Simultaneously Installation, Validation and Maintenance of Water System used in Health Industry

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Abstract— Water is part of each pharmaceutical product [1]. It is used in the pharmaceutical industry in various ways, for example, for example, as a raw material, inactive pharmaceuticals, pharmaceutical agents, pharmaceutical intermediates, pharmaceutical analysis, cleaning solvents, etc. In the formulation of a medicine, it is necessary to use water of high purity in each phase of the formulation of each medicine. Water because it is impossible to obtain pharmaceutical water from an external pharmaceutical supplier. Water is used in the preparation of all pharmaceutical forms, but parenteral drugs are very dangerous. Today, each pharmaceutical production unit has a purified water system, while the parenteral drug manufacturing unit needs water for injection systems [4] (WFI system). Most drug regulatory authorities cite guidelines for various types of water, such as purified water, sterile water for injections, bacteriostatic water for injections, etc., which can be used in several ways. Any means of pharmaceutical production. The quality of pharmaceutical water depends to a large extent on the quality of the water system [9-10]. However, before the water produced in a unit can be used, the water supply system [2] must be validated and the reliability of water treatment, storage and distribution confirmed. The continuous monitoring of the water system is a clear regulatory requirement and an important financial burden for the personnel and resources of the company. Proper planning of the water supply system with personal skills in all physical, chemical, technical and microbiological areas related to water is essential. The correct pharmaceutical water system must respect and respect the requirements of the Pharmacopoeia. Have the correct scanning system in the right places and at the correct frequency.

Key words: Water System Validation, Validation, Purified Water System Validation, Validation, Pharmaceutical

I. INTRODUCTION

Water is mostly used substances, raw material, or ingredient in the production, processing, and formulation of Compendial articles. Control of the microbiological quality [3] of this water is important because proliferation of microorganisms ubiquitous to water may occur during the purification, storage and distribution of this storage sub- stance. If water is used in the finished product, these microorganisms or their metabolic products may finally cause adverse consequences. Water that is used in the initial stages of the production of drug substances and that is the source or feed water for the preparation of the numerous types of purified water must meet the requirements of the National Primary Drinking Water Regulations (NPDWR) (40 CFR 141) issued by the Environmental Protection Agency (EPA). Comparable regulations for drinking water of the European Union or Japan are acceptable. These requirements ensure the absence of coliforms, which if determined to be of fecal origin, may portend or indicate the presence of other microorganisms of fecal origin, including viruses that may be pathogenic for humans. On the other hand, meeting these National Primary Drinking Water Regulations would not rule out the for other uses Dechlorination Ultrafiltration [6-8].

II. DIFFERENT GRADES OF WATER FOR PHARMACEUTICAL PURPOSES:

A. Drinking water:

Drinking water must meet the criteria of national and international water regulations, such as WHO, ISO and other regional authorities. Drinking water is not changed, with the exception of limited treatment of water from natural or stored sources. Normally natural sources contain wells, wells, rivers, lakes and the sea. It is mandatory for the user to test the supply water at the site to ensure that water quality is to be monitored. conform to the required standard.

B. Purified water:

Purified water produced by an appropriate method (RO, UV, electro-deionization, ultrafiltration, vapor compression, etc.) of water regulating the EU's drinking water regulation, WHO, Japan, the US Environmental Protection Agency. It must be protected from recontamination and microbial growth.

C. Water for Injection (WFI):

The WFI was prepared by an appropriate process from the water that makes up the purified water regulation of the EU, WHO, Japan and the United States. UU and other international organizations for the elimination of chemicals and microorganisms. It must be protected from recontamination and microbial growth.

D. Sterile water for injection:

Irrigation, inhalation: Sterile water for injection, irrigation, inhalation is prepared from WFI, which is sterilized and properly packaged. Contains no additional antimicrobial agent

E. Sterile Bacteriostatic Water for Injections:

Bacteriostatic water for injection is prepared from sterilized and appropriately packaged water for injection that may contain one or more appropriate antimicrobials.

