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ANALYSIS OF OPERATION *PURIFIED WATER SYSTEM* IN THE PHARMACEUTICAL FIELD OF PT. NULAB PHARMACEUTICAL INDONESIA

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ABSTRACT

Health is an indicator of the level of human welfare so that it becomes a priority in the national development of a nation. This is related to efforts to improve the quality of the nation's resources. With quality human resources, it will further increase the nation's competitiveness in the current era of global competition. The main form of the application of technology is as a driving force for the advancement of science and technology and the times, in making work more efficient. Currently, many factories in the pharmaceutical industry have used a purified water system, for example a water management system in the manufacture of drugs. The objectives of this study are (1) to determine the Purified Water System process in the pharmaceutical sector. (2) knowing the performance system in the Purified Water System process in the pharmaceutical sector, (3) analyzing the results of the Regeneration of the Purified Water System in the pharmaceutical sector. The research method used is qualitative research with a descriptive approach. The data collection techniques include observation, interviews, literature study and documentation. The data analysis technique used an interactive method developed by Miles & Huberman. The results of this study indicate that the working mechanism of the Purified Water System is a water treatment system that can remove various contaminants (ions, organic matter, particles, microbes and gases) in the water to be used for production. Water (raw water) water treatment can be obtained from PDAM water (city water), Shallow well (shallow well) with a depth of 10-20 m, or from deep wells (deep wells) with a depth of 80-150 m. Variations in the quality of raw water supplies that meet the requirements are determined from the water quality target to be produced. Likewise, water quality determines the equipment needed for water treatment.

Keywords: *Purified water system, pharmacy, analysis, operation*

INTRODUCTION

Water treatment can be carried out in various ways, for example conventional treatment, namely by adding alum and also filtering using cloth or sand. However, this traditional water treatment is not optimal and clean water is obtained that meets the requirements. Currently the development of water treatment has grown rapidly. There are already enough agencies that need clean water in large quantities, establishing independent clean water treatment plants to get rid of dependence on PDAM. This independent water treatment was developed by following the development of existing clean water filtration technology, of course also influenced by the ability of the agency both in terms of technology availability and in terms of finance. The working mechanism of the purified water system is a water treatment system that can remove various contaminants (ions, organic matter, particles, microbes and gases) contained in the water that will be used for production.

Water*(rawwater)*water treatment can be obtained from tap water*(city water*), *Shallow well* (shallow wells) with a depth of 10-20 m, or derived from Deep well (deep wells) with a depth of 80-150 m. Variations in the quality of supply of raw water*(rawwater)*are eligible is determined by water quality targets that will be generated. Likewise, water quality determines the equipment needed for water treatment. *The purified water system* consists of: *Multimedia filter*, Carbon *filter*, *Water softener*, *Heat Exchanger* (HE), *Micro filter*, *Ultra filtration* (RO = *Reverse Osmosis*), and *Electro Deionization* (EDI). The aims of this research are (1) to know the process of *Purified Water System* in the pharmaceutical sector. (2) knowing the performance system in the process *Purified Water System* in the pharmaceutical sector and (3) analyzing the results of the *Purified Water System Regeneration* in the pharmaceutical sector.

PT Nulab Pharmaceutical Indonesia is a branch of the pharmaceutical industry parent PT Guardian Pharmatama which was established in September 1992 to replace Hasto Husodo's Pharmaceutical Industry. Based on a notarial deed, PT Nulab Pharmaceutical Indonesia was established on October 17, 2008. While the company's operations began on January 2, 2018. The head office of PT Nulab Pharmaceutical Indonesia is located in the Green Ville Maisonette complex, Block FA 18-19, Jakarta 11510. While the factory is located in Sweet Industrial Estate, Jl. Sweet Raya, Ex. Gandasari, Kec. Jatiuwung, Tangerang City, Banten Province. Since 1994, PT Guardian Pharmatama which is the parent of the industry has received CPOB (Good Manufacturing Practices) certificate for:

1. Ordinary antibiotic
2. tablets Non-antibiotic ordinary
3. tablets Antibiotic
4. coated tablets Non-antibiotic coated tablets
5. Oral fluids Oral fluids antibiotics
6. Non-antibiotic oral liquid Non-antibiotic
7. oral powder Non-antibiotic
8. external powder AntibioticNon-antibiotic
9. hard capsules hard
10. capsule Non-antibiotic
11. external medicine Liquid Non-antibiotic
12. ointment/cream

The products produced by PT Nulab Pharmaceutical have gone through a production process that refers to the GMP guidelines and the ISO 9001: 2008 management system to get high quality, safe, and efficacious drugs. Water treatment can be carried out in various ways, for example conventional treatment, namely by adding alum and also filtering using cloth or sand. However, this traditional water treatment is not optimal and clean water is obtained that meets the requirements (Kurniawan, 2014). Currently the development of water treatment has grown rapidly. There are already enough agencies that need clean water in large quantities, establishing independent clean water treatment plants to get rid of dependence on PDAM. This independent water treatment was developed by following the development of existing clean water filtration technology, of course also influenced by the ability of the agency both in terms of technology availability and in terms of finance.

Water Treatment System (SPA) is a system to obtain water with the quality required by each type of drug that is made and meets the requirements of the pharmacopoeial monograph. Water plays an important and critical role in the pharmaceutical industry because it is the starting material to ensure the production of quality and safe drugs for users. Because of their important role, these SPAs need designed, manufactured,*commissioned to* be properly, qualified, operated and maintained to achieve their intended use. The replacement of the water treatment system from manual to automatic also needs to be qualified which will later be able to guarantee the quality of the water used in drug production, as well as other activities in the pharmaceutical industry (Priyambodo, 2007).

