

DIALYSATE BAGS

FIELD OF THE INVENTION

The invention relates to the field of dialysate bags useful in dialysis treatment, and to systems and methods involving the dialysate bags.

BACKGROUND TO THE INVENTION

Dialysis fluid (also known as dialysate) is an aqueous solution used in both haemodialysis and peritoneal dialysis. Dialysis fluid is used in dialysis treatment, where toxins and other species may be removed from a patient's body by diffusion across a semi-permeable membrane. This process may take place within a patient's body, in the peritoneum (peritoneal dialysis), or outside of a patient's body, in a dialyser (haemodialysis). In both cases, dialysis fluid may be provided as a pre-made sterile solution.

Typically, dialysis fluid is provided as a ready to use solution packaged in a bag. However, a major disadvantage with this is that the ready to use solutions, which contain large amounts of water, are very heavy and bulky. For example, the typical patient undergoing automated peritoneal dialysis (APD) is required to use from 60 to 120 L of dialysis fluid per week. This results in a very large amount of dialysis fluid being required, which takes up a lot of space and causes logistical challenges due to the weight of the fluid. Furthermore, bags that are full of dialysis fluid may be liable to bursting or breaking during transport or storage.

If dialysis fluid is provided as a powder or liquid concentrate for reconstitution immediately prior to dialysis treatment, it is essential to ensure that the solution is completely dissolved/reconstituted and thoroughly mixