In order to use these time-pressure-filling systems for a wide range of different liquid drug products, specifically for multi-product-filling lines, the system has to be cleaned and sterilized extensively. This implies great challenges, in particular for pharmaceutical drug products, such as liquid drug products for subcutaneous application and/or high-potent liquid drug products: The permissible toxicological residual concentrations of liquid drug products being filled after a cleaning of the system often are below an analytical detection limit. Further, very few analytical detection methods having a sufficient sensitivity are available.

Therefore, it is a major challenge to provide methods and devices, which allow for filling a wide range of many different liquid drug products using the same time-pressure-filling system while enabling the highest possible level of patient security and further avoiding possible cross contaminations.

Problem to be solved

It is therefore desirable to provide methods and devices, which address the above-mentioned technical challenges of filling at least one liquid drug product into containers. Specifically, it is desirable to provide methods and devices, which allow for filling a wide range of many different liquid drug products using the same time-pressure-filling system while enabling the highest possible level of patient security. Further, methods and devices shall be proposed which overcome the need for an extensive cleaning of the time-pressure-filling system.

Summary

This problem is addressed by a time-pressure-filling system and a time-pressure-filling method for filling at least one liquid drug product with the features of the independent claims. Advantageous ~~embodiments~~examples which might be realized in an isolated fashion or in any arbitrary combinations are listed in the dependent claims.

As used in the following, the terms “have”, “comprise” or “include” or any arbitrary grammatical variations thereof are used in a non-exclusive way. Thus, these terms may both refer to a situation in which, besides the feature introduced by these terms, no further features are present in the entity described in this context and to a situation in which one or more further features are present. As an example, the expressions “A has B”, “A comprises B” and “A includes B” may both refer to a situation in which, besides B, no other element

is present in A (i.e. a situation in which A solely and exclusively consists of B) and to a situation in which, besides B, one or more further elements are present in entity A, such as element C, elements C and D or even further elements.

Further, it shall be noted that the terms “at least one”, “one or more” or similar expressions indicating that a feature or element may be present once or more than once typically will be used only once when introducing the respective feature or element. In the following, in most cases, when referring to the respective feature or element, the expressions “at least one” or “one or more” will not be repeated, non-withstanding the fact that the respective feature or element may be present once or more than once.

Further, as used in the following, the terms "preferably", "more preferably", "particularly", "more particularly", "specifically", "more specifically" or similar terms are used in conjunction with optional features, without restricting alternative possibilities. Thus, features introduced by these terms are optional features and are not intended to restrict the scope of the claims in any way. The ~~invention~~disclosure may, as the skilled person will recognize, be performed by using alternative features. Similarly, features introduced by "in an ~~embodiment~~ example of the ~~invention~~disclosure" or similar expressions are intended to be optional features, without any restriction regarding alternative ~~embodiments~~examples of the ~~invention~~disclosure, without any restrictions regarding the scope of the ~~invention~~disclosure and without any restriction regarding the possibility of combining the features introduced in such way with other optional or non-optional features of the ~~invention~~disclosure.

In ~~a first aspect of~~ the present ~~invention~~disclosure, a time-pressure-filling system is disclosed. The time-pressure-filling system is configured for filling at least one liquid drug product into containers. The time-pressure-filling system comprises:

A. at least one storage vessel for storing the liquid drug product;

B. at least one surge vessel, wherein the surge vessel is configured for single use, wherein the surge vessel is at least partially made of at least one rigid plastic material;

C. at least one supply line for feeding the liquid drug product from the storage vessel into the surge vessel in a pressurized fashion;

D. at least one pressure control line for applying a control pressure to the surge vessel;

E. at least one dispenser for dispensing the liquid drug product into the containers;

F. at least one dispensing line connecting the surge vessel to the dispenser;

G. at least one pressure sensor for determining a pressure in the dispensing line; and

H. at least one valve for controlling a flow of the liquid drug product through the dispensing line.

In one aspect, the present disclosure provides a time-pressure-filling system for filling at least one liquid drug product into containers, comprising:

A. at least one storage vessel for storing the liquid drug product;

B. at least one surge vessel, wherein the surge vessel is configured for single use, wherein the surge vessel is at least partially made of at least one rigid plastic material;

C. at least one supply line for feeding the liquid drug product from the storage vessel into the surge vessel in a pressurized fashion;

