The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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CPMP Position Statement on the Quality of Water used in the production of Vaccines for parenteral use

Background

This document aims at giving advice on the quality of water to be used in the preparation of antigens used in the manufacturing process of vaccines. It takes into account the new European Pharmacopoeia monographs, which were introduced in 2002 as well as the QWP Note for Guidance on the Quality of Water for pharmaceutical use, which was adopted by the CPMP in November 2001

Recommendation

In the European Pharmacopoeia 4. ed., 2002, three different qualities of water are described: Purified water (PW), Water, highly purified (HPW) and water for injection (WFI). The HPW standard came into force 1 January 2002.

The three main discriminating parameters are

1. the method of production

2. the limit for bacterial endotoxin content

3. the limit for bioburden.

HPW and WFI have the same limits for endotoxin and bioburden, but the methods for production are different. For endotoxins, no limit is normally applied to PW, while for HPW and for WFI in Bulk, the limit is < 0.25 IU/ml. For bioburden, a 1000 times higher action limit during production and subsequent storage is accepted for PW compared with the requirements for HPW and WFI in Bulk.

The general monograph on VACCINES FOR HUMAN USE 0153 states that “The methods of preparation are designed to maintain adequate immunogenic properties, to render the preparation harmless and to prevent contamination with extraneous agents.” and “Vaccines are as far as possible free from ingredients known to cause toxic, allergic or other undesirable reactions in man.”

Taking the “Guideline on quality of water for pharmaceutical use", the new HPW standard and what has been accepted for production of sterile vaccines in the past into account, WFI or HPW should be used for the final purification step. For any other steps in the production (e.g. fermentation, initial purification) PW, HPW or WFI may be used.

For the final formulation of vaccines, WFI must always be used.

As a general recommendation, the better water quality is preferable for production of vaccines, but the conditions and storage period of the intermediates should be taken into account when choosing the water quality. It is essential that a water quality is chosen, which has no deleterious effect on cell cultures, vaccine antigen and their production.

Regarding water to be used for cleaning/rinsing of equipment, containers and closures, the Guideline on quality of water for pharmaceutical use gives adequate advice.

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