The invention relates to a method of distributing a fluid. According to the invention, the following elements are connected simultaneously to a valve (1) which comprises multiple inlets and outlets and which is equipped with a check valve, namely: a fluid sampling and injecting device, such as a syringe (2); a gas (e.g., air) supply conduit; a supply conduit for the liquid to be distributed; and a discharge conduit (6). The inventive method consists in: drawing in the liquid to be distributed in order to transfer same to the sampling and injecting device (2), injecting the liquid into the discharge conduit (6), drawing in the gas in order to transfer same to the sampling and injecting device (2), and injecting the gas into the discharge conduit (6) in order to push the remaining liquid into the discharge conduit (6). The invention also relates to a device and kit for implementing said method.
METHOD AND DISPOSABLE DEVICE FOR SAMPLING AND DISTRIBUTING A LIQUID, FOR EXAMPLE, IN STERILE CONDITIONS

[0001] The present invention relates to a method and disposable device for sampling and apportionment of liquid, in particular under sterile conditions.

[0002] In the fields in particular of food, medicine, pharmaceuticals or biotechnology, there is the problem of the repeated transfer of fluids in particular in a sterile manner, and apportionment of a reproducible, precisely measured volume.

[0003] Today, this type of operation is carried out by separate, successive actions which multiply the connection/disconnection operations. The multiplication of these connections/disconnections leads to a high risk of contamination, either by exposure to the air, or because of incorrect handling by the operator.

[0004] A standard application is, for example in parenteral nutrition, the preparation of batches of nutritive mixtures to be administered subsequently to the patient, from a certain number of stock solutions such as: a solution of amino acids, a glucose solution, a lipid emulsion, to which are added small volumes of complementary substances such as trace elements, mineral salts and vitamins.

[0005] In pediatrics and neonatology in particular, the composition of these mixtures is varied from day to day as a function of the nutritive state of the patient and the need to ensure that he has a suitable calorie intake.

[0006] The need to vary this mixture from day to day does not allow the use of standard mixtures supplied by the pharmaceuticals industry, the composition of which does not vary by definition.

[0007] These mixtures must therefore be prepared in the hospital, under perfectly aseptic conditions. This operation is generally carried out on a laboratory table under a laminar air flow.

[0008] A standard application is, for example in biotechnology, the repeated taking of samples from a solution in cell culture, throughout this same culture which extends over several days. This repeated sampling makes it possible to ensure counting of the cells in a given volume and thus to follow their growth curve, and even to carry out sterility tests on the samples taken in order to ensure the absence of any contamination.

[0009] According to the method stage, this operation is generally carried out either on a laboratory table, or under a laminar air flow, or in controlled production zone.

[0010] In cell therapy, cells potentized by genetic engineering have to be apportioned and then cultured in multiple reproducible individual doses, for subsequent administration to the patient (autologous vaccine).

[0011] This apportionment requires the reproducibility of each of the doses and the transfer of the latter in sterile mode. This operation is generally carried out on a laboratory table, under a laminar air flow.

[0012] It would therefore be desirable to have a simple method which is easy to implement, for distribution and apportionment of a fluid, in particular under sterile conditions.

[0013] After prolonged research the Applicant has developed such a method.

[0014] This is why a subject of the present Application is a method for distribution of a fluid characterized in that

[0015] a) there are connected simultaneously to a multiple inlet and outlet valve equipped with a non-return valve

[0016] a fluid sampling and injection device such as a syringe,

[0017] an inlet pipe for gas such as air,

[0018] an inlet pipe for liquid to be distributed

[0019] an outlet pipe preferably equipped with a branch towards a waste container,

[0020] b) the liquid to be distributed is drawn off in order to be transferred into the sampling and injection device,

[0021] c) it is injected into the outlet pipe,

[0022] d) gas is drawn off in order to be transferred into the sampling and injection device,

[0023] e) the gas is injected into the outlet pipe in order to push the liquid remaining in the outlet pipe.

[0024] The multiple inlet and outlet valve equipped with a non-return valve is arranged in order to let in the liquid to be distributed, to let it out towards the sampling and injection device, to let it in from the sampling and injection device without the possibility of apportionment by the entry of the liquid to be distributed (effect of the non-return valve), to let it out towards the outlet pipe. Such non-return valves are well known. For example the valves marketed by the company Fillertek Inc (USA) under the name 3-way check valve can be mentioned.

[0025] The inlet pipe of liquid to be distributed is connected to a container containing said liquid to be distributed. This container can be for example a bottle or a pouch. This liquid inlet pipe is preferably equipped with a valve allowing or not allowing communication between the container and said inlet.

