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(54) METHOD AND APPARATUS FOR CLEANING CONTAINERS TO BE SEALED AND CONTAINING A FILLER FROM OXYGEN GAS

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(57) ABSTRACT

The method of manufacturing a sealed container for containing a non-gaseous filler, which filler is to be protected from Oxygen gas, comprises the following steps in the indicated sequence: 1.) filling said filler into said container; 2.) evacuating said container substantially without evaporating parts of said filler; 3.) filling Nitrogen gas into said container; 4.) sealing the container. The method can be used in-line. The apparatus for cleaning filled containers containing a non-gaseous filler, comprises at least one holder for holding said containers; at least one pump adapted for evacuating said containers; a Nitrogen reservoir for supplying Nitrogen gas to be filled into said containers; a process control unit adapted to allowing for an evacuation of said containers by means of said at least one pump and subsequentially filling said Nitrogen gas into said containers.

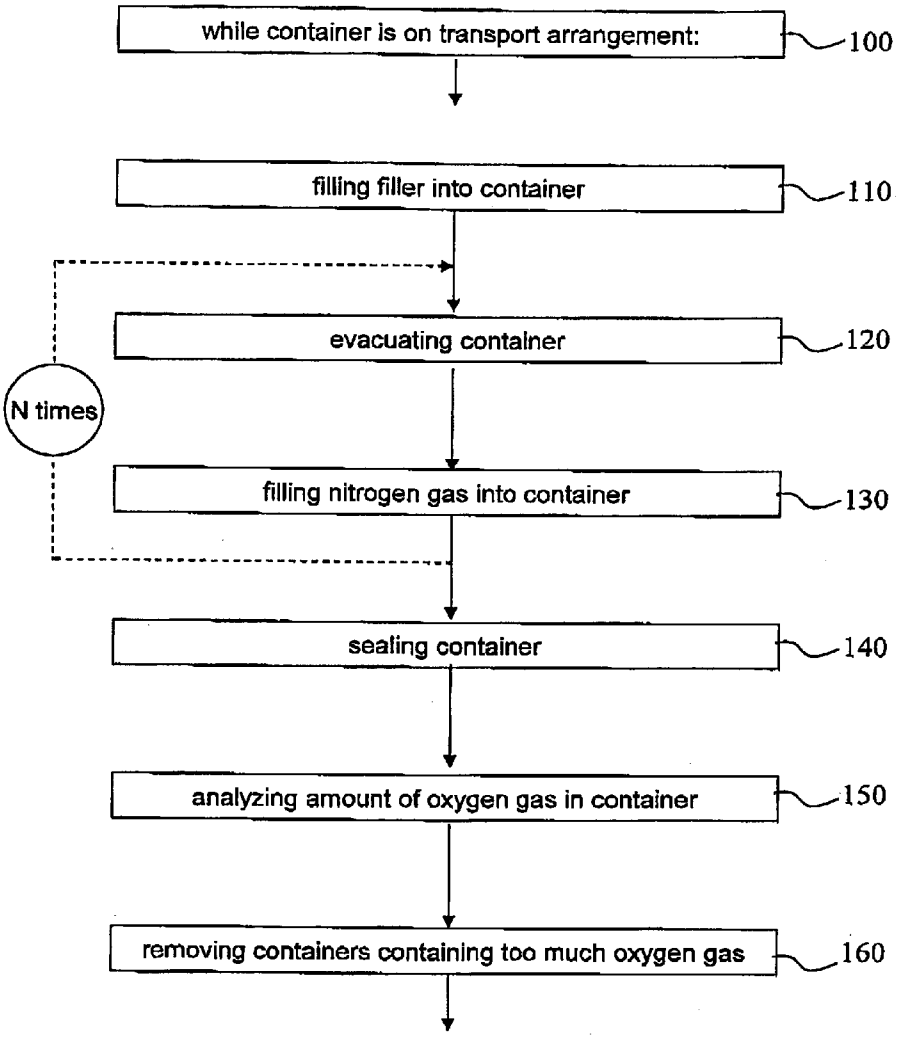
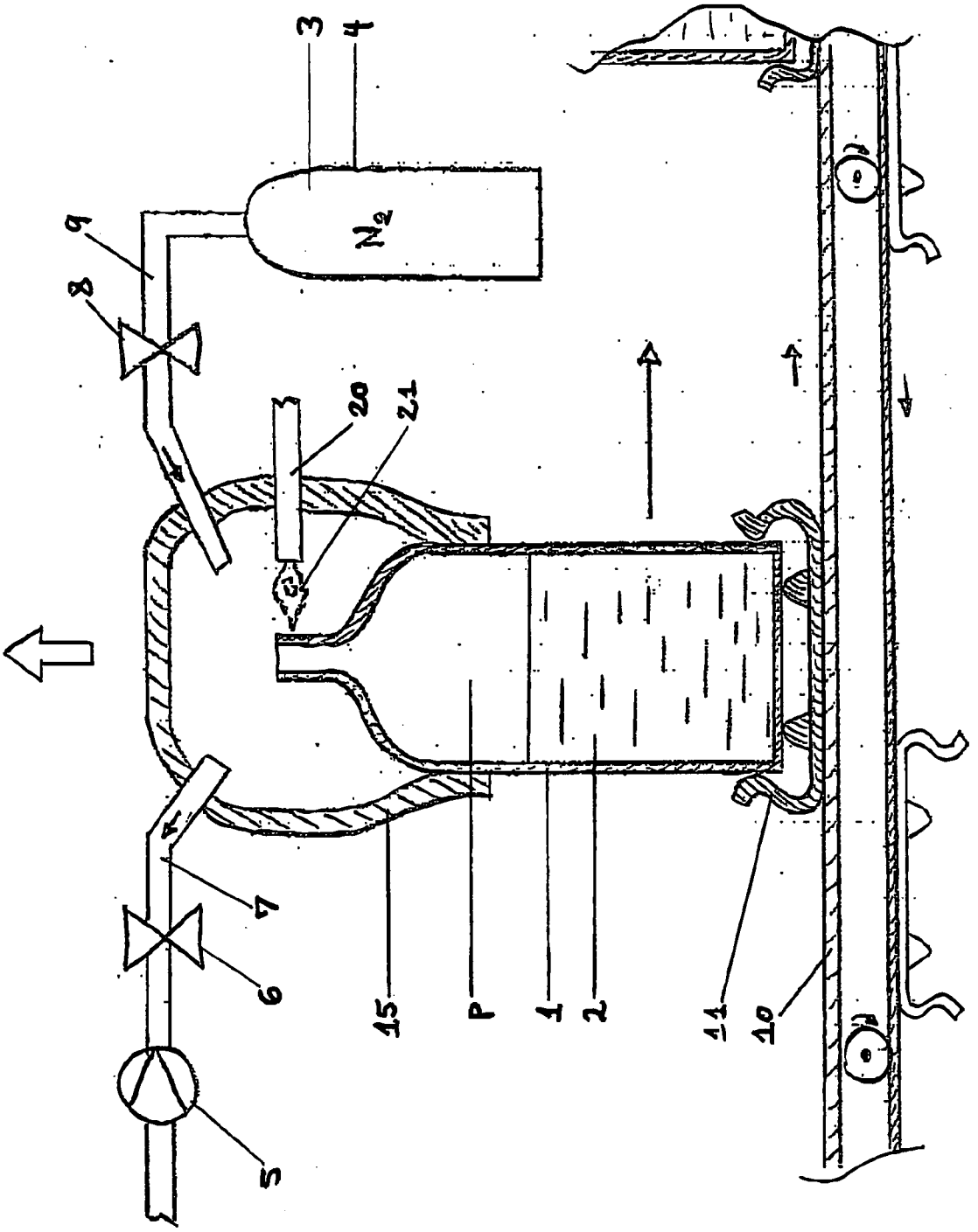