Figure 1. Water Management System (Source: SPA Book, 2014)

Water Treatment System is a critical system that has a direct impact on quality, so the critical quality parameters of the system must be qualified. The qualifications to be carried out must follow the validation rules which include Design Qualification (KD), Installation Qualification (KI), Operational Qualification (KO) and Performance Qualification (KK) in accordance with GMP Guidelines. KD, KI and KO are very dependent on each system installed by each pharmaceutical industry, so the type of GMP does not provide specific guidelines. Technical Guidelines for CPOB (and also POPP CPOB) only provide guidelines regarding the implementation of KK (Performance Qualification) with a 3 phase approach, namely phase 1, phase 2 and phase 3. Water treatment is a technical effort carried out to provide protection to water sources by improving quality the origin of the water to the desired quality with the aim of making it safe for use by the water user community (Siregar, 2005). In the water treatment system, there are 2 (two) types of treatment (Sutrisno, 1987), including:

1. Physical Treatment, is water treatment that aims to reduce or eliminate coarse impurities, removal of mud and sand and reduce organic substances in water. to be processed.
2. Chemical Treatment, is a processing process with the addition of certain chemicals with the aim of improving water quality. The addition of these chemicals in the form of:

a. Coagulant. The coagulant needed in the drinking water treatment process aims to form flocs of suspended particles and non-settled colloids. The coagulant added is usually in the form of Al2SO4, FeCl3, or Poly Aluminum Chloride (PAC), and others.
b. Neutralizing material. Alkali application is intended to neutralize the pH, because in general the pH will decrease after the addition of an acidic coagulant. Alkali application is required when the treated raw water has a low alkalinity.
c. Disinfectant. Aims to kill pathogenic bacteria that are still present in water that has gone through the filter stage. *The disinfectants* used are chemical substances which are strong oxidizing agents such as chlorine and chlorine.
d. Porous carbon or better known as activated carbon, is used as an adsorbent for color removal, waste treatment, and water purification. Activated carbon will form amorphous which consists mostly of free carbon and has a hollow inner surface, black color, odorless, tasteless, and has a much greater absorption capacity than carbon that has not undergone the activation process. Activated carbon is a carbon compound, which can be produced from materials containing carbon or from charcoal that is treated in a special way to get a wider surface. The surface area of activated carbon ranges from 300-3500 m2/gram and this is related to the internal pore structure which causes activated carbon to act as an adsorbent. Activated carbon can adsorb gases and certain chemical compounds or its adsorption properties are selective, depending on the size or volume of the pores. -pores and surface area (Awalludin, 2007).

Pure water systems can be used for various purposes in pharmaceutical manufacturing. For non-parenteral products it can be used in product formulation and final washing of process equipment and containers. In the manufacture of parenteral products it can be used in washing starting containers and for WFI systems. To produce Purified Water, it is important to remove organic matter, high and medium molecular weight ions and bacteria/pyrogens to a level that meets Eur.Ph, USP or JP requirements. Pure Water is obtained by further purification of RO or Pre-Treated Water via Ion Exchange Deionization/Demineralization (DI), Electro Deionization (EDI/CEDI) and UV light treatment depending on the level required. Honeyman Water has built a market-leading reputation for designing Pure Water systems that work for you, regardless of level, capacity or desired application. Our water systems are designed to ensure:

1. Capacity varies from 100 to 20,000 lph (liters per hour).
2. Compliance with GMP, Eur.Ph, USP and JP regulatory requirements or site-specific requirements.
3. Sanitary in-line instrumentation to monitor critical product parameters such as conductivity, temperature, Ozone in water, TOC and Ph.

This grade purified water is widely used as raw materials, ingredients, and solvents in the processing, formulation and manufacture of pharmaceutical products, active pharmaceutical ingredients (APIs) and intermediates, compendial articles, and analytical reagents. Purified Water is used as an excipient in the production of non parenteral preparations. and in other pharmaceutical

applications, such as cleaning of certain equipment and nonparenteral product contact components. Minimum quality of source or feed water for pure drinking water production (Asmadi, 2011). Cloudy water is water that contains solid materials and pollutes the environment so that it can cause health problems. Turbid water is also polluted and dirty water, so it can cause infectious diseases and health problems. Turbidity is not necessarily due to the dangerous nature of water, but people generally think that cloudy water is polluted and dirty water, so there is concern that infectious diseases and other health problems arise. Very cloudy water will accelerate the occurrence of blockages in the cracks. filter media, resulting in an unsatisfactory filtering performance. Filtration is one of the physical water treatment. Filtration is a solid-liquid separation process by passing liquid through a porous medium or materials to remove or remove as many fine particles of suspended solids as possible from the liquid (Varonika, 2009).

The multi-media water filter system is very suitable for binding sediment, iron, manganese, and other particles, including removing unwanted colors, removing unpleasant odors, removing turbidity in water. This filter system is also very suitable for use as a*pre-treatment*in reverse osmosis and ultrafiltration systems. Multi-media filter systems are also ideal for use in the process of filtering water from wastewater treatment.

In a multimedia filter, there are several stratified layers. The heavier layers are layered at the bottom and the lighter layers are layered at the top. Usually, lighter layers are designed to have a larger grain size. In this way, larger contaminants are filtered out of the water before smaller contaminants, and the filtration efficiency for the filter media volume is increased. The most common multimedia filters consist of sand and anthracite as filtration media. Sand has smaller grains and is heavier than anthracite. This ensures that a layer of sand settles beneath the anthracite and provides a smoother filtration. A properly operated Multimedia filter can remove particles up to 20 microns. Multimedia filters that use the addition of a coagulant (which induces small particles to join together to form particles large enough to be filtered) can remove particles up to 10 microns.

The main reason that filters in service may need to be re-washed is that contaminants can build up in such a way that water flow is obstructed or the quality of the filtered water is no longer acceptable. This condition can be monitored with a differential pressure gauge or switch to indicate that the filter needs to be re-washed. Backwash should be performed when the differential pressure is greater than 10-15 psi. Carbon filtration is commonly used in water filtration systems. In this illustration, activated carbon is in the fourth level (counted from below). There are two main types of carbon filters used in the filtration industry: powder activated block filters and granular filters. In general, carbon block filters are more effective at removing large amounts of contaminants, based on the increased surface area of the carbon. Many carbon filters also use a secondary medium, such as silver, to prevent bacterial growth in the filter. Carbon filters have been in use for several hundred years and are considered one of the oldest means of purifying water. Historians have shown evidence that carbon filtration may have been used in ancient Egyptian culture for both air and water sanitation. Today, carbon filters are used in individual homes as point-of-use water filters and, occasionally, in municipal water treatment facilities. They are also used as pre-treatment devices for reverse osmosis systems and filters specifically designed to remove chlorine-resistant cysts, such as giardia and cryptosporidium.

The water filter method that we will use is the addition of a porous filter with sizes of 0.5 micron and 0.3 micron and activated carbon. Activated carbon is used for water purification, gas

purification, beverage industry, pharmaceuticals, catalysts, and various other uses (Kirisitset, 2001). To reduce the hardness of water, filtration (filtering) with activated carbon media has chemical and physical properties, including being able to absorb organic and inorganic substances, can act as a cation exchanger, and as a catalyst for various reactions. Special research is needed to be able to determine the content and amount of sediment in the water. Therefore, research on the use of water filters and laboratory tests will be carried out in this research. It is also hoped that this research can overcome the problem of water deposition and purify water.

