

GMP requirements for pure steam generators

An important purpose of using pure steam generators is to remove the bacterial endotoxin. This steam has the same internal quality as the water for injection, except for its different physical states. For example, when the conductivity of water is within $10 \mu S / \Omega$, the pure steam conductivity is usually $0.20.5 \mu S / \Omega$, and the maximum is $1 \mu S / \Omega$. Normally, the design level of a pure steam generator; a condensate of pure steam removed from a pure steam generator with a gas-liquid separation unit. The pyrogen level should be 34 log less lower than the source water with a pure steam generator.

Most pure steam generators are vertical, and their principle flow is shown in Figure 5-8 and Figure 5-9. Separate evaporation space and gas-liquid separation device can be used as evaporators in the same- -containers or in different containers. All pure steam generators, with evaporators and heat exchangers, all use boiler steam as a heat source. The heat exchanger

(including evaporator) is a double plate design to prevent contamination from boiler steam.

(1) operational principle. The source water is pumped into a pipe for the distillation (column) and the heat exchanger. Through the liquid level controller

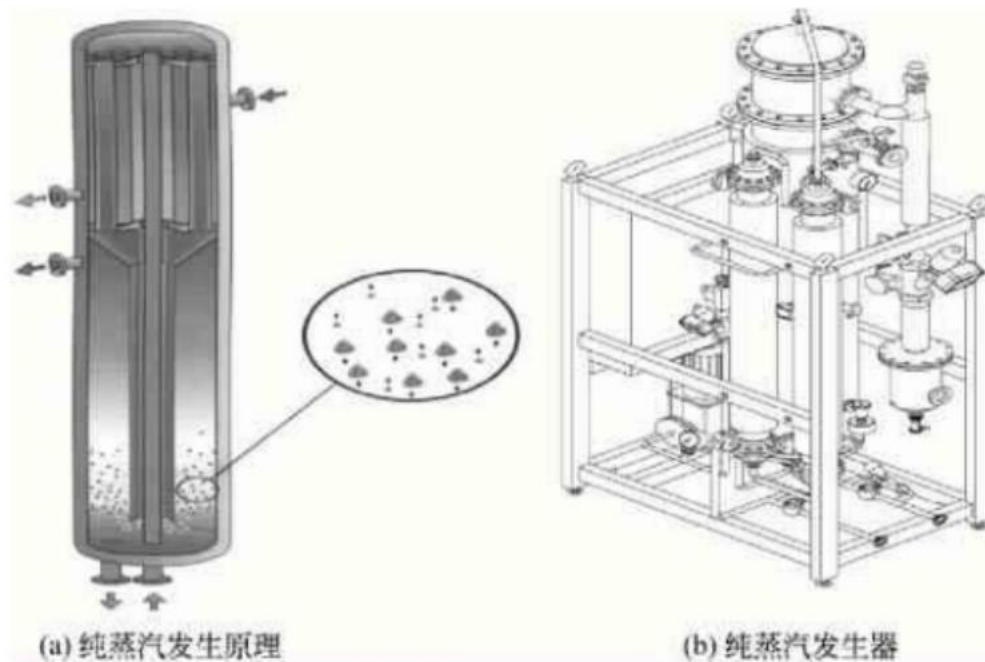


图 5-8 纯蒸汽发生原理

Make the hydraulic pressure in the still machine to reach the verification level. Boiler steam or hot water into the heat exchanger, the water in the distillation to evaporation temperature, steam and unfinished evaporation of tiny droplets

mixture, in the cyclone spin at high speed, make contain no volatile pyrogen substances and impurities tiny droplets produce a large centrifugal force, is thrown to the outside and fall by gravity, into the bottom, the evaporation water is in the form of steam up, into the distribution system. Source water continues to enter, waste water continues to discharge, pure steam continues into the distribution system. The pressure of the pure steam produced by the pure steam generator is like 0~0.6MPa. Suitable for online sterilization of process water system and other process equipment. Within a certain range, the steam production volume and steam pressure of the pure steam generator can be realized by adjusting the pressure and water intake of the boiler steam.

(2) Structural characteristics. The pure steam generator consists of two parallel main components: one is a double expansion heat exchanger tube end pull shell and seamless tube beam distillation, the other is the purification column.

The two main components are manufactured from 316L stainless steel. The material for the sealing washer is manufactured with injection-grade PTFE. The housing and seamless tube still can be removed for necessary maintenance and inspection. The still and heat exchanger use mineral cotton as insulation material, and

the surface of the protective layer is covered with AISI304 stainless steel polished plate.