FIG. 1



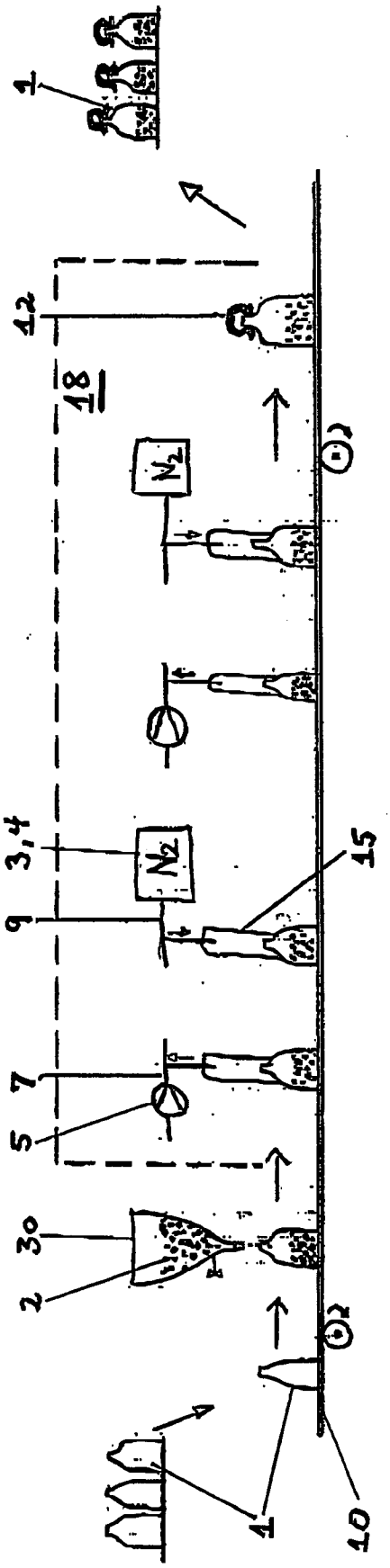


FIG. 2

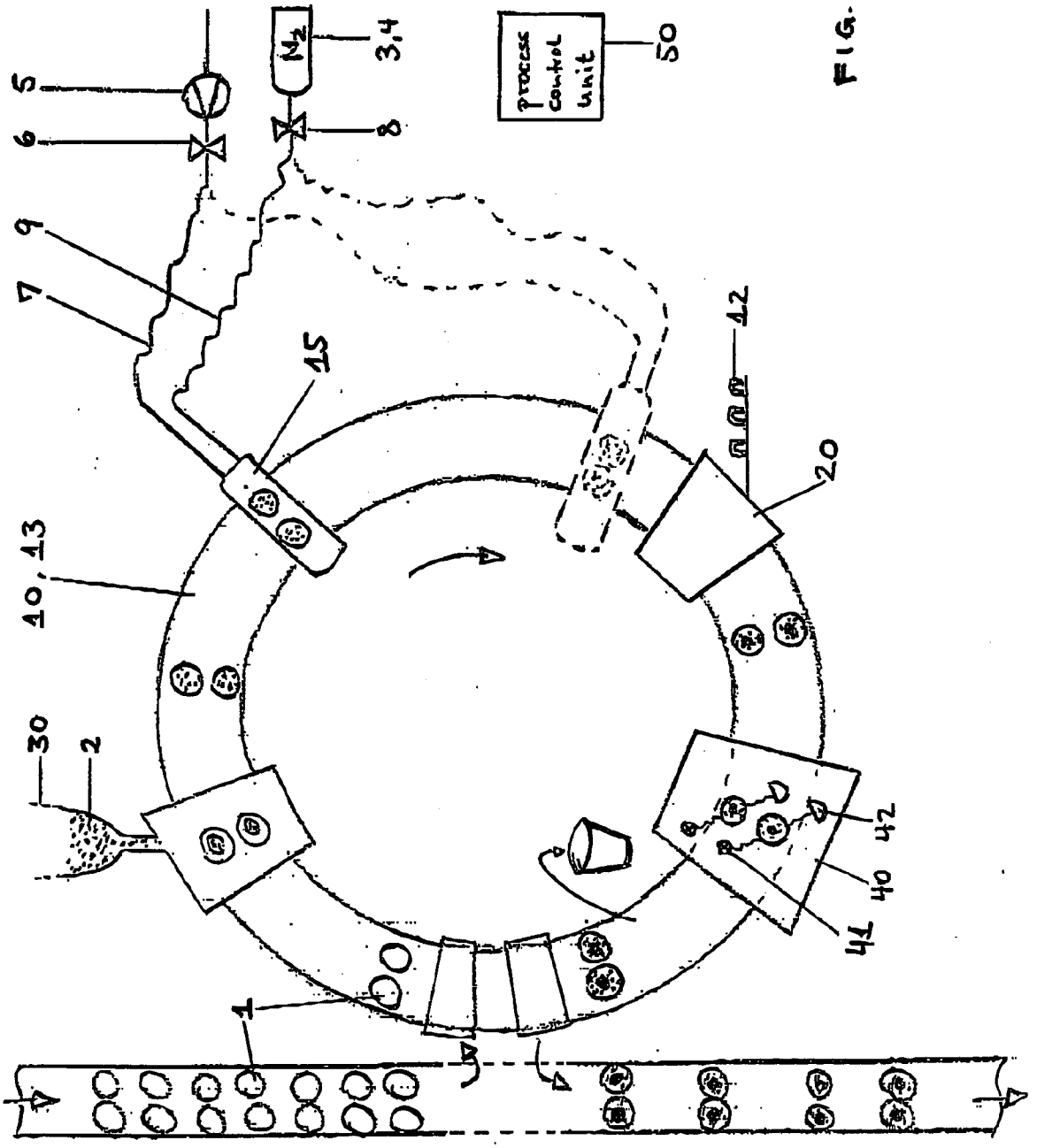


FIG. 3

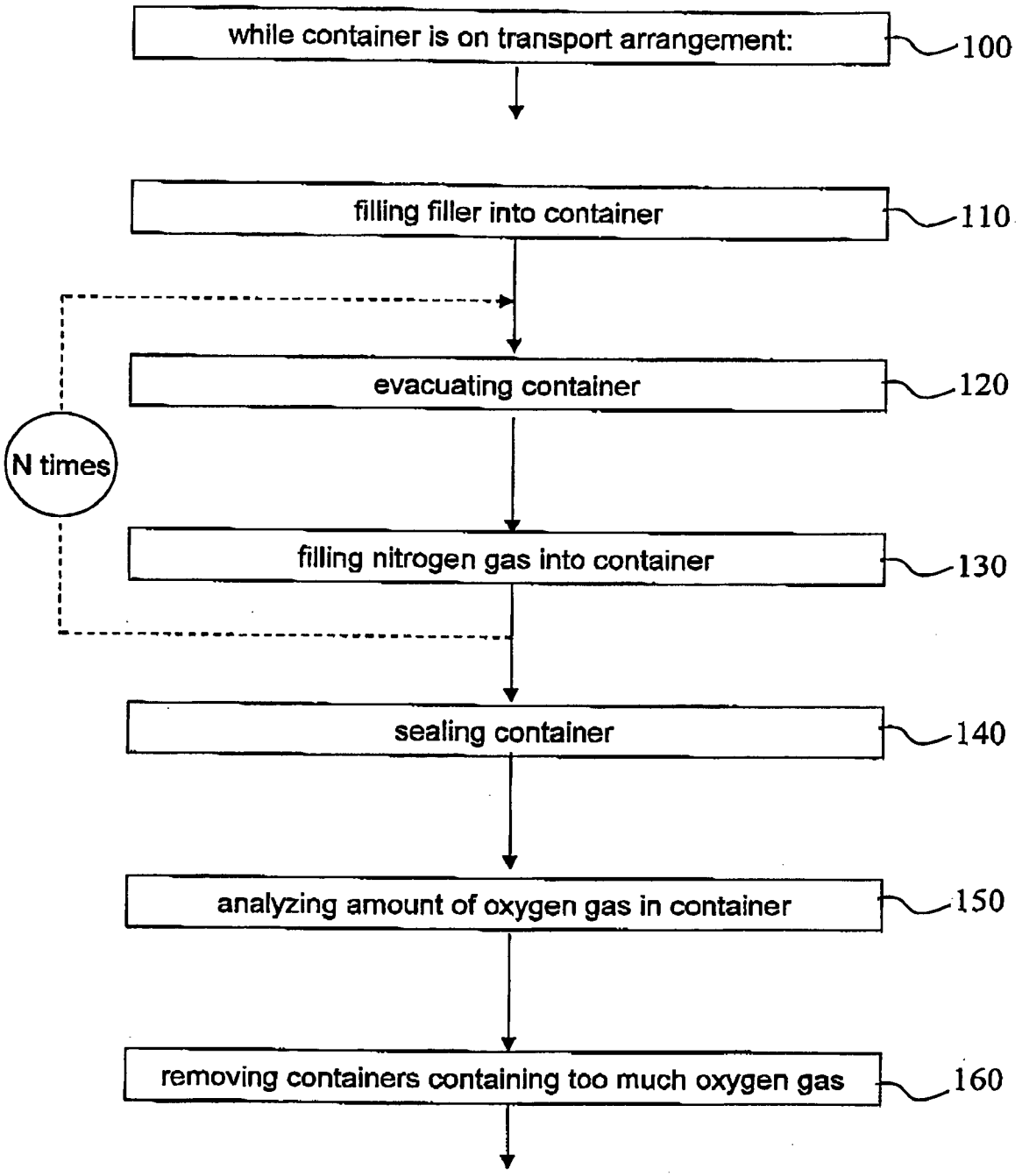

while container is on transport arrangement:
100
filling filler into container
110
evacuating container
120
N times
filling nitrogen gas into container
130
sealing container
140
analyzing amount of oxygen gas in container
150
removing containers containing too much oxygen gas
160