D. at least one pressure control line for applying a control pressure to the surge vessel;

E. at least one dispenser for dispensing the liquid drug product into the containers;

F. at least one dispensing line connecting the surge vessel to the dispenser;

G. at least one pressure sensor for determining a pressure in the dispensing line; and

H. at least one valve for controlling a flow of the liquid drug product through the dispensing line.

The term "time-pressure-filling system" as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to an arbitrary system for dispensing, releasing or conducting an arbitrary liquid, such as a pure liquid, a liquid mixture, a solution, a suspension, a dispersion or an emulsion, such as into receptacles or containers. The time-pressure filling system may be configured for controlling the volume flow of the liquid by applying a pressure to the liquid and controlling an opening time of a valve. Thus, the time-pressure-filling system may be configured for supplying a pre-defined amount of the liquid by providing the liquid at a controlled or pre-defined pressure via a line and by opening a valve for a pre-defined time span. Thus, the time-pressure-filling system may comprise at least one element containing the liquid and being configured for applying a pressure to the enclosed liquid. Further, the time-pressure-filling system, as will be outlined in further detail below, may comprise at least one valve, wherein the opening time of the valve may be controlled. The volume flow of the liquid may depend on the applied pressure, on the opening time of the valve and on the dimension or geometry of the valve, such as a diameter or a cross-section of the valve.

Therefore, the time-pressure-filling system may be configured for controlling a filling volume of the liquid into the receptacles or containers. Further, the time-pressure-filling system may be configured for filling a plurality of containers in a sequential and/or in a parallel fashion via the at least one dispenser of the at least one dispensing line. As an example, the time-pressure-filling system may comprise a number of N dispensers for simultaneously filling the liquid into a batch of N containers, followed by a subsequent batch of N containers and so forth. The time-pressure-filling system may be used for filling a predetermined amount of the liquid into containers. Thus, the time-pressure-filling system may be used in industrial applications, such as for filling at least one liquid drug product into containers.

The term “liquid drug product” as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to a liquid, such as a pure liquid, a liquid mixture, a solution, a suspension, a dispersion or an emulsion, wherein the liquid is usable as a medication or that may be used or prepared in the process of producing a medication or a preparation or that may be used or prepared as an interstage, a precursor or a compound of a medication or a preparation. Thus, the drug

ing line and the at least one pressure control line comprised by reinforced silicone tubes, may be configured for being sterilized, specifically by means of gamma radiation.

Further, the control pressure applied to the surge vessel may be in the range of 50 to 1000 mbar, specifically 50 to 400 mbar.

The time-pressure-filling system according to the present ~~invention~~disclosure specifically may comprise the at least one surge vessel according to the present ~~invention~~disclosure, such as according to any one of the ~~embodiments~~examples disclosed herein and/or as disclosed in further detail below. Thus, for optional ~~embodiments~~examples of the surge vessel of the time-pressure filling system, reference may be made to the disclosure of the surge vessel given in further detail below.

The time-pressure-filling system may further comprise at least one control unit. The control unit may specifically be configured for at least one of: controlling a filling level of the surge vessel; controlling the control pressure applied to the surge vessel; controlling an opening time of the valve. The term “control unit” as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to an electronic device configured, specifically by hardware and/or by software programming, for controlling the functionality of the time-pressure-filling system. Specifically, the control unit may be or may comprise a computer configured for receiving a signal, such as a signal from the at least one optical sensor and/or a signal from the at least one pressure sensor, and for further evaluating the received signal. For example, the control unit may be configured evaluating a signal from the at least one optical sensor for detecting a filling level of the surge vessel. As another example, the control unit may be configured for evaluating a signal from the at least one pressure sensor for determining a pressure in the at least one dispensing line. Further, the control unit may be configured for controlling the control pressure applied to the surge vessel and/or for controlling the pressure applied to the storage vessel for feeding the surge vessel with the liquid drug product. Thus, the control unit may be configured for controlling the filling level of the surge vessel in range of 30 percent to 60 percent. The control unit may further be configured for controlling the opening time of the valve. For example, the control unit may control the opening time of the valve in conjunction with the control pressure applied to the surge valve for controlling the filling volume of the liquid drug product into the containers.

In ~~a further aspect of~~ the present ~~invention~~disclosure, as indicated above, a surge vessel for use in a time-pressure-filling system is disclosed, such as for use in a time-pressure-filling system

according to any one of the ~~embodiments~~ examples disclosed above and/or according to any one of the ~~embodiments~~ examples disclosed in further detail below. The surge vessel is configured for single use. The surge vessel is at least partially made of at least one rigid plastic material. The surge vessel comprises:

a. a rigid cylindrical vessel sidewall;
b. a rigid vessel bottom plate;
c. a rigid vessel top plate;
d. at least one supply pipe penetrating the rigid vessel bottom plate, wherein the supply pipe has at least one portion protruding into an interior space of the surge vessel and wherein the supply pipe further has at least one inlet connecting branch protruding from the vessel bottom plate outside the interior space for connecting a supply line to the supply pipe;
e. at least one outlet connecting branch protruding from the vessel bottom plate outside the interior space for connecting at least one dispensing line; and
f. at least one pressure control branch protruding from the vessel top plate outside the interior space for connecting at least one pressure control line.