[0026] Under preferential conditions for implementing the invention, the inlet pipe for liquid to be distributed is connected to several containers containing several liquids to be distributed and preferably to a container containing a rinsing liquid.

[0027] To this end, said liquid inlet pipe can be supplied by several supply tubes, each preferably being equipped with a valve.

[0028] The gas inlet pipe can open directly into the multiple inlet and outlet valve.

[0029] Under preferential conditions for implementing the invention, the gas originates from a branch pipe provided on the liquid inlet pipe. This branch pipe is itself also preferably equipped with a valve allowing or not allowing communication between the air intake and the liquid inlet pipe.

[0030] Under other preferential conditions for implementing the invention, a filter, preferably a sterilizing filter is provided on the gas inlet pipe. The gas, for example the nitrogen or air coming from this pipe, is therefore sterile.
[0031] The fluid sampling and injection device can for example be a pump in particular a dosing pump, but is preferably a syringe.

[0032] The outlet pipe opens into a collecting container such as a flexible pouch and preferably into several collecting containers. To this end, said outlet pipe can be separated into several tubes, each being preferably equipped with a valve.

[0033] The collecting container is advantageously pre-connected, i.e., the container comprises connections allowing the direct mounting of said collecting container onto the outlet pipe(s).

[0034] A fraction of a single liquid to be distributed or a mixture of several fractions of different liquids can be collected.

[0035] This outlet pipe is preferably equipped with a branch leading to a waste container, equipped with a valve. In particular a rinsing fluid can thus be eliminated.

[0036] Under yet other preferential conditions for implementing the invention, the multiple inlet and outlet valve is equipped with a pipe for a rinsing liquid.

[0037] However, the rinsing liquid can be contained in one of the containers of liquid to be distributed. This avoids the use of an additional inlet on the multiple inlet and outlet valve.

[0038] Under yet other preferential conditions for implementing the method described above, the multiple inlet valve is connected by a pipe to a rinsing liquid, a rinsing liquid is drawn off in order to be transferred into the sampling and injection device, and it is injected into the outlet pipe in order to be transferred towards a waste-recovery container.

[0039] Under further other preferential conditions for implementing the method described above, the inlet pipe for liquid to be distributed is supplied for example by 1, 2, preferably 3 and particularly 4 containers of liquid to be distributed or more.

[0040] The outlet pipe opens for example into 1, 2, preferably 3 and particularly 4 or more collecting containers of the liquid or liquids distributed.

[0041] Apart from the multiple inlet and outlet valve, the other valves the function of which is to direct the flows of liquid and gas during the implementation of the method can for example be taps or preferably reversible clamps.

[0042] Under further other preferential conditions for implementing the invention, the above liquid sampling and apportionment method is implemented under sterile conditions, particularly using disposable components.

[0043] A subject of the present Application is also a device which can be used in an above method for distribution of a fluid characterized in that it comprises a multiple inlet and outlet valve equipped with a non-return valve, said inlet and outlet valve being provided

[0044] with an adapter for receiving the fluid sampling and injection device such as a syringe (Luer-lock® type for example).

[0045] with an inlet pipe for gas (for example air),

[0046] with an inlet pipe for liquid to be distributed

[0047] with an outlet pipe preferably equipped with a branch leading to a waste container,

[0048] Under preferential conditions for implementing the invention, the above inlet pipe for liquid to be distributed moreover includes an adaptation system for cooperating with a container containing a liquid to be distributed. This adaptation system can be perforating, self-perforating, be screw or bayonet fitting, have aseptic connections etc.

[0049] Under other preferential conditions for implementing the invention, the gas inlet pipe is a branch from the inlet pipe for liquid to be distributed.

[0050] Under further other preferential conditions for implementing the invention, the inlet pipe for liquid to be distributed comprises a shared section on the side of the multiple inlet and outlet valve and moreover a set of tubes for several containers containing a liquid to be distributed.

[0051] The gas inlet pipe is preferably connected onto the shared section of the inlet pipe for liquid to be distributed.

[0052] Under yet other preferential conditions for implementing the invention, the outlet pipe comprises a shared section on the side of the multiple inlet and outlet valve and moreover a set of tubes for several containers having to contain a liquid to be distributed.

[0053] The pipe towards the waste container is preferably connected onto the shared section of the outlet pipe.

[0054] In the case of a single stock solution, the inlet pipe is also the supply tube, advantageously in a single piece.