Fig. 4

FIG. 6

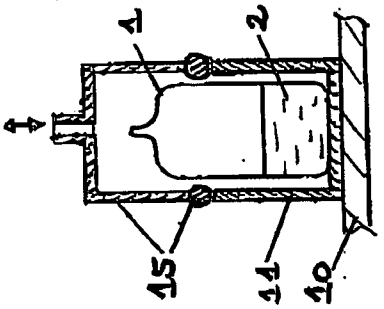


FIG. 5

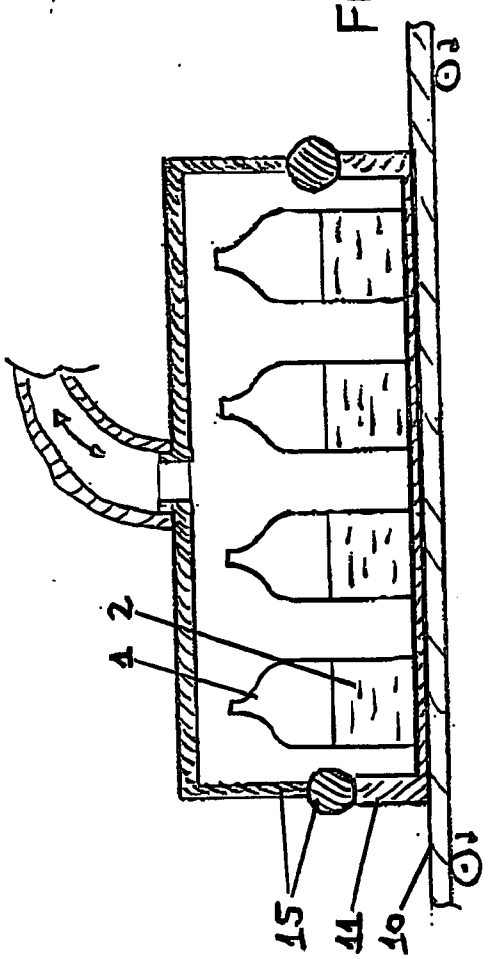
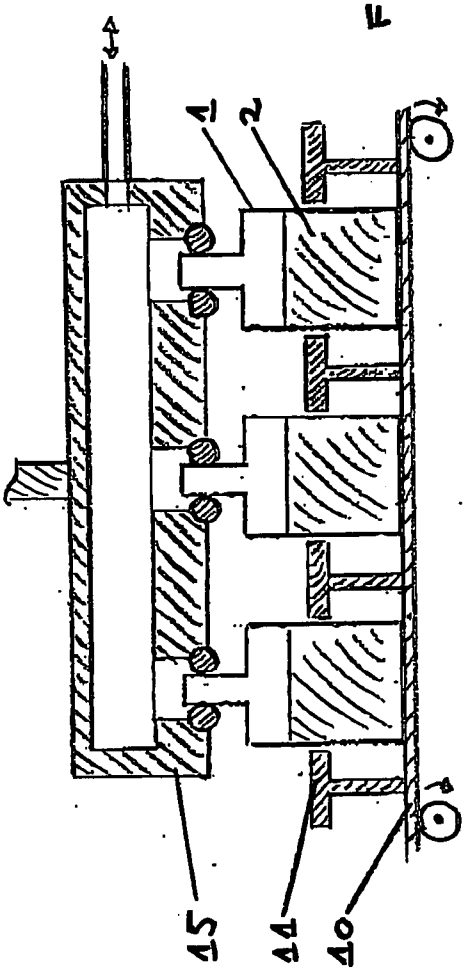


FIG. 7



METHOD AND APPARATUS FOR CLEANING CONTAINERS TO BE SEALED AND CONTAINING A FILLER FROM OXYGEN GAS

TECHNICAL FIELD

[0001] The invention relates to the packaging of chemical or pharmaceutical products in sealed containers. It relates to a method and apparatuses according to the opening clauses of the claims. Such devices and methods find application, e.g., in the chemical and in the pharmaceutical industry. The invention resulted from the desire for a rapid way to produce vials or like containers, which contain a non-gaseous filler and shall contain only a low amount of Oxygen gas.

BACKGROUND OF THE INVENTION

[0002] Many chemical and pharmaceutical products are oxidation-sensitive, i.e., they change properties when oxidized, e.g., through exposure to Oxygen gas. Therefore, such substances are often contained in sealed containers, like vials, so as to avoid a contact of the substance with the environment, in particular to Oxygen in the air. Typical amounts of Oxygen that are acceptable are of the order of 1% by volume.

[0003] Often, single-portion containers, e.g., containing as much of a drug as required for one shot, are used. Typical volumes enclosed by envisaged containers are of the order of 1 cm^3, of the order of 10 cm^3, or of the order of 100 cm^3.

[0004] It is known to batch-wise temper the containers after having them filled with the drug. In that case, for typically one to three days, a large number (of the order of hundreds to tenthousands) of substance-filled and not-yet sealed containers is put into an autoclave in order to dry them and reduce the Oxygen gas content. Such a process is very time-consuming and requrires to take said large number of containers out of the process chain.

SUMMARY OF THE INVENTION

[0005] Therefore, a goal of the invention is to create a method and an apparatus that does not have the disadvantages mentioned above. A method and an according apparatus shall be provided, which allows for a rapid production of filled sealed containers containing little Oxygen gas.

[0006] Furthermore, a method and an according apparatus shall be provided, which allow an in-line integration of a cleaning step, during which the Oxygen-content of said container is reduced.

[0007] These objects are achieved by methods and by apparatuses according to the patent claims.

[0008] The method for cleaning a container containing a non-gaseous filler, which filler is to be protected from Oxygen gas, and which container is to be sealed, comprises the following steps in the indicated sequence:

[0009] A) evacuating said container substantially without evaporating parts of said filler;

[0010] B) filling Nitrogen gas into said container.

[0011] The steps can be perfomed at substantially or approximately ambient (room) temperature. Process temperatures can be between 290 K and 300 K. It is also possible to run the process at higher temperatures, e.g., 300 K to 350 K, or to run the process at lower temperatures, e.g., 250 K to 270 K.

[0012] The steps are usually applied before providing the container with a final seal.