In another aspect, the present disclosure provides a surge vessel for use in a time-pressure-filling system as described herein, wherein the surge vessel is configured for single use, wherein the surge vessel is at least partially made of at least one rigid plastic material, the surge vessel comprising:

a. a rigid cylindrical vessel sidewall;
b. a rigid vessel bottom plate;
c. a rigid vessel top plate;
d. at least one supply pipe penetrating the rigid vessel bottom plate, wherein the supply pipe has at least one portion protruding into an interior space of the surge vessel and wherein the supply pipe further has at least one inlet connecting branch protruding from the rigid vessel bottom plate outside the interior space for connecting a supply line to the supply pipe;
e. at least one outlet connecting branch protruding from the rigid vessel bottom plate outside the interior space for connecting at least one dispensing line; and
f. at least one pressure control branch protruding from the rigid vessel top plate outside the interior space for connecting at least one pressure control line.

The term “rigid cylindrical vessel sidewall” as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to an arbitrary cylindrical enclosure of the surge vessel which is at least partially made of at least one rigid plastic material. Thus, the rigid cylindrical vessel sidewall may be at least partially transparent, specifically for light in the visible and/or infrared spectral range. The rigid cylindrical vessel sidewall may be configured for attaching at least one optical sensor to the outside of the rigid cylindrical vessel sidewall, wherein the optical sensor may be configured for detecting the filling level of the surge vessel. Further, the rigid cylindrical vessel sidewall may have a wall thickness of at least 0.5 mm, specifically of at least 1 mm, such as a thickness of 0.5 mm to 5 mm, e.g. a thickness of 1.0 mm to 3 mm. Further, the enclosure of the surge vessel may also have other shape than a cylindrical shape, such as a conical shape or a cubic shape. Other options are feasible.

The term “rigid vessel bottom plate” as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to an arbitrary enclosure at the bottom end of the surge vessel which is at least partially made of at least one rigid plastic material. The rigid vessel bottom plate comprises the at least one outlet connecting branch. As an example, the rigid vessel bottom plate may

light in the visible and/or infrared spectral range. Further, the optical sensor may also be sensitive to an interval of wavelength in the visible and/or infrared spectral range.

The term "visible spectral range" as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to a wavelength interval of visible light. Specifically, the visible spectral range may refer to visible light having a wavelength of 380 nm to 760 nm. Consequently, the term "infrared spectral range" as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to a wavelength interval of infrared light. Specifically, the infrared spectral range may refer to infrared light having a wavelength of 760 nm to 1 mm.

Further, the at least one optical sensor may be configured for detecting a filling level of the surge vessel. Specifically, the surge vessel and/or the time-pressure-filling system may comprise the at least one control unit, wherein the control unit may be configured for detecting a filling level by evaluating at least one signal generated by the optical sensor.

The rigid cylindrical sidewall of the surge vessel may have a wall thickness of at least 1 mm. Thus, the surge vessel may be pressure-stable in the above-identified pressure range. The surge vessel may further comprise a plurality of outlet connecting branches. The plurality of outlet connecting branches may have at least two diameters, wherein the at least two diameters may be equal or different to each other. Thus, the time-pressure-filling system comprising the surge vessel may be configured for filling a plurality of containers. The plurality of containers may be filled by using at least one manifold in at least one dispensing line. As another example, the plurality of containers may be filled by using a plurality of dispensing lines connected to the plurality of outlet connecting branches. The time-pressure-filling system may further be configured for filling different sizes of containers by using the plurality of dispensing lines connected to the plurality of outlet connecting branches having a different diameter.

In ~~a further aspect of~~ the present ~~invention~~disclosure, a time-pressure-filling method for filling at least one liquid drug product into containers is disclosed. The time-pressure-filling method comprises the following steps which specifically may be performed in the given order. It shall be noted, however, that a different order is also possible. Further, it is also possible to perform one or more of the method steps once or repeatedly. Further, it is possible to per-

form one or more of the method steps simultaneously or in a timely overlapping fashion. The method may comprise further method steps which are not listed.

The time-pressure-filling method comprises:

i. providing the time-pressure-filling system according to the present ~~invention~~disclosure, such as according to any one of the ~~embodiments~~ examples disclosed above and/or according to any one of the ~~embodiments~~ examples disclosed in further detail below referring to a time-pressure-filling system, specifically comprising at least one surge vessel according to the present ~~invention~~disclosure, such as according to any one of the ~~embodiments~~ examples disclosed above and/or according to any one of the ~~embodiments~~ examples disclosed in further detail below referring to a surge vessel;

ii. feeding the liquid drug product from the storage vessel into the surge vessel in a pressurized fashion;

iii. controlling the pressure in the surge vessel by applying a control pressure to the surge vessel;

iv. determining the pressure in the dispensing line by using the pressure sensor; and

v. dispensing predetermined amounts of the liquid drug product into the containers by controlling an opening time of the valve.