Water softener is a method or process with a function to reduce the concentration of magnesium, calcium and other ions that are categorized as hard *water*. In this case,*hard ions*can cause various unwanted effects, such as difficulty forming foam on soap and causing Limescale, which is white crust on the hot water pipes of boilers and boilers. When used manually, the operator will open and close the faucet to control the rate, frequency and timing of regeneration. Meanwhile, if the softener filter is used semi-automatically, the operator will only see the regeneration cycle, and the button will be pressed when the softener must be regenerated, then the unit will control the regeneration process. This softener tank can also be operated automatically through the completeness of the timer starting the regeneration and each stage of the process itself. Where the operator itself only needs to adjust the time and add salt based on needs. Filter media is carried out when the media has weakened or died so that dirt and ions contained in the water cannot be completely filtered out.

Procedure Softener Resin Water can be said as a water filtration tank that functions to remove hardness and water hardness using cation resin. Where this water softening technology utilizes 2 types of equipment, namely a softener tank for resin storage and a brine tank for salt or NaCl storage. In this case, the cation resin in the softener functions to absorb lime and after the resin is saturated or filled with lime, it can be reactivated using only NaCl salt. The softener tank can be operated differently according to the type of valve itself (Setyo, 2007). The function of Cation Resin is to remove lime (CaCO3), Magnesium (Mg), Calcium (Ca) content in drinking water or ground water or PDAM water or mountain water. Cation resin is commonly used as a softener for water with a high level of hardness (high total hardness). Water with high hardness contains a lot of lime (CaCO3) and elements of Calcium (Ca), Magnesium (Mg) in large quantities. Water with high hardness will cause the function of the water for the washing or cleaning process to be disrupted. For example, if it is used to wash clothes with detergent or detergent, the soap or detergent cannot produce a lot of foam, in other words, it has little foam. Likewise, if used for bathing using bath soap, the foam will be a little and feel slippery. The same thing happens when used to wash hair using a hair cleansing shampoo. Therefore, water with high hardness like this needs to be repaired first (= softener/softener) by using cation resin. This high hardness water also cannot be filtered using an RO membrane, therefore it is necessary to use a cation resin softener before being processed through an RO (Reverse Osmosis) machine.

This is done with the aim that the work of the RO membrane (reverse Osmosis) is not quickly clogged. Together with anion resins, cation resins are used for demineralization purposes, namely to produce water with very minimal mineral levels. In the field of drinking water treatment using an RO machine, this process is usually carried out before the water enters the RO (Reverse Osmosis) machine so that the RO membrane work is not too heavy. This process is carried out with the aim of producing pure water with a TDS level close to 0, where this pure water is often

needed for health purposes such as oxy water and others. This pure water is also commonly used in industrial steam boilers, boilers, synthetic fiber factories in fabrics such as nylon, rayon, TV electronics factories, computers and pharmaceuticals. Finally, nuclear power plants (NPP) and coal also require demin water for feed water purposes (Wahyuningrum, 2010).

The function of demineralization itself is the ability to make pure water that is designed not only for water that will be consumed by humans, but also for water that will be used in industrial machines. Excess levels of minerals in water move through the pipes, more and more minerals stick to the pipes, and cause corrosion. Demineralizers help avoid problems like this with pipes. So in other words demineralization is a process to remove certain minerals from water, such as calcium and magnesium. They perform this function by replacing calcium and magnesium atoms (Alphonsia, 2012). Water will naturally exert pressure from a higher water surface (concentrated solution) to a lower water surface (dilute solution). This pressure is what we call the osmotic pressure. At a certain water level in the concentrated solution), this large osmotic pressure will cause the osmosis process to stop (Idaman Said Nusa, 2003).

Osmosis Is a natural phenomenon that occurs in living cells where solvent molecules (usually water) will flow from an area of low concentration to an area of high concentration through a semipermeable membrane. This semipermeable membrane refers to the cell membrane or any membrane that has a similar structure to or part of the cell membrane. The movement of the solvent continues until an equilibrium concentration is reached on both sides of the membrane. Reverse osmosis is a process of reversing an osmosis process. Osmosis is the process of moving a solution from a solution with a low solute concentration to a solution with a higher solute concentration until a concentration equilibrium occurs (Etikasari, 2009).

The process of osmosis is a natural process that occurs in an effort to balance the salt concentration on both sides. This osmosis process will cause the water level in the concentrated solution to be higher than the surface in the dilute solution.

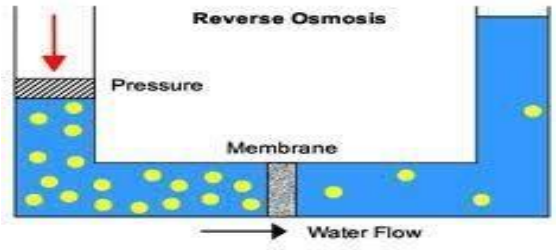

Figure 2. Reverse Osmosis Process (Source: Kimia.com)

The process of Reverse Osmosis technology uses a semipermeable membrane whose diameter is smaller than 0.0001 microns (500,000 times smaller than a hair or the same as a micron filter, functions to remove various impurities, micro materials, bacteria, viruses and so on) and is given high pressure so that the filtering process can run. This process can remove salt particles and other polluting particles where the size of these particles is larger than the Reverse Osmosis membrane, therefore, Reverse Osmosis is called the most effective water purification method. Working Principle of Mix Bed Deionization technology is a process to remove dissolved ions in water using an ion-exchange process using either an ion exchange resin or an electrical deionizer.

In ion exchange resins there will be a process of capturing positively charged ions by the cation resin (*cation replacement resin*) and negatively charged ions will be captured by the anion resin (*anion replacement resin*). A device for removing ions using the principle of deionization technology is called a deionizer. One example of deionization technology is the mixed-bed deionizer (Anonymous, 2012).

The method used to increase the supply of demin water and reduce the amount of waste production during regeneration is to increase the remaining mix bed production. Remaining is the operational capacity of a mix bed and is expressed in volume units of tons or m3. If before this innovation, if the remaining value has reached 0 and the conductivity is still < 0.8 S/cm, regeneration is immediately carried out. With this innovation, it is done by adding the initial setting or design remaining (5100) if the mix bed has reached remaining zero (0) but the conductivity value is still 0.8 S/cm. Due to the maximum limit value of the conductivity value for hot well adding water in the form of demin water is 0.8 S/cm. The addition of the Remaining value is done automatically using software. The addition of remaining is done in stages, because there is no definite reference for the addition of remaining in each mix bed. The addition is made of 500 if it has reached a value of 0 (zero).