[0055] The method for distributing a fluid, which is the subject of the present invention has very useful qualities. In its version made from plastic, which is sterile and disposable:

[0056] it minimizes the number of connections under aseptic conditions and therefore reduces the risk of contamination by contact with the operator;

[0057] it implements the concept of the closed system, independent of the ambient air and therefore reduces the risk of bacterial contamination;

[0058] it is disposable, thus eliminating any risk of cross-contamination, batch by batch;

[0059] it allows the precise measurement of the volume sampled or transferred;

[0060] it allows the reproducibility of the volume transferred.

[0061] These qualities justify the use of the method for distributing a fluid described above, in the applications referred to above.

[0062] The preferential conditions for implementing the methods described above also apply to the other subjects of the invention referred to above, in particular to the devices for their implementation.

[0063] The invention will be better understood with reference to the attached drawing (FIG. 1) which is a diagrammatic representation of an example of an assembly of the invention with multiple inlets and outlets.
In FIG. 1 it is possible to discern the central element of the method and device according to the invention, a valve 1 with multiple inlets and outlets equipped with a non-return valve. This non-return valve allows the introduction of the liquid drawn off into the rigid body of a syringe 2 and its transfer, without returning downstream, towards the apportionment line.

It is then possible to discern from upstream to downstream in the circulation of the liquids:

1) Upstream, an inlet line with multiple tubes 3 provided for connecting to flasks, one or more pouches, a reactor or a tank, containing the stock solution or solutions to be filled (not represented). They join together into an inlet pipe 4 in the valve 1 with multiple inlets and outlets, and constitute a shared section.

2) The valve 1 with multiple inlets and outlets.

3) The syringe 2—which may or may not be pre-connected—with a capacity for example of 10 ml to 500 ml allowing the precise measurement (with a tolerance close to the measurement on the syringe body) of the volume drawn off.

4) Downstream, a distribution line with multiple tubes 5 allows the transfer and apportionment of the fluid drawn off towards the collecting pouches. They join together into an outlet pipe 6 of the valve 1 with multiple inlets and outlets, which constitutes a shared section.

5) One or more collecting pouches 7 pre-connected or not pre-connected to the distribution line, allowing the collection of the volumes of stock solutions transferred.

6) On the inlet line, upstream, a sterilizing hydrophobic filter 8 is pre-connected in a branch. Its function is to allow the introduction of filtered air into the device and to evacuate all of the dead volume of liquid which could remain there. The dead volume of this closed system being constant, purging it makes it possible to reproduce the drawing-off and transfer operation as many times as desired, in reproducible manner.

7) On the distribution line, downstream, a waste pouch 9 pre-connected to a branch, with a volume for example of 1 to 5 litres, makes it possible to collect either air, or part of the liquid transferred serving as rinsing liquid between each transfer, if necessary.

8) Reversible sealing clamps. On all the branches of the device, a reversible sealing clamp 10 is installed wherever necessary in order to direct the flow of liquid or air during use. 10S means that the clamp is installed on an outlet tube, 10F that the clamp is installed on an inlet tube, 10E that the clamp is installed on the filter tube and 10R that the clamp is installed on the waste pouch tube.

The above device can be used according to the following method:

1) The clamp on the desired inlet line is opened, the desired volume of stock solution is drawn off by aspiration into the syringe 2, measuring this volume on the body of the syringe.

2) The clamp 10E on the inlet line is closed, the clamp 10S on the apportionment line is opened, the measured volume of stock solution is transferred into the apportion line as far as the collection pouch 7.

3) The clamp 10E on the inlet line is closed, the clamp 10F downstream of the hydrophobic filter 8 is opened, air is drawn through the filter 8, using the syringe 2.

4) The stock solution trapped in the dead volume is pushed by means of the filtered air introduced up to the apportionment line is emptied into the collection pouch 7.

5) The clamp 10E on the inlet line is opened, a volume of stock solution is drawn into the syringe 2.

6) The clamp on the distribution line is closed, the clamp 10R of the waste pouch is opened, the volume of stock solution is transferred into the waste pouch 9, in order to rinse the pipes.

The above sequence is recommended as many times as necessary in order to ensure the repeated and reproducible transfer of the measured volume of stock solution.

As may be understood by a person skilled in the art, a device such as that above can be produced in modules from separate optionally multi-purpose elements. In addition to the valve 1 with multiple inlets and outlets, pipes can be found which are equally suitable for the inlet and the outlet, branched or not branched. For example, the same type of branched pipes is equally suitable for mounting the filter and the waste pouch. Moreover, a pipe suitable for the inlet and the outlet can be mounted on a piece provided with a set of channels allowing the same number of tubes to be mounted.