In another aspect, the present disclosure provides a time-pressure-filling method for filling at least one liquid drug product into containers, comprising:

i. providing the time-pressure-filling system as described herein referring to a time-pressure-filling system;

ii. feeding the liquid drug product from the storage vessel into the surge vessel in a pressurized fashion;

iii. controlling the pressure in the surge vessel by applying a control pressure to the surge vessel;

iv. determining the pressure in the dispensing line by using the pressure sensor; and

v. dispensing predetermined amounts of the liquid drug product into the containers by controlling an opening time of the valve.

The term “feeding the liquid drug product” as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to a supply of the liquid drug product and/or a transfer of the liquid drug product from the storage vessel into the surge vessel by applying a pressure to the storage vessel.

The term “controlling the pressure in the surge vessel” as used herein is a broad term and is to be given its ordinary and customary meaning to a person of ordinary skill in the art and is not to be limited to a special or customized meaning. The term specifically may refer, without limitation, to one or more of assessing, verifying, maintaining or setting the pressure in the surge vessel. Specifically, the pressure in the surge vessel may be set by applying the control pressure to the surge vessel. The pressure applied thereto may be verified by determining the pressure in the dispensing line by using the pressure sensor, as will be described in further detail below. Further, controlling the pressure in the surge vessel may also involve a regulation of the applied control pressure after determining the pressure in the dispensing line. Thus, step iii. and step iv. may be subsequently repeated until a predetermined pressure value in the dispensing line is realized.

mined amount of the liquid drug product, wherein the method may comprise exchanging the surge vessel after filling the batch of the liquid drug product into the containers and disposing of the surge vessel. Further, the time-pressure-filling system may comprise a plurality of the surge vessels, wherein the surge vessels may be used subsequently one after the other for different batches, wherein used surge vessels may be disposed of.

In ~~a further aspect of~~ the present ~~invention~~disclosure, a use of at least one of the time-pressure-filling system and the surge vessel is disclosed. The at least one time-pressure-filling system and the at least one surge vessel are used for filling at least one of the following liquid drug product into containers: a pharmaceutical product; a steroid product; a liquid drug product for subcutaneous application; a liquid drug product for intravenous application; a high-potent liquid drug product; an aqueous protein solution, such as an antibody drug product solution.

In another aspect, the present disclosure provides a use of at least one of the time-pressure-filling system as described herein referring to a time-pressure-filling system and the surge vessel as described herein referring to a surge vessel, for filling at least one of the following liquid drug product into containers: a pharmaceutical product; a steroid product; a liquid drug product for subcutaneous application; a liquid drug product for intravenous application; a high-potent liquid drug product; an aqueous protein solution.

A pressure-stable surge vessel may be realized by using the at least one rigid plastic material, for example polypropylene and/or polyethylene, to construct the surge vessel, wherein the rigid vessel sidewall may have a thickness of at least 1 mm. The rigid plastic material may be transparent and, thus, may allow for determining the filling level of the surge vessel by using the at least one optical sensor. The determination of the filling level may avoid overfilling of the surge vessel. Further, a filling level in the range of 25% to 75%, specifically 30% to 60%, may ensure a sufficient dwell time of the liquid, for example of the liquid drug product, in the surge vessel. During the dwell time, the liquid, such as the liquid drug product, may outgas the gas which is absorbed when pressure is applied to the liquid, for example the pressure applied to the liquid in the storage vessel. The outgassing of the liquid may enhance the filling accuracy of the time-pressure-filling system.

The surge vessel may further be in a cylindrical shape to ensure a homogeneous pressure distribution in the interior space of the surge vessel. The supply line may have at least one portion protruding the rigid vessel bottom plate configured for enabling a soft and turbulence-free inflow of the incoming liquid, such as the liquid drug product.

The liquid, such as the liquid drug product, may be transported to the storage vessel and/or out of the storage vessel through platinum reinforced silicone tubes which may be connected to the at least one inlet connecting branch and/or the at least one outlet connecting branch. Specifically, braid reinforced silicone tubes may be used to prevent pressure loss in one or more of the supply line or the dispensing line.

Further, the number and/or the diameter of the at least one connecting branch may be adjusted to the number and/or the diameter of the at least one dispensing line as well as to the predetermined filling volume of the liquid, such as the liquid drug product. The predetermined filling volume and/or the filling speed may be dependent on the container to be filled with the liquid, such as the liquid drug product. The predetermined filling volume may be in a range of 100 µl to 100 ml.

Further, the time-pressure-filling system may comprise the at least one manifold, at least one choke and/or at least one adapter configured for reducing the tube´s diameter for enhancing the filling accuracy of the liquid, such as the liquid drug product.

