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Declarations under Rule 4.17: 

[Continued on nextpage]

(54) Title: A METHOD FOR AN ASEPTIC ASSEMBLY OF A MULTI-COMPONENT MEDICAL DEVICE AND A KIT THEREOF

(57) Abstract: The invention concerns a method for an aseptic assembly of a multi-component medical device (60) comprising the steps of: -providing a first component (12) of the medical device (60) in a first container (10) and a second component (40) of the medical device (60) in a second container (38), wherein each of the separated containers (10,38) comprises a ruptureable portion (28.52), -sterilizing the first component (12) in the first container (10) using a first sterilization technique and sterilizing the second component (40) in the second container (38) using a second sterilization technique, -joining the first and second container (10,38) while arranging the ruptureable portions (28.52) in an overlapping configuration which is aseptically sealed against the surrounding -ings, -transferring one of the components through the ruptureable portions (28.52) and aseptically assembling the components to form the medical device (60) as a sterile package.
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A method for an aseptic assembly of a multi-component medical device and a kit therefor

Description

The invention concerns a method for an aseptic assembly of a multi-component medical device, in particular a skin-mountable sensor device for example as a system for continuous glucose monitoring. The invention further relates to an aseptic kit for providing such a multi-component medical device.

US 2014/20348703 A1 notes that it is important for devices that are to be implanted in the body or positioned below a skin surface of a user, to be sterile upon insertion. In this context, said document discloses methods and systems for the sterilization of medical devices, including devices for the continuous or automatic monitoring of analytes, such as glucose, in bodily fluid. There is provided assembling an analyte sensor with an analyte sensor insertion device, packing the assembled analyte sensor and sensor insertion device in a container which may optionally include a substantially airtight seal, and irradiating the packaged assembled analyte sensor and sensor insertion device at a dose effective to sterilize the package. However, this sterilization approach leads into a dilemma when electronic units, such as signal amplifiers, and adherent coatings are impaired by ionizing radiation.

Present applicants have observed that it is difficult to shield sensitive units from ionizing radiation. Disadvantageously in radiation screening is also the necessary shielding material mass, which increases costs of manufacture and volume of packaging. On the other hand, additional components such as enzyme-containing sensor elements may become deactivated by reactive sterilization gases. A problem associated therewith lies in the fact that the commonly used ethylene dioxide gas dissolves in usual packaging materials, thus requiring overpackaging for the gas-sensitive system parts.
On this basis the object of the invention is to further improve the known methods and devices and to provide easy-to-use and reliable arrangements for sterilized multi-component medical devices.

The combination of features stated in the independent claims is proposed to achieve this object. Advantageous embodiments and further developments of the invention are derived from the dependent claims.

The invention is based on the idea of providing a sterile port in an aseptic package of separately sterilized components. Accordingly it is proposed according to the invention that the method mentioned at the outset comprises the steps of

- providing a first component of the medical device in a first container and a second component of the medical device in a second container, wherein each of the separated containers comprises a ruptureable portion,
- sterilizing the first component in the first container using a first sterilization technique and sterilizing the second component in the second container using a second sterilization technique,
- joining the first and second container while arranging the ruptureable portions in an overlapping configuration which is aseptically sealed against the surroundings,
- transferring one of the components through the ruptureable portions and aseptically assembling the components to form the medical device as a sterile package.

In this way, the invention provides a simple method to separately sterilize sensitive system components such that they can be assembled aseptically. The utility of a two- or multi-piece separated but combinable container arrangement enables to apply respective sterilization techniques which are not impairing the operativeness and reliability of the sterilized components. Still other advantages may exist, where in case of different shelf-life the
sterilization processes may be adjusted accordingly. Advantageously, the provisions according to the invention result in a reduction of costs as the sterilization volume for radiation sterilization is reduced, not further shield need to be included and the assembly within the container arrangement can be carried out side of a clean room potentially even by a user.

According to a preferred embodiment, the first and second sterilization techniques are different from each other and are selected from the group consisting of gas sterilization (preferably using ethylene oxide gas), irradiation sterilization (preferably using an electron beam) and thermal sterilization. This allows also that the packaging can be adapted to the respective sterilization technique.

