

A STERILE REAGENT PREPARATION DEVICE AND THE METHOD OF USING THE SAME

The present application relates to a sterile reagent preparation device for preparing a
5 stock solution of a toxic reagent. The sterile reagent preparation device comprises one
or more liquid reservoirs for storing solvents and one or more reagent containers for
containing reagents., Each liquid reservoir comprises a flipper, a head and two or more
cannulas; and each reagent container comprises a body, a cap, a cap cover (i.e. cover)
and a membrane. The method of using the sterile reagent preparation device is also
10 disclosed in the present application.

In particular, the membrane of the reagent container in the present application has
several advantages. Firstly, the membrane is made of chemically stable materials that
can resist highly toxic reagents and various solvents. Secondly, the membrane can be
15 pierced through by the cannulas before the solvent is injected into the reagent
container. Thirdly, the membrane has a textured surface and a predetermined
thickness such that the membrane can substantially recover to its original state as an
intact membrane for sealing the reagent container again after withdrawal of the
cannulas from the reagent container. After the stock solution is prepared in the reagent
20 container, the cap cover and the membrane are both closed to provide a double sealing
mechanism for preventing the stock solution from leakage.

In addition, the two or more cannulas of the liquid reservoir are used for air exchange
between the liquid reservoir and the reagent container so that no toxic air originally
25 encapsulated inside the reagent container would come out into the surrounding

environment during the injection of the solvent. Instead, the toxic air is transferred into the reagent container in the process of preparing the stock solution.

Many pharmaceutical reagents require preparation in a hygienic environment prior to use. Conventional reagent preparation device under a sterile condition such as in a hospital is a syringe having a nozzle and a piston. When in use, a syringe needle such as a steel needle is further installed onto the nozzle. An injection medicine in either liquid state or solid state is stored and sealed in a container and pure water or medical saline solution is kept in another bottle. Pure water or medical saline solution is first extracted by inserting the syringe needle into the bottle and pulling the piston backward. Then the extracted pure water or medical saline solution is injected into the container by pushing the piston forward; and the medicine is dissolved in the pure water or medical saline solution inside the container. However, the syringe with syringe needle as a reagent preparation device may have several drawbacks. Firstly, the medical reagents are handled by some personnel such as a nurse at the point of use. The quality of the reagents is easily compromised because of any error made during the preparation procedures. Even small errors may lead to an improperly prepared reagent, including but not limited to misusing the reagent, mis-measuring the reagent and mis-diluting the reagent. Secondly, the syringe and the syringe need to be completely sterilized and disinfected before usage and also kept away from any contamination from surrounding environment during the preparation procedures. Thirdly, some lyophilized reagents cannot be prepared by the syringe because the freeze-dried reagents would decrease their biological and chemical activities and thus damage the effectiveness by being exposed at room temperature for a relative long time. Therefore,

a novel sterile reagent preparation device is needed to replace the syringe with syringe needle. resolve the existing challenges.

Modern medical and pharmaceutical research and development such as cancer,
5 genetic engineering or oncology diagnostics involves more and more highly toxic or
even deadly reagents in solid state. The toxic solid reagents are usually prepared into
sterile stock solutions by means of micro-filtration. But the current preparation method
also has a major drawback. The toxic solid reagents must be frequently weighed by a
research or an assistant before the micro-filtration process. The research or assistant
10 may be dangerously exposed to the highly toxic reagents although a suitable personal
protective equipment (PPE) has to be properly selected according to special toxicity of
each of the reagents. The above method also needs laborious efforts to investigate the
toxicity of each reagent in detail and arranges a great variety of PPEs if a large number
of toxic reagents are used. Thus, the toxic reagents are often sold in sterile stock
15 solutions that are less noxious. However, the stock solutions also have issues of
stability and shipping. For example, a mixture of penicillin sodium and streptomycin
sulfate is commonly used as an antibiotic in mammalian cell culture. Although the
mixture is stable and potent in a solid state at room temperature, many people are
allergic to penicillin powder. Hence, a stock solution of the mixture is often preferred
20 for less risk. But penicillin is unstable in an aqueous solution such that its shelf life is
less than two weeks at room temperature. It is so required to store the solution at 20
degrees below the freezing point (-20°C) with help of dry ice. But shipping the solution
at -20°C is very troublesome and costly. Even if properly and carefully handled, the
shelf life of the solution is still much shorter than that of the penicillin stored in a solid
25 powder form. In addition, the quality of the reagents solution (the amount of the