The control pressure may be applied via the pressure control line to the pressure control branch at the rigid vessel top plate. The applied pressure may be determined in the at least one dispensing line using the at least one pressure sensor. The pressure sensor may be integrated into the at least one dispensing line and may also be configured for single use. The control unit may control the applied pressure within predetermined pressure limits.

As outlined above, the time-pressure-filling system may be fully or partially enclosed by the at least one isolator. The components of the time-pressure-filling system may be sterilized, such as by using at least one of gamma radiation and/or gaseous ethylene oxide, and may be transferred into the isolator via the sterile port. The assembly of the components of the time-pressure-filling system may take place inside the isolator via couplings, such as quick-release couplings.

The methods and devices according to the present ~~invention~~disclosure provide a large number of advantages over similar methods and devices known in the art. Specifically, the methods and devices according to the present ~~invention~~disclosure may allow using the time-pressure-filling systems for a wide range of different liquid drug products, specifically for multi-product-filling lines. The time-pressure-filling system, specifically the surge vessel, may be configured for single use and, thus, may be disposed of after filling a batch of the liquid drug product. Therefore, by using the time-pressure-filling system, specifically the surge vessel according to the present ~~invention~~disclosure, the need for extensive cleaning of the time-pressure-filling system may become obsolete. Thus, the methods and devices according to the present ~~invention~~disclosure may allow for filling a wide range of many different liquid drug products using the same time-pressure-filling system while enabling the highest possible level of patient security and further avoiding possible cross contaminations.

Further, the assembly of the time-pressure-filling system inside the at least one isolator may provide an easy handling to the worker as well as further compliance and product stability advantages. Thus, the sterile filtration may take place in close proximity to the point of fill and is, thus, in accordance with regulations and safety guidelines. Further, the sterile filter may be installed inside the at least one isolator and, thus, an H_2O_2 absorption into the liquid drug product by the decontamination process may be avoided. This may enhance additionally the product safety.

An integration of the time-pressure-filling system and/or of the surge vessel as proposed herein may also take place into an existing or established time-pressure-filling system so far made of stainless steel. The automation of the existing filling system may be used without further adjustments. Only minor mechanical and electrical adjustments may be necessary. These adjustments may refer to an extension of the pressure supply to the surge vessel configured for single use and a determination of the pressure in the dispensing line by using the pressure sensor configured for single use.

Summarizing and without excluding further possible ~~embodiments~~examples, the following ~~embodiments~~examples may be envisaged:

~~Embodiment~~Example 1: A time-pressure-filling system for filling at least one liquid drug product into containers, comprising:

A. at least one storage vessel for storing the liquid drug product;

B. at least one surge vessel, wherein the surge vessel is configured for single use, wherein the surge vessel is at least partially made of at least one rigid plastic material;

C. at least one supply line for feeding the liquid drug product from the storage vessel into the surge vessel in a pressurized fashion;

D. at least one pressure control line for applying a control pressure to the surge vessel;

E. at least one dispenser for dispensing the liquid drug product into the containers;

F. at least one dispensing line connecting the surge vessel to the dispenser;

G. at least one pressure sensor for determining a pressure in the dispensing line; and

H. at least one valve for controlling a flow of the liquid drug product through the dispensing line.

~~Embodiment~~Example 2: The time-pressure-filling system according to the preceding ~~embodiment~~example, wherein the at least one storage vessel and the at least one surge vessel are pressure-stable vessels.

~~Embodiment~~Example 3: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the at least one supply line, the at least one pressure control line and the at least one dispensing line comprise pressure-stable tubes.

~~Embodiment~~Example 4: The time-pressure-filling system according to the preceding ~~embodiment~~example, wherein the pressure-stable tubes comprise reinforced silicone tubes, specifically braid reinforced silicone tubes, more specifically platinum reinforced silicone tubes.

~~Embodiment~~Example 5: The time-pressure-filling system according to any one of the three preceding ~~embodiments~~examples, wherein the components of the time-pressure-filling system are pressure-stable in a pressure range of 50 to 5000 mbar, specifically 50 to 3000 mbar more specifically 50 to 1000 mbar.

~~Embodiment~~Example 6: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the pressure sensor is arranged in the at least one dispensing line.

~~Embodiment~~Example 7: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the time-pressure-filling system comprises at least one manifold, specifically at least one manifold for single use, wherein the manifold provides one inlet port and a plurality of outlet ports.

~~Embodiment~~Example 8: The time-pressure-filling system according to the preceding ~~embodiment~~example, wherein the plurality of outlet ports of the manifold have a smaller diameter than the inlet port.

~~Embodiment~~Example 9: The time-pressure-filling system according to any one of the two preceding ~~embodiments~~examples, wherein the at least one manifold is installed in the at least one dispensing line.

~~Embodiment~~Example 10: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the time-pressure-filling system comprises at least one sterile filter, specifically in one or both of the supply line and the dispensing line.

