USP Standards for Sodium Chlorine Injection for IVGEN and IVGEN Mini

The United States Pharmacopeia (USP) is the authoritative source for medicine and healthcare product standards. IVGEN and IVGEN Mini follow the guidance of USP-standardized Sodium Chloride Injection. USP defines Solidum Chloride Injection as a sterile solution of Sodium Chloride in Water for Injection. It contains no antimicrobial agents, not less than (NLT) 95.0%, and not more than (NMT) 105.0% of the labeled amount of sodium chloride (NaCl). USP details each standard for Sodium Chloride Injection in the form of a monograph which can include process-oriented descriptions, sterility requirements, usage, and final product packaging. Not all standards for Sodium Chloride Injection are exactly specified in USP documentation. For example, three major water processing steps are required before Sodium Chloride Injection can be manufactured. These steps include generating or sourcing drinking water, purified water, and water for injection (WFI). The USP standard for purified water requires that source water meet Environmental Protection Agency (EPA) National Primary Drinking Water Regulations (NPDWR). To meet USP requirements for WFI distillation, reverse osmosis, or an equivalent or superior process is acceptable; however, there are no quantifiable values for assessment. (Process displayed in Figure 1)

Eights tests were conducted on the IVGEN-generated IV fluid before and after flight. The IV solution was tested for Sterile Sodium Chloride for Injection concentration, endotoxin concentration, heavy metal concentration, identification of sodium and chloride, the concentration of iron, particulate matter analysis, sterility, and pH testing. IVGEN Mini plans to test for all these items and test for total organic carbon (TOC) concentration and solution conductivity. Table 1 includes each test name, specification, and USP general chapter (USP Ch).

Water Purification Processes

The USP specifies distillation and Reverse Osmosis (RO) are the “acceptable” methods to produce Sterile Water for Injection (SWI); however, provisions are included that other processes may be utilized, provided that these processes deliver water of equivalent quality. Common water purification processes and their descriptions include:

Distillation - The process of separating substances from water by a phase change using selective boiling and condensation collection.

Reverse Osmosis – A filtration process that involves using a semipermeable membrane to remove ions, molecules, and larger particles from water. A solvent diffuses across the membrane from a region of low concentration to a region of higher concentration

Absorption - Impurities are chemically absorbed onto a packing material.

Ultrafiltration - Water is forced through a semipermeable membrane with very small pore diameters that physically block the passage of impurities.

Deionization - Cation and anion resin beads exchange unwanted ions with pure hydrogen and hydroxide molecules to form pure water. The ion-exchange resin binds with unwanted mineral salts such as sodium, potassium, chloride, fluoride, etc.

Test	Specification	USP Ch
Sterile Sodium Chloride for Injection	Contains NLT 95.0% and NMT 105.0% of the labeled amount of sodium chloride (NaCl) (Ref: for 0.9% Saline: NLT 0.855% and NMT 0.945% NaCl by mass.)	USP NS Monograph
Endotoxin Concentration	NMT 0.5 USP Endotoxin Unit/mL where the labeled amount of sodium chloride in the Injection is between 0.5% and 0.9%, and NMT 3.6 USP Endotoxin Units/mL where the labeled amount of sodium chloride in the Injection is between 3.0% and 24.3%	<85>
Heavy Metals by USP	NMT 0.001%	<231>
Identification Sodium by USP	Sample responds to tests for sodium	<191>
Identification Chloride by USP	Sample responds to tests for chloride	<191>
Iron by USP	NMT 2 ppm	<241>
Particulate Analysis by USP	≤25 particles per mL larger than 10 μm ≤3 particles per mL larger than 25 μm	<788>
Sterility by USP	No growth	<1>,<71>
pH Testing by USP	4.5 to 7.0	<791>
TOC	**The solution should be prepared to an accuracy of +/- 0.005 mg/L of carbon	<643>

Table 1: Table of USP standards for IV fluid

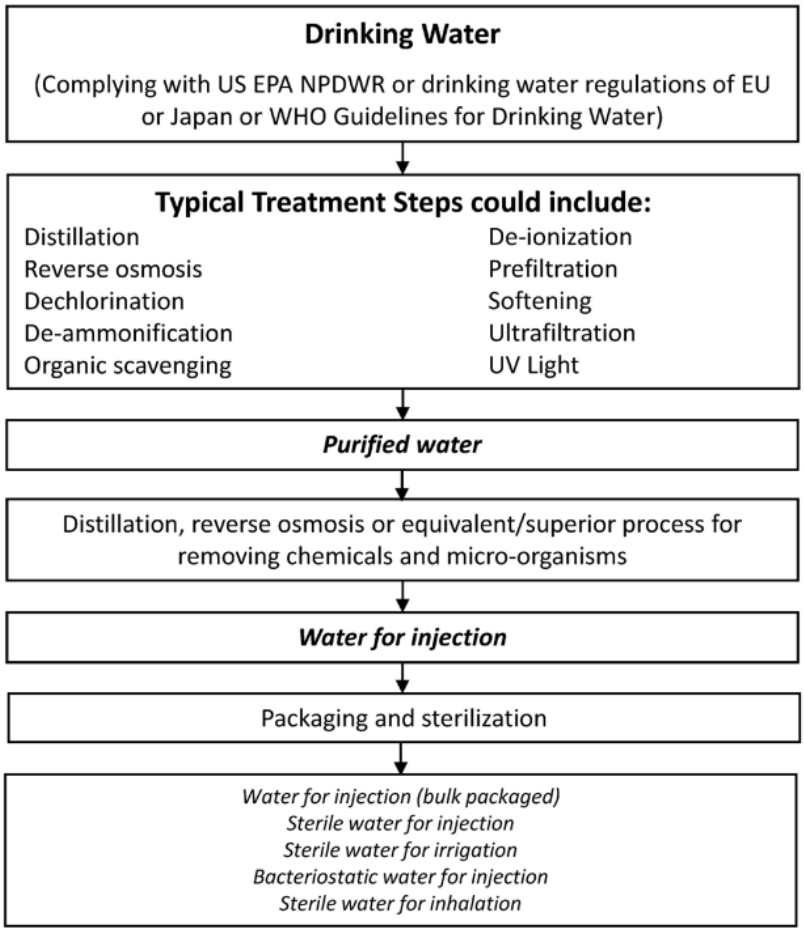

Figure 1: The process to produce IV fluid