Reducing Organism Counts In RO Product Waters

By: Dr. Theodore H. "Ted" Meltzer

The reliance upon Reverse Osmosis operations in the manufacture of process waters in both the pharmaceutical and semiconductor industries is well established. Curiously, the RO methods in these applications, although directed to the same objective---namely, the preparation of ultrapure water---differ significantly in some important respects. Water in the pharmaceutical industry is an area of particular concern because of the potential presence of organisms. Electronic rinse waters eschew microbes for their interference with fine line integrity. Ironically, the limits prescribed by the USP for the drug industry are more generous than those accepted in the electronics industry.

Originally, RO was strongly directed towards brackish water desalination. Some salinity could be tolerated in waters intended for agricultural purposes. This may explain the early RO membranes' occasional lack of integrity. "Leakers" could be encountered and tolerated to some extent. However, it is difficult today to ascribe the finding of organisms in RO product waters to poor quality. There is concern about the fact that RO treatments cannot be depended upon to reliably prepare sterile water.

It is noteworthy that in the manufacture of pharmaceutical waters, microporous membranes provide more sterile effluent than RO devices despite the greater tightness, the smaller diameters of the "pores" of the RO membranes. The intersegmental spaces of the polymeric membranes through which the water permeates in RO operations are small enough to stop the passage of hydrated ions yet cannot assuredly prevent the passage of much larger microbes where drug waters are concerned. But apparently it can be prevented, or almost entirely so, in the case of the electronic rinse waters. Why should this be the case? Given the health implications of organisms in pharmaceuticals, it seems reasonable to suggest that this apparent contradiction deserves investigation.

The microporous membranes, usually rated as being 0.2 µm in pore size, undergo integrity testing before they are used in pharmaceutical filtrations. This is to make certain that they are qualified to produce sterile effluent when properly handled. This is not done for RO filters even though vacuum and air pressure testing is performed by RO manufacturers before the device is released for distribution. Other tests can also be performed to ascertain the integrity of RO membrane devices. For example, comparisons of sulfate and chloride ion rejections can be performed as in-service integrity tests. Equal parts of sodium chloride and sodium sulfate at a 500-ppm concentration can be processed by an RO at a differential pressure of 60 psi. About 89% of the sodium chloride and 99% of the sodium sulfate will be rejected. At 400 psi and a total salt concentration of 200 ppm, about 95 to 97% sodium chloride and 99.9% of the sulfate will be rejected. Leakage in RO membranes will be made evident by lower rejections of the chloride and sulfate ions, and their differences will be minimized in proportion to the seriousness of the imperfections, if any. A particularly meaningful integrity test would result from a correlation of the loss of chloride-sulfate ion discrimination with organism passage. This would not be a casual undertaking.

A second area worthy of investigation by those dedicated to the use of RO in pharmaceutical settings would be a review of the TOC standard for product water. The 500 ppb standard set by the USP was adopted to harmonize with that established by the Japanese pharmaceutical industry. The standard is meant to serve as a part of the definition of the final product water, be it Purified Water or Water for Injection (WFI). It is completely innocent of implications regarding health. Thus, a water of lower TOC content would be purer for having less total organic carbon, but need not necessarily be more salubrious in use. The pharmaceutical industry is believed generally to prepare waters with a TOC value of less than 250 ppm. However, FDA investigators have been known to observe, correctly, that a well-operated system will be below a 20 ppb count.

In the making of silicon chips, the electronics industry holds to very low TOC values, namely, to about 5 ppb.

Since TOC can serve as nutrient for the microbes, the colony-forming unit count measuring the water's bio-burden can be kept to less than one cfu per liter. However, this does require a superior pretreatment effort. This goal is surely one that the pharmaceutical industry should have because it could contribute significantly to maintaining lower organism counts in RO waters.

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