DEFINING OF ASEPTIC TANK POSITION IN THE PRODUCTION PROCESS OF COSMETIC AND PHARMACEUTIC PRODUCTS

***Rasheva Violeta, Valtchev Georgy, Tasheva Stanislava**

University for Food Technologies – Plovdiv, Bulgaria

***Rasheva Violeta, v_rasheva@abv.bg**

Abstract: A survey for the use of aseptic processes in the production of cosmetic and pharmaceutical products is carried out. It is turned out that the aseptic filling is one of the most critical processes in these industries. The requirements of this process and for establishing of the aseptic conditions for its conducting are examined. An investigation of the installations for production of liquid cosmetic and pharmaceutical products, their main components and characteristics and the technology for production of studied products is carried out. The place and the function of the aseptic tank in these installations are defined. The advantages of the aseptic tank, its technical characteristics and requirements for its production are presented.
Keywords: aseptic tank, aseptic filling, cosmetic and pharmaceutical products

Introduction:

Aseptic filling of sterile medicines (also known as a sterile filling) is one of the most critical processes in biopharmaceutical industry. This is due to its highly technical driven process and the potential impact of the security to the end user, usually placed in an advance risk patients. There are only indirect protective measures for sterility of the filled medicine after its filling and sealing in a clean room.

In the method of aseptic filling, the product and the packaging are sterilized separately, and then cooled product is filled ("cold filling") and hermetically sealed under conditions that exclude re-contamination by microorganisms (aseptic conditions). This method is characterized by two specific process stages - pasteurization (sterilization) of the product and creating of the required conditions for a sterile transport, packaging and storage of the product. Heat treatment of the product intended for aseptic filling is carried out according to the principle of the high temperature short-term heating. Two methods of product heating (indirect and direct) have application in this process.

Aseptic filling is an aseptic process which requires good coordination and complex interaction between personnel, sterilized product, technological equipment for filling (final treatment), clean rooms, attaching equipment and sterilized filling components. Micro contaminations have infinitesimal dimensions and the surfaces, which look clean and sterile, in fact may are not so clean and sterile. Therefore the aseptic filling (final processes) are highly dependent on the equipment, detail technological procedure and control. The more unique are the products or the packing system, the greater technical and operational requirements have to be provided.

Creating of aseptic conditions

A necessary precondition for successful implementation of the method of aseptic filling is to create sterile conditions for transport, packaging and storage of the product. The secondary microbiological contamination of sterile products should be totally excluded.

A specific preparation of the technical equipment for the process of aseptic filling of the packaging is required to achieve this purpose. The achievement of absolute purity and

sterility of all industrial facilities that come into contact with the sterile product during the process of aseptic filling is extremely important. The sanitary processing should ensure the implementation of two major tasks: 1 - mechanical separation of the dirt - product residue, sludge, scale, scaling, etc., 2 - separation of the residual micro flora.

Installations for liquid pharmaceutical or cosmetic products:

Different liquid pharmaceutical and cosmetic products are manufactured and stored in fully automated installations (Fig. 1 shows an installation for liquid pharmaceutical products, and Fig. 2 shows a scheme of the operation of such unit.) Each of the three production vessel with content of 500, 1000 and 2000 liters respectively, can be connected with each of the five vessel for product's storage (2x1000, 3x2000 liters), which means possibility for change and a flexible system. Up to three different manufacturing steps are possible.

The installation is designed in accordance with good manufacturing practice (GMP) and is approved by the Administration of food and medicines (FDA). The design and construction of the installation are in accordance with the latest directives and standards. The product transfer from the preliminary tank to the storage tank, cleaning in place (CIP), sterilization in place (SIP) and drying up in the different sections of the aseptic installations could be performed at the same time. Each preserver vessel is set for a filling machine.

Fig. 1. An installation for liquid pharmaceutical products

An automatic cleaning and drying up process of all, wetted from the operating liquids, components and sections is provided.

The full transfer length of the installation is 1,000 meters. The equipments are made from a high-quality stainless steel. All components, which could be wetted from the working fluids are mechanically grinded or electrolytic polished with aim to achieve a smoothness of the inside surfaces, and all links are orbital welded.

Each of the preliminary tanks is placed on a bearing construction in an individual clean room. In such way cross-contamination with active substances from other products is eliminated. The active substances and the working liquids are added to the aseptic vessels through a direct connection or through vacuum suction from the reservoirs. All installed, manually or pneumatically controlled, valves from DN8 to DN50 (with the exception of a few valves in the transferring section) are membrane (diaphragm) valves.

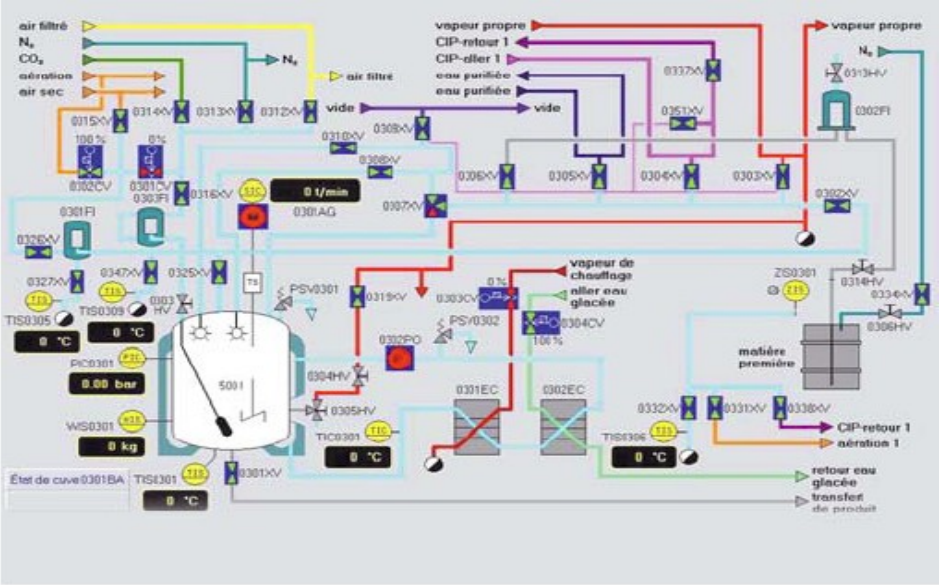

Fig. 2. Operation scheme of the installation for liquid pharmaceutical products

Aseptic tank for pharmaceutical and cosmetic applications (Fig. 3 and 4):

Aseptic tank, as a part of these installations, is widely used for intermediate hermetic storage of different pharmaceutical, biotechnological and cosmetic semi-manufacture products under aseptic conditions or as a process vessel. It may be used as a one separated piece or as a component in an aseptic line. In the second case it is located after the sterilization equipment and before the filling machines.

The aseptic vessel, used in the pharmaceutical industry, must meet certain requirements depending on the stored in it product. These vessels require optimal outside species, easily maintained surface of stainless steel with a polished inner surface and the roughness height of the surfaces, which are in contact with the manufactured product from 0.1 μm to 0.3 μm.

The aseptic vessel must be produced according to requirements of the specific technological regime, consistent with the process thermal parameters (temperature and pressure). Strength design of the tank must meet the corresponding absolute pressure in the vessel designated by the given technological regime. The pressure in the tank ranges from perfect vacuum to 0.3 MPa gauge pressure. The vessels usually have a double jacket for cooling water circulation and it is sterilized with steam. They must have safety valves on steam and sterile air lines, cleaning in place (CIP) system and an agitator at customer's request. The aseptic tanks are also equipped with all the necessary accessories – an access hatch, system of

inlets and outlets with taps for loading and unloading of the products, for steam or compressed air supply, for mounting of the measuring devices.