reagents solution, the purity of the reagents solution and the alike) cannot be guaranteed if a precise dosage is needed. Therefore, a novel sterile reagent preparation device is provided to resolve the existing challenges.

- 5 Many active reagents are commonly used for preparing stock solutions of the toxic reagents under a sterile condition in a laboratory, especially a cell culture laboratory for growing cell lines or a microbiology laboratory for growing microorganism. The stock solution is much more concentrated than an active reagent solution used in a laboratory. To prepare the active reagent solution, a portion of the stock solution is first
- 10 transferred by using a pipet into a volumetric flask; and then the portion of the stock solution is precisely diluted to the mark of the volumetric flask for a pre-determined volume. Therefore, a novel device and the method of using thereof is needed for preparing a stock solution of the toxic reagent safely, quickly and precisely.
- 15 The sterile reagent preparation device of the present application is mainly used for preparing a stock solution of a toxic reagent under a sterile condition in a laboratory, especially a cell culture laboratory or a microbiology laboratory. The sterile reagent preparation device has several significant advantages over any of the conventional devices mentioned above. Firstly, the sterile reagent preparation device can deal with
- 20 highly toxic reagents used in the cell culture lab or the microbiology lab. In particular, the sterile reagent preparation device adopts a flipper for covering a cap so that the highly toxic reagents are safely contained in the sterile reagent preparation device without any leakage during preparation. Secondly, many components of the sterile reagent preparation device are made of chemically stable plastics such that a great
- 25 variety of reagents with different physical and chemical properties can be handled

safely and properly. For example, a plastic cannula (i.e. needle) is used instead of a conventional steel needle for transferring stored solvents to be mixed with the toxic reagents, because the steel needle is not chemically stable to certain solvents having chlorides. In addition, the plastic cannula is not as sharp as the steel needle so that a human operator or anyone around the human operator can be better protected. Thirdly, the sterile reagent preparation device is applicable for preparing the stock solution in a wide range in terms of volume, ranging from 0.01 millilitre to several hundred millilitres. In particular, the stock solution has to be prepared in a quick manner. The sterile reagent preparation device can meet this requirement by adjusting a diameter of the plastic cannula to a certain range. Meanwhile, the cap also has a hole that matches the size of the plastic cannula. In this way, the plastic cannula can penetrate through the hole smoothly and safely. In summary, the sterile reagent preparation device is suitable for preparing stock solutions of highly toxic reagents used primarily in laboratories due to the novel features mention above. Therefore, the present application is distinguishably different from any of the existing reagent preparation in a laboratory and/or dispensing device in the medical and pharmaceutical field.

Essential features of the present application are provided by one or more independent claims, whilst advantageous features are presented by their dependent claims respectively.

According to a first aspect of the present application, a sterile reagent preparation device is disclosed comprising one or more liquid reservoirs such as an antiseptic cylinder for storing solvents and one or more reagent containers such as an antiseptic test tube for containing reagents. The liquid reservoirs and the reagent containers exist

as individual components that are kept separately before mixing the reagents with the solvents stored in the liquid reservoirs (i.e. stored solvents).

