Water Purification and Validation Systems in Pharmaceuticals

Gautam Tomar*, Meenakshi Bhatt,
Shri Guru Ram Rai University,
College of Pharmaceutical sciences, Dehradun, Uttarakhand, India

Abstract:
Water is known as the "elixir of life": in the pharmaceutical industry, water quality is an essential and priority ingredient of various pharmaceutical preparations and is also used to clean process equipment and, therefore, performs a fundamental role in the pharmaceutical industry: it is the most used raw material in the production of active pharmaceutical ingredients (API), in intermediate products, in the finished dosage forms, making it an important raw material in GMP and in the validation of the manufacturing process.
The objective of purifying and validating water is to demonstrate that the process, when operating within certain limits, produces the product with a high degree of guarantee of consistency and specified quality. To achieve high quality, the purity and security of water system validation is essential. The validation process not only provides high quality water, but also provides a standard framework for monitoring the safety, effectiveness and outcome of the process. The purpose of this discussion is an attempt to look at the various aspects of purification and validation that include components of water treatment systems, equipment qualification, different qualification stages, documentation, validation, preventive maintenance, change control and post- monitoring.

Keywords: Validation; API; Water treatment systems.

➢ Introduction:

Water is the solvent most used in the production, processing and formulation of various pharmaceutical preparations such as tablets, capsules, suspensions and emulsions. The control of the microbiological contamination of this water is important because during the purification the diffusion of microorganisms in the water can occur. If contaminated water is used in the final product, these microorganisms or their metabolic products may eventually have negative consequences. [1]

The water that is used in the initial phases of the production of pharmaceutical substances and which is the source or feed water for the preparation of the various types of purified water must meet the requirements of the national standards on primary drinking water (NPDWR).(40 CFR 141) issued by the Environmental Protection Agency (EPA). Water is classified into different groups based on source, quality, treatment or use. [2]

Water is classified into different groups based on its origin, quality, treatment or use. Different types of water are classified according to the minimum quality requirements, particularly in relation to the expected chemical and microbiological purity. [3][4][5]

Fig .1 Classification of water System.

Level	Water Types
Level 1	Well Water

Level 2	Potable Water
Level 3	Potable Water used for general batch applications
Level 4	Food and Drug Administration (FDA) water for final rinse, formulation, and WFI

- **Level I Water:-**

Level I is untreated water used for utilities (fire protection, lawn sprinklers, etc.) and may be from a well or surface source.

- **Level II Water:-**

Level II (potable) is drinking water, which must meet EPA requirements for quality. Its source can be a private or municipal supply that has a variable degree of hardness and added chlorine for microbial control.

- **Level III Water:-**

Level III is purified water, which is the most difficult to control from a microbial standpoint. It is usually used for bulk batch application where there is no reasonable alternative and for non-parenteral product formulation. It is sometimes used as the initial cleaning agent for some processes.

- **Level IV Water:-**

Level IV water is the most critical quality level. It is commonly used in final formulation for parenteral applications and it is also used as final rinse water for critical product contact surfaces. This water must satisfy the specifications for water for injection as defined by current USP requirements.

1. Types of Water Systems :

Water is used as an ingredient for pharmaceutical preparations. It should meet the requirements for purified water, water for injection or one of the sterile forms of water covered by the pharmacopoeia. The pharmacopoeia is useful guide because it contains not only water information tests and minimum water quality standards, but also information on the manufacture of the various types of pharmaceutical waters, microbial control validation of water systems. [6]

Broadly, the pharmaceutical water can be divided into two groups: the loose water produced on the spot and the bottled water produced, packaged, and sterilized. The Bulk water is typically produced for use in same site in large volume by a multi-unit operation water system and employs a distribution system for its use in production purposes. Purified water and water for injection WFI are widely used in pharmaceuticals manufacture. [7]

1.1 Purified and Highly Purified Water:

These waters are used as an excipient in the production of non-sterile products non-parenteral products or preparations such as syrups, suspension, emulsions and in others pharmaceutical applications, such as cleaning equipment, apparatus and glassware's. [8]

1.2 Laboratory Water:

Laboratory water is used, where there is a need for the preparation of reagents for analytical tests evidence. The quality of laboratory water used to prepare the laboratory reagents should meet and fulfill the requirements of the analytical test methods. The laboratory water used should be purified using

different techniques like deionization, distillation, ion exchange, reverse osmosis (RO), filtration, or other suitable purification procedures. [9]