[0013] It is in principle also possible to use the method with other inert gases than Nitrogen gas, e.g., with a noble gas, e.g., Neon or Argon.

[0014] It is in principle also possible to use the method for cleaning a container from other residual gases than Oxygen gas.

[0015] The vapor pressure of such a part of a filler, which would be evaporated during evacuating, can be used as a lower limit for the pressure to be achieved during the evacuation step. In other words, the highest vapor pressure of an outwardly exposed part of the filler can be used as a lower limit for the evacuation pressure. Whereas: if, e.g., the filler is a granulate consisting of solid particles with a liquid inside, the vapor pressure of said liquid is not relevant for the evacuation pressure, since it is not outwardly exposed; only the vapor pressure of the solid, which contains the liquid, is (theoretically) limiting the evacuation pressure (vapor pressures of such solids are usually very low, thus usually not posing a practical limit to the evacuation pressure).

[0016] Often, fillers are liquids, and particularly often, aqueous (water-based) solutions. The vapor pressure of an aqueous solution is typically of the order of 5 mbar to 10 mbar.

[0017] The gas contained in the container before evacuation (step A)) can be ambient air.

[0018] In one embodiment, the sequence of the steps A) and B) is performed at least two times. After the first sequence A), B), the Oxygen content is already strongly reduced. After the second sequence A), B), the Oxygen content is very strongly reduced. This is sufficient for a large number of applications (pharmacutics-typical vials with water-based solution; evacuation pressure of the order of **50** mbar; less than about 1% by volume of Oxygen after sealing).

[0019] A step B) after which a step A) will follow, can be considered a purging step, purging the filler-containing container with Nitrogen.

[0020] The number of required A)-B) sequences depends, amongst others, on the porosity of the filler (powder or granulate fillers).

[0021] The evacuation pressures to be used during the first and during the second A)-B) sequence (and during possible further sequences) can be different or the same. Also the pressure with which the container is filled with Nitrogen may be different or the same during the first and during the second A)-B) sequence (and during possible further sequences).

[0022] It can be advantageous to perform the sequence A)-B) at least three times, i.e., A)-B)-A)-B)-A)-B).

[0023] In one embodiment, the method further comprises the step

[0024] C) leaving said Nitrogen gas in the container for at least 0.2 s after a first and before a second sequence of steps A) and B).

[0025] It can be advantageous to leave the Nitrogen gas for at least 0.2 s, for at least 0.4 s, for at least 0.6 s, for at least 0.75 s in the container between subsequent A)-B) sequences (before evacuating). It is possible to extend that time to at least 1 s or at least 2 s. Usually, it is not necessary to extend that time to more than 1 s or more than 5 s or even more than 15 s. Often, the whole A)-B)-C) cycle will last for of the order of 1 s to 10 s. This is so rapid, that the whole process sequence can be integrated in an in-line process.

[0026] In one embodiment, after said second sequence of steps A) and B), a sequence C),A),B) is performed. The sequence is, accordingly, A),B),C),A),B) C),A),B).

[0027] Depending on the filler an the process parameters, another C),A),B) sequence can be added.

[0028] The length of time during which the Nitrogen remains in the container before evacuating again can be varied or be constant.

[0029] The length of time during which the container is evacuated can vary, e.g., from parts of a second to some seconds.

[0030] In one embodiment, said container is a vial.

[0031] In one embodiment, the container is a container for containing pharmaceutical or chemical substances.

[0032] In one embodiment, said container is made substantially of a glass.

[0033] In one embodiment, said container is substantially made of a polymer material.

[0034] In one embodiment, the filler comprises a drug (or a medicine or a pharmaceutical substance) or is a drug (or a medicine or a pharmaceutical substance).

[0035] The filler can be a test filler, e.g., clean (or purified) water or sand or polymer balls or the like.

[0036] Typically, the filler or a part of it is oxidation-sensitive.

[0037] In one embodiment, the filler is or comprises a liquid. The filler can be a solution, can be an aqueous solution, can be an alcoholic solution or others.

[0038] In one embodiment, the filler is a granulate or a powder. The filler can be in pulverized form or granulated. It can be or comprise a liquid, a pulverized or a granular material.

[0039] In one embodiment, the method comprises the step of transporting said container during said steps A) and B). Since the cleaning process is so fast, it is possible to have the container attached to a transport assembly during the cleaning (steps A),B), possibly C)).

[0040] In one embodiment, said Nitrogen gas is purified Nitrogen gas. This reduces the danger of contaminating the filler. In one embodiment, the Nitrogen gas is of at least 99.9% purity, in particular of at least 99.999% purity.

[0041] In one embodiment, said Nitrogen gas contains at most 1 ppm Oxygen gas.

[0042] In one embodiment, the pressure at which the Nitrogen gas is filled into the container is generally atmospheric pressure or slightly above atmospheric pressure. In particular, that pressure can be between 900 mbar and 1300 mbar or between 970 mbar and 1100 mbar. It is possible to keep the container under even stronger underpressure or overpressure.

[0043] In one embodiment, for the evacuation pressure p is valid $p \leqq 300$ mbar, in particular $p \leqq 200$ mbar or $p \leqq 120$ mbar. It can be advantageous to use an evacuation pressure p with $p \leqq 100$ mbar, $p \leqq 80$ mbar, $p \leqq 65$ mbar, or even $p \leqq 50$ mbar or $p \leqq 30$ mbar. Often it will be possible or advisable to use evacuation pressures with $p \leqq 5$ mbar, $p \leqq 10$ mbar, $p \leqq 20$ mbar or $p \leqq 30$ mbar. One lower limit can be a vapor pressure of the filler. Another limit can be the (maximum) time that shall be spent on achieving the evacuation pressure. It can be advisable (time- or effort-saving) to add another sequence of steps A),B) instead of skipping another such sequence, but work with a lower evacuation pressure.

[0044] In one embodiment, the method's steps are performed while said container is on a transport arrangement.