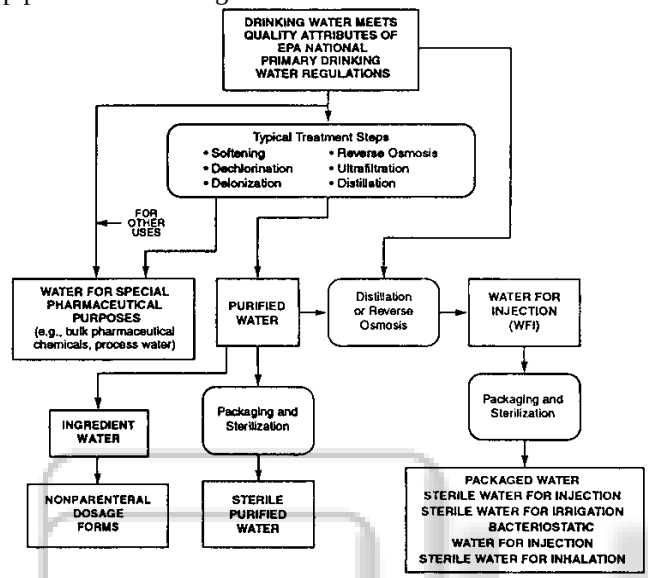
F. Water Purification Systems:

When purifying water, any suitable qualified cleaning method or series of techniques may be used. The cleaning technique depends on the quality of the feed water. Normally, purified water can be obtained by sequences of techniques such as ion exchange, reverse osmosis, ultrafiltration with water, electrode ionization techniques, and distillation.

III. MISCELLANEOUS TECHNIQUES FOR THE TREATMENT [4] OF WATER.

A. Chlorination:

The chlorination can be carried out with LPG, sodium hypochlorite solution or calcium hypochlorite granules and chlorine gas generators. Chlorine belongs to the group of halogens in the periodic table. Chlorine is a very effective disinfectant. It can kill pathogenic pathogens such as bacteria, protozoa and viruses that are common in water supply basins, pipe walls and storage tanks.



B. Softening:

The process of removing water hardness is called water softening. The raw water transports the Ca and Mg ions, which cause the total hardness of the raw water. Hard water is very dangerous.

The calcium (Ca 2+) and magnesium (Mg 2+) ions can be removed by an ion exchange procedure. Water softeners are generally cation exchange devices. Cations refer to positively charged ions that dissolve in water. The exchange of cations involves the replacement of hardness ions by ions without hardness.

Water softeners generally use sodium (Na +) as an exchange ion. In the ion exchange process, sodium ions are used to coat a replacement agent in the plasticizer. The replacement medium may be natural "zeolites" or synthetic resin beads resembling wet sand.

When hard water passes through a softener, calcium and magnesium are replaced by sodium ions. Sodium ions are poorly preserved and can easily be replaced by calcium and magnesium ions. During this process, the "free" sodium ions are released into the water.

C. Dosing (SMBS, Antiscalent, NaOH):

Sodium metabisulfite (SMBS) reacts mainly with water to form sodium bisulfite (SBS). This SBS reacts with hypochlorous acid to form byproducts without free chlorine: any of these byproducts can be easily eliminated with the RO system.

D. Filtration:

The purpose of the filtration is to remove solid contaminants from the water supply and protect other modules in the particulate system that can affect the performance of the equipment and its useful life.

E. CEDI:

CEDI removes ions from water through a unique combination of ion exchange membranes, ion exchange resins and electricity. Water contains cations and anions as positive and negative charges. When a pair of electrodes is applied between the water and the electric current, the ions are attracted through an ion exchange membrane to their respective electrodes. In this system, the ion exchange resin acts as an ion transport bridge.