Figure 3. Mix Bed Water (Source: PT. Nulab Pharmaceutical Indonesia)

Mixed-Bed Deionizer is a device for removing dissolved ions in water using cation and anion resins, where both resins are in one container (tank). One of the industries that use Mixed-Bed Deionizer the most is the pharmaceutical industry, because the water used for the washing process must be clean of ions. The loop control system, especially the closed loop control, is a feedback control system where the value of the output will also affect the control action. Closed loop control is applied to the water tank filling process. The process in the loop system requires precise control. Manual control has many drawbacks. EDI has a working principle similar to the electrodialysis (ED) process, where the salt ions in the feed solution are moved with the help of an electric field

and separated by an ion-selective membrane. The difference between the two processes is the use of ion exchange resin in the EDI module which reduces the overall resistance of the module.

Figure 4. Lopping Tank Water (Source: Looping Systemotomation, 2018)

Some of them are that the water heating process will take a relatively longer time, and the user's tank filling will be constrained because the water heating process is too long. The design of the looping control system for filling the water tank uses an automation control system. There are three sensors used, namely temperature sensors, flow sensors and level sensors. The PLC program in the looping system utilizes PID control in the heating process, the temperature sensor is used to control the regulating valve which functions as a heating steam opening valve. The volume of water that enters the user's tank is monitored by a flow sensor. The level sensor serves as an indicator to turn on the filling pump for the softwater storage tank and process safety (Ogata, 1996).

There are 4 steps in the user tank filling process. The first process is Step 1 which is the process of heating water (water circulation), Step 2 is the process of filling the user's tank, step 3 is the finishing process and the last stage is step 31 where all systems will be turned off. Storage tanks must be protected from the entry of contaminants by suitable ventilation filters. Pure water is continuously recirculated and cooled to maintain purity. UV disinfection is often used to maintain microbial purity in the distribution circle. Ozone disinfection is gaining popularity because it is produced in-situ and is twice as strong as an oxidant than chlorine.

The production of high-purity water has traditionally used a combination of membrane separation and ion exchange processes. EDI is a process that combines semi-impermeable membrane technology with an ion exchange medium to produce a high-efficiency demineralization process. Electro dialysis uses an electric current and a specially prepared membrane that is semi permeable to ions based on their charge, electric current, and ability to reduce ions based on their charge. Through electro dialysis, the electric potential transports and separates charged aqueous species. An electric current is used to continuously regenerate the resin, eliminating the need for periodic regeneration (Nagarale, 2006).

The EDI stack has the basic structure of a deionization chamber. The chamber contains the ion exchange resin, packed between the cationic exchange membrane and the anionic exchange membrane. Only ions can pass through the membrane, the water is blocked. When the flow enters the resin filled dilution compartment, several processes will move. Strong ions are removed from the feed stream by the mixed bed resin. Under the influence of a strong direct current field applied across the stack of components, charged ions are drawn from the resin and drawn towards each of the oppositely charged electrodes. In this way these strongly charged ionic species are continuously transported and transferred to the adjacent concentrating compartment. As the ions

enter the membrane, they can pass through the concentration chamber but cannot reach the electrode. They are blocked by adjacent membranes, which contain resins of the same charge.

EDI is able to reject salt up to more than 99.5% with a resistivity of 1–18 MΩ.cm and a TOC of less than 0.05 mg/L. Bacterial levels can also be minimized because the presence of electric current in the system can inhibit the growth of microorganisms in the water. Electrodeionization has several advantages when compared to conventional ion exchange systems, namely a continuous process with stable product quality, and does not require regeneration (Wenten, 2014). In EDI, the ionization process takes place in two stages, namely (1) electropermutation where the ions in the feed solution are attached to the ion exchange resin, and (2) electroregeneration where the ions attached to the resin are released due to substitution by H+ and OH- ions from the breakdown of water molecules. with the voltage difference as the main driving force. This regeneration stage maintains the stability of the EDI instrument by minimizing changes in pH so as to avoid the polarization phenomenon. Only by supplying electricity, all resins in the compartment can regenerate their alkaline and acidic ion content automatically without the need to involve the addition of external chemicals.

METHOD

The research used is a qualitative research with a descriptive approach. Sugiyono (2012) also suggests qualitative research as a research method based on the philosophy of postpositivism, used to examine the condition of natural objects, where the researcher is the key instrument, data collection techniques with triangulation, data analysis is inductive or qualitative, and qualitative research results are more emphasize meaning rather than generalization. As for what is meant by qualitative research, namely research that intends to understand the phenomenon of what is experienced by the research subject holistically, and by way of description in the form of words and language, in a special natural context and by utilizing various scientific methods (Moleong, 2003). 2007).

Data collection techniques are the most important part of a study, because with data researchers can find out the results of the research. In this study, data were obtained from various sources, using various data collection techniques and carried out continuously until the data was saturated. In accordance with the characteristics of the data required in this study, the data collection techniques carried out are:

1. Observation

Observation is a fundamental technique in non-test research. Observations are made with clear, detailed, complete, and conscious observations about the actual behavior of individuals in certain circumstances. The importance of observation is the ability to determine the initial factors of behavior and the ability to accurately describe the reactions of individuals observed under certain conditions. Observations in qualitative research are carried out on real situations that are reasonable, without being prepared, changed or not held specifically for research purposes. Observations are made on the object of research as a source of data in the original state or as in everyday situations. Marshall in Sugiyono (2010) stated that "through observation, the researcher learned about behavior and he meaning attached to those behavior".

2. Interview

Interview is the process of obtaining information for research purposes by means of question and answer while looking face to face between the questioner or interviewer and the answerer or respondent using an interview guide. In this study, the researcher recorded all the answers from the respondents as they were. The interviewer occasionally interspersed the respondent's answers, both to ask for an explanation and to straighten out if there were answers that deviated from the questions. The type of interview used in this study is a structured interview. That is, in conducting interviews, researchers have prepared research instruments in the form of written questions.

3. Documentation

According to Djam'an Satori (2011), documentation studies are collecting documents and data needed in research problems and then examining them intensely so that they can support and increase trust and proof of an incident.

Data Analysis Techniques According to Sugiyono (2009) data analysis is a process of systematically searching and compiling data obtained from interviews, observations, and documentation, by organizing data into categories, breaking down into units, synthesizing, compiling into patterns, choosing what is important and what will be studied, and making conclusions so that they are easily understood by themselves and others. Data analysis in qualitative research is carried out before entering the field, while in the field and after finishing in the field.