Each of the liquid reservoirs comprises a movable shell, a flipper inside the movable
5 shell, two or more cannulas outside the movable shell and a head connecting the flipper and the cannula. The movable shell defines a bottom side, a left side and a right side of the liquid reservoir. The movable shell can move between a full position denoting the liquid reservoir is filled with a stored solvent and an empty position denoting the stored solvent is completely drained off. When the stored solvent is
10 drained off from the liquid reservoir, the movable shell moves from the full position to the empty position. The flipper is located inside the movable shell and used as a sealing layer for isolating the stored solvent from outside environment. When not in use, the liquid reservoir is positioned vertically with the head and cannulas on the top; and the flipper is used for sealing the solvent that is inside the liquid reservoir and
15 below the flipper. When in use that the two or more cannulas are inserted into the reagent container, the flipper is pushed open by sliding the movable shell forward or pulling the head backward. In this way, the stored solvent is released from the liquid reservoir and flows into the reagent container. The head is used for connecting the flipper and the cannulas. The cannulas are used for draining off the stored solvent and
20 releasing the toxic gas in the reagent container. If two or more types of stored solvents are needed, more liquid reservoirs can be used in the sterile reagent preparation device accordingly. Each of the reagent containers comprises a body and a cap. The body defines a bottom side, a left side and a right side of the reagent container. When not in use, the reagent container is positioned vertically with the cap on the top; and
25 the cap has a double sealing mechanism for sealing the toxic reagent stored inside the

reagent container. In the present application, the body of the reagent container has distinctive functions in different stages. The body is used for containing the reagent before usage, for acting as a reactor during mixing the reagent with the stored solvent, and for storing the reagent-solvent mixture as a stock solution after usage. Therefore, the body of the reagent container has to be made of a chemically inert material that can resist the reagent, the solvent and the mixture or the stock solution. The cap completely covers the top side of the body for sealing the reagent or the stock solution inside the body. The cap is configured for receiving the two or more cannulas of the liquid reservoir.

The head of each liquid reservoirs has a frame and a conduit. The frame is connected to the movable shell such that the movable shell can move along the frame within a limited distance from the full position to the empty position. In detail, the frame further has a first portion, a second portion and a dent for connecting the first portion and the second portion. The first portion of the frame is always located outside the movable shell and defines the outside boundary of the liquid reservoir with the movable shell. The second portion of the frame may become gradually enclosed inside the movable shell when the movable shell moves from the full position to the empty position. When the movable shell is fixed at the full position, the second portion of the frame is almost completely exposed outside the movable shell. On the contrary, when the movable shell moves to the dent of the frame where the empty position is denoted, the second portion of the frame is almost completely enclosed inside the movable shell. The second portion of the frame and the movable shell need to be precisely matched in the way that the solvent stored inside the liquid reservoir would not leak outside when the movable shell moves along the frame of the head. In other words, the external surface

of the second portion need to be in direct and tight contact with the internal surface of the movable shell. The conduit of the head is completely formed inside the movable shell and the head. Particularly, the conduit is connected beneath the flipper such that the conduit pushes the flipper open when the movable shell moves from the full position
5 to the empty position. Hence, the solvent stored in the liquid reservoir can flow across the flipper, along the conduit and to the cannula by simply moving the movable shell.

The liquid reservoir may have two or more cannulas, each of which is almost completely or partially outside the movable shell. Each of the cannulas has a first end
10 connected to the conduit and a second end located outside the movable shell. The second end is required to be sharp enough to penetrate through the corresponding part (i.e. the membrane) of the reagent container, but not too sharp for safety consideration. The sterile reagent preparation device is mainly used for preparing a stock solution of a toxic reagent under a sterile condition in a laboratory, such as a cell
15 culture laboratory or a microbiology laboratory. A lab technician has to work in a safety hood where internal space is usually very limited. Thus, a very sharp second end of cannula may be dangerous to the technician or any person around him or simply passing by him. To meet both the requirements above, the second end has a cut angle ranging from 10 degrees to 45 degrees. In addition, a protective lid may be installed
20 onto the second end of the cannula for avoiding any accident and particularly safeguarding an operating staff while the stored solvent is harmful to human. Meanwhile, the protective lid also protects the second end of the cannula from external contamination and damage. The cannula also needs to resist the solvent stored in the liquid reservoir and the reagent contained in the reagent container. In contrast to the
25 steel syringe needle conventionally used in the syringe, the cannulas are preferably

made of chemically stable plastics, such as polypropylene (PP), polytetrafluoroethene (PTFE), polyethylene terephthalate (PETG) or any combination thereof.

