

Method of preparing containers for blood-derived productsDESCRIPTION

5 This patent application discloses a method of preparing containers for blood-derived products which has novel characteristics which are advantageous compared to known characteristics.

One of the viral inactivation methods known in the prior art for this technological sector relating to blood-derived products consists in heat treatment by submerging the containers or bags of product in
10 water. The water is heated until the product reaches a target temperature which depends on the requirements of the blood-derived product, and from that time a viral inactivation cycle using a water bath begins. During this cycle which lasts many hours, the temperature must be maintained within a very limited range. Once said cycle has ended, the product is rapidly cooled again to prevent the product from being over-exposed to high temperatures.

15 In the sector concerned with the preparation of blood-derived product containers, a quality control test is carried out thereon to detect possible defects in the container. However, visual inspection of the containers is not sufficient as it is difficult to detect defects, which means that many containers arrive at the end user in poor condition. On many occasions, said containers, which may be bags made of a
20 plastics material, have defective sealing which cannot be detected with the naked eye, owing to defects such as defective welding on the container, breaks in the container, splits and porosities in the walls of the container, as well as other types of defect that cannot be seen with the naked eye. Said defects are sometimes manifested when the containers have already been made available to the customer.

25 The present invention aims to overcome this drawback. This is achieved by subjecting the containers to a stress test during the viral inactivation phase of the product in order to amplify any defect therein so as to facilitate the detection of defects in the quality control phase by a visual inspection of the product. Said stress test has the additional advantage of replacing the viral inactivation method previously used in the sector relating to blood-derived products.

30 The object of the present invention is to achieve a more effective and simpler quality control whilst also replacing the conventional viral inactivation methods for blood-derived product containers.

The present invention discloses a method of carrying out a stress test simultaneously with the viral
35 inactivation of the blood-derived product containers, which aims to overcome some of the drawbacks found in the prior art.

More particularly, the present invention discloses a method of preparing containers for blood-derived products which comprises at least:

- 40
- a filling phase of the blood-derived product containers with the blood-derived material,
 - a viral inactivation phase of the blood-derived product containers,
 - a quality control phase for detecting possible defects in the blood-derived product containers,

in which the viral inactivation phase is carried out by placing the blood-derived product containers in contact with steam at a sub-atmospheric pressure in a chamber adapted for that purpose.

- 5 Preferably, said method comprises an additional cooling phase after the viral inactivation phase of the blood-derived product containers. More preferably, the cooling phase is carried out by recirculating cold air.

10 More preferably, in the viral inactivation phase the steam is 'clean', in other words, said steam has no contaminant particles. Still more preferably, the steam used in the viral inactivation phase is sanitary quality steam. The contaminant particles found in the steam may be rust, scale, dirt and sediments which may be carried by the water used to produce the steam. Sanitary quality steam is understood as steam produced from sanitary quality water, the parameters and parametric values of which meet those established by the World Health Organization in its Guidelines for drinking-water quality.

15 More preferably, the steam used in the viral inactivation phase is saturated steam. Alternatively, superheated steam may be used.

20 Preferably, the quality control phase comprises a visual inspection of the blood-derived product containers in order to locate defects in said containers. More preferably, the object of said visual inspection is to locate any containers that have defective sealing.

25 More preferably, the blood-derived product is albumin and the viral inactivation phase is carried out at a temperature of between 55°C and 65°C and at an absolute pressure of between 190 mbar and 210 mbar. Still more preferably, the blood-derived product is albumin and the viral inactivation phase is carried out at a temperature of between 59.5°C and 60.5°C at an absolute pressure of 200 mbar. When the blood-derived product is albumin, the viral inactivation phase preferably lasts between 10 and 11 hours.

30 Alternatively, the blood-derived product is FACTOR VIII and the viral inactivation phase is carried out at a temperature of between 80°C and 82°C at an absolute pressure of between 450 and 550 mbar.

These pressure and temperature conditions in the viral inactivation phase are such that the steam is in the gaseous phase.

35 Preferably, the containers are bags made of a plastics material. Alternatively, the containers are vials. In an alternative form, the containers are made of another material that allows the blood-derived product to be contained while meeting the health standards in this respect.

40 For a better understanding, the accompanying diagram of an embodiment of the present invention is provided as an explanatory but non-limiting example.

Figure 1 is a diagram showing the phases of the method according to the present invention.

Figure 1 shows a filling phase -1- of the container for a blood-derived product, a second viral inactivation phase -2-, with an access inlet -2'- for steam at sub-atmospheric pressure, and a third quality control phase -3- with subsequent storage -4-.

5 In a first embodiment by way of example, the method of preparing containers for blood-derived product uses albumin as said product. In the filling phase -1-, the container is filled. In this embodiment, the containers are preferably bags made of a plastics material. In the viral inactivation phase -2-, the viral inactivation is carried out using steam in direct contact with the bags made of a plastics material at sub-atmospheric pressure. Said phase is carried out at a temperature of between 55°C and 65°C and at
10 an absolute pressure of between 190 mbar and 210 mbar. In a more preferred embodiment, said phase is carried out at between 59.5°C and 60.5°C and at an absolute pressure of 200 mbar.

