

Revised European Pharmacopeia (Ph. Eur.) monograph for Water for Injection (0169)

PHARMACEUTICAL

From April 2017, the revised European Pharmacopoeia monograph 0169 will allow the generation of Water for Injection (WFI) by distillation or by a purification process that is equivalent to distillation such as reverse osmosis(RO) coupled with appropriate secondary membrane system.

Towards a greater choices of techniques

- ▶ Historically distillation has been the preferred method for producing WFI in the biopharmaceutical industry even though the US and Japan Pharmacopoeias have allowed alternatives for some years. The authorisation of equivalent techniques to distillation by Ph. Eur. offers the industry more choice.

Production Techniques

- ▶ Distillation offers the reassurance of a phase change from water to steam that removes impurities and results in product water compliant with microbial and endotoxin limits for WFI. RO based systems achieve compliance through the use of CEDI and Ultrafiltration (UF) downstream of the RO. UF reduces endotoxin levels and removes any prevailing microorganisms.

Storage & Distribution

- ▶ Regardless of production technique, a storage and distribution system should be well designed so as to minimize risk of microbial growth and facilitate regular sanitization. The advantage offered by distillation is that it is possible to operate the loop at a continuous high temperature thus ensuring microbial control. RO system loops run at ambient temperatures therefore require regular hot water sanitization or ozonation (coupled with UV) to control the risk of microbial contamination.

Cost vs Risk

- ▶ The selection of WFI production method is ultimately about finding the correct balance between cost and risk. Multiple effect distillation (MED) is seen as less risky than Vapour Compression Distillation (VCD) as there are no moving parts. Likewise both distillation techniques are viewed as less risky than RO based systems, which may be susceptible to biofilm formation if not maintained correctly. However, in a market where margins are under pressure the OPEX savings offered by RO based system and VCD units are highly attractive and an increasing number of clients are looking at ways to reduce operating costs without affecting the integrity of the system.




Overcoming Risks

- ▶ Any system for WFI production - regardless of technology - must be well designed by an experienced company in line with the current regulatory guidelines, correctly installed and then monitored and maintained to a high standard. For RO based systems, some extra care and attention is required to monitor the condition of the membranes. This would include regular sanitization of the membranes using hot water and multi-point in-line monitoring of TOC, conductivity and possibly rapid microbiological testing. As cited above, storage and distribution risks also need to be assessed and controlled appropriately.

Veolia, 30 years of pharmaceutical experience

Whether you decide to produce Water for Injection using distillation with the Polaris range or with the Orion RO based system, you can be assured that the system will produce EP, USP and JP compliant WFI. Performance optimization, risk reduction, compliance and preventative maintenance are second nature to Veolia.

Quick Comparison table

DESCRIPTION	POLARIS VCD Vapour Compressor Distiller	POLARIS MED Multi Effect Distiller	ORION™ RO, CEDI & UF
WFI compliant with EP, USP and JP	High efficiency distillation, with high compression ratio's and ultra low droplet separation. 	Multiple effect stills with energy efficient falling film technology. 	Skid mounted multi-technology system. Comprising of softening, reverse osmosis, CEDI & UF. 
Up to 20,000 litres/hour production	✓	✓	✓
WFI production with membrane based system	✗	✗	✓
WFI production by distillation/water to steam phase change	✓	✓	✗
Product monitoring with calibrated instruments	✓	✓	✓
cGMP validation documents including IQ/OQ/commissioning	✓	✓	✓
Cold WFI production	✓	✗	✓
Hot WFI production	✓	✓	✗
Combined WFI and Clean Steam production	✗	✓	✗
Independent PLC control with 21CFR Part 11 Compliance	✓	✓	✓
Pressurised discharge	✓	✗	✓
Low water footprint	✓	✗	✓
Hot water sanitisation capability	✓	✓	✓
Low steam pressure requirement	✓	✗	✓

Veolia also has extensive experience in Storage & Distributions and Turn-Key Projects.