5 The two or more cannulas are used for draining off the solvent stored in the liquid reservoir and releasing the toxic gas in the reagent container for avoiding any toxic materials leaking out of the reagent container to the surrounding environment. Since the sterile reagent preparation device is applicable for preparing the stock solution in a wide range from 0.01 millilitre to several hundred millilitres a quick manner, the cannula can be too small in radial size. If the diameter is too small, the stored solvent
10 may not smoothly and easily flow out of the cannulas due to surface tension at the second end of the cannula; and the preparation process may take a longer period particularly when the stored solvent has a high viscosity. The diameter of the cannula preferably ranges from 1 mm to 5 mm according to a specific design. Two or more cannulas are adopted, each of the cannulas may have a same diameter or different
15 diameters because at least one of the cannulas is exclusively used for releasing the toxic gas from the reagent container to the liquid reservoir. Therefore, the cannula is one of the key technical features of the subject application.

The cap of the reagent container has a left portion, a top portion and a right portion
20 such that the cap is contoured for completely sealing the opening of the body. The top portion of the cap has two or more holes, each of which would be peered through by one of the cannulas during preparation of the stock solution. The cap cover of the reagent container comprises two or more protruding parts located on the bottom surface of the cap cover. Each of the two or more protruding parts is used for blocking
25 and covering one of the two or more holes. Thus, the number and the layout of the

protruding parts are the same as these of the holes. To tightly block each of the holes, the protruding part has a same shape of the hole with such a slightly larger size that the protruding part can just tightly fit into the hole. The cap cover has distinctive functions at different stages of operation. Before usage, the cap cover is integrated with the cap as a whole to prevent the reagent contained inside the reagent container from leakage as well as contamination by the surrounding environment. Right before preparing the stock solution, the cap cover with the two or more protruding parts is first removed from the reagent container; as a result, the two or more holes are exposed. Meanwhile, the membrane of the reagent container below the cap is partially exposed from the holes. The cannulas are then inserted into the holes, peered through the membrane and finally pushed into the reagent container. Therefore, the protruding parts are so designed to match the layout of the cannulas in terms of number, location and size.

The cap cover is another key technical features of the subject application. In contrast to the conventional rubber cap cover that is unstable to many reagents or solvents, the cap of the reagent container here is preferably made of chemically stable plastics, such as polypropylene (PP), polytetrafluoroethene (PTFE), polyethylene terephthalate (PETG) or any combination therefore.

The membrane of the reagent container is located near the opening of the body and below the cap cover. The reagent is contained below the membrane that protects the reagent from leakage as well as contamination. The membrane of the present application has several advantages. Firstly, since the membrane may be in direct contact with the toxic reagent and the solvent, the membrane is particularly made of

chemically stable plastics, such as polypropylene (PP), polytetrafluoroethene (PTFE), polyethylene terephthalate (PETG) or any combination thereof. Secondly, the membrane should not so hard and stiff such that it can be peered through by the plastic cannulas before the solvent is injected into the reagent container. Thirdly, the

5 membrane has a textured surface and a pre-determined thickness such that the membrane can substantially recovers to the original state as an intact membrane and then seals the reagent container again after the cannulas are withdrawn from the membrane. After the stock solution is prepared in the reagent container, the cap cover and the membrane are both closed to provide double sealing mechanisms for

10 preventing the stock solution from leakage. Preferably, the membrane may have a thickness ranging from 0.1 mm to 5 mm. In addition, the membrane may have a plurality of pores that help the membrane to recover after the cannulas are withdrawn from the membrane. Preferably, the size of the pore ranges from 0.1 micrometre to 10 micrometres. The membrane can also be selected or designed according to the

15 specific reagent and solvent in terms of material, thickness and pore size.