F. Reverse osmosis[6-8]:

Reverse osmosis membranes consist of a flat membrane, which is divided into three layers: polyester base, polysulfone layer, polyamide layer and 0.2-micron barrier layer that protects chemicals, bacteria and viruses. Water. The flat arc membrane is a spacer combination for the feed channel that creates turbulence and provides space for the membrane sheets for the feedwater. The feed is forced through the spacer of the feed channel and into the barrier layer of the membrane. The water passes through the surface of the membrane in the first channel, which flows in a spherical direction, and accumulates in the central tube. This water is the final water of recycling.

G. UV Treatment:

Bacteria, which cause some of our most common diseases, are unicellular organisms. There are seven main groups of bacteria that differ in their shape and cell wall. When we look at a bacterium, the simplicity of the cell is obvious. The cell contains DNA, ribosomes and other basic proteins, and this simplicity increases sensitivity to UV light. UV-induced damaged DNA can affect the production of proteins and enzymes with lethal effects. However, if you look in a cell, ultraviolet light can cause fatal damage. As UV rays pass through the water, the production of reactive oxygen species that react with the cell wall increases. Cell walls and other cellular components are severely damaged, cell growth stops and the immune response increases.

IV. EQUIPMENT AND DIFFERENT COMPONENTS FOR THE WATER SYSTEM:

The material used in the water system is very important for the quality of the product. Materials that interact with purified water, such as pumps, pipes, meters, etc., must be compatible, resist corrosion and prevent leaching. Some important components of the water system are listed below.

A. Pipes:

Pipes are very important in water systems. In hydraulic systems, the state of stiffness of the steel must be at least 316L.

B. Valves:

Valves, fittings and flanges must be hygienic. Once purified, the water is susceptible to microbial contamination and the

system is subject to the development of biofilms when using storage and cold circulation.

C. Pumps:

Pumps play an important role in the circulation in the water system. Pumps must be ready or successful to avoid blockages in the system.

D. Carbon Beds:

Carbon beds remove organic compounds from the feed water. One of the most commonly eliminated organic compounds is chlorine, which allows communities to control the growth of bacteria in drinking water. Because carbon beds filter the organic matter required for bacterial growth, this material is concentrated in carbon beds. If the beds are not well maintained, they may contain bacteria and endotoxins. Hot water or steam should be used regularly to clean the system of such contaminants. It is important that Standard Operating Procedures (SOPs) include these maintenance procedures.

E. Storage tanks:

The air filter is the design element of greatest concern to the collection bin. Most new tanks use double jacketed aeration filters to prevent condensate or water from clogging the hydrophobic filter. It is important that maintenance SOPs include procedures to periodically check the integrity of the aeration filter. For this reason, the filter must be in a position allowing easy access to the tests. SOPs should also regularly include full washing or emptying of holding tanks.

F. Capacitors:

It is important that the condenser be designed with double-plate tubes to prevent the distillate from coming into contact with the refrigerant, thus avoiding further contamination. Another aspect of the distillation burners is the quality of the steam supplied to the process. The quality of the steam must be controlled to avoid any recontamination.

G. Heat exchangers:

Heat exchangers play a very important role in water systems. When heat exchangers are used to heat or cool purified water in a system, protective devices must be used to prevent the heating or cooling tool from contaminating the water. The safest types of heat exchangers should be considered for the double tube plate or double plate and the frame or tube and cover.

V. INSTALLATION, ASSEMBLY MATERIAL AND SELECTION OF COMPONENTS:

Installation techniques are important because they can affect the mechanical, corrosive and hygienic integrity of the system. The installation position of the valve should promote drainage by gravity. Pipe brackets must provide suitable slopes for drainage and must be designed to sufficiently support pipes under the most adverse thermal conditions. The methods of connecting system components, including control panels, reservoirs and manifolds, require special attention to avoid potential problems.