[0045] The method of manufacturing a sealed container for containing a non-gaseous filler, which filler is to be protected from Oxygen gas, comprises the following steps in the indicated sequence:

[0046] 1.) filling said filler into said container;

[0047] 2.) evacuating said container substantially without evaporating parts of said filler;

[0048] 3.) filling Nitrogen gas into said container;

[0049] 4.) sealing the container.

[0050] The steps 2.) and 3.) of this method correspond to the steps A) and B), respectively of the above-mentioned method. Both methods are closely related, and particular embodiments described above can also be embodiments of this method.

[0051] The filling-in of the filler can be done in any thiankble way, in particular any thinkable way used today for filling pharmaceutical or chemical products in a suitable container, e.g., into a vial.

[0052] The sealing can be done in any thinkable way, in particular any thinkable way used today for sealing containers suitable for fillers under discussion. The sealing can be done, e.g., by plugging, by pressing-in, by adding a membrane (e.g., a rubber membrane) to the container's opening, by applying a lid (lid made of a polymer, a metal; a flexible or a hard.lid), by applying a metal top, by melting a part of the container or by melting a sealing material, or by adding some other cover.

[0053] In one embodiment, the method furthermore comprises, after step 3.), another step 2.) followed by another step 3.).

[0054] In one embodiment, the method furthermore comprises, after step 4.), the step of analyzing an amount of Oxygen gas contained in said container. This way, it is possible to monitor whether or not a prescribed maximum Oxygen content in the container is exceeded. Containers that contain too much Oxygen gas can be removed from further processing. If not every container is analyzed in that way, but only one or some of a batch, the whole batch can be discarded if the tested container(s) has excessive Oxygen gas inside.

[0055] One possible method for analyzing the residual gas content is described in US 2005/0022603 A1 of the same applicant. All details on such a residual gas analysis (method and apparatus) can be taken from that document. Therefore, that document (US **2005/0022603** A1) is hereby incorporated in this application by reference in its entirety.

[0056] Other possible methods for analyzing the residual gas content can be used, too. Preferably, the method is in-line compatible.

[0057] In one embodiment, the method's steps (or at least part of them) are performed while said container is on a transport arrangement. Such transport arrangement can be a conveyor, in particular a screw conveyor. The container is subjected to a transport arrangement while the method's steps are performed. The method's steps (or some of them) are performed while said container is moved on a transport arrangement, e.g., a conveyor.

[0058] The method for achieving. an oxygen percentage by volume below a threshold percentage in a container containing an oxidation-sensitive non-gaseous filler, wherein the container is to be sealed, comprises the following steps in the indicated sequence:

[0059] A) evacuating said container substantially without evaporating parts of said filler;

[0060] B) filling Nitrogen gas into said container.

[0061] The steps A) and B) of this method correspond to the steps A) and B), respectively, of the above-mentioned method. Both methods are closely related, and particular embodiments described above can also be embodiments of this method.

[0062] In one embodiment, said threshold percentage is 2%. The threshold percentage can also be 3%, 4% or 1.5% or 1% or 0.7% or another value.

[0063] Often, the pressure to be finally in the container is around 1 atm. Accordingly, the method can be considered a method for achieving an Oxygen partial pressure below a threshold pressure in a container containing an oxidation-sensitive non-gaseous filler, wherein the container is to be sealed, comprising the following steps in the indicated sequence:

[0064] A) evacuating said container substantially without evaporating parts of said filler;

[0065] **2**) filling Nitrogen gas into said container.

[0066] Corresponding threshold pressures can, e.g., be 50 mbar, 20 mbar, 15 mbar, 10 mbar or 5 mbar or another value.

[0067] According to the invention, the apparatus for cleaning filled containers containing a non-gaseous filler, comprises

[0068] at least one holder for holding said containers;

[0069] at least one pump adapted to evacuating said containers;

[0070] a Nitrogen reservoir for supplying Nitrogen gas to be filled into said containers;

[0071] a process control unit adapted to allowing for an evacuation of said containers by means of said at least one pump and subsequentially filling said Nitrogen gas into said containers.

[0072] Since this apparatus and the above-described methods are closely related, so that particular embodiments described above can easily be transformed into embodiments of this apparatus.

[0073] The apparatus can also be understood as an apparatus for manufacturing sealed containers.

[0074] Furthermore, the "apparatus" may as well be considered to be a "system".

[0075] In one embodiment, the apparatus comprises a filling apparatus for filling said filler into each of said containers.

[0076] In one embodiment, the apparatus comprises a sealing apparatus for sealing said containers.

[0077] In one embodiment, said filler is sensitive to Oxygen gas, and the apparatus furthermore comprises a residual gas monitor for obtaining a quantity representative of an amount of Oxygen gas contained in said container.

[0078] The analysis will typically take place after providing the container with a final Nitrogen filling. The analysis will typically take place after finally sealing the container.

[0079] In one embodiment, the apparatus comprises a transport arrangement for moving said containers.

[0080] In one embodiment, said transport arrangement comprises a conveyor.

[0081] In one embodiment,said transport arrangement comprises a carrousel.

[0082] The invention can make a tempering step of the container after filling-in of the filler superfluous. It is usually not necessary to provide for a (separate) drying step (of a duration of greater than 1 hour, greater than 6 hours, greater than 1 day or greater than 2 days).

[0083] The invention reduces the Oxygen gas content in the container. The Oxygen partial pressure is reduced; Oxygen gas is removed from the container.

[0084] The sequential process comprises evacuating, and purging with Nitrogen, before sealing.

[0085] Containers do usually not have to be removed from a transport arrangement for more than 10 minutes or more than 3 minutes, if at all.

[0086] Containers may be transported by the transport arrangement during the cleaning procedure (evacuating, Nitrogen filling) or during part of it.

[0087] The cleaning process can be fully in-line integrated.

[0088] There is no need to interrupt the manufacturing process (at least not for hours or days) for the desired Oxygen removal

[0089] The cleaning process is adaptable to production lines, at typical transport speeds.

[0090] Containers may be transported (moved) during the cleaning process.