1.3 High Purity Water:

The European Medicines Agency (EMEA) has introduced the concept of high purity water. The high purity water is defined as high quality water for use in the preparation of pharmaceutical products where a high quality of water is needed except where WFI is used. [10]

1.4 Water for Injection(WFI):

Water for injection is high quality water without significant contamination. A sterile version is used to make solutions that will be given by injection. Before such use, other substances must generally be added so that the solution is more or less isotonic. It can be given by injection into a vein, muscle or under the skin. A non-sterile version can be used in production and sterilization takes place later in the production process. [11]

2. Design Requirements for Purification of Pharmaceutical Water System:-

2.1 The Incoming Municipal Water:

The inward water is usually a public water supply system that is being supplied from the storage tanks or either from the ground water. The public water supply should be constantly monitored for the quality of water, flow rates and pressure. The incoming public water should meet the criteria set by the Environmental Resource council (ERC-2) and the EPA guidelines for drinking water. The data in the Fig. 2 shows the major contaminants found in the city water: [12]

Fig.2 Major Contaminants in City Water Systems

Contaminants	City Feed Water Results
Total Dissolved Solids (TDS)	125.74 mg/l
Total Hardness	77.71 mg/l
Total Organic Carbon (TOC)	10.45 ppm
pH	9.23
Microbial Limits	500 cfu/ml

2.2 Pre Management of the incoming water:

To prevent the contamination and to maintain a high level of biological and chemical control there is a necessity for the management and pretreatment of the incoming water before it is used for some purpose. The different components that are being used in this process are: [13] [14]

a) Multi-media sieve,
b) Duplex water softener with brine tank and brine feed pump,
c) Hot water sanitizable Carbon Filter Skid (CFS) with circulation pump,
   - ✓ Heat exchanger
   - ✓ Activated carbon filter

d) Multi-cartridge filters,

a) Multi-Media Sieve:

A multi-media sieve is a type of sieve used to remove or reduce the turbidity, suspended solids, and residue from the supply water (incoming city water). The multi-media separation also removes particles with a nominal size of 10 microns or greater.

b) Duplex Water Softener:

The duplex water softner system produces a sodium cycle that will remove scaling and other trace materials from the water to improve the reverse osmosis process that will improve the life of the membrane.

c) Carbon Filter Skid:

The carbon filter skid is used to eliminate the organic matter and chlorine from the filtered water. The carbon bed is fitted on a loop of circulation pump, heat exchanger and activated carbon filters. To minimize the risk of microbial contamination the system and loop are periodically heated with the help of heat exchanger at a temperature about 176^0F to sanitize it.

The standards for the incoming water are summarized in Fig.3:

Fig.3 Pre- Treatment Water Specifications.

Contaminant	Specification
Conductivity	< 5 micro siemens/cm
Endotoxins	< 25 EU/ml
Microbial	< 500 cfu/ml
pH	5.5 to 7.0
Total Solids	< 5 mg/L
Chlorine	Non-Detected

2.3 Water Purification System:

Usually, the components associated with purification systems are similar to WFI systems with the exception of the method of water production (distillation versus RO/DI) and the final quality output. Along with the water pre-treatment system described above, these are the components that comprise a Purified Water System:

a) System Elements:-

i. RO feed tank with break tank and vent filter; RO feed pump,
ii. Single pass reverse osmosis unit,
iii. Deionization (DI) bottles(Filter - 0.5 micron),
iv. Ultra-Violet (UV) sterilizer(Final filter - 0.2 micron),
v. Storage tank (still)(Tank vent filter).

b) System Details:-

i. Water Pretreatment System,
ii. Break Tank System,

A 100 gallon RO feed break tank provides an air break and reserve capacity for the RO system. The pump delivers feed water through two 1.0 micron multi-cartridge filters, which are used to remove carbon fines or other particulate matter from the water before it passes through the RO unit.

iii. Reverse Osmosis,

A single pass (RO unit is used to remove 99% of particulate matter, silica, bacteria, and endotoxins.) The operation of the RO unit is continuous in order to minimize bacterial load. When the still does not require feed water, the RO unit will operate in a high recovery mode in order to minimize water consumption.

iv. Deionization System,

The DI recirculation loop provides pressurized RO/DI water to the still feed system. The water in this system flows constantly through the DI recirculation pump, which consists of two deionization bottles in series, an ultra-violet sterilizer, and a 0.5 micron resin trap filter.

v. UV Sterilizer and Final Filtration System.