Miles and Huberman in Sugiyono (2009: 337-338) argue that data analysis in qualitative research is carried out during data collection, and after data collection is completed after completing data collection within a certain period. At the time of the interview, the researcher had analyzed the answers of the interviewees. If the interviewee's answers after being analyzed feel unsatisfactory, the researcher will continue again to a certain stage until data that is considered credible is obtained. In addition, activities in qualitative data analysis are carried out interactively and continuously until complete, so that the data is saturated. The steps of data analysis are shown in the following figure:

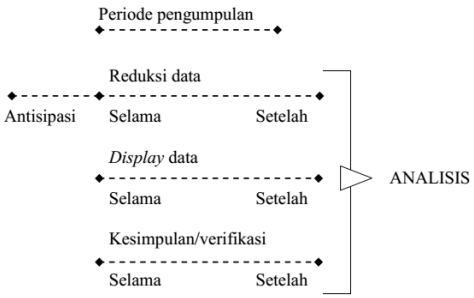

Figure 5. Components in Data Analysis (Flow Model)

Based on the picture, it can be seen that, after the researchers collected data, the researchers carried out anticipatory measures before reducing data. In addition, it can also be concluded that the steps of data analysis between one another are related to each other. These steps can not be separated or done in order. In order to produce good data, the researcher in analyzing the data must be in accordance with the existing steps. Furthermore, the interactive model in data analysis is shown in the figure below:

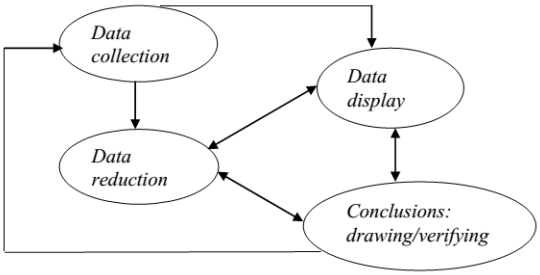

Figure 6. Components in Data Analysis (Interactive Model)

Figure 6 shows the steps taken in data analysis according to Matthew B. Miles and A. Michael Huberman (2009), which are as follows:

1. Data Reduction as a process of selecting, concentrating, paying attention, simplifying, abstracting, and transforming rough data that emerges from field notes, so that the data provides a clearer picture of the results of observations, interviews, and documentation;
2. Data Display (presentation of data), which is a set of structured information giving the possibility of drawing conclusions and taking action. In qualitative research, the data is presented in the form of brief descriptions, charts, tables, graphs, pictograms, and the like. Through the presentation of the data, the data is organized so that it will be easier to understand;
3. Conclusion Drawing or Verification, researchers make conclusions based on data that has been processed through data reduction and display. The conclusions put forward are temporary and will change if no strong evidence is found to support the next stage of data collection. However, if the conclusions raised at an early stage are supported by valid and consistent evidence when the researcher returns to the field to collect data, then the conclusions put forward are credible conclusions.

Data Validity Check The implementation of the data validity checking technique in this study is based on certain criteria. According to Lexy J. Moleong (2009), to determine the validity of the data, an examination technique is needed based on a number of certain criteria. There are four criteria used, namely credibility (degree of trust), transferability, dependence, and conformability.

RESULTS AND DISCUSSION

Research conducted at PT. Nulab Pharmaceuntical Indonesia is a field research in the engineering department which is carried out directly on the analysis of the operation of the purified water system used in the water purification process in the manufacture of drugs in the pharmaceutical industry, namely a water treatment system that can remove various contaminants (ions, organic matter, particles, microbes and gas) contained in the water that will be used for production. I made these observations directly and through interviews about how the Purified Water System operating system can control the water that comes out of this process is called softwater, softwater is usually used for boilers to be used as steam. The technology used for the production of pure water is generally based on ion removal (deionization), because one of the important parameters in pure water quality is the conductivity value which is closely related to the presence of ions in the water. This conductivity is measured by the ability of water to pass electricity. This ability is directly related to the concentration of ions in the water. The ions in water come from dissolved salts and inorganic compounds such as alkalis, chlorides, sulfides, and

carbonate compounds. In the field, researchers are guided by industry supervisors and employees to see and understand how to operate the Purified Water System.

The working mechanism of the Purified Water System is a water treatment system that can remove various contaminants (ions, organic matter, particles, microbes and gases) contained in the water that will be used for production. Water (raw water) for water treatment can be obtained from PDAM water (city water), Shallow well (shallow well) with a depth of 10-20 m, or from Deep well (deep well) with a depth of 80-150 m. The variation in the quality of the raw water supply that meets the requirements is determined from the water quality target to be produced. Likewise, water quality determines the equipment needed for water treatment. The purified water system consists of: Multimedia filter, Carbon filter, Water softener, Heat Exchanger (HE), Micro filter, Ultra filtration (R.O = Reverse Osmosis), and Electro De-Ionization (EDI). From the previous explanation, it can be explained with a flow chart regarding the working principle of the Purified water system which is arranged as an overview of the working mechanism as follows:

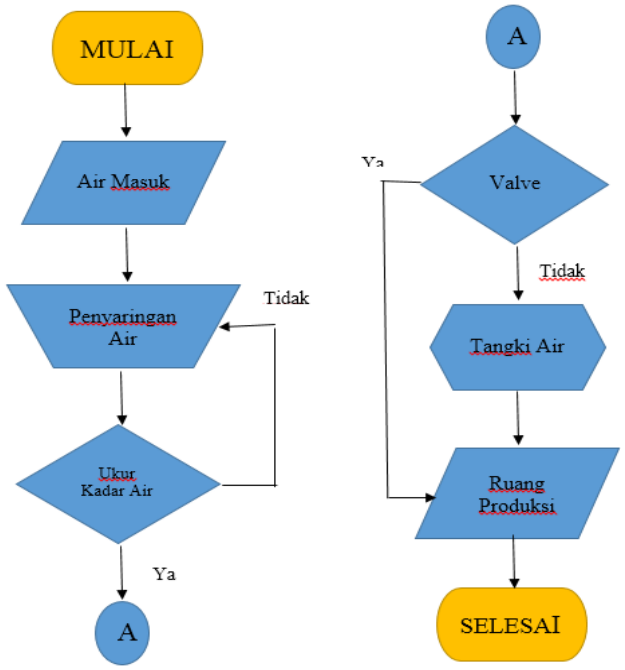

Figure 7. Flowchart of Purified Water System Working Principle

In Figure 7 Flowchart of the working principle of the purified water system, it can be explained that the process begins with the following flow:

a. Multimedia filters

Multimedia filter serves to remove mud, sediment and particles contained in raw water. Multimedia filter consists of several filters with a porosity of 6-12 mm; 2.4 – 4.8 mm; 1.2-2.4 mm; and 0.6-1.2 mm. These filters are arranged in one vessel (tube) with the bottom of the tube given gravel or sand as the base of the vessel (so it is often also called a sand filter).