The pure steam generator has the function of automatically eliminating refractory gas and has an appropriate control system with the following functions:

① Automatic adjust the water volume through the liquid level control inside the distillation. When the water intake is insufficient or too large, there is an alarm and automatic shutdown device;

② By automatically adjusting the pressure of the boiler steam valve to adjust the pure steam pressure required for production within the 0~0.6MPa;

③ The steam production process of the pure steam generator can be automatically controlled by the programmable controller (PLC).

(3) Performance characteristics. The pure steam generator used in the online sterilization of the pharmaceutical water system can be adjusted within the steam production range of

0100% according to the production requirements. Ability to adjust the stills automatically

The water inflow and the pressure of the boiler steam are in a matching running state to ensure that the pure steam generator achieves the set capacity of removing pyrogenics.

The temperature speed and water storage in the distillation unit can meet the pure steam generator in a very short time from the normal state.

The operation process noise is small, the equipment maintenance is convenient, do not need a special space and height.

Factors affecting the pure steam quality. The operation of the pure steam generator is relatively simple. The production of pure steam needs to control the pressure and water inflow of the boiler steam, so it needs a boiler steam control valve and the liquid level control device inside the evaporator. The pressure of boiler steam must be higher than the pressure of pure steam, and the greater the pressure difference, the more the production of pure steam. In order to obtain suitable pure steam output, the steam pressure of boiler source steam should be at least 0.3

~0.4MPa higher than that of ordinary pharmaceutical boiler steam pressure (such as the heating steam used in general sterilization equipment), and the consumption of boiler steam should be 10% and 20% higher than the pure steam obtained. In the matching case, the temperature difference of the heat exchange surface of the evaporator is close to the maximum value to maintain the maximum output of the steam generator. If the steam pressure of the boiler is near the maximum value, while the pure steam pressure is at the lowest value, the steam flow speed through the steam-liquid separator is too large, which will bring the mist beads containing endotoxin into the pure steam, affecting the steam quality. Therefore, the equipment with the alarm installation automatic shutdown function, to prevent the flow rate is too large, to ensure the quality of pure steam.

In addition, when the amount of purified water is too large, the small water droplets too late to evaporate are more likely to entrain into the pure steam, resulting in the loss of pure steam mass. Will cause product quality risks.

(5) Pure steam quality monitoring. Pure steam purity needs to be controlled at the point of process use. Sampling can use a special sampling device, which consists of a sampling valve and a condensing heat transfer device. Laboratory condensers may also be used, but with safety attention. When sampling, with pure steam flow steam flushing sampling, and make the pure steam sample cool, become condensed water (should be injection water). The quality of condensate is inspected and evaluated according to the standard of injection water.

(6) Pretreatment of the source water. Pure steam generator uses purified water or injection water as its source water, mainly for the following two reasons.

① Prevent scale formation inside the pure steam generator. The operating temperature of the pure steam generator is high, and the total dissolution of the source water is solid

The body must be at a very low level, especially the silicon content in the source water. The content of silicon in the pure steam design specification shall be less than 10×10^{-6} , Moreover, the hardness of the source water should be undetectable.

② Prevent the corrosion of the steam generator and its pipe system. Under high temperature conditions, water is very corrosive, and chloride ion is more corrosive to stainless steel materials. According to literature reports, free chloride ions are usually concentrated in pure vapor generators and some areas in the system pipeline, which can reach tens of hundreds of 10^{-6} . In the steam flowing in the generator, the concentration of free chloride ions is much less than 10^{-6} . In some of the above areas of the small gap, immersed in stainless steel material in high temperature water corrosion, with the passage of time, the beginning of the corrosion, can be changed into linear material rupture, usually called corrosion rupture, at this time, the pipeline will leak, endanger the quality of the product.

③ Prevent volatile substances from endangering product quality. It is difficult to separate volatiles in distillation, such as ammonia, hydrazine, aldehyde, etc. Although distilled water machine and pure steam generator have exhaust devices, but they-into the source water, will bring quality risks.

The latter two are related to drug quality, so the requirements for source water can be traced back to the pharmacopoeia. This is the fundamental reason that the pure steam must use purified water and water for injection as the



source water, and it is also the reason for conducting alarm and automatic control equipment at the water inlet of the pure steam generator.



Tel +86 15951082997

E-mail biocell@biocell-pharma.com

Room 1904, Building 10, No.218, Jiqingmen Street,

Jianye District, Nanjing, Jiangsu, China