Stainless steel welds are designed to provide reliable, smooth and corrosion-free connections in the interior. Low carbon stainless steel wire filters compatible with inert gas, automatic welding machines and regular inspections and documentation guarantee acceptable welding quality. Subsequent cleaning and passivation are important to remove the products of contamination and corrosion and restore the corrosion resistant passive surface. Plastics can sometimes be welded (welded) and also require smooth and even interior surfaces. Adhesives should be avoided because of the risk of vacuum and chemical reactions. Mechanical assembly methods, such. Flange connections, require precautions to avoid generation of offsets, voids, penetrations and voids. Control measures include proper alignment, seals of sufficient size, sufficient space, uniform sealing force and avoiding screw connections.

The building materials must be chosen so that they are compatible with control measures such as hygiene, cleaning and passivation.

System / Equipment: Classification is a critical factor in the selection of appropriate materials as the surfaces may be required to withstand high operating and disinfecting temperatures.

The material must be able to withstand turbulent flow and high speeds without wear during the impact of the corrosion barrier, such as the chromium oxide surface associated with the passivation of stainless steel.

VI. VALIDATION SEQUENCE:

A. Design Qualification (DQ):

The design of the equipment that constitutes the water purification system must be a priority. This is the result of the requirements of the water purification process. The capabilities of the process must be defined, for example. For example, the total volume required per hour or per day, average consumption, maximum demand, reversion capacity, minimum circulation and if high temperature storage is required. Participation of all appropriate groups, such as design, manufacturing operations, quality assurance, analytical services, etc. This is necessary because of the complexity of the business. Material selection, equipment suitability, functional checks, design techniques, cleaning and disinfection procedures, component compatibility, preventive maintenance, sterilization programs, sampling and regulatory requirements. The design qualification lists the activities required for the consistent production of the specified water quality. It also allows calibration of critical instruments. Design qualification establishes microbial impact and alert limits, provides sampling plans and connections for chemical and microbial testing, defines disinfection methods, and defines a method for data analysis and recording. The basic design package must contain the following elements:

The water system flow diagrams proposed with all instruments, controls, valves and components must be numbered for reference.

A complete description of the features and functions of the system. This is essential to ensure that production and quality control personnel, who are not familiar with technical terminology, can fully understand the design, construction, operation, control and sterilization of the system.

Detail of specifications for water treatment and pre-treatment equipment.

Detailed specification for all other system components such as storage tanks, heat exchangers, pumps, valves and pipe components.

Detailed specifications of controls of the sanitary system and description of how it works.

Specification of construction techniques used when quality is critical.

Cleaning process of the system both after construction and regularly.

Preliminary standard operating instructions for use, collection and sterilization. These procedures are referenced with the number of valves and components in the system diagrams.

Preliminary SOPs for filter change, integrity and maintenance tests.

Preliminary sampling procedures to control water quality and equipment operation.

Preliminary system certification procedures.

Preventive maintenance procedures.

B. Installation qualification (IQ):

This is the first qualification document. It includes the description of the system that follows in the Procedures section. Correct installation and assembly of various equipment should be checked. After a careful review of each ordered and verified device, the similarity must be examined and recorded. Note that all components of the device are installed according to the specifications and design drawing. IQ provides a design check that meets the specified specifications. This also includes instrument connections, verification of instrument drawings, verification and verification of the MOC, inspection and documentation of welds, trapping of tibial inclination and tubes, verification of passivation of stainless steel and other information. IQ conforms to the drawing "as built" and guarantees the adequacy of the finished system. The absence of leakage must also be taken into account. IQ should include why and how the water purification system is described with a full description of the system and cleaning system. The feed water must be specified at this stage. List the main components of the system, such as: pump, filters, UV lamps, controls, valves, drains, control system, etc., and verify that they meet the design specifications. Create the list of instruments and controls. The calibration of these instruments should be based on national and international standards. Instrument calibrations can be performed at the end of the IQ process and can be recorded as part of the IQ or at the beginning of the operational qualification. Once IQ is complete, the system is recommended for QO.