According to a second aspect of the present application, a method of using the sterile reagent preparation device is also disclosed. The method comprises the following steps. Firstly, remove the cap cover from the cap of the reagent container. In the first

20 step, the protruding parts are removed from the holes of the cap. Secondly, remove the protective lid from the second end of each cannula of the liquid reservoir. Thirdly, insert the one or more cannulas into the holes of the cap accordingly, and further peer through the membrane. Fourthly, open the flipper by pushing the movable shell forward or pulling the head backward from the full position to the empty position. Fifthly, the

25 stored solvent is injected into the reagent container by flowing across the flipper to the

conduit and the one or more cannulas. Meanwhile, the toxic air inside the reagent container is transferred into the liquid reservoir through the cannulas, the conduit and across the flipper. The toxic air is prevented from leakage outside to the surrounding environment. Sixthly, withdraw the liquid reservoir from the reagent container by
5 extracting the cannulas out of the membrane and the holes of the cap. After the sixth step, the cannulas exposed outside the head may undergo an antiseptic process and/or a drying process. And seventhly, reset the flipper by pulling the movable shell backward from the empty position to the full position. In the seventh step, another same or different solvent may be refilled into the liquid reservoir such that the sterile reagent
10 preparation device is reusable without any contamination.

The accompanying figures (Figs.) illustrate embodiments and serve to explain principles of the disclosed embodiments. It is to be understood, however, that these figures are presented for purposes of illustration only, and not for defining limits of
15 relevant applications.

Fig. 1 illustrates a cross-sectional view of a sterile reagent preparation device with a separated cap according to a first embodiment of the present application.

20 Fig. 2 illustrates a method of using the sterile reagent preparation device according to a second embodiment of the present application.

Exemplary, non-limiting embodiments of the present application will now be described with references to the above-mentioned figures. Embodiments of the application
25 comprise parts or method steps that are similar or identical to each other. These parts

or method steps are thus denoted with similar or identical names or reference numerals. Description of these relevant parts of method steps is hereby incorporated by reference, wherever relevant or appropriate.

5 Fig. 1 shows the first embodiment 100 of a sterile reagent preparation device 102 of the subject application. The sterile reagent preparation device 102 comprises a liquid reservoir 104 for storing a solvent 106 and a reagent container 108 for containing a reagent 110. The liquid reservoir 104 and the reagent container 108 exist as individual components that are not connected before mixing the reagent 110 with the solvent 106
10 stored in the liquid reservoir 104 (i.e. stored solvent 106).

The liquid reservoir 104 comprises a movable shell 112, a flipper 114 inside the movable shell 112, a first cannula 116 and a second cannula 118 outside the movable shell 112 and a head 120 connecting the flipper 114 and the first and second cannulas
15 116 and 118. The movable shell 112 defines a bottom side 122, a left side 124 and a right side 126 of the liquid reservoir 104. The movable shell 112 can move between a full position 128 (not shown) denoting that the liquid reservoir 104 is fully filled with a stored solvent 106 and an empty position 130 (not shown) denoting that the stored solvent 106 is completely drained off. When the stored solvent 106 is drained off from
20 the liquid reservoir 104, the movable shell 112 moves from the full position 128 to the empty position 130. The flipper 114 is located inside the movable shell 112 and used as a sealing layer for isolating the stored solvent 106 from the outside environment. When in use, the flipper 114 can release the stored solvent 106 in the liquid reservoir 104. The head 120 is used for connecting the flipper 114 and the cannulas 116 and
25 118. The first cannula 116 is used for draining off the stored solvent 106; while the

second cannula 118 is used for releasing toxic gas in the reagent container 108. The reagent container 108 comprises a body 132, a cap 134, a cap cover 162 and a membrane 164. The body 132 defines a bottom side 136, a left side 138 and a right side 140 of the reagent container 108. In the present application, the body 132 is used for containing the reagent 110 before preparation, acting as a reactor during mixing the reagent 110 with the stored solvent 106, and for storing the reagent-solvent mixture as a stock solution after preparation. Therefore, the body 132 of the reagent container 108 is made of a chemically inert material that can resist the reagent 110, the solvent 106 and the stock solution. The cap cover 162 and the membrane 164 completely cover the opening of the body 132 at the top side 142 for sealing the reagent 110 inside the body 132. The cap 134 is configured for receiving the two cannulas 116 and 118 of the liquid reservoir 104 at the same time.