Advantageously, one of the containers has a gas-permeable and aseptically sealing membrane, wherein a sterilization gas is introduced and released through the membrane such that no potentially harmful gas remains after achieving a desired sterility level. This may be further facilitated by use of a pressure alternating procedure.

It is also preferred to arrange a plurality of first or second containers including respective components in a sterile-tight outer covering before the sterilizing step, thereby reducing operating expense and allowing for sterile intermediary transport.

In this context, it is also advantageous when the first and second container are joined in a sterile environment.

According to a preferred implementation, at least one of the first and second containers has an adhesive portion, and the containers are adhered to each other using the adhesive portion.
For further improvement of sterile assembly it is advantageous when an aseptic seal is formed around the ruptureable portions by bonding together sealing portions of the first and second container.

Another mounting improvement provides that the step of transferring one of the components includes rupturing both of the ruptureable portions.

In this connection, it is also advantageous when the component to be transferred is used to rupture the ruptureable portions.

Advantageously, at least one of the first and second components may be manipulated by handling means provided within the containers.

A particular embodiment further comprises providing one of the first and second containers as a flexible bag or bellow and compressing the flexible bag or bellow to move the component included therein.

Another handling improvement may be achieved when at least one of the first and second containers has a flexible wall, and when at least one of the first and second components is manipulated through the flexible wall to form the medical device.

From the manufacturing point of view it is advantageous when forming at least a part of the containers from a plastic material preferably by means of injection moulding or blow moulding or deep drawing.

For further improvement of the usability it is advantageous to form at least one of the ruptureable portions from a foil material, preferably a metal foil.

Another aspect of the invention concerns an aseptic kit for a multi-component medical device, in particular a skin-mountable sensor device, comprising a first component of the medical device in a first container and a second
component of the medical device in a second container, wherein the components are maintained sterile within the containers, characterized in that each of the containers comprises a ruptureable portion, and that the first and second container are connected to each other such that the ruptureable portions are arranged in an overlapping configuration which is aseptically sealed against the surroundings.

The invention is further elucidated in the following on the basis of an embodiment example shown schematically in the drawings, where

Fig. 1 is a section view of a first container including an applicator unit of a continuous blood glucose measuring device;

Fig. 2 is a top view of a cover lid of the first container having a ruptureable portion;

Fig. 3 is a section view of a second container including a skin-insertable sensor unit of the measuring device;

Fig. 4 is a section view of the joined first and second container;

Fig. 5 - 7 illustrate the assembling of the measuring device under sterile conditions within the joined containers.

Fig. 1 shows a first container 10 including a first component 12 of a multi-component medical device. In this embodiment, the first component 12 includes an applicator unit 13 which is combined with a patch 14 containing electronic components 16 and an adhesive pad 18. The first container 10 has a rigid wall 20, a transparent flexible wall 22, a gas-permeable membrane 24 and a cover lid 26 which is provided with a first ruptureable portion 28 and which is coated with an adhesive layer 30 covered by a liner 32.
As apparent from Fig. 2, the first ruptureable portion 28 is formed as a circular insert preferably from aluminum foil and is reinforced by a central flap 34 providing a bendable connecting link 4 to the lid 26. Advantageously, the lid 26 is configured with lateral cutaways 36 as positioning aids to be explained further below.

In the state illustrated in Fig. 1, the first component 12 can be sterilized using a gas sterilization technique without impairing the adhesiveness of the pad 18 and without damaging the electronics 16. In a certain embodiment, ethylene dioxide as sterilizing gas is introduced and released through the gas-permeable membrane 24 by use of a pressure alternating procedure. For further efficiency improvement of this sterilization procedure, a plurality of first containers 10 comprising respective first components 12 may be arranged in a sterile-tight outer covering (not shown).

Turning now to Fig. 3, a second container 38 holds a second component 40 of the multi-component medical device. In one embodiment, the second component 40 includes an inserter unit 42 for a skin-implantable sensor which is combined with a carriage 44 designed for a connection to applicator 13 and with a transport sleeve 46 provided as a handling aid.