UV Sterilizer and Final Filtration System a 0.5 micron filter is used to decrease the bioburden levels and to prevent resin particles from the DI bottles from being deposited onto the surface in the UV sterilizer. A UV sterilizer and a 0.2 micron final filter are used to decrease the bioburden levels in the water before it enters into the still. [15]

2.4 Purified Water Storage System:

The Purified water is being supplied to the storage tanks after the purification process. The quality of the purified water is being maintained by the continuous supply of the water to the tanks. The purified water is being discarded after a period of 24 hrs. to prevent the bacterial growth in the purified water. The purified water distribution loop returns to the storage vessel after being further polished and filtered. A 0.2 micron hydrophobic vent filter is usually employed on the purified water storage vessel to filter out any air coming into the storage vessel during purified water system draw down. [16]

2.5 Purified Distribution Loops:

The generated purified water is distributed throughout in a continuous loop. In distribution systems, where the water circulates at a specified controlled temperature, dead legs and low flow should be avoided, and valve tie in points should have length-to-diameter ratios of six or less. Components and distribution lines should be sloped and fitted with drain points. The distribution loop tubing may be composed of stainless steel or plastic. The purification system is designed to purify water to meet USP specifications. [17][18]

Fig.4 Purified water Specifications.

Contaminants	Specifications
Conductivity	USP Specifications
Endotoxins	No Specifications
Bacteria	100 cfu/ml
pH	5.0-7.0
Total Organic Carbon	500 ppb

3. Design Requirements for Purification of Water for Injection:-

The components that are used in the purification of the water for injection system are:

a) Multiple-effect distillation unit,
b) Vapor compression distillation,
c) Jacket storage tank,
   - Vent filter
d) Cold, hot, and ambient WFI distribution loops with associated pumps,

- Heat exchanger with cooling water
- Heat exchanger with chilled glycol
- Heat exchanger with chilled water

a) Multiple-Effect Distillation Unit:

Multiple Effect Distillation (ME) System it is a method as much known. Multiple-effect stills are mainly noted for their multiple column design which re-uses steam energy through the process, requiring minimal moving parts, but requiring cooling water for final distillation of product. In case of low capacities required (since MED systems absorbing much energy and cooling water) you can also get WFI from Single Effect Distiller (BRAM-COR Mod. DPSG),that is both a still and a Pure Steam Generator. [19][20]

b) Vapor Compression Distillation:

Vapor Compression Distillation (VC) System is also known as thermo vapor recompression or thermal / mechanical vapor compression. It is a technology similar to the evaporation systems used for the water desalination. Vapor compression is also common term in the refrigeration industry. VCD units are driven by a more mechanical process than MED, involving a compressor and other moving parts to compress steam and increase its pressure/temperature for evaporation; they are powered by either steam or electric heating, and have a minimal feedwater quality requirement due to lower operating temperature. [21]

c) Storage Tanks for Water for Injection:

Purified water for injection is supplied to multi-effect storage tanks. The quality of the water is maintained by continuously recirculating the contents of the storage system beyond the temperature of 800 ° C. An external covering in the tanks keeps the temperature above 800 ° C. The WFI hot distribution circuit returns to the WFI storage container via a spray ball. The sprayer ball constantly irrigates the dome and the side walls of the storage container with the WFI hot water to keep the cleaning inside the storage tank.

Typically a 0.2 micron hydrophobic vent filter is used in the WFI storage vessel to filter the air entering the tank during the WFI extraction. The filter is equipped with a steam jacket coming from the low pressure system to prevent filter obstruction. Valves and ports are provided on the vent filter to clean the steam disinfectant from the vent filter after cartridge replacement. A rupture disk in the storage container protects it from overpressure. A burst monitor indicates overpressure of the rupture disk and triggers an alarm. The temperature of the WFI storage tank is continuously monitored. [22][23]

d) Distribution Loops for Water for Injection:

The generated WFI distributed during installation can be in three different loops: hot distribution, environmental distribution or cold distribution. In distribution systems where water circulates at high temperatures, dead legs and low flow must be avoided and the valve connection points must have a length / diameter ratio of six or less. The components and the distribution lines must be inclined and equipped with drainage points. [22]

Fig.5 Water for Injection Specifications.

Contaminants	Specifications
Conductivity	USP Specifications
Endotoxins	0.25 EU/ml
Bacteria	10 cfu/100ml
pH	5.0-7.0

Total Organic Carbon	500 ppb

4. **Other Additional Methods and Techniques used for Purification of Pharmaceutical Water System:**

In the normal osmosis process, the solvent naturally moves from an area of low solids concentration through a membrane to an area with a high concentration of solids. Reverse osmosis is applying external pressure to reverse the natural flow. RO is more commonly known for its use in the purification of water from seawater (that is, the removal of salt and other substances from water molecules).