Some Important Verification during Installation Qualification:

1) Inspection of welds:

1) All welding joints in the system must be carefully checked for the following parameters:
2) Missing needle points or Pin holes.
3) The appearance of the weld must be uniform and uniform.
4) Thermal cracks must be absent.
5) The color of the welding is missing.
6) The thickness of the weld must not exceed 20% of the thickness of the pipe.
7) Stainless steel oxidation products are missing.
8) Welded pipe sections must be aligned correctly.
9) The shape of the weld should be substantially convex.

2) Checking the slope:

This is verified to verify the inclination of the pipes at the time of installation. The ratio of the slope to the length of the pipe should not exceed 1: 100. The slopes of the pipes are maintained so that the water can drain from the system to a low drain point.

3) Dead legs:

A common problem with the placement of pipes in hot or cold water systems with high quality circulation are the "dead legs". and therefore is not subject to the benefits of the continuous circulation of water. Water can accumulate in dead legs and provide the opportunity for the formation of biofilms and the growth of microorganisms. Water circulation systems must be removed from the bodies and routine hygiene procedures must be performed to ensure proper cleaning and maintenance of the system.

4) Pressure Test:

This test is performed to check if the system is integrated. Perform hydraulic tests at pressures that are at least twice the expected maximum operating pressure or 150 psig.

5) Remarks:

After the qualification of the successful installation, a report will be created. The second step is operational qualification to ensure that the system meets the requirements defined in the system design. Key activities to be carried out include:

C. Operational Qualification (OQ):

once the IQ is completed successfully, the QO system is possible. The system must be thoroughly cleaned and all constructions must be removed to minimize the risk of contamination and corrosion. Once the cleaning is complete, the appliance should be put into operation and should be carefully checked for proper operation. OQ checks if the processing units are functioning satisfactorily within the operating limits. The water quality of the system capacity, the temperature control and the flow rates are included in the OQ. Concentrate the elements and critical parameters during the QO. The control of the service alarm must be checked, such as the vapor pressure (high / low) and the differential pressure limits. The calibration requirement is determined for each limit. The system must present challenges with the minimum and maximum effort and operational results. The results are verified and are within the limits of acceptance. Use, cleaning and preventive maintenance The standard operating procedures must be complemented with operation, operation and maintenance manuals. The training of SOP technical staff will be covered at the end of the SOP in QO. Any change can be processed through a system of control and approval of changes. Any discrepancy must be approved and registered. Make sure that all operational and operational parameters meet the acceptance criteria and complete the QO documents. Review and approve the magazine and the OQ report. The system is ready for performance qualification (PQ) or validation.

D. Performance Qualification (PQ):

The objective of PQ is to perform rigorous tests to demonstrate the efficiency and reproducibility of the entire

integrated process. Three approaches are needed to achieve the goal of ensuring the reliability and robustness of the operating system over a long period. The validation of three phases is a regular expectation.

1) PHASE 1:

The test phase lasts 2 to 4 weeks (at least 14 days) to closely monitor the system. During this time, the system must operate continuously without errors or performance deviations. The following should be included in the test approach. Perform chemical and microbial testing according to a specified schedule. Show the incoming water daily to check the quality. Sample after each cleaning step daily. Develop suitable work areas. Development and completion of operation, cleaning, disinfection and maintenance procedures. Demonstration of the production and supply of water of a product in the required quality and quantity. Check preliminary alarms and action levels. Use and optimize the SOP for problems in operation, maintenance, disinfection, and screaming. Develop and refine the test error procedure.

2) PHASE 2:

An additional test period of 2 to 4 weeks (30 days) must be completed for additional intensive monitoring while all refined POEs are developed after successful completion of Phase 1. The sampling procedure should generally be the same as in Phase 1. During this phase water can be used for manufacturing purposes. The approach must also demonstrate consistent operation within the specified ranges and demonstrate the production and constant delivery of water in the quantity and quality required when operating the system in accordance with the SOP.