The second container 38 comprises a bellow 48 and a connector lid 50 which is provided with a second ruptureable portion 52 and lateral joining portions 54. The ruptureable portion 52 consists of aluminum foil and covers an outlet of the bellow 48. If necessary, a drying agent or sorbent may be included in the second container 38.

In the state illustrated in Fig. 3, the second component 40 can be sterilized using an irradiation sterilization technique. All elements in the second container 38 are radiation-proof and reveal low outgassing. In one embodiment, electron beam irradiation is applied. The electron beam may be configured to irradiate the second container 38 at a dosage of approximately
25 kGy which results in an adequate sterility assurance level. Preferably, a plurality of second containers 38 is packed densely in a sterile-tight outer covering during the sterilization process. In this case, any shielding of the scanning electron beam should be avoided.

After separate sterilization of the first and second components 12, 40, the first and second containers 10 and 38 may be joined in order to allow the assembly of the medical device. This should take place in a sterile environment, e.g. in a flow-box provided with a sterile filter and UV-lamp, wherein the containers 10, 38 are withdrawn from the respective outer covering and are adhered to each other using the adhesive layer 30 after removing the liner 32.

In the joined configuration shown in Fig. 4, the joining portions 54 of the connector lid 50 engage the lateral cutaways 36 of the cover lid 26 in a form-locking manner, such that a defined mutual orientation is achieved in which the ruptureable portions 28, 52 overlap each other. Due to the planar adhesive connection via the adhesive layer 30, an aseptic seal around the ruptureable portions 28, 52 is formed which is sterile-tight against the surroundings or environment of the joined container configuration. In this way, as sterile kit is formed which allows to separately store the components 12, 40 in their respective containers 10, 38 and to assemble the complete system only at the time of use. In the case of putting together the components by the user himself, the handling aid 46 and guiding means 56 are provided to allow the correct accomplishment of the necessary steps while considerably reducing the possibility of errors.

As the case may be, the final aseptic assembly is carried out as described hereinafter in connection with Fig. 5 to 7.

According to Fig. 5, the second component 40 is transferred through the ruptureable portions 28, 52 into the first container 10. For this purpose, the
free end of the handling aid 46 has to be grasped through the bellow 48 to
allow for moving the second component 40 in direction to the first component
12. Thereby, the carriage 44 is used to rupture or tear-open both of the
rupturable portions 28, 52 and to establish an open port 58 without
interfering sterility within the containers 10, 38.

Potentially present germs which may have been deposited onto one of the
lids 26, 50 after the sterilization steps will be immobilized by the adhesive
layer 30. Germs which were able to reach the airspace inside one of the
containers when the ruptureable portions 28, 52 are broken, can settle down
only onto the transport sleeve 46 or other uncritical surfaces. The probability
of a viable germ to settle down onto a body contacting surface during
assembly is extremely low due to additional protection by liners and/or
protective covers.

Now, once introduced into the guiding means 56 of the first component 12,
the carriage 44 links with the applicator 13, as illustrated in Fig. 6. This allows
to withdraw the transport sleeve 46, which remains in the bellow 48.
Subsequently the patch 14 may be swiveled against the applicator 13, where
the flexible wall 22 allows the necessary manipulation. Then, the assembly is
completed, resulting in a sterile arrangement of the combined first and
second components 12, 40.

Turning now to Fig. 7, the assembled medical device 60 consisting of first
and second components 12, 40 is shown ready to use, when the cover lid 26
has been removed from the first container 10. The user removes the liner 62
from the adhesive pad 18 and adheres the device 60 to the skin of a body
part. Then, the applicator 13 is triggered and the inserter unit 42 implants the
sensor in the skin. After separating the applicator 13, the skin-mounted pad
14 is ready for docking a reusable processor unit, which as such is not
sterilized.
Patent Claims

1. A method for an aseptic assembly of a multi-component medical device (60), in particular a skin-mountable sensor device, comprising the steps of:
   a) providing a first component (12) of the medical device (60) in a first container (10) and a second component (40) of the medical device (60) in a second container (38), wherein each of the separated containers (10,38) comprises a ruptureable portion (28,52),
   b) sterilizing the first component (12) in the first container (10) using a first sterilization technique and sterilizing the second component (40) in the second container (38) using a second sterilization technique,
   c) joining the first and second container (10,38) while arranging the ruptureable portions (28,52) in an overlapping configuration which is aseptically sealed against the surroundings,
   d) transferring one of the components through the ruptureable portions (28,52) and aseptically assembling the components to form the medical device (60) as a sterile package.