~~Embodiment~~Example 11: The time-pressure-filling system according to the preceding ~~embodiment~~example, wherein the sterile filter is installed in close proximity to a point of fill.

~~Embodiment~~Example 12: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the components of the time-pressure-filling system are connectable via couplings, specifically via plug-in couplings, more specifically via quick-release couplings.

~~Embodiment~~Example 13: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the time-pressure-filling system is surrounded by at least one isolator, such as a box isolator and/or a restricted area barrier system, wherein the isolator provides a sterile surrounding for the time-pressure-filling system.

~~Embodiment~~Example 14: The time-pressure-filling system according to the preceding ~~embodiment~~example, wherein the isolator comprises at least one sterile port, wherein the sterile port is configured for unidirectionally or bidirectionally exchanging components of the time-pressure-filling system in a sterile fashion.

~~Embodiment~~Example 15: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the materials used for the time-pressure-filling system are configured for being sterilized by means of radiation, specifically by gamma radiation.

~~Embodiment~~Example 16: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the control pressure applied to the surge vessel is in the range of 50 to 1000 mbar, specifically 50 to 400 mbar.

~~Embodiment~~Example 17: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the time-pressure-filling system comprises at least one surge vessel according to any one of the following ~~embodiments~~examples referring to a surge vessel.

~~Embodiment~~Example 18: The time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the time-pressure-filling system further comprises at least one control unit, wherein the control unit specifically is configured for at least one of: controlling a filling level of the surge vessel; controlling the control pressure applied to the surge vessel; controlling an opening time of the valve.

~~Embodiment~~Example 19: A surge vessel for use in a time-pressure-filling system, specifically for use in a time-pressure-filling system according to any one of the preceding ~~embodiments~~examples, wherein the surge vessel is configured for single use, wherein the surge vessel is at least partially made of at least one rigid plastic material, the surge vessel comprising:

a. a rigid cylindrical vessel sidewall;
b. a rigid vessel bottom plate;
c. a rigid vessel top plate;
d. at least one supply pipe penetrating the rigid vessel bottom plate, wherein the supply pipe has at least one portion protruding into an interior space of the surge vessel and wherein the supply pipe further has at least one inlet connecting branch protruding from the vessel bottom plate outside the interior space for connecting a supply line to the supply pipe;
e. at least one outlet connecting branch protruding from the vessel bottom plate outside the interior space for connecting at least one dispensing line; and
f. at least one pressure control branch protruding from the vessel top plate outside the interior space for connecting at least one pressure control line.

~~Embodiment~~Example 20: The surge vessel according to the preceding ~~embodiment~~example, wherein the at least one rigid plastic material comprises at least one material selected from the group consisting of: polypropylene; polyethylene; polycarbonate.

~~Embodiment~~Example 21: The surge vessel according to any one of the preceding ~~embodiments~~examples referring to a surge vessel, wherein the rigid plastic material is at least partially transparent, specifically for light in the visible and/or infrared spectral range.

~~Embodiment~~Example 22: The surge vessel according to the preceding ~~embodiment~~example, wherein the surge vessel comprises at least one optical sensor, wherein the at least one optical sensor is disposed outside the interior space, specifically wherein the optical sensor is attached to the outside of the rigid cylindrical vessel sidewall, and wherein the optical sensor specifically is sensitive in at least one of the visible and the infrared spectral range.

~~Embodiment~~Example 23: The surge vessel according to the preceding ~~embodiment~~example, wherein the at least one optical sensor is configured for detecting a filling level of the surge vessel specifically, the surge vessel and/or the time-pressure-filling system may comprise at least one control unit, wherein the control unit is configured for detecting a filling level by evaluating at least one signal generated by the optical sensor.

~~Embodiment~~Example 24: The surge vessel according to any one of the preceding ~~embodiments~~examples, wherein the rigid cylindrical sidewall has a wall thickness of at least 1 mm.

~~Embodiment~~Example 25: The surge vessel according to any one of the preceding ~~embodiments~~examples, wherein the surge vessel comprises a plurality of outlet connecting branches.

~~Embodiment~~Example 26: The surge vessel according to the preceding ~~embodiment~~example, wherein the plurality of outlet connecting branches has at least two diameters, wherein the at least two diameters are equal or different to each other.

~~Embodiment~~Example 27: A time-pressure-filling method for filling at least one liquid drug product into containers, comprising:

i. providing the time-pressure-filling system according to any one of the preceding ~~embodiments~~examples referring to a time-pressure-filling system, specifically comprising at least one surge vessel according to any one of the preceding ~~embodiments~~examples referring to a surge vessel;
ii. feeding the liquid drug product from the storage vessel into the surge vessel in a pressurized fashion;
iii. controlling the pressure in the surge vessel by applying a control pressure to the surge vessel;
iv. determining the pressure in the dispensing line by using the pressure sensor; and
v. dispensing predetermined amounts of the liquid drug product into the containers by controlling an opening time of the valve.