[0091] During evacuation (typically also during Nitrogen-filling), a temporary seal will typically be applied to containers. It is possible to foresee one temporary seal per

container or one temporary seal per a number (e.g., 1 . . . 5, 1 . . . 12, or 1 . . . 40) containers.

[0092] It is possible to provide for the evacuation of single containers or of groups (e.g., 1 . . . 40) of containers.

[0093] A test (analysis) for residual Oxygen in the container after sealing can be done for every single container or for one or a number of containers of a batch, e.g., of a group of containers that were evacuated and/or Nitrogen-filled together.

[0094] The time of transport of containers can be used for cleaning the container's inner volume from Oxygen gas.

[0095] The advantages of the methods correspond to the advantages of corresponding apparatuses.

[0096] Further preferred embodiments and advantages emerge from the dependent claims and the figures.

BREIF DESCRIPTION OF THE DRAWINGS

[0097] Below, the invention is described in more detail by means of examples and the included drawings. The figures show:

[0098] FIG. **1** a cross-section of a detail of an apparatus for cleaning filled containers, schematically;

[0099] FIG. **2** a cross-section of a detail of an in-line apparatus for manufacturing sealed containers, schematically;

[0100] FIG. **3** a cross-section of a detail of an in-line apparatus for manufacturing sealed containers, schematically;

[0101] FIG. **4** a diagram of steps of a method of manufacturing a sealed container;

[0102] FIG. **5** an example how to realize a temporary seal;

[0103] FIG. **6** an example how to realize a temporary seal;

[0104] FIG. **7** an example how to realize a temporary seal.

[0105] The reference symbols used in the figures and their meaning are summarized in the list of reference symbols. The described embodiments are meant as examples and shall not confine the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0106] FIG. **1** shows a schematic cross-section of a detail of an apparatus for cleaning filled containers. A container **1** containing a liquid filler **2**, e.g., an aqueous solution of a drug, which is sensitive to oxidation, is helt in a holder **11** of a conveyor **11**. The small arrows indicate the directions of movement of container **1** and conveyor **10**. On top of the container a temporary seal **15** has been placed, e.g., a cap with rubber lips. Through a gas line **7**, in which a valve **6** is arranged, gas, typically ambient gas, contained in the container **1**, can be removed from the container **1** by means of a pump **5**. By means of this evacuation, a pressure p in the container **1** is reduced to about 50 mbar. Thereupon, Nitrogen gas **3** from a gas cylinder **4** is filled into the container via a gas line **9** in which a valve **8** is arranged. Either then the container **1** is sealed by means of a sealing apparatus **20** having a flame **21** (sealing by melting), or the container **1** is sealed after another evacuation of the container **1** and another filling with Nitrogen gas **3**. Sealing glas vials by melting is well-known in the art.

[0107] It has been found that, under typical conditions for the production of pharmaceutic vials, an Oxygen content in the sealed vial of less than 1% can readily be achieved by two times evacuating to about 50 mbar and each time subsequently filling with Nitrogen gas **3** (to about ambient pressure, 1 atm, in particular to slightly above 1 atmosphere).

[0108] Said temporary seal **15** can be connected to the container **1** and removed from it, as indicated by the open arrow above said temporary seal.

[0109] FIG. **2** shows diagrammatically a cross-section of a detail of an in-line apparatus for manufacturing sealed containers. Empty, unsealed containers **1** are, as indicated on the left-hand side of FIG. **2**, put onto a conveyor **10**. By means of a filling apparatus **30**, a filler **2** is filled into a container. As very schematically indicated, the container is then evacuated, filled with Nitrogen gas **3**, evacuated again and filled with Nitrogen gas **3** again, like described in conjunction with FIG. **1**. The small arrows show the direction of gas flow.

[0110] The container **1** is sealed with a seal **12** (e.g., a metal cap **12**) and then removed from the conveyor **10** (as shown in FIG. **2**) or the container will remain on the conveyor for further processing.

[0111] In FIG. **1** the sealing apparatus was (partially) integrated in the temporary seal **15**. It is possible to do this in an embodiment according to FIG. **2**, too. But, as symbolized by the dashed lines in FIG. **2**, it is possible to create a purified-nitrogen-atmosphere **18** at least near the place where the sealing takes place, so that the temporary seal **15** can be taken off the container for sealing the container without oxygen (or other undesired gases or substances) slipping into the container **1**.

[0112] FIG. **3** shows schematically a cross-section of a detail of an in-line apparatus for manufacturing sealed containers. From a transport band (or conveyor) on the left hand side empty containers are taken and put onto a carrousel **13** (arrow indicates rotation-direction). The containers are filled with filler **2** in a filling apparatus. It is indicated in FIG. **3** that always two containers **1** are being moved next side-by-side and commonly processed. It is also possible to treat each container singly. It is also possible to have larger batches trated simultaneously, comprising at least 3, 4, 5, 8, 12, 15, 24 or more containers (typically less than 100 or 400). This depends mainly on the size of the conveyor and on the size of the containers.

[0113] A temporary seal **15** is applied to the containers, which is connected to a pump **5** and to a Nitrogen bottle **4** via gas lines **7** and **9**, respectively, containing valves **6** and **8**, respectively. While the containers **1** are cleaned (evacuating and Nitrogen-filling, see above), they move on the conveyor. The position, in which the temporary seal **15** is removed from the containers **1**, is indicated by dashed lines (also the gas lines in that position are indicated by dashed lines). There can be more than one (set) of temporary seals **15**, so as to allow for a higher rotation speed of the carrousel **13**.

[0114] After cleaning and being filled with Nitrogen, the containers **1** are sealed with seals **12** by means of a sealing apparatus **20**.

[0115] The sealed containers **1** move on to a residual gas monitor **40**, in which all of the containers or a part of them are analyzed as to their oxygen contents. The residual gas monitor **40** comprises at least one light source **41** and at least one light detector **42**. Details of the residual gas monitor **40** can be taken from the above-mentioned incorporated US 2005/0022603 A1.

[0116] Containers with excessive oxygen content (or containers belonging to a batch comprising at least one container with excessive oxygen content) are discarded as indicated by the trash can. They are removed from the further processing (possibly, they can be further analyzed for fault-finding).

