Depyrogenation of buffer or purified water

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Depyrogenation of buffer or purified water

The situation

Pyrogens, substances that cause fever, must be removed from purified water and a host of buffers and small molecular solutions used in pharmaceutical research and production. Pyrogens take two forms, exogenous and endogenous. For the most part, exogenous pyrogens are microbes, microbial products or toxins, such as gram-negative endotoxin (bacterial lipopolysaccharides [LPS]) or toxins from Staphylococcus strains. Endogenous pyrogens are cytokines (polypeptides [PPs]) produced generally by monocyte macrophages but also by skin, endothelial, epithelial, and glial cells.

Maximum safety is enhanced by depyrogenating solutions immediately prior to use. Simple sanitization by heat does not remove the toxic compounds associated with LPS or PPs. Sterilization via bactericides or other chemicals results in unwanted chemical residue. A simple, consistent means of removing pyrogens at the point of use—one that does not permit last-minute contamination—is mandatory for many R&D and medical settings.

The solution: GE Healthcare hollow fiber ultrafiltration cartridges

One of the most effective ways of water depyrogenation is via membrane separations, which removes contaminants and pyrogens at the molecular level using an easily-configured system. Cross flow membrane separations lend themselves to closed systems that provide good protection against contamination.

General guidelines

- Suited to depyrogenation of purified water, buffers, and solutions of small molecules
- Pyrogens can be endotoxins or other entities
- Endotoxins (LPS) readily aggregate to a molecular weight (MW) of 250,000 kD+
- Subunits are 10 kD
- Ultrafilters can reduce endotoxin levels > 4 logs
- Sanitize and depyrogenate equipment beforehand
- Confirm with WFI rinse
- Sanitize frequently
- Maintain flow in water systems—even when not in use (Fig. 2)

Pyrogen removal from municipal water using a 10,000 nominal molecular weight cutoff (NMWC) hollow fiber ultrafiltration membrane

Membrane: 10,000 NMWC
Model number: GE Healthcare UFP-10-C-85
Feed: 0.2 µm filtered tap water
Inlet pressure: 1.03 barg (15 psig)
Outlet pressure: 0.97 barg (14 psig)

Time (minutes)	Feed	Bleed	Reject	Permeate
0	93	93	104	0.023
30	119	119	183	0.031
60	125	125	189	0.039
90	155	155	268	0.049
120	159	296	-	0.02
150	159	304	-	0.034
180	157	327	-	0.019

Figure 1. Typical depyrogenation results (in eu/ml) showing a consistently low level in the filtrate despite a 3× increase in the LPS level in the feed

Depyrogenation of USP water

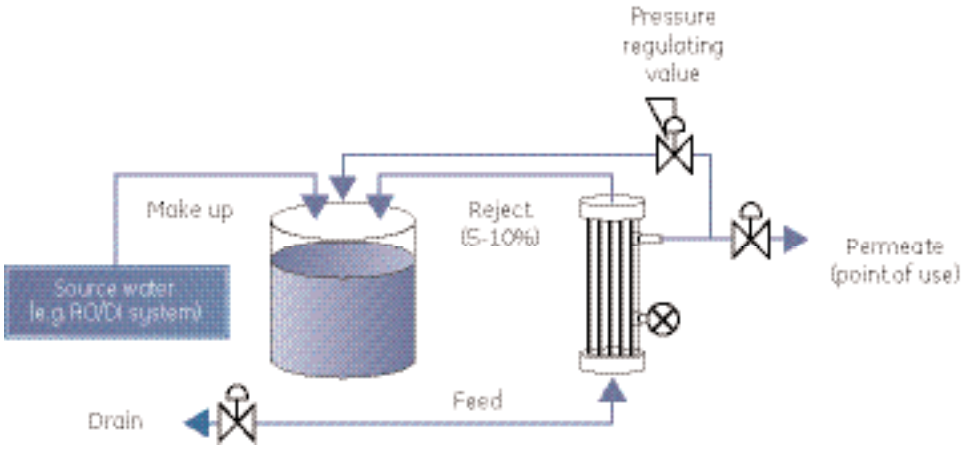

Figure 2. Typical depyrogenation system utilizing ultrafiltration. This is a closed system, with no element exposed to the environment. Water from a reverse osmosis/deionization (RO/DI) system is fed to a reservoir, which then is circulated through a hollow fiber ultrafiltration cartridge. Water flows continuously, both via a reject line in the retentate circuit and a shunt in the permeate circuit that recirculates permeate when it is not being drawn off. Valves and pressure gauge are shown; necessary pumps are not.

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