~~Embodiment~~Example 28: The method according to the preceding ~~embodiment~~example, wherein the time-pressure-filling system comprises further at least one control unit, wherein the control unit is configured for at least one of: controlling the filling level of the surge vessel; controlling the control pressure applied to the surge vessel; controlling the opening time of the valve.

~~Embodiment~~Example 29: The method according to the preceding ~~embodiment~~example, wherein the control unit is configured for controlling the opening time of the valve to at least one time value in a range of 1 to 2000 ms, specifically of 1 to 400 ms.

~~Embodiment~~Example 30: The method according to any one of the two preceding ~~embodiments~~examples, wherein the control unit is configured for controlling the filling level of the surge vessel to

at least one level value in a range of 30 percent to 60 percent of a maximum filling capacity of the surge vessel.

~~Embodiment~~Example 31: The method according to any one of the preceding method ~~embodiments~~examples, wherein a batch of the liquid drug product is defined by a predetermined amount of the liquid drug product, wherein the method comprises exchanging the surge vessel after filling the bench batch of the liquid drug product into the containers and disposing of the surge vessel.

~~Embodiment~~Example 32: The method according to the preceding ~~embodiment~~example, wherein the time-pressure-filling system comprises a plurality of the search surge vessels, wherein the search surge vessels are used subsequently one after the other for different batches, wherein used surge vessels are disposed of.

~~Embodiment~~Example 33: A use of at least one of the time-pressure-filling system according to any one of the preceding ~~embodiments~~examples referring to a time-pressure-filling system and the surge vessel according to any one of the preceding ~~embodiments~~examples referring to a surge vessel, for filling at least one of the following liquid drug product into containers: a pharmaceutical product; a steroid product; a liquid drug product for subcutaneous application; a liquid drug product for intravenous application; a high-potent liquid drug product; an aqueous protein solution, such as at least one antibody drug product solution.

Short description of the Figures

Further optional features and embodiments will be disclosed in more detail in the subsequent description of embodiments, preferably in conjunction with the dependent claims. Therein, the respective optional features may be realized in an isolated fashion as well as in any arbitrary feasible combination, as the skilled person will realize. The scope of the invention is not restricted by the preferred embodiments. The embodiments are schematically depicted in the Figures. Therein, identical reference numbers in these Figures refer to identical or functionally comparable elements.

In the Figures:

Figure 1 shows an embodiment of a time-pressure-filling system for filling at least one liquid drug product into containers in a schematic view;

Claims

1. A time-pressure-filling system ~~(110)~~ for filling at least one liquid drug product into containers ~~(111)~~, comprising:
   A. at least one storage vessel ~~(112)~~ for storing the liquid drug product;
   B. at least one surge vessel ~~(114)~~, wherein the surge vessel ~~(114)~~ is configured for single use, wherein the surge vessel ~~(114)~~ is at least partially made of at least one rigid plastic material;
   C. at least one supply line ~~(116)~~ for feeding the liquid drug product from the storage vessel ~~(112)~~ into the surge vessel ~~(114)~~ in a pressurized fashion;
   D. at least one pressure control line ~~(118)~~ for applying a control pressure to the surge vessel ~~(114)~~;
   E. at least one dispenser ~~(120)~~ for dispensing the liquid drug product into the containers ~~(111)~~;
   F. at least one dispensing line ~~(122)~~ connecting the surge vessel ~~(114)~~ to the dispenser ~~(120)~~;
   G. at least one pressure sensor ~~(124)~~ for determining a pressure in the dispensing line ~~(122)~~; and
   H. at least one valve ~~(126)~~ for controlling a flow of the liquid drug product through the dispensing line ~~(122)~~.

2. The time-pressure-filling system according to the preceding claim, wherein the time-pressure-filling system ~~(110)~~ comprises at least one manifold ~~(134)~~, wherein the manifold ~~(134)~~ provides one inlet port ~~(156)~~ and a plurality of outlet ports ~~(158)~~, wherein the plurality of outlet ports ~~(158)~~ of the manifold ~~(134)~~ have a smaller diameter than the inlet port ~~(156)~~.

3. The time-pressure-filling system ~~(110)~~ according to any one of the preceding claims, wherein the time-pressure-filling system ~~(110)~~ comprises at least one sterile filter ~~(130)~~.

4. The time-pressure-filling system ~~(110)~~ according to any one of the preceding claims, wherein the components of the time-pressure-filling system ~~(110)~~ are connectable via couplings.

5. The time-pressure-filling system ~~(110)~~ according to any one of the preceding claims, wherein the time-pressure-filling system ~~(110)~~ is surrounded by at least one isolator ~~(128)~~, wherein the isolator ~~(128)~~ provides a sterile surrounding for the time-pressure-filling system ~~(110)~~.