During said viral inactivation phase -2-, the bags are subjected to the above-mentioned temperature and pressure conditions for a prolonged period of between 10 and 11 hours. A prolonged time under these
15 temperature and pressure conditions implies a stress test and a sealing test for the bags in which small, existing defects are magnified. If the bags have any defect, the steam used would be capable of penetrating said bags, said penetration being visible with the naked eye, making the visual detection of defects easier.

20 Next, a process of cooling the bags made of a plastics material takes place. Said cooling process is an air-cooling process. In addition, it is advisable to incorporate an air venting system. Preferably, the air is filtered through a sterilising filter.

Finally, the quality control phase -3- comprises a visual inspection. In this phase, among other things,
25 sealing defects are inspected, said defects being, for example, defective welding in the container, breaks in the container, splits and porosities in the walls of the container, as well as other types of defects.

The object of the quality control is to discard defective containers. To do this, means for artificial viewing and image processing, for example, may be used. According to the present invention, defects may be
30 detected by detecting water in the containers.

Alternatively, in this first embodiment, glass containers may be used.

In a second embodiment by way of example, the method of preparing containers for blood-derived
35 products uses FACTOR VIII as said product. In the filling phase -1-, the container is filled. In this embodiment, the containers are usually vials. Alternatively, said containers may be of any other type. After filling, the product is lyophilised and after said lyophilisation a viral inactivation phase -2- is carried out. In the viral inactivation phase -2-, the viral inactivation is carried out by means of steam in direct contact with the bags made of a plastics material at sub-atmospheric pressure. Said phase is carried out
40 at a temperature of between 80°C and 82°C and at an absolute pressure of between 450 and 550 mbar.

During said viral inactivation phase -2-, the bags are subjected to the above-mentioned temperature and pressure conditions for a prolonged period of between 72 and 74 hours. A prolonged time under these

temperature and pressure conditions implies a stress test and a sealing test for the bags in which small, existing defects are magnified. If the bags have any defect, the steam used would be capable of penetrating said bags, said penetration being visible with the naked eye, making the visual detection of defects easier.

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Next, a process of cooling the vials takes place. Said cooling process is an air-cooling process. In addition, it is advisable to incorporate an air venting system. Preferably, the air is filtered through a sterilising filter.

- 10 Finally, the quality control phase -3- comprises a visual inspection. In this phase, among other things, sealing defects are inspected, said defects being, for example, defective welding in the container, breaks in the container, splits and porosities in the walls of the container, as well as other types of defects.

- 15 The object of the quality control is to discard defective containers. To do this, means for artificial viewing and image processing, for example, may be used. According to the present invention, defects may be detected by detecting water in the containers.

- 20 Various tests have been carried out using bags with no defects and control bags with defects and it was demonstrated that for the bags with defects, steam penetrated therein, and for the bags with no defects the steam did not penetrate, which demonstrates the viability of the method described in this application, both for the viral inactivation phase and for the detection of defects.

- 25 Although the invention has been described and illustrated on the basis of various representative examples, it should be understood that said embodiments given by way of example in no way limit the present invention, and therefore any of the variations included directly or as an equivalent in the content of the accompanying claims should be considered as included within the scope of the present invention.

CLAIMS

1. Method of preparing containers for blood-derived products which comprises at least:

- 5 - a filling phase of the blood-derived product containers with a blood-derived product,
 - a viral inactivation phase of the blood-derived product containers,
 - a quality control phase for detecting possible defects in the blood-derived product containers,

10 characterised in that the viral inactivation phase is carried out by placing the blood-derived product
containers in contact with steam at a sub-atmospheric pressure in a chamber adapted for that purpose.

2. Method according to claim 1, characterised in that it comprises an additional cooling phase after the
viral inactivation phase of the blood-derived product containers.

15 3. Method according to the preceding claim, characterised in that the cooling phase is carried out by
placing the containers for blood-derived products in contact with purified water.

20 4. Method according to any of the preceding claims, characterised in that the steam used in the viral
inactivation phase is sanitary quality steam.

5. Method according to any of the preceding claims, characterised in that the steam used in the viral
inactivation phase is saturated steam.

25 6. Method according to any of the preceding claims, characterised in that the quality control phase
comprises a visual inspection of the containers in order to locate defects in said containers.

30 7. Method according to any of the preceding claims, characterised in that the blood-derived product is
therapeutic albumin and the viral inactivation phase is carried out at a temperature of between 55°C and
65°C at an absolute pressure of between 190 mbar and 210 mbar.

8. Method according to any of the preceding claims, characterised in that the blood-derived product is
therapeutic albumin and the viral inactivation phase is carried out at a temperature of between 59.5°C
and 60.5°C and at an absolute pressure of 200 mbar.

35 9. Method according to any of the preceding claims, characterised in that the viral inactivation phase lasts
between 10 and 11 hours.

40 10. Method according to any of claims 1 to 6, characterised in that the blood-derived product is FACTOR
VIII and the viral inactivation phase is carried out at a temperature of between 80°C and 82°C at an
absolute pressure of between 450 and 550 mbar.

11. Method according to claim 10, characterised in that the viral inactivation phase lasts for between 72
and 74 hours.

12. Method according to any of the preceding claims, characterised in that the containers are bags made of a plastics material.

5 13. Method according to any of claims 1 to 11, characterised in that the containers are vials.