Figure 8. Multimedia Water Filter (Source: Deltapuro.com)

High suspended solids in feed water can cause a decrease in water pressure and reduce the effectiveness of filtration equipment such as reverse osmosis membranes, EDI electrodeization, UV sterilization and water softener or demineralization, if multimedia filtration is not used as a pre-treatment (Asmadi, 2011).

a. Active Carbon Filter

Activated carbon is carbon that has been activated using high pressure steam or carbon dioxide (CO2) derived from materials that have very high adsorption capacity. Usually used in granular form (granules).

Figure 9. Carbon Filter (Source: PT. Nulab Pharmaceuntical Indonesia)

Active carbon functions as a pre-treatment before the de-ionization process to remove chlorine, chloramine, benzene, pesticides, organic materials, color, odor and taste in water. Activated carbon is commonly used in filters, because it has been treated to have a much higher surface area than untreated carbon. One gram of activated carbon has a surface area of more than 3,000 m2 32,000 square feet (Budiyanto, 2006).

a. Water Softener Filter

The water softener filter contains anionic resin which functions to remove and reduce water hardness by binding to Ca++ and Mg++ ions which cause high levels of water hardness. In this case the cation resin in the softener functions to absorb lime and after the resin is saturated or filled with lime, it can be reactivated using only NaCl salt. In the softener tube itself there is a cation resin, which will attract ions such as magnesium, calcium, iron and so on and release sodium ions.

Figure 10. Softener Filter (Source: PT. Nulab Pharmaceuntical Indonesia)

The softener tank can be operated differently according to the type of valve itself (Elrina L, 2007).

a. Reverse Osmosis

Reverse osmosis is a technique for making purified water that can reduce up to 95% of Total Dissolve Solids (TDS) in water. Reverse osmosis consists of a very fine (up to 0.0001 micron) filter layer.

Figure 11. Reverse Osmosis (Source: PT. Nulab Pharmaceuntical Indonesia)

This pressure is what we call the osmotic pressure. At a certain water level in the concentrated solution), this large osmotic pressure will cause the osmosis process to stop (Idaman Said Nusa, 2003).

a. EDI (Electronic De-Ionization)

EDI is the development of the ion exchange system where as a binder of (+) and (-) ions are also used in addition to the resin electrode. This electrode is connected to a direct current so that the water purification process can take place continuously without the need for regeneration. After passing through the EDI, the purified water produced is then stored in a storage tank equipped with CIP (cleaning in place) and a looping system and ready to be distributed to the production room. Electrodeionization has several advantages when compared to conventional ion exchange systems, namely a continuous process with stable product quality, and does not require regeneration (Wenten, 2014).

Table 1. Comparison of Purified Water (PW) Parameters FI VI USP 41 and EP

Parameter	FI VI	USP 41	EP 9th
Water Conductivity	≤ 1,3 µS/cm	≤ 1,3 µS/cm	≤ 4,3 µS/cm
Carbon Total Organic	≤ 0,5mg / L together with 500 ppb	500 ppb	≤ 0,5 mg/L
Microbial limit test	ALT ≤ 100 cfu / mL	< 100 cFu/ml	< 100 cFu/ml

The following is the reason for choosing USP 41 as a reference for pure water requirements: Minimum water specification requirements, this means less costs are required for inspection. For TOC examination, it is relatively more expensive. Conditions that are slightly automated, examination is faster, except for microbiology, microbial incubation is at least 3 days. EP 9 and FI VI also require a microbial limit of < 100 cfu/ml. The water filtration and purification process takes problem water and turns it into clean water free of odors, tastes, sediments, and contaminants. With physical filtration, water is filtered, often through a membrane such as gauze, to remove larger particles. The purpose of this pretreatment process is so that the removal of dissolved minerals that occurs in the R/O can be more optimum and the R/O membrane is not damaged quickly.

a. Chlorinasl (In Raw Water Storage Tank)

Deep well water is pumped into the raw water storage tank which is first injected with Sodium hypochlorite, this Sodium hypochlorite in the Raw Water Storage Tank will release chlorine, where this chlorine breaks organic bonds, oxidizes iron and other oxygen and at the same time acts as a catalyst. The disinfectant kills the bacteria present.

b) Multimedia Filters

Multimedia Water Filter is a type of water filtration consisting of several layers of filter media. Each layer is progressively composed of several measures of layer roughness and depth. Layers of filter media are progressively stacked with the coarsest and densest media such as gravel at the bottom and lighter and finer media at the top. Multimedia filters are used to reduce the level of SDI (Silt Density Index), TSS (Total Suspended Solids) in the incoming feed water or raw water. Suspended solids consist of small particles such as silt, soil, sand, organic matter, algae and other microorganisms. The graph on the pressure gauge is shown in Figure 12 below.

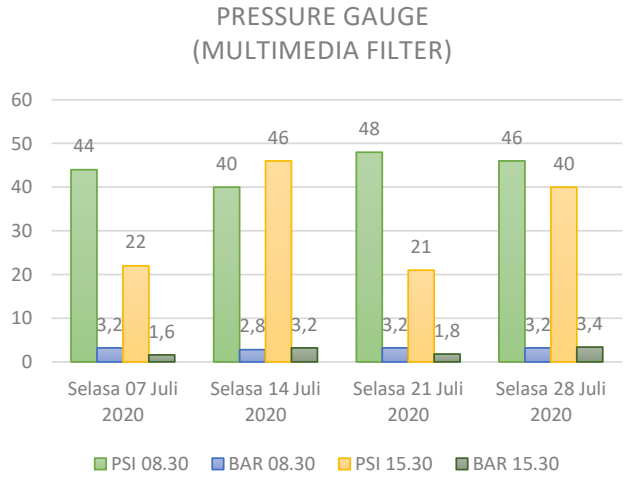

Figure 12. Comparison of Pressure Gauge Graph (Multimedia Filter).

From Figure 12 above, a comparison of the pressure gauge graph (Multimedia Filter) can be explained, if the filter is checked 4 times in 1 month. When the check is divided into 2 sessions, namely in the morning at 08.30 in the afternoon 15.30. This Filler function reduces dirt and particles in the water. Inside the Multimedia Filter contains anthracite and silica gravel media as supporting media. This absorption process takes place continuously so that one day there will be

a pressure difference due to the accumulation of dirt/particles across the filter media, at this time it is necessary to wash the filler. Backwash which functions to remove dirt and (2) Rinsing which functions to rinse the remnants of dirt in the filter. The working process of this filter is as follows:

Operation Process

Water will flow from the top of the filter, through the filter media and filter pores, out of the bottom of the filter. This will cause the dirt particles to be trapped in the top filter, so that the water that comes out is clearer. The presence of dirt stuck in the filter will cause the inlet pressure to increase and inhibit the absorption of chlorine, so that the filtering and absorption process does not take place properly. At this time the filter needs to be washed.