The UV sanitation systems use a UV light source (lamp) enclosed in a transparent protective cover (usually quartz). The lamp is mounted in such a way that the water passing through a flow chamber is exposed to UV-C light rays. When microbes are exposed to UV rays, they become sterile and can no longer reproduce. The microbes are now considered dead.

The treatment with UV water does not introduce any chemical into the water, does not produce by-products and does not alter the taste, pH or other properties of the water.

The use of UV lamps is not recommended as the main means of controlling microbial growth. UV lights can be used in combination with other pretreatment units (such as 0.2 micron filters) to provide secondary microbial control. Normally, the UV lamps are installed after the EDI unit. UV intensity should be monitored and documented. [24][25][26]

Validation of Purified Pharmaceutical Water:-

Validation is the process of establishing documentary evidence to demonstrate that a procedure, process or activity performed in the tests and then in production maintains the desired level of compliance at all stages. In the pharmaceutical industry, it is very important that in addition to final tests and product compliance, it is guaranteed that the process constantly produces the expected results. The desired results are established in terms of specifications for the outcome of the process. The qualification of systems and equipment is therefore part of the validation process. In common words, validation involves testing of: [27]

1. Engineering design
2. Operational procedures and acceptable ranges for control parameters.
3. Maintenance procedures

To achieve this, the system must be designed, installed and tested sensibly during and after construction, and therefore for a prolonged period of time under all conditions. There are two basic validation approaches:

1. Depending on the evidence obtained through the tests: prospective and simultaneous validation
2. Depending on the analysis of the (historical) data accumulated: retrospective validation

1. Validation Plan:

This document is not an FDA requirement, but has become almost an industry standard. The validation plan must contain all the information concerning the water purification system. Which are positive for basic information about design, plans, specifications, procedures and protocols. Indicate the reasons for the choice of equipment, for the cleaning and disinfection frequencies, for the replacement and renewal of the components. It will contain the records of equipment changes and procedural alterations. It will have records of equipment and filters and recertification data. In short, it will be the main reference file for the

entire water production and purification system. As such, it will be used for internal research purposes and will form the basis for external regulatory reviews.

The validation plan is used to establish the limits for validation, to define the scope of the project and the systems included and not included in the qualifications and what the project is going to demonstrate. For example, if the project involves the use of deionized water to feed a clean steam generator, the validation plan will define which components would be involved in the preparation of that water; which attributes of general quality should be achieved by each unit of purification; and the sampling time of the system at which frequency.

Issues related to options need to be addressed in the validation plan, including the reasons for the options. The reason why the selected decisions are appropriate should be clear. The validation plan must be consistent with the company's quality control policies and must be included in the POS. [28]

2. Validation Steps:

A sequence of steps is involved in the validation of the pharmaceutical water system. Traditionally these steps areidentified as

1. Design Qualification (DQ)
2. Installation Qualification (IQ)
3. Operational Qualification (OQ)
4. Performance Qualification (PQ)

The final validated condition is a sum total of the proceeding qualification. It is necessary that the efficacy and proof of the tests trials and experiments be performed successfully at least three consecutive times to constitute positive conformation satisfactory to the FDA validation requirement. [29]

3. Validation Sequence

3.1 Design Qualification

These are the design documents that define the standards and objectives of the hardware. The design qualification will list the activities necessary for the consistent production of the established water level. It will contain a complete description of the system by specifying its acceptable ranges and operating limits. It will provide complete diagrams of electrical, mechanical and water flows for subsequent verification of its correct installation. Identify the specific purification units, the various control devices and the safety and alarm systems, which will specify the sampling plans and the doors for chemical and microbial tests , establish the disinfection methods and define the procedures for analysis and tracking The DQ data is prepared in accordance with the URS (User Requirements Specifications) and Pharmacopoeia standards. [30][31][32][33]

The various components of water generation systems that need to be validated include the following:

Fig .6 Component of water generation system.