The head 120 of the liquid reservoir 104 has a frame 144 and a conduit 146. The frame 144 is connected to the movable shell 112 such that the movable shell 112 can move along the frame 144 within a limited distance. In detail, the frame 144 further has a first portion 148, a second portion 150 and a dent 152 for connecting the first portion 148 and the second portion 150. The first portion 148 of the frame 144 is always located outside the movable shell 112 and defines the outside boundary of the liquid reservoir 104 with the movable shell 112. The second portion 150 of the frame 144 may become gradually enclosed inside the movable shell 112 when the movable shell 112 moves from the full position 128 to the empty position 130. When the movable shell 112 is fixed at the full position 128, the second portion 150 of the frame 144 is almost completely exposed outside the movable shell 112. On the contrary, when the movable shell 112 moves to the dent 152 of the frame 144 where the empty position 130 is

denoted, the second portion 150 of the frame 144 is almost completely enclosed inside the movable shell 112. The second portion 150 of the frame 144 and the movable shell 112 need to be just matched in the way that the stored solvent 106 inside the liquid reservoir 104 would not leak outside when the movable shell 112 moves along the frame 144. In other words, the external surface of the second portion 150 needs to be in direct and tight contact with the internal surface of the movable shell 112. The conduit 146 is completely inside the movable shell 112 and the frame 144. Particularly, the conduit 146 is connected beneath the flipper 114 such that the conduit 146 pushes the flipper 114 open when the movable shell 112 moves from the full position 128 to the empty position 130. Hence, the stored solvent 106 in the liquid reservoir 104 can flow across the flipper 114 and the conduit 146 to the cannula 116 by simply pushing the movable shell 112 forward.

As shown in Fig. 1, the liquid reservoir 104 has two cannulas 116 and 118, each of which has a first end 154 connected to the conduit 146 and a second end 156 always located outside the movable shell 112. The second end 156 is required to be sharp enough to penetrate through the membrane 164, but not too sharp for safety consideration. To meet the requirements, the second end 156 has a cut angle ranging from 10 degrees to 45 degrees. In addition, two protective lids 158 (not shown) are installed onto the second ends 156 of the cannulas 116 and 118 for avoiding any accident and particularly safeguarding an operating staff. Meanwhile, the protective lids 158 also protects the second ends 156 of the cannulas 116 and 118 from external contamination. The cannulas 116 and 118 also need to resist the stored solvent 106. Thus the cannulas 116 and 118 are preferably made of chemically stable plastics, such

as polypropylene (PP), polytetrafluoroethylene (PTFE), polyethylene terephthalate (PETG) or any combination thereof.

In the first embodiment 100, the first cannulas 116 is used for draining off the stored
5 solvent 106 in the liquid reservoir 104; while the second cannula 118 is used for
conducting an air exchange 160 between the reagent container 108 and the liquid
reservoir 104. Thus, the cannulas 116 and 118 can have a same or a different diameter
that preferably ranges from 1 mm to 5 mm. Since the first cannula 116 is used for
draining off the stored solvent 106, the diameter of the first cannula 116 is usually
10 determined by a viscosity of the stored solvent 106. The higher the viscosity is, the
larger the diameter of the first cannula 116 should have for an easy outflow.