Washing Process

Backwash (Wash Back) the water flow is changed from bottom to top so that the dirt that is stuck on the filter media will be lifted upwards for a while this backwater flow is maintained so that all retained dirt can come out Rinsing (Rinsing) the water flow from top to bottom like the operating process but disposed of the drain so that it can remove the remaining dirt in the filter tube.

Mixed Bed Exchanger

Mixed bed is a tool to remove dissolved ions in water using cation and anion resins, where both resins are in one container (tank). One of the industries that use mixed bed the most is the drug industry, because the water used for the drug manufacturing process must be clean of ions. The regeneration graph on the mixed bed is shown in Figure 13 below.

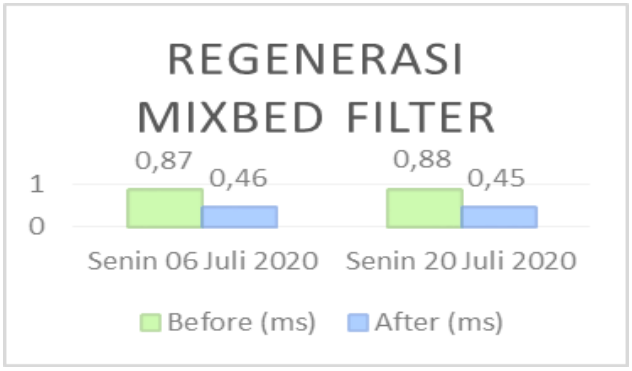

Figure 13. Mixbed Filter Regeneration Graph.

In Figure 13, it is explained that in checking there are 2 times in 1 month. If the Mixbed Filter has increased milliseconds from 0.85 the maximum limit to 0.45 the normal limit. Mixed Bed Exchanger is an ion removal polisher to get a high final quality pure water with electrical conductivity below 1.3 microsimens/cm. This Mixed Bed Exchanger column contains cation resin and anion resin which are mixed evenly to get high water quality. The resin column has two types, namely Single Bed and Mixed Bed Ion Exchange Resin. Single bed means that in one column there is only one type of resin, namely cation resin or anion resin. While the Mixed Bed column contains a mixture of cation and anion resins. There are 2 main processes in the mix bed, namely Operational and Regeneration. Cation resin serves to bind positive ions dissolved in raw water. Examples of ionic reactions between resins and NaCl compounds are as follows:

$$\mathbf{R\text{-}H + + Na+ \rightarrow R\text{-}Na+ + Cl-}$$

Anion resin is used to bind negative ions dissolved in raw water. Examples of ionic reactions between resins and NaCl compounds are as follows:

R-OH- + Cl- → R-Cl- + Na+

When the resin is saturated, it will regenerate. Negative ions will be regenerated with NaOH while for positive ions will be regenerated using HCl. The regeneration reaction of the cation resin is as follows:

R-Na+ + HCl → R-H + + Cl-

S-As for the anion resin as follows:

T-Cl- + NaOH → R-OH- +Na+

Operations Manual Water Softener Filter

The water supply for this process comes from PDAM water or well water which contains high enough hardness so that it can be problematic for reverse osmosis. For this reason, the Asian water is flowed through a softener filter which is filled with Cation resin media which functions to filter the hardness levels (Ca and Mg) contained in the water which can be reduced so that the water becomes soft. Below is how the resin cation works:

Resin Cation

Ca++ Ca

R- Na + Mg++ --- R- Mg +Na+

After some time of use, the softener filter will eventually become saturated. For this reason, a washing or regeneration process must be carried out so that the resin can become active again. For this process, salt must be provided for cation resin. This process consists of several steps that must be carried out one by one. This is detected from the hardness content that exceeds the limit and a regeneration process must be carried out. Here there are several stages of the regeneration process, namely (backwash, regeneration, rinsing).) and then return to the filter position as table 2 below.

Table 2. Softener Filter Operation

OPERATION MANUAL			
No	Process	Valve Open	Duration
1	Operation	1, 4	5 minutes
2	Backwash	2, 3	5 minutes
3	Regeneration	5, 6, 7	30 minutes
4	Rinsing	1, 5	10 minutes

From table 2 it can be explained that the softener filter operation is carried out once a week in which there are 4 operating processes, namely operation, backwash, regeneration, and rinsing. The way it works when the operation process is to open valve 1,4 which lasts for 5 minutes then backwash open valve 2,3 for 5 minutes after that regeneration open valve 5,6,7 for 30 minutes and finally rinsing open valve 1.5 for 10 minutes. The way it works when the operation process is to open valve 1,4 which lasts for 5 minutes then backwash open valve 2,3 for 5 minutes after that regeneration open valve 5,6,7 for 30 minutes and finally rinsing open valve 1.5 for 10 minutes. How to calculate regeneration, calculate the amount of water that passes

Formula: Amount of resin (liter) x 1800

28,3 (cu feet)

Original water hardness

= A m3

So it is found that every A m3 of water that passes in the cation filter must be regenerated.

Calculation of the amount of salt needed for each regeneration

Formula: Resin Amount x 7 kg Nacl

28,3

Resin Calculation Method

That the standard ion exchange capacity of the softener resin is 1.9 eQ/L Resin. Then we will get further data as follows:

Water Volume until Regen = 100 x 72 = 7200 Liter

Number of Ions exchanged = 7200 x 12.95 = 93240 Milli Ions Eqvalent. Then the resin requirement

is = 93240 Mili Ion Eqivalen / 1.9eQ/L = 49 Liter Resin.

Replacement of the filter media is carried out when the media has weakened or died so that the impurities and ions contained in the water cannot be completely filtered out or the physical properties of the media change color, shape becomes smaller and so on. This can be determined by examining the water in the laboratory. The resistance of the media to water is determined by the nature of the original water that will pass through it (1-2 years).

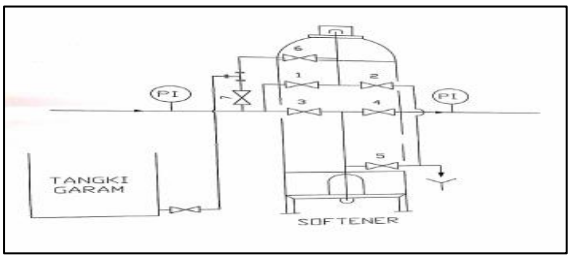

Figure 14. Operation manual for water softener (Source: PT. Nulab Pharmaceuntical Indonesia)

Implementation Method:

a. Open the top distributor above and remove the strainer then remove the media from the top hole of the tank
b. Clean the inside of the filter by spraying water into the filter and draining it
c. Put the strainer back in and insert the new media through the top hole. Reinstall the inlet and outlet pipes and do the washing (backwash, regeneration and rinsing) manually.

