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EMA/CHMP/CVMP/QWP/BWP/428135/2016
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on the need for revision of note for guidance on quality of water for pharmaceutical use (H+V)

Agreed by Quality Working Party	September 2016
Agreed by Biologics Working Party	September 2016
Adopted by CHMP for release for consultation	15 December 2016
Adopted by CVMP for release for consultation	19 January 2017
Start of public consultation	06 March 2017
End of consultation (deadline for comments)	06 June 2017

The proposed guideline will replace the “Note for guidance on quality of water for pharmaceutical use” (CPMP/QWP/158/01 EMEA/CVMP/115/01)

Comments should be provided using this [template](#). The completed comments form should be sent to qwp@ema.europa.eu

Keywords	Guideline, water, Ph. Eur.
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1. Introduction

This concept paper addresses the need to update and revise the Note for Guidance on Quality of water for pharmaceutical use (CPMP/QWP/158/01 EMEA/CVMP/115/01). This guideline was originally adopted in May 2002 and came into operation on 1st June 2002.

Since then, there have been ongoing discussions for many years as to whether there is a need to include non-distillation technologies as a method for production of water for injections (WFI) and eventually, during its 154th Session, the Ph. Eur. Commission adopted a revision of the monograph for Water for Injections (0169) allowing the use of non-distillation technologies for WFI production (the revised monograph will be published in the Ph. Eur. Supplement 9.1 and will become effective in April 2017).

2. Problem statement

The current guideline needs to be updated to reflect imminent changes in European Pharmacopoeia. The text of guideline needs to be updated to take into account manufacturing practices using methods other than distillation for producing water of injectable quality and the consequent deletion of the monograph Water, highly purified. A new Ph. Eur. monograph "Water for preparation of extracts" (2249) is also published.

Consequently, the opportunity will be taken to review current requirements to ensure that they are still appropriate and, if necessary, to amend.

3. Discussion

The objective of the Guideline is to provide guidance to the Industry on the pharmaceutical use of different grades of water in the manufacture of active pharmaceutical ingredients and medicinal products for human and veterinary use.

The intention of the revision is to be in line with the revised Ph. Eur. monograph for Water for Injections (0169) and the consequent future deletion of the monograph Water, highly purified (1927).

The monograph (0169) revision is the result of extensive consultations with stakeholders.

Up to now, the production of Water for Injections (WFI) had been limited to distillation only. The revision of the monograph for Water for Injections (0169) allows for production of WFI by a purification process equivalent to distillation such as reverse osmosis, coupled with appropriate techniques. This brings the Ph. Eur. more closely in line with the US Pharmacopeia and the Japanese Pharmacopoeia which allow for production of WFI by distillation or a purification process proven being equal or superior to distillation, and by distillation or reverse osmosis followed by ultrafiltration, respectively.

The information in the guideline will be updated accordingly.

In addition, the European Pharmacopoeia Commission adopted a new policy for the test for bacterial endotoxins, reflected in the revision of chapter 5.1.10 "Guidelines for using the test for bacterial endotoxins", published in Pharmeuropa 26.4. As a consequence, new monographs on substances for pharmaceutical use will no longer include the test for bacterial endotoxins (with possible exceptions);

this aspect will now be covered by the general monograph, which will include recommendations for establishing limits and information on how to evaluate the pyrogenicity of substances.

Therefore, it would be the manufacturer's responsibility to decide whether or not the requirements for bacterial endotoxins have to be applied and, if so, to calculate the corresponding limits. In addition, according to the monographs on Parenteral preparations (0520) and Preparations for irrigation (1116), the requirements apply to the finished product. To ensure that a preparation complies with the requirements, the manufacturer may therefore use substances that comply with the test for bacterial endotoxins and/or demonstrate that the process includes an appropriate procedure for the removal of bacterial endotoxins, where the decision will be part of the overall control strategy.

The opportunity will be taken to generally review the content of the current guideline in terms of the currently specified minimum acceptable quality of water requirements, for different grades of water quality, in the manufacture of active pharmaceutical ingredients and medicinal products for human and veterinary use. However, considering the acknowledged possibility for risk based approaches to be applied as part of an overall control strategy to the control of bacterial endotoxins, particular consideration will be given to the specified minimum standard for quality of water used for the final processing steps of non-sterile drug substances used in sterile parenteral products.

The opportunity will also be taken to revise the CPMP Position Statement on the Quality of Water used in the production of Vaccines for parenteral use and to merge its content with the Note for Guidance on Quality of water for pharmaceutical use.

4. Recommendation

The Quality Working Party recommends revision of the Note for Guidance on Quality of water for pharmaceutical use in order to be in line with the revised Ph. Eur. monograph for Water for Injections (0169) and the consequent future deletion of the monograph Water, highly purified (1927).

The revision is recommended also to consider possible amendment on the requirements of different grades of water quality in the manufacture of active pharmaceutical ingredients and medicinal products for human and veterinary use.

5. Proposed timetable

January 2017 – Adoption of concept paper at CHMP/CVMP

May 2017 – End of public consultation on the concept paper

October 2017 – Draft revision of the guideline released for public consultation

6. Resource requirements for preparation

The revision will involve the EMA-QWP Secretariat, the Joint CHMP/CVMP Quality Working Party, the GMP/GDP Inspectors Working Group, the Biologics Working Party (BWP), the CHMP and CVMP. The QWP should appoint a rapporteur and a drafting group from the members of QWP, BWP and IWP, as necessary.

7. Impact assessment (anticipated)

No adverse impact on Industry with respect to either resources or costs is foreseen. The updated guidance will reflect current requirements.

8. Interested parties

Pharmaceutical Industry, EU Competent Authorities, GMP/GDP Inspectors Working Group.

9. References to literature, guidelines, etc.

1: Note for Guidance on Quality of water for pharmaceutical use (CPMP/QWP/158/01-EMEA/CVMP/115/01).

2: Ph. Eur. monograph for Water for Injections (0169)

3: CPMP Position Statement on the Quality of Water used in the production of Vaccines for parenteral use (EMA/CPMP/BEP/1571/02 Rev.1)