



Sterile Products



WFIQ: A New Designation of Sterile Alcohols for Cleanroom Disinfection. Equivalent WFI Bacterial Endotoxin Limits are Assured Through Documented USP End-Product Testing.

-Charlotte Veloski

Water for Injection (WFI) is defined by USP 24 as water purified by distillation or reverse osmosis that contains not more than 0.25 USP Endotoxin Units (EU) per mL. The term endotoxins, in the pharmaceutical industry, refers to the cell wall components of gram-negative bacteria released during bacterial growth, or subsequent to death and lysis of the cell. Also termed pyrogens, bacterial endotoxins are of great concern to the parenteral pharmaceutical industry. When injected in sufficient quantity, bacterial endotoxins cause a specific, fever-producing response (giving them their pseudonym “pyrogens”, a Greek term meaning fire producing) as well as more clinically significant pathogenic effects including hypotension, and even fatal septic shock. As a result the FDA has established critical limits of pyrogen load for parenteral products.

There can be several sources of pyrogens in parenterals including raw materials, equipment used in manufacturing, or water used as a solvent or in processing. Since gram-negative bacteria are the most common bacteria found in water this is the most common source. Therefore, USP WFI is the grade of water used in the manufacture of parenterals. The USP has set the endotoxin limit for WFI at 0.25 EU/mL due to a concern that there might be an additive effect of the low level pyrogens in a drug product and its vehicle (WFI). This concern over the additive effect of endotoxins in ingredients has carried over into all aspects of parenteral pharmaceutical manufacture including cleaning and disinfection. While the use of WFI in parenterals addresses a very realistic concern for the specifications of an *ingredient*, the use of WFI in non-ingredient applications, such as cleanroom disinfection, is only relevant with respect to endotoxin levels. What is critical here is not whether a disinfectant is prepared with WFI as an ingredient, but rather that end-product testing is conducted, and more importantly documented, to ensure an endotoxin level equivalent to WFI.

In order to establish a standard for sterile alcohols for cleanroom disinfection applications, the designation WFIQ, water for injection quality, has been developed by Decon Labs to indicate that these products are end-product tested according to USP methods to meet or exceed the endotoxin level criterion set forth by the USP for WFI. In addition to being sterility tested, Decon Lab's sterile alcohol products are tested using the LAL test, the compendial method for bacterial endotoxins.

The LAL test is recognized by both the USP and FDA as the test method proven to be a sensitive, reliable indicator of bacterial endotoxins (pyrogens). In the 1980s it was substituted for the USP Pyrogen Test (rabbit fever test) whereby the development of a fever in the subject rabbits in response to the injected test product indicated the presence of pyrogens. The LAL assay reagent is derived from an aqueous (non-lethal) extract of blood from the horseshoe crab. It originated from the observation of Dr. Fred Bang, who was studying blood circulation using horseshoe crabs, that the entire volume of blood in his crabs clotted into a gel-like mass in response to contact with both live and dead gram-negative bacteria. The LAL test, Limulus (horseshoe crab), Amebocyte (blood cell), Lysate (aqueous extract), reenacts the natural horseshoe crab immune response to bacterial endotoxins. The test is available in sensitivity ranges from 0.03 to 0.5 EU/mL depending upon the test application. Decon Labs' sterile alcohols are tested at a sensitivity level of 0.125EU/mL, twice below the endotoxin limit of 0.25 EU/mL set forth by the USP for WFI.

While WFI is not used as an ingredient in the manufacture of Decon Labs' sterile alcohol products, the most crucial WFI water quality criteria, sterility and bacterial endotoxin levels, are assured through documented USP end product testing. It must be remembered that the specification of WFI as an ingredient in the manufacture of parenteral pharmaceuticals is intended to maintain a low pyrogen load so that the critical endotoxin limits for the final product are met. Although the use of WFI in the manufacture of disinfectants occurs, it is somewhat misleading since endotoxins can theoretically come from the chemicals/active ingredients that are blended with the WFI, or from the containers used to mix or dispense the product. The only relevant factor is not that WFI is used but rather that the *finished product* endotoxin levels meet or exceed WFI requirements. WFIQ is offered as the new standard for sterile alcohols for cleanroom disinfection where documented USP testing of our end-products assures that the WFI endotoxin level criterion of 0.25 EU/mL is met or exceeded.

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