Fig. 3. Aseptic fermentation vessel

Fig. 4. Pharmaceutical aseptic tank

The spectrum of demand is from small mobile vessels with working volume of 10 l to larger volumes of technological and storing vessels with a diameter from 1.8 to 4.2 m and a height from 3 to 7.8 m. The large aseptic containers are mainly used for storage of various pharmaceutical and biotechnology products as a semi-manufactured product with aim of their subsequent processing into finished product pieces. This allows to be extended the production season and sharply reduces production costs. Furthermore this allows to be eliminated the need of expensive additional equipment for creation of artificial cold.

So the advantages of the aseptic tank as a buffering vessel are: The production season could be prolonged and the production costs could be sharply decreased; There is no requirement from the additional use of expensive apparatuses for product cooling; The aseptic tank secures safety of the sterile products through constant pressure and temperature, and guarantees products stabile quality during the whole production season; The repeatedly product heating, due to the stopping of the production process or to the shortage of the filling machine capacity could be avoided; The sterile intermediate storage of the aseptic product ensures continuously operation of the filling machine, even during the process of cleaning in place; The aseptic tank ensures flexible connections between one or more technological processes and filling lines, and also different products could be filled and packed at the same time without manual intervention; Excellent quality of the product; Steady regulation of the sterilization process at using of different storage volumes; Possibilities for manufacturing of more than one product.

The tank (Figs. 5 and 6) is designed for operation at pressures up to 0.31 MPa and at a perfect vacuum. All interior surfaces are polished with a maximum roughness of 25 Ra. The vessel is sterilized with steam and has double walls for circulating of cooling water under atmospheric pressure. There is a high speed washing turbine for washing out of the vessel and an agitator at the bottom of the vessel. An aseptic connection and an aseptic

filling hole with a steam barrier are also provided. The sterility of the vessel is provided by its connecting and inlet openings. The connecting holes have size from 1 to 6 inches, and the feeding hole is 20 inches.

Fig. 6 a, b. Aseptic tanks

Technical specification of an aseptic stainless steel vessel (Fig. 7): Volume - 2000 liters; Material - stainless steel; Orientation - horizontal; Shape - round; Supports - 4; Working pressure - 0,5 bar; Operating temperature - 111 0C; Agitator - yes; Dimensions: 2700 mm x 1500 mm x 2400 mm overall height.

Fig. 7. Aseptic tank

Conclusion:

1. The process of aseptic filling of sterile medicines is one of the most critical processes in the biopharmaceutical manufacturing. The advantage of the aseptic filling of different products over the methods of hot filling or refrigeration is proven.

2. The role of the aseptic tank in cosmetics and pharmaceutical industry is for intermediate storage of different products in aseptic conditions or to be used as a technological vessel. It could be used as a separate vessel or as a component of an aseptic

line. In the second case the aseptic vessel is placed after the sterilization equipment and before the filling section.

3. The advantages of the aseptic tank for storages purposes are:

Excellent product quality;

Efficiency of utilization line (possibilities for running of the sterilization process simultaneously with the filling process or the process stopping);

High-flexibility of the production process (easy transfer of the product between the sterilization equipment and filling line);

Possibility for more than one product processing;

Energy consumption and product loss reduction;

The aseptic buffered product prevention;

Steady regulation of sterilization process, when aseptic vessels with different volume are used.

4. A module for aseptic storage of liquid food products has been worked out and a prototype has been developed in the company "Biomashinostroene AD" - Plovdiv on the base of this study.

References

1. Stockdale D. Overview of Aseptic Fill/Finish Manufacturing. American Pharmaceutical Review, issue September/October 2004
2. www.traderscity.com
3. www.bolz-edel-tank.com/pharma.htm
4. www.gemue.de
5. www.tankki.fi/pdf/tankki.pdf
6. This study is carried out with a financial support of the National Innovation Fund by the Science-applied research project "Working out of module for aseptic storage of liquid food products and prototype developing" developed jointly of the companies "Biomashinostroene AD" in Plovdiv, "Thermohran engineering" in Stara Zagora and University of Food Technologies (contract № НИФ – 02-89/04.04.2008 г.)