Component	Desired Features/Functions
Piping	Selected material: stainless steel; should be designed for reliability, pressure control, nullifying presence of extractable contaminants.
Holding Tanks	Optimal size/capacity: 2000-4000 gallons, Hydrophobic air filters-restrict entrance of microbes in tanks.
Filters	Removes undissolved solids and bacterial contaminants Control

	measures: Pressure and flow monitoring, backwashing, sanitizing and replacing the filter media etc.
Deionizers and Reverse Osmosis	Removes dissolved solids, resins must be periodically regenerated.
Carbon Beds	Removes organic chlorine compounds and low molecular weight carbon compounds, required design features: selection of proper particle size, avoidance of hydraulic channeling etc.
UV Lights	Biocidal wavelength: 254 nm; UV dose variables: lamp intensity, residence time distribution and water transmittance should be properly measured.
Distillation Still	Deactivates bacterial endotoxins and removes dissolved solids not otherwise removed by RO units and deionizers.
Ozone and Heat Sterilants	Strong oxidizing agent, effective at low concentration. Both are used as biocidal.

The basic design package should include the following,

- Flow schematics for the proposed water system showing all of the instrumentation, controls and valves and component should be numbered for reference.
- A complete description of features and functions of the system. This is of critical importance to enable production and quality assurance personnel, who may be unfamiliar with engineering terminology, to fully understand the manner in which the system is to be designed, built, operated, monitored and sterilized.
- Detail specification for the equipment to be used for water treatment and pretreatment.
- Detail specification for all other system components such as storage tanks, heat exchangers, pumps, valves and piping components.
- Detailed specifications for sanitary system controls and description of their operation.
- Specification for construction techniques to be employed where quality is of critical importance.
- Procedure for cleaning the system, both after construction and on a routine basis.
- Preliminary standard operating procedures (SOP's) for operating, sampling and sterilization. These procedures will be cross referenced to the valve and component numbers on the system schematics.
- Preliminary SOP's for filter replacement, integrity testing and maintenance.
- Preliminary sampling procedures to monitor both water quality and operation of the equipment.
- Preliminary system certification procedures.
- Preliminary preventive maintenance procedures.

Fig .7 Numerical Interpretation of USP Standard

Component	Purified water	Water-for-injection
pH	5.0–7.0	5.0–7.0
Chloride (mg/L)	0.2	0.2
Sulfate (mg/L)	1.0	1.0
Ammonia (mg/L)	0.1	0.1
Calcium (mg/L)	1.0	1.0
Carbon dioxide (mg/L)	5.0	5.0
Heavy metals (mg/L	0.1 as Cu	0.1 as Cu
Oxidizable substances	Pass USP Permanganate test	_
Total solids (mg/L)	10.0	10.0

Pyrogens (EU/mL by limulus amebocyte lysate)	_	0.25

3.2 Installation Qualification:

The IQ protocol will consist of a description of the system followed by a section of the standard operating procedure. Before being able to examine the operating characteristics of the system, it is necessary to verify the correct installation and assembly of the various components of the equipment. Subsequently, it is carefully checked that every equipment ordered and received is identical to that stipulated in the system design. The qualification of the installation confirms the "incorporated" plans and guarantees the adequacy of the whole system. As stated in the guidelines provided by the Food and Drug Administration. The installation qualification phase includes the examination of equipment design, the determination of calibrations, maintenance and regulation requirements and identification of critical elements Characteristics that could influence the process and the product. The information obtained from these studies should be used to establish written procedures that cover equipment calibration, maintenance, monitoring and control. "For an IQ of the water generation system, the following would be the typical key elements: Controls include compressed air, steam, feed water and electricity. Everything must be verified when installing the equipment for the systems Water generation Calibration of all process control tools according to written procedures and certification that meet the tolerance limits specified for accuracy and also in terms of selectivity or specificity must be performed and documented. system design, including material data and calibration certificates.[27][34]

3.3 Operational Qualification:

When the installation of the equipment has been verified as correct, it is possible to execute the system OQ documentation. The purpose of OQ is to establish documented evidence through system tests that all critical components are able to operate within established limits and tolerances. It is the functional test of the system components mainly the critical components. The purpose of OQ is also to verify and document that the water generation system provides an acceptable operational control under "rest" conditions. The Qualification Operation verifies the ability of the water purification system to provide sufficient water with a high degree of quality to ensure compliance with specifications, to maintain general parameters such as pressure, temperature, flow at established points, to maintain any critical parameter (pH, TOC, endotoxin, microbial level, conductivity, etc.) includes tests that have been developed from process knowledge, from the equipment system and from tests including a condition or set of conditions with operational limits lower, sometimes referred to as the "worst case" conditions. [35]

3.4 Performance Qualification:

The purpose of the PQ protocol is to provide a rigorous test to demonstrate the reproducibility and effectiveness of the total integrated system. System setpoints, control sequences and operating parameters are detected. The process is repeatedly challenged to demonstrate its constant performance. All acceptance criteria must be met at the conditions of the "worst case" process. When faults occur they must be identified and corrected. Tests must be performed again to respond to the elimination of the causes of failure. Look for the consistency of the acceptable water quality of the product.

