

Overview of the New USP <1231> Water for Pharmaceutical Purposes



by Fritz Röder

The new version of USP <1231> will go into effect on 01 December 2016. The final version has been available in the relevant editions of the pharmacopoeia since 01 June. With 37 pages, the new USP <1231> is very lengthy, but at the same time it contains concise instructions for action.

What has changed compared to the last version? Are there new requirements that did not previously exist? Can some things be omitted in the future?

The following article takes a look at these questions while giving a compact overview of the contents of the chapter.

What is USP<1231> and what is new?

Chapter <1231> is very detailed and describes diverse **aspects of designing, operating and monitoring water systems**. "USP <1231> Water for Pharmaceutical Purposes" is "non-binding" (as are all USP chapters from <1000> onwards). However, references are made to it repeatedly whenever a water system is being inspected. Moreover, the requirements also coincide with diverse other existing regulations and recommendations on this topic (e.g., U.S. FDA Guide to inspections of high purity water systems, ISPE Guide Water & Steam Systems, WHO-Technical Report 970 (2012) water for pharmaceutical use (Technical Report Series, Annex 2), USP 85/643/645/797).

Another point - and the most important one - is that USP <1231> offers an extensive and very useful **guide for action to control water systems**. Following these tips makes it possible to recognise potential problems early on. Especially the topic of biofilm formation often gives rise in practice to questions to which the monograph can supply a number of answers.

The document has been completely revised and restructured. The old version had a narrative style with large text bodies. The new version contains many layout changes and makes greater use of chapter numbers and lists. A very welcome change is that all **procedural topics** are explained in terms of content, then they are dealt with separately with regard to "**areas of concern**" and the **corresponding control mechanisms**. Both topics were already included in the old version, but now they are more clearly organised. This makes the document easier to understand.

One new part is in **Performance Qualification**: In the future it will be possible to use the water, at a risk, as soon as phase 1 of the PQ has been completed. However, exceeding the action level would render batches produced during phase 2 unsalable.

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The **recommended temperature in hot sanitising** has also changed. The previous recommendation of at least 80°C has been lowered to 65-80°C. Now temperatures far in excess of 80°C are explicitly deemed inadvisable.

From the “Sampling” chapter onwards the guideline has been reorganised and completely rewritten. This includes the topics of “Chemical Tests”, “Microbiological Tests” and “Alert and Action Levels”. The key items remain the same in content, although they have generally been moved to other locations and new aspects have been added. That is a welcome development insofar as the previous guidelines on the topic of “**Sampling and Water Monitoring**” were not overly detailed. For example, the following information is new concerning:

- Sampling plans for validation
- Sampling plans for routine operations
- Differentiation and explanation of the sampling concepts for drinking water, process water, purified water, water for injections and for sampling outside of the routine

On the whole, Chapters 6-8 now contain very good **instructions on action** to establish a **monitoring concept** in the company and to have long-term, adequate control of the system.

The topic of and relating to **alert and action levels** has also been newly developed and supplemented in detail. There is now information in USP <1231> on two and three-stage levels, how they are determined, what is permitted and what is not and what rationales can be applied for the specification to a certain level.

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