The reagent container 108 comprises a body 132, a cap 134, a cap cover (i.e. cover)
162 and a membrane 164. The cap cover 162 has a cage 166, a first protruding part
15 168 and a second protruding part 170. The cage 166 further has a left portion 172, a
top portion 174 and a right portion 176 so that the cage 166 is contoured for completely
sealing the opening of the body 132 near the top side 142 of the reagent container 108.
The protruding parts 168 and 170 are located on the bottom surface of the top portion
174. The right portion 176 of the cage 166 is tied to the right side 140 near the opening
20 with a rope 178. Before usage, the cap cover 162 is attached to the cap 134 for
covering the opening of the body 132 and sealing the reagent 110. During usage, the
cap cover 162 is removed from the cap 134 by rotating cap cover 162 around the rope
178 and then flipped upside down with the bottom surface of the top portion pointing
upward. A first hole 180 and a second hole 182 are exposed from the cap 134. During
25 the process, the first protruding part 168 and the second protruding part 170 are taken

out of the first hole 180 and the second hole 182 respectively. When the cannulas 116 and 118 are pushed toward the reagent container 108, the first cannula 116 and the second cannula 118 would be inserted into the first hole 180 and the second hole 182 respectively, and further peered through the membrane 164.

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The membrane 164 is located inside the body 132 and below the cap cover 162. The reagent 110 is contained below the membrane 164 that protects the reagent 110 from contamination. Since the membrane 164 may be in contact with the reagent 110, the membrane 164 is particularly made of chemically stable plastics, such as
10 polypropylene (PP), polytetrafluoroethene (PTFE), polyethylene terephthalate (PETG) or any combination thereof. The membrane 164 should not so hard and stiff such that it can be peered through by the plastic cannulas 116 and 118 before the stored solvent 106 is injected into the reagent container 108. In particular, the membrane 164 has a textured surface and a pre-determined thickness such that the membrane 164 can
15 substantially recovers to the original state as an intact membrane and then seals the reagent container 108 again after the cannulas 116 and 118 are withdrawn from the membrane 164. After the stock solution is prepared in the reagent container 108, the cap cover 162 and the membrane 164 are both closed to provide a double sealing mechanism for preventing the stock solution from leakage. Preferably, the membrane
20 may have a thickness ranging from 0.1 mm to 5 mm. In addition, the membrane may have a plurality of pores that help the membrane to recover after the cannulas are withdrawn from the membrane. Preferably, the membrane 164 may have a thickness ranging from 0.1 mm to 5 mm. In addition, the membrane 164 may have at least one pore 184 for helping the membrane 164 to recover. The size of the pore 184 ranges
25 from 0.1 micrometre to 10 micrometres.

Fig. 2 shows a method of using the sterile reagent preparation device 102 according to a second embodiment 200 of the present application. The method comprises a first step 202 of removing the cap cover 162 from the cap 134 of the reagent container 108.

5 In the first step 202, the protruding parts 168 and 170 are removed from the holes 180 and 182 of the cap 134. The method comprises a second step 204 of removing the protective lid 158 from the second end 156 of each cannula 116 or 118 of the liquid reservoir 104. The method comprises a third step 206 of inserting the cannulas 116 and 118 into the holes 180 and 182 of the cap 134 accordingly, and further peer
10 through the membrane 164. The method comprises a fourth step 208 of opening the flipper 114 by pushing the movable shell 112 forward or pulling the head 120 backward from the full position 128 to the empty position 130. The method comprises a fifth step 210 of injecting the stored solvent 106 into the reagent container 108 by flowing across the flipper 114 to the conduit 146 and the first cannula 116. Meanwhile, the toxic air
15 inside the reagent container 108 is transferred into the liquid reservoir 104 through the second cannula 118, the conduit 146 and across the flipper 114. The toxic air is prevented from leakage outside to the surrounding environment. The method comprises a sixth step 212 of withdrawing the liquid reservoir 104 from the reagent container 108 by extracting the cannulas 116 and 118 out of the membrane 164 and
20 the holes 180 and 182 of the cap 134. And the method may comprise a seventh step 214 of resetting the flipper 114 by pulling the movable shell 112 backward from the empty position 130 to the full position 128.

As used herein, the term "about", in the context of concentrations of components of
25 the formulations, typically means +/- 5% of the stated value, more typically +/- 4% of

the stated value, more typically +/- 3% of the stated value, more typically, +/- 2% of the stated value, even more typically +/- 1% of the stated value, and even more typically +/- 0.5% of the stated value.