[0117] Finally, the tested containers **1** are taken off the carrousel **13** to be placed, e.g., on another transport device (e.g., on the same which already transported the empty containers).

[0118] A process control unit **50**, typically computer-driven, is also shown in FIG. **3**. For reasons of clarity, the various connections of the process control unit **50** to other parts of the apparatus have not been indicated in FIG. **3**.

[0119] FIG. **4** shows in a diagram steps of somewhat elaborate a method of manufacturing a sealed container. The steps **100** to **160** are self-explaining and have (at least implicitely) already been discussed above. The steps **120** and **130** can be repeated a number of times.

[0120] FIGS. **5**, **6** and **7** show some examples, how the temporary seal **15** can be realized, schematically and in cross-section.

[0121] In FIG. **5** a number (four; any number possible) of containers are arranged on a holder **11** of a conveyor **10**. The temporary seal **15** seals towards the holder **11**. The whole enclosed volume is evacuated or filled with oxygen (as indicated by the two-way arrow).

[0122] FIG. **6** is similar to FIG. **5**, but only one single container **1** is enclosed in the temporary seal **15**. in FIG. **7** the temporary seal **15** tightens against every single container **1** of the three containers **1** (any number possible). This way, the volume to be evacuated and filled with Nitrogen, is much smaller than in FIGS. **5** and **6**.

[0123] A single pump and a single Nitrogen supply line is sufficient to operate the embodiments of FIGS. **5**, **6** and **7**.

List of Reference Symbols

[0124] **1** container, vial

[0125] **2** filler, liquid, powder, granulate, drug, oxidation-sensitive filler

[0126] **3** inert gas, Nitrogen gas, N_2

[0127] **4** inert gas reservoir, gas cylinder

[0128] **5** pump, vacuum pump

[0129] **6** valve

[0130] **7** gas line

[0131] **8** valve

[0132] **9** gas line

[0133] **10** transport arrangement, moving apparatus, conveyor, screw conveyor, part of transport arrangement

[0134] **11** holder, container holder

[0135] **12** seal

[0136] **13** transport arrangement, moving apparatus, carrousel, part of transport arrangement

[0137] **15** removable seal, temporary seal

[0138] **18** Nitrogen atmosphere

[0139] **20** sealing apparatus

[0140] **21** flame, flame for sealing container, flame for sealing vial

[0141] **30** filling apparatus

[0142] **40** residual gas monitor

[0143] **41** light source

[0144] **42** light detector

[0145] **50** process control unit

[0146] **100 - 170** steps

[0147] p pressure

1. Method for cleaning a container containing a non-gaseous filler, which filler is to be protected from Oxygen gas, and which container is to be sealed, the method comprising the following steps in the indicated sequence:

A) evacuating said container substantially without evaporating parts of said filler;

B) filling Nitrogen gas into said container.

2. Method according to claim 1, wherein the sequence of the steps A) and B) is performed at least two times.

3. Method according to claim 2, further comprising the step

C) leaving said Nitrogen gas in the container for at least 0.2 s after a first and before a second sequence of steps A) and B).

4. Method according to claim 3, wherein after said second sequence of steps A) and B), a sequence C),A),B) is performed.

5. Method according to claim 1, wherein said container is a vial.

6. Method according to claim 1, wherein said container is made substantially of a glass.

7. Method according to claim 1, wherein the filler comprises a drug.

8. Method according to claim 1, wherein the filler is liquid.

9. Method according to claim 1, wherein the filler is a granulate or a powder.

10. Method according to claim 1, comprising the step of transporting said container during said steps A) and B).

11. Method according to claim 1, wherein said Nitrogen gas is purified Nitrogen gas.

12. Method according to claim 1, wherein for said pressure p is valid $p \leqq 300$ mbar.

13. Method according to claim 1, wherein for said pressure is valid $p \leqq 80$ mbar.

14. Method according to claim 1, wherein the method's steps are performed while said container is on a transport arrangement.

15. Method of manufacturing a sealed container for containing a non-gaseous filler, which filler is to be protected

from Oxygen gas, said method comprising the following steps in the indicated sequence:

1.) filling said filler into said container;

2.) evacuating said container substantially without evaporating parts of said filler;

3.) filling Nitrogen gas into said container;

4.) sealing the container.

16. Method according to claim 15, furthermore comprising, after step 3.), another step 2.) followed by another step 3.).

17. Method according to claim 15, furthermore comprising, after step 4.), the step of analyzing an amount of Oxygen gas contained in said container.

18. Method according to claim 15, wherein the method's steps are performed while said container is on a transport arrangement.

19. Method for achieving an Oxygen percentage by volume below a threshold percentage in a container containing an oxidation-sensitive non-gaseous filler, wherein the container is to be sealed, comprising the following steps in the indicated sequence:

A) evacuating said container substantially without evaporating parts of said filler;

B) filling Nitrogen gas into said container.

20. Method according to claim 19, wherein said threshold percentage is 2%.

21. Apparatus for cleaning filled containers containing a non-gaseous filler, comprising

at least one holder for holding said containers;

at least one pump adapted to evacuating said containers;

a Nitrogen reservoir for supplying Nitrogen gas to be filled into said containers;

a process control unit adapted to allowing for an evacuation of said containers by means of said at least one pump and subsequentially filling said Nitrogen gas into said containers.

22. Apparatus according to claim 21, furthermore comprising a filling apparatus for filling said filler into each of said containers.

23. Apparatus according to claim 21, furthermore comprising a sealing apparatus for sealing said containers.

24. Apparatus according to claim 21, wherein said filler is sensitive to Oxygen gas, the apparatus furthermore comprising a residual gas monitor for obtaining a quantity representative of an amount of Oxygen gas contained in said container.

25. Apparatus according to claim 21, furthermore comprising a transport arrangement for moving said containers.

26. Apparatus according to claim 25, wherein said transport arrangement comprises a conveyor.

27. Apparatus according to claim 25, wherein said transport arrangement comprises a carrousel.

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