Operations Manual Mixbed Filter

The Mixedbed Filter as a polisher unit gets its water supply from the Reverse Osmosis Storage Tank. Inside the Mixedbed Filter Tube is filled with mixed Cation and Anion resin media which functions to remove positive and negative ions in the water. So that the resulting ALR is of high quality (low conductivity value). For this reason, a washing or regeneration process must be carried out so that the resin can become active again. For this process, HCL for cation resin and NAOH for Anlon resin must be provided.

CATION RESIN

Qty Resin : 40 liter Cation Resin
Qty Regen : 12 kg HCL 32% 10,4 liter
Waktu Kontak : 30 menit

Atur kecepatan Flow Rate pada saat injeksi HCL pada posisi 20,8 liter/hour agar kontak waktu dengan chemical mencapal 30 menit.

ANION RESIN

Qty Resin : 60 liter Anion Resin
Qty Reagen : 12 kg Naoh 48% = 8,4 liter
Waktu Kontak : 30 menit
ANION RESIN : 12 kg NaOH 48%

Set the Flow Rate at the time of NAOH injection at 11.2 liters/hour so that the contact time with the chemical reaches 45 minutes. For this process consists of several stages that must be done one by one. MixedBed is a combination of two types of resin, Cation and Anion, which functions as a polishing unit after demineralizer (Cation-Anion). This process can produce pure water with a Conductivity value < 1 microsiemens/cm2. The chemical reaction that occurs in this column is by exchanging the ions contained in the water where the positive ions are bound by the cation resin, while the cation resin will release hydrogen ions and the negative ions are bound by the anion resin while the anion resin releases hydroxide ions. If the hydrogen ions and hydroxide ions contained in the resin have been completely exchanged for positive and negative ions contained in the water flowing into this mixed bed exchanger column, the water quality will be reduced and this indicates a mixed bed exchanger needs to be done. regeneration to get good quality results again. Water demineralization is a process of absorbing mineral ions in water using an ion exchange resin. The demineralized water is used for various needs, especially for industry. Industries that use demineralized water include steam power plants, the semiconductor industry, and also the pharmaceutical industry, as shown in Figure 15 below.

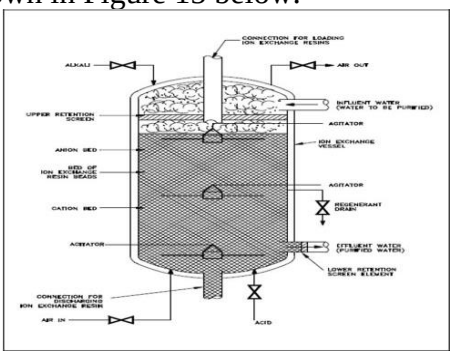

Figure 15. Mix Bed Column Schematic (Source: demineralised water, 2020)

Demineralization is a system that aims to bind the ions contained in Raw Water so that the results of the mix bed will have a low conductivity value (< 0.8 S/cm). In general, resin columns are used in the water demineralization process. The resin column has two types, namely Single Bed and Mixed Bed Ion Exchange Resin. Single bed means that in one column there is only one type of resin, namely cation resin or anion resin. While the Mixed Bed column contains a mixture of cation and anion resins. Calculation of the use of NaOH and HCl To find out whether the use of HCl and NaOH has met the capacity of the resin to capture chemicals or not, the PT. Nulab pharmaceuntical Units 1 and 2 recommended that we calculate the most efficient amount of NaOH

and HCl for PT. Nulab pharmaceuntical Units 1 and 2 were due to the difference in tonnage from 2,200 kilograms to 2,000 kilograms. The data needed for the calculation results in:
1) Total Absorption of Sodium Hydroxide (HCl) HCl adsorbed by resin = Required reagent – Residual HCl = 2,355 kg – 647.79 kg = 1,687.21 kg
2) Total Absorption of Sodium Hydroxide (NaOH) NaOH absorbed by resin = Reagent requirement – NaOH residue = 2173.5 – 854.77 kg = 1.318.77 kg

Table 3 Mixbed Filter Operation

MANUAL OPRATION				
No.	Process	Valve Open	Duration	Information
1.	Backwash	1, 4, 5	15 minutes	-
2.	Setlle	2, 3, 5	5 minutes	-
3.	Anion Regeneration	7, 8, 9, 14	45 minutes	NAOH 48%
4.	Rinsing Anion	1, 14	10 minutes	-
5.	cation regeneration	10, 11, 12, 14	30 minutes	HCL 32%
6.	Rinsing Cation	3, 5, 14	10 minutes	-
7.	Fast Rinse	1, 3, 5, 14	5 minutes	-
8.	Drain Down	13, 14	2 minutes	-
9.	Mixing	2, 15	10 minutes	Compress Air
10.	Final Rinse	1, 6	5 minutes	conduct low
11.	Operation	1, 4, 5	5 minutes	conduct high

CONCLUSION

Based on the results of the research conducted, it can be concluded as follows: (1) This purified water system process can remove salt particles and other polluting particles where the size of these particles is larger than the Reverse Osmosis membrane, the process of filtering and purifying water takes water problem and turn it into clean water that is free from odor, taste, sediment, and contaminants. Purified water system consists of: Multimedia filter, Carbon filter, Water softener, Heat Exchanger (HE), Micro filter, Ultra filtration (RO = Reverse Osmosis) , and Electro De-Ionization (EDI). (2) The working mechanism of the Purified Water System is a water treatment system that can remove various contaminants (ions, organic matter, particles, microbes and gases) contained in the water to be used for production. Water (raw water) for water treatment can be obtained from PDAM water (city water), Shallow well (shallow well) with a depth of 10-20 m, or from Deep well (deep well) with a depth of 80-150 m. The variation in the quality of the raw water supply that meets the requirements is determined from the water quality target to be produced. Likewise, the water quality determines the equipment needed for the water treatment. (3) Regeneration Water Treatment is a reciprocal exchange process between ions contained in water with ions present in the resin, ion exchange resin ion exchange is an organic compound with a three-dimensional structure with cross-links and has functional groups that can be ionized, with the results of the Regeneration Purified Water System itself, it can remove various impurities (ions, organic matter, particles, microbes, and gases) so that the water becomes clearer which is used for production.

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