This is why a subject of the present Application is a fluid distribution unit characterized in that it comprises a multiple inlet and outlet valve equipped with a non-return valve, said valve being equipped with a fluid sampling and injection device such as a syringe or an adapter such as a cone for attaching a syringe, and two pipes, one being equipped with a branch (Y-shaped pipe), or four pipes and a branch end piece (3 pipes connected onto a branch end piece corresponding to a pipe equipped with a branch).

Method for distribution of a fluid characterized in that:

a) there are connected simultaneously to a multiple inlet and outlet valve (1) equipped with a non-return valve a fluid sampling and injection device such as a syringe (2), an inlet pipe for gas such as air, an inlet pipe for liquid to be distributed an outlet pipe (6),

b) the liquid to be distributed is drawn off in order to be transferred into the sampling and injection device (2),

c) it is injected into the outlet pipe (6),

d) gas is drawn off in order to be transferred into the sampling and injection device (2),

e) the gas is injected into the outlet pipe (6) in order to push the liquid remaining in the outlet pipe (6).
2. A method according to claim 1, characterized in that the inlet pipe (4) for liquid to be distributed is connected to several containers containing several liquids to be distributed.

3. A method according to claim 1, characterized in that the inlet pipe (4) for liquid to be distributed is connected to a container containing a rinsing liquid.

4. A method according to claim 1, characterized in that the liquid inlet pipe (4) is supplied by several supply tubes (3), each being equipped with a valve (10E).

5. A method according to claim 1, characterized in that the gas originates from a branch pipe provided on the liquid inlet pipe (4).

6. A method according to claim 1, characterized in that a filter (8), for example a sterilizing filter, is provided on the gas inlet pipe (4).

7. A method according to claim 1, characterized in that the fluid sampling and injection device (2) is a dosing pump or a syringe.

8. A method according to claim 1, characterized in that the outlet pipe (6) opens into one or more collecting containers (7).

9. A method according to claim 1, characterized in that the outlet pipe (6) separates into several tubes (5), each being equipped with a valve (10S).

10. A method according to claim 1, characterized in that the collecting container (7) is pre-connected (or the collecting containers).

11. A method according to claim 1, characterized in that a mixture of several fractions of different liquids is collected.

12. A method according to claim 1, characterized in that the outlet pipe (6) is equipped with a branch towards a waste container (9), equipped with a valve (10R).

13. A method according to claim 1, characterized in that the multiple inlet valve (1) is connected by a pipe to a rinsing liquid, a rinsing liquid is drawn off in order to be transferred into the sampling and injection device (2), and it is injected into the outlet pipe (6) in order to be transferred towards a waste-recovery container (9).

14. A method according to claim 1, characterized in that the inlet pipe (4) for liquid to be distributed is supplied by 3 containers for liquid to be distributed or more.

15. A method according to claim 1, characterized in that the outlet pipe (6) opens into 3 collecting containers of the liquid or liquids distributed or more.

16. A method according to claim 1, characterized in that it is implemented under sterile conditions, for example using disposable components.

17. A device which can be used in a method as defined in claim 1 characterized in that it comprises a multiple inlet and outlet valve (1) equipped with a non-return valve, said valve being provided with an adapter for receiving the fluid sampling and injection device such as a syringe (Luer-lock® type for example), with an inlet pipe for gas (for example air), with an inlet pipe (4) for liquid to be distributed with an outlet pipe (6).

18. A device according to claim 17, characterized in that the outlet pipe (6) is equipped with a branch towards a waste container (9).

19. A device according to claim 17, characterized in that the inlet pipe (4) for liquid to be distributed comprises an adaptation system for cooperating with a container containing a liquid to be distributed.

20. A device according to claim 17, characterized in that the inlet pipe (4) for liquid to be distributed comprises a shared section on the side of the multiple inlet and outlet valve and a set of tubes (3) for several containers containing a liquid to be distributed.

21. A device according to claim 17, characterized in that the gas inlet pipe is connected onto the shared section of the inlet pipe (4) for liquid to be distributed.

22. A device according to claim 17, characterized in that the outlet pipe (6) comprises a shared section on the side of the multiple inlet and outlet valve and a set of tubes (5) for several containers having to contain the liquid distributed.

23. A fluid distribution unit characterized in that it comprises a multiple inlet and outlet valve (1) equipped with a non-return valve, said valve being equipped with a fluid sampling and injection device such as a syringe or an adapter such as a cone for adapting a syringe, and two pipes (4, 6), one being equipped with a branch, or four pipes and a branch end piece.