The purpose of QP is to verify, test and document that the water generation system provides acceptable control under "full operation" conditions. QP must follow successful completion of QI and OQ. According to the FDA opinion: "The observed variability of the equipment between and within the runs can be used as a basis for determining the total number of trials selected for subsequent PQ trials of the process." parameters over time (such as pH, TOC, conductivity). The PQ and OQ tests are sometimes performed together with others. [36][37]

4. Qualification Phases:- [38]

WHO recommend three phase approach to WHO Technical Report Series 929 to prove heftiness and reliability.

4.1 Phase I:

This requires a 2 to 4 week trial period to monitor the deviation from the enactment. The periodic sampling together with the tests in pre-determined test tests is performed in the samples according to the defined plan. This phase also involves the development of appropriate operating intervals together with the completion of the cleaning, disinfection and maintenance procedures. At the end of this phase, the systems are simulated to operate under stress conditions such as starting after a power failure or emergency stop. The system is also tested in standard maintenance restorations, filter changes, etc.

4.2 Phase II:

This phase includes the same sampling scheme as in step I. It must include additional system monitoring during a 2-4 week trial period. After the completion of phase I, all the improved SOPs are implemented. During this phase the water is used for production purposes. This passage establishes that the system is under control, within predetermined specifications. The tests in this phase also ensure the constant production and supply of water of the required quantity with a high degree of quality when the system operates in compliance with the SOPs.

4.3 Phase III:

This is a confirmation phase in which the frequency and number of sampling positions are lower than the previous steps and shows that the system has a reliable and prolonged performance and is under control for a prolonged period of time. It takes about a year to complete after phase II has been successfully completed. During this phase, water can be used for production purposes. Periodic deviations of feedwater are also examined at this stage. This final phase should only start after having satisfied the requirements mentioned in the Phase I and II test protocols. At this stage, a complete microbiological and chemical analysis should be performed and the results should

It will be presented graphically using various computer applications. A completed validation report, reviewed and approved must be prepared according to company procedures. The validation project is considered only after approval of the final reports by the competent authorities.

5. Preventive Maintenance [38]

This element is often considered the responsibility of the site's Maintenance and Operations department and is often given a low priority within a technical design team. There is a clear requirement to maintain a structure in a qualifying state. A preventive maintenance program is an essential component of a work program to achieve this goal. The general validation plan must identify the necessity of this program and, therefore, indicate its importance for the designers. The role of sellers and suppliers is very important in this sector. Operational and maintenance manuals should be considered a fundamental part of the specifications

program. This task must be performed during the design phase and the required documentation must be included in the application. The execution of a preventive maintenance program can become more relevant during the pre-commissioning and commissioning phases, which shows that, once qualified, a unit has been adequately maintained and in accordance with the supplier's instructions.

6. Change Control [28][39]

A water system that works without problems can suffer exits for reasons other than alterations in its water reserve. These must be explained, defined and documented correctly. Since water purification units, such as ion-exchange beds, can be depleted, RO membranes will require cleaning, reservoirs and piping may require remediation, etc. In general, the devices and accessories that make up the system will periodically require activities related to maintenance, such as replacement, restoration, cleaning, disinfection, replacement and renewal of different types. Furthermore, the various elements require attention at different times. The necessary

Therefore, the system documentation will also include a series of information related to the proper maintenance of each component of the equipment. Much of this will initially come from equipment suppliers and could, in fact, form clauses related to the performance guarantees of your equipment. The relevant documentation includes the standard maintenance procedures necessary for the proper functioning of the system.

7. Revalidation [40]

The revalidation and evaluation must be made on the basis of the impact of the change in the water generation system. Routine monitoring and examination will continue under the same conditions as those existing during the original validation. Ordinary maintenance or replacement of parts must provide a specific written procedure, which must be validated at the time of initial validation.

Conclusion

It can be concluded that the water purification system is effective for eliminating organic, inorganic and microbial contamination and since water is a universal solvent used in the pharmaceutical industries for the production, processing and cleaning of all equipment, it must be pay special attention for its purification.

The system qualification and validation must be performed over a period of time to demonstrate its reliability and robustness of the system to produce water of specific quality with a high degree of safety. And each of the reports must be documented for a better job.

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