- 5 Throughout this disclosure, certain embodiments may be disclosed in a range format. The description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the disclosed ranges. Accordingly, the description of a range should be considered to have specifically disclosed all the possible sub-ranges as well as individual numerical values within that
- 10 range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed sub-ranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 3, 4, 5, and 6. This applies regardless of the breadth of the range.
- 15 It will be apparent that various other modifications and adaptations of the application will be apparent to the person skilled in the art after reading the foregoing disclosure without departing from the spirit and scope of the application and it is intended that all such modifications and adaptations come within the scope of the appended claims.

	100	first embodiment
	102	sterile reagent preparation device
	104	liquid reservoir;
	106	(stored) solvent
5	108	reagent container
	110	reagent
	112	movable shell
	114	flipper
	116	first cannula
10	118	second cannula
	120	head
	122	bottom side
	124	left side
	126	right side
15	128	full position (not shown)
	130	empty position (not shown)
	132	body
	134	cap
	136	bottom side
20	138	left side
	140	right side
	142	top side
	144	frame
	146	conduit
25	148	first portion

	150	second portion
	152	dent
	154	first end
	156	second end
5	158	protective lid (not shown)
	160	air exchange (not shown)
	162	(cap) cover
	164	membrane
	166	cage
10	168	first protruding part
	170	second protruding part
	172	left portion
	174	top portion
	176	right portion
15	178	rope
	180	first hole
	182	second hole
	184	pore (not shown)
	200	second embodiment
20	202	first step
	204	second step
	206	third step
	208	fourth step
	210	fifth step
25	212	sixth step

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214 seventh step

Claims

1. A sterile reagent preparation device for preparing a stock solution of a toxic reagent comprising:

- 5 ➤ at least one liquid reservoir for storing a solvent, comprising
- a movable shell;
 - a flipper for sealing and releasing the solvent,
 - a head, and
 - at least two cannulas for draining off the solvent and relieving a
- 10 gas,
- wherein the head is used for connecting the liquid flipper and at least one of the cannulas;
- at least one reagent container for containing a reagent;
- wherein
- 15 • the reagent container comprises a cap; and
- the cap is configured for receiving the cannulas.

2. The head of the liquid reservoir of claim 1 further comprising:

- a conduit for pushing the flipper open and draining off the solvent; and
- 20 ➤ a frame for enclosing the conduit.

3. The cannula of the liquid reservoir of claim 1 or 2 further comprising:

- a first end connected to the head; and
- a second end with a cut angle ranging from 10 degrees to 45 degrees.

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4. The cannula of the liquid reservoir of any of the preceding claims, wherein the cannula is made of chemically stable plastics, such as polypropylene (PP), polytetrafluoroethene (PTFE), polyethylene terephthalate (PETG) or any combination thereof.

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5. The cannula of the liquid reservoir of any of the preceding claims, wherein the cannula has a diameter ranging from 1 mm to 5 mm.

6. The reagent container of any of the preceding claims further comprising:
a cap cover and a membrane wherein

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- the cap cover has at least two hole for receiving the cannulas;
and
- the membrane protects the reagent from contamination.

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7. The membrane of the claim 6 wherein the membrane is made of chemically stable plastics, such as polypropylene (PP), polytetrafluoroethene (PTFE), polyethylene terephthalate (PETG) or any combination thereof.

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8. The membrane of claim 6 or 7 wherein the membrane has a thickness ranging from 0.1 mm to 5 mm.

9. The membrane of any of the preceding claims 6 to 8 further comprising:
at least one pore with a size ranging from 0.1 micrometer to 10 micrometers for
the solvent flowing into the reagent container.

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10. A method of using the sterile reagent preparation device of the preceding claims comprising:

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- removing the cap cover from the cap of the reagent container;
- inserting the at least two cannulas into the cap;
- peering the at least two cannulas through the membrane;
- injecting the solvent into the reagent container; and
- withdrawing the liquid reservoir from the reagent container.