6. The time-pressure-filling system ~~(110)~~ according to any one of the preceding claims, wherein the time-pressure-filling system ~~(110)~~ further comprises at least one control unit ~~(123)~~, wherein the control unit ~~(123)~~ specifically is configured for at least one of: controlling a filling level of the surge vessel ~~(114)~~;

controlling the control pressure applied to the surge vessel ~~(114)~~; controlling an opening time of the valve ~~(126)~~.

7. A surge vessel ~~(114)~~ for use in a time-pressure-filling system ~~(110)~~ according to any one of the preceding claims, wherein the surge vessel ~~(114)~~ is configured for single use, wherein the surge vessel ~~(114)~~ is at least partially made of at least one rigid plastic material, the surge vessel ~~(114)~~ comprising:
   a. a rigid cylindrical vessel sidewall ~~(138)~~;
   b. a rigid vessel bottom plate ~~(140)~~;
   c. a rigid vessel top plate ~~(142)~~;
   d. at least one supply pipe ~~(144)~~ penetrating the rigid vessel bottom plate ~~(140)~~, wherein the supply pipe ~~(144)~~ has at least one portion ~~(146)~~ protruding into an interior space ~~(148)~~ of the surge vessel ~~(114)~~ and wherein the supply pipe ~~(144)~~ further has at least one inlet connecting branch ~~(150)~~ protruding from the rigid vessel bottom plate ~~(140)~~ outside the interior space ~~(148)~~ for connecting a supply line ~~(116)~~ to the supply pipe ~~(144)~~;
   e. at least one outlet connecting branch ~~(152)~~ protruding from the rigid vessel bottom plate ~~(140)~~ outside the interior space ~~(148)~~ for connecting at least one dispensing line ~~(122)~~; and
   f. at least one pressure control branch ~~(154)~~ protruding from the rigid vessel top plate ~~(142)~~ outside the interior space ~~(148)~~ for connecting at least one pressure control line ~~(118)~~.

8. The surge vessel ~~(114)~~ according to the preceding claim, wherein the at least one rigid plastic material comprises at least one material selected from the group consisting of: polypropylene; polyethylene; polycarbonate.

9. The surge vessel ~~(114)~~ according to any one of the preceding claims referring to a surge vessel ~~(114)~~, wherein the rigid plastic material is at least partially transparent.

10. The surge vessel ~~(114)~~ according to the preceding claim, wherein the surge vessel ~~(114)~~ comprises at least one optical sensor ~~(117)~~, wherein the at least one optical sensor ~~(117)~~ is disposed outside the interior space ~~(148)~~, and wherein the optical sensor ~~(117)~~ specifically is sensitive in at least one of the visible and the infrared spectral range.

11. The surge vessel ~~(114)~~ according to the preceding claim, wherein the at least one optical sensor ~~(117)~~ is configured for detecting a filling level of the surge vessel ~~(114)~~.

12. A time-pressure-filling method for filling at least one liquid drug product into containers ~~(111)~~, comprising:

i. providing the time-pressure-filling system ~~(110)~~ according to any one of the preceding claims referring to a time-pressure-filling system ~~(110),~~;

ii. feeding the liquid drug product from the storage vessel ~~(112)~~ into the surge vessel ~~(114)~~ in a pressurized fashion;

iii. controlling the pressure in the surge vessel ~~(114)~~ by applying a control pressure to the surge vessel ~~(114)~~;

iv. determining the pressure in the dispensing line ~~(122)~~ by using the pressure sensor ~~(124)~~; and

v. dispensing predetermined amounts of the liquid drug product into the containers ~~(111)~~ by controlling an opening time of the valve ~~(126)~~.

13. The method according to the preceding claim, wherein a batch of the liquid drug product is defined by a predetermined amount of the liquid drug product, wherein the method comprises exchanging the surge vessel ~~(114)~~ after filling the batch of the liquid drug product into the containers ~~(111)~~ and disposing of the surge vessel ~~(114)~~.

14. The method according to the preceding claim, wherein the time-pressure-filling system ~~(110)~~ comprises a plurality of the surge vessels ~~(114)~~, wherein the surge vessels ~~(114)~~ are used subsequently one after the other for different batches, wherein used surge vessels ~~(114)~~ are disposed of.

15. A use of at least one of the time-pressure-filling system ~~(110)~~ according to any one of the preceding claims referring to a time-pressure-filling system ~~(110)~~ and the surge vessel ~~(114)~~ according to any one of the preceding claims referring to a surge vessel ~~(114)~~, for filling at least one of the following liquid drug product into containers ~~(111)~~: a pharmaceutical product; a steroid product; a liquid drug product for subcutaneous application; a liquid drug product for intravenous application; a high-potent liquid drug product; an aqueous protein solution.