2. The method of claim 1, wherein the first and second sterilization techniques are different from each other and are selected from the group consisting of:
   - gas sterilization, preferably using ethylene oxide gas,
   - irradiation sterilization, preferably using an electron beam,
   - thermal sterilization.

3. The method of claim 1 or 2, wherein one of the containers (10,38) has a gas-permeable and aseptically sealing membrane (24), and wherein a sterilization gas is introduced and released through the membrane (24) preferably by use of a pressure alternating procedure.
4. The method according to any of claims 1 to 3, further comprising arranging a plurality of first or second containers \((10,38)\) including respective components \((12,40)\) in a sterile-tight outer covering before the sterilizing step.

5. The method according to any of claims 1 to 4, wherein the first and second containers \((10,38)\) are joined in a sterile environment.

6. The method according to any of claims 1 to 5, wherein at least one of the first and second containers \((10,38)\) has an adhesive portion \((30)\), and wherein the containers \((10,38)\) are adhered to each other using the adhesive portion \((30)\).

7. The method according to any of claims 1 to 6, further comprising forming an aseptic seal around the ruptureable portions \((28,52)\) by bonding together sealing portions of the first and second container \((38)\).

8. The method according to any of claims 1 to 7, wherein the step of transferring one of the components \((12,40)\) includes rupturing both of the ruptureable portions \((28,52)\).

9. The method according to any of claims 1 to 8, wherein the component \((12,40)\) to be transferred is used to rupture the ruptureable portions \((28,52)\).

10. The method according to any of claims 1 to 9, further comprising manipulating at least one of the first and second components \((12,40)\) by handling means \((46)\) provided within the containers \((10,38)\).
11. The method according to any of claims 1 to 10, further comprising providing one of the first and second containers (10,38) as a flexible bag or bellow and compressing the flexible bag or bellow to move the component included therein.

12. The method according to any of claims 1 to 11, wherein at least one of the first and second containers (10,38) has a flexible wall (22), and wherein at least one of the first and second components (12,40) is manipulated through the flexible wall (22) to form the medical device (60).

13. The method according to any of claims 1 to 12, further comprising forming at least a part of the containers (10,38) from a plastic material preferably by means of injection moulding or blow moulding or deep drawing.

14. The method according to any of claims 1 to 13, further comprising forming at least one of the ruptureable portions (28,52) from a foil material, preferably a metal foil.

15. An aseptic kit for a multi-component medical device (60), in particular a skin-mountable sensor device, comprising a first component (12) of the medical device (60) in a first container (10) and a second component (40) of the medical device (60) in a second container (38), wherein the components (12,40) are maintained sterile within the containers (10,38), characterized in that each of the containers (10,38) comprises a ruptureable portion (28,52), and that the first and second container (10,38) are connected to each other such that the ruptureable portions (28,52) are arranged in an overlapping configuration which is aseptically sealed against the surroundings.
## A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

- A61M
- A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

- EPO-Internal
- WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>wo 2008/070220 AI (GAMBR0 BCT INC [US]; FEKT THOMAS [US]) 12 June 2008 (2008-06-12) page 6, lines 7-14 page 7, line 15 - page 8, line 17 figures 1-3</td>
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<tr>
<td>A</td>
<td>wo 2012/114105 AI (TECHNOLOGY PARTNERSHIP [GB]; ROGERS SAMSON SALMAN [GB]; KATZ DAVID MIC) 30 August 2012 (2012-08-30) page 2, lines 15-31; figures 1-6</td>
<td>1-15</td>
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<tr>
<td>A</td>
<td>US 4 019 512 A (TENCZAR FRANCIS J) 26 April 1977 (1977-04-26) column 6, line 65 - column 7, line 15; figures 7-11</td>
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Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:
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