3) PHASE 3:

Phase 3 usually ends one year after the successful completion of Phase 2. In this phase, water can be used for production purposes, with the following goals and features: Increased reliable performance. Make sure that seasonal fluctuations are evaluated. Sample locations, sampling frequencies and assays should be reduced to the normal routine pattern according to the procedures tested in Phase 1 and 2. After completing Phase 3 of the Water System Qualification Program, this should be set up a routine plan based on the results of Phase 3.

4) REVALIDATION:

Revalidation may only be performed if the system or operating parameters have changed significantly. Routine monitoring and inspection will continue under the same conditions as the original validation. Routine maintenance or parts replacement must have a specific written procedure that must be validated at the time of original validation.

5) SANITATION:

Microbial control in water supply systems is mainly achieved through sanitation. The system can be disinfected thermally or chemically. In-line UV light with a wavelength of 254 nm can also be used to permanently disinfect the water in the system. Chemical processes, if compatible, can be applied to a wide range of construction materials. These processes usually use oxidants such as halogenated compounds, hydrogen peroxide, ozone or peracetic acid. Halogenated compounds are effective disinfectants, but are difficult to remove from the system and tend to cause acidic biofilms to oxidize bacteria and biofilms through the formation of reactive peroxides and free radicals (especially hydroxyl radicals). The short half-life of these compounds, especially ozone, may require a continuous addition during the disinfection process. Hydrogen peroxide and ozone decompose rapidly in water and oxygen. Peracetic acid is degraded in acetic acid in the presence of ultraviolet rays.

6) ALARM AND ACTION LEVELS:

The single monograph Pure water and water for injection does not contain specific microbial limits. These have been deliberately omitted since most of the current microbiological techniques require at least 48 hours to reach the final results. At this time, the water from which the sample was taken was already used in the production process. Failure to comply with the specifications of the compendium would require the rejection of the relevant product batch. And this is not the intention of a policy of alarm or action. The definition of a quantitative microbiological guide for water for pharmaceutical purposes is appropriate, as this Directive establishes procedures that should be applied in case of significant deviations beyond those limits.

Warning levels are levels or ranges beyond which a process may have deviated from its normal operating conditions. The warning levels are a warning and do not necessarily require corrective action.

Levels of action are levels or ranges that, when exceeded; Indicates that a process has left its normal operating range. Exceeding a level of action means that corrective action must be taken to bring the process back into the normal operating range.

E. Operation, Maintenance and Control:

A preventive maintenance program must be established to ensure that the water supply system remains under control.

1) Operational Procedures: Operating procedures for the water supply system and maintenance and corrective operations must be documented and the point at which the action is required. The process must be well documented, describe the function of each job in detail, determine who is responsible for the work and describe how the work is to be done.
2) Monitoring Program: Critical quality characteristics and operational parameters should be documented and monitored. The program may include a combination of on-line sensors or receivers (eg, a conductivity meter and a logger), manual documentation of operational parameters (such as a pressure drop in a carbon filter), and laboratory tests.
3) Disinfection: Depending on the design of the system and the selected operating units, regular disinfection may be necessary to maintain the system in a microbial control state. Disinfection technologies are described above.
4) Preventive Maintenance: A preventive maintenance program must be effective. The program must determine what preventive maintenance should be done, how often, and how the work should be documented.
5) Change control: Mechanical configuration and operating conditions must be checked. The proposed changes must be evaluated for their impact on the entire system. The need to requalify the system for modifications needs to be identified. After the decision to change a water system, the plans, manuals and procedures involved must be reviewed. intact compounds such as hydrogen

VII. DISCUSSION

There are many types of purified water systems used in pharmaceutical plants. Although most have common features, each system is tailor-made for a particular application. Developing a suitable design requires a good understanding of how the system works and attention to detail. Simple compliance with the general rules does not necessarily guarantee a reliable system, no matter how much is spent. On the other hand, with good understanding, it is often possible to design, install, and validate a purified, functional, and reliable water system with less investment and lower cost of ownership.

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