TECHNICAL PAPER

WFI Liquid Monitoring for Pharma

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LIGHTHOUSE
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Pharmaceutical Water Quality requirements for use in the Cleanroom

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Water is one of the major utilities used by the pharmaceutical industry. Different grades of water quality are required depending on the different pharmaceutical uses. Control of the quality of water, in particular the microbiological quality, is a major concern and the pharmaceutical industry devotes considerable resource to the development and maintenance of water purification systems.

Water for Injection (WFI) may be present as an excipient or used for reconstitution of products, during synthesis, during production of the finished product or as a cleaning agent for rinsing vessels, equipment, primary packaging materials, etc. Therefore sterile water which is free of viable contamination is a necessity for the quality of the end pharmaceutical product.

Fig 1. Water for Injection (WFI) production system image courtesy of Bram-Cor

In April 2017 the production of Water for Injections (WFI) had been limited to production by distillation only. However with the revision of European Pharmacopeia monograph for Water for Injections (0169). The production of WFI by a purification process using reverse osmosis using electro-deionization, or nano filtration.

Pharmaceutical Grade Water

There are four main types of water graded for pharmaceutical use. These grade have been defined by United States Pharmacopeia (USP) and European Pharmacopeia (Ph.Eur).

- Portable (Mains) Water
- Purified Water
- Highly Purified Water
- WFI

What is Portable (Mains) Water

Portable or mains water is typically the primary source for all other grades of water. This type of water has no direct contact with the product.

What is WFI?

Water for Injections (WFI) is water for the preparation of medicines for parenteral administration when water is used as a vehicle (water for injections in bulk) and for dissolving or diluting substances or preparations for parenteral administration (sterilised water for injections). Water for injection is water of extra high quality without significant contamination. A sterile version is used for making solutions that will be given by injection.

What is Purified Water?

Purified water is water that has been mechanically filtered or processed to remove impurities and make it suitable for use. Distilled water has been the most common form of purified water, but, in recent years, water is more frequently purified by other processes including capacitive deionization, reverse osmosis, carbon filtering, microfiltration, ultrafiltration, ultraviolet oxidation, or electro deionization. Combinations of a number of these processes have come into use to produce ultrapure water of such high purity that its trace contaminants are measured in parts per billion (ppb) or parts per trillion (ppt).

1. Categories of Sterile Products and minimum acceptable quality of water.

Sterile medicinal products	Minimum acceptable quality of water
Biologics (including vaccines and ATMP)	WFI
Parenteral	WFI
Ophthalmic (excluding ATMP)	Purified Water
Haemofiltration Solutions Haemodiafiltration Solutions	WFI
Peritoneal Dialysis Solutions	WFI
Irrigation Solutions	WFI
Nasal/Ear Preparations	Purified Water
Cutaneous Preparations	Purified Water

Table 1. Sterile Medicinal Products and Water Quality

2. Categories of non-Sterile Products and minimum acceptable quality of water.

Non-sterile medicinal products	Minimum acceptable quality of water
Vaccines for non-parenteral use	Purified Water*
Oral Preparations	Purified Water
Nebuliser Solutions	Purified Water**
Cutaneous Preparations	Purified Water***
Nasal/Ear Preparations	Purified Water
Rectal/Vaginal Preparations	Purified Water

Table 2. Non Sterile Medicinal Products and Water Quality

* WFI is recommended in order to ensure the vaccines' safety and product quality (avoid introduction of undesirable microorganisms in the finished product formulation) unless otherwise justified (i.e. for some non-sterile veterinary vaccines for non-parenteral use, purified water might be accepted).

**In certain disease states (e.g. cystic fibrosis), medicinal products administered by nebulization are required to be sterile and non-pyrogenic. In such cases, WFI should be used.

*** For some products such as veterinary teat dips, it may be acceptable to use potable water where justified and authorized taking account of the variability in chemical composition and microbiological quality.

WFI and Purified Water System with online particulate monitoring

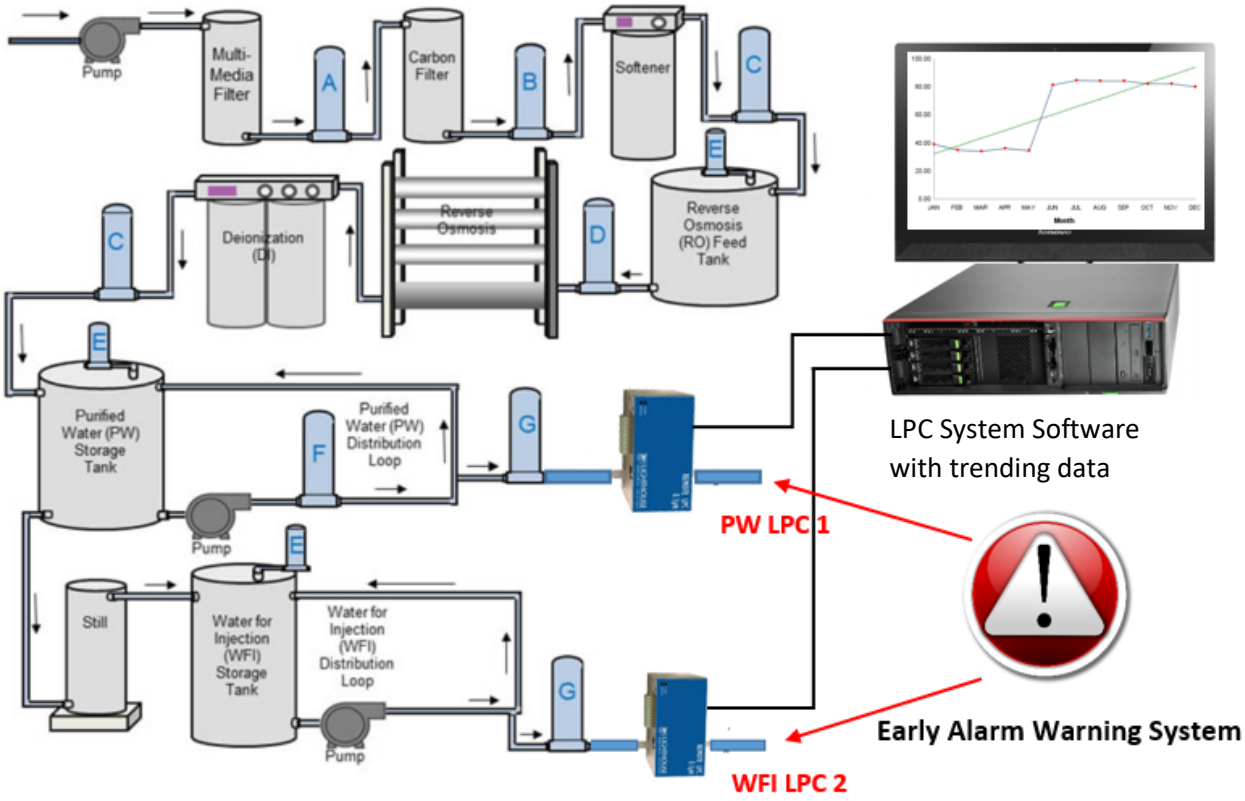

Fig 2. WFI and Purified Water System with LPC Monitoring System

With GMP new updates pushing for a complete facility **Contamination Control Strategy** outlined in the recent EU GMPAnnex1: 2021 update. Monitoring Purified Water and WFI systems using liquid particle counters (LPC) enables fast notification of contamination. With continuous sampling of loop systems operators and managers can be notified immediately if base levels rise which can compromise product quality and safety. With a Liquid Particle Monitoring System. The system above shows two monitoring point's one on the Purified Water distribution loop (LPC1) and the WFI distribution loop (LPC2).

More monitoring points can be added to other pre-filtration stages to get an earlier indication of failure points for a more robust system which can act as an early warning system. The last thing an operator needs is contaminated WFI or Purified water circulating around sterile products.

Online Liquid Particle Monitoring

Point of use remote liquid particle counters can be easily connected online and capture important data in real time. Notifications can be issued immediately to end users.

Fig 3. Remote LPC (0.1µm)

Remote LPC's can be easily installed along the water systems based on a risk assessment. Multiple points can be monitored to look at filtration or system failures. Most pharmaceutical water systems use process filtration and reverse osmosis with deionized systems with filtration pore sizes of 0.2µm with some down to 0.1µm.

"EARLY SYSTEM FAILURE DETECTION ENABLES A MORE STRATEGIC CONTAMINATION CONTROL STRATEGY"

Why use a LPC Monitoring System?

- Implement a real time contamination control solution
- Establish base line trends and set alarm notifications
- Real Time data – apply data analytics to set system service strategies
- Helps maximize system uptime and save costs
- Improved quality yield of product
- Reliable data to make informed process decisions
- Prevents contaminated water accidental usage
- Easy to install and manage
- Vendor remote technical support

References

1. Note for Guidance on Quality of water for pharmaceutical use (CPMP/QWP/158/01- 193 EMEA/CVMP/115/01).
2. CPMP Position Statement on the Quality of Water used in the production of Vaccines for parenteral use (EMEA/CPMP/BWP/1571/02 Rev.1).
3. Ph. Eur. monograph "Water for Injections" (0169).
4. Ph. Eur. monograph "Water, purified" (0008)