6 month consultation period.

It is expected that the guideline will come into operation six months after publishing the final adopted guideline. The current Note for Guidance for medicinal products for human use and its annex are expected to be withdrawn when the new guideline comes into operation. The current annex (only) to the veterinary Note for Guidance would be expected to be withdrawn when the new guideline comes into operation

6. Resource requirements for preparation

The revision will involve the EMA secretariat, the Joint CHMP/CVMP Quality Working Party, the CHMP, the CVMP, and GMP/GDP Inspectors Working Group, who would be consulted, as necessary. The QWP should appoint a rapporteur and a drafting group.

7. Impact assessment (anticipated)

No adverse impact on industry with respect to either resources or costs is foreseen.

The guideline will clarify requirements for regulators and industry with respect to the choice of sterilisation processes for medicinal products for human and veterinary use. The guideline will further elaborate current expectations on the choice and justification of sterilisation processes for medicinal products.

8. Interested parties

Pharmaceutical industry, EU competent authorities, joint CHMP/CVMP Quality Working Party, GMP/GDP Inspectors Working Group, EDQM.

9. References to literature, guidelines, etc.

1: CPMP/QWP/054/98 Annex to development pharmaceutics: Decision trees for selection of sterilisation methods and the development of a new guideline on sterilisation procedures

2: EMEA/CVMP/065/99 Annex to note for guidance: Development pharmaceutics for veterinary medicinal products: Decision trees for the selection of sterilisation methods

3: CPMP/QWP/155/96 Note for Guidance on Development Pharmaceutics

4: ICH Q8 (R2) Pharmaceutical Development

5: CHMP/QWP/396951/06 Excipients in the Dossier for Application for Marketing Authorisation of a Medicinal Product

6: CPMP/EWP/QWP/1401/98 Rev. 1/ Corr ** Guideline on the investigation of bioequivalence/CPMP/EWP/QWP/1401/98 Rev. 1 Investigation of bioequivalence

7: CHMP/QWP/49313/2005 Pharmaceutical Quality of Inhalation and Nasal Products

8: EMEA/CVMP/315/98 Note for Guidance: Development pharmaceutics for veterinary medicinal products

9: Ph. Eur. 5.1.1, Methods of preparation of sterile products

10: EMA/CHMP/QWP/811210/2009 Guideline on Real Time Release Testing (formerly Guideline on Parametric Release)

11: CPMP/QWP/486/95 Note for guidance on manufacture of the finished dosage form

12: EMEA/CVMP/QWP/339588/2005 Guideline on Parametric Release

13: EMEA/CVMP/126/95 Note for Guidance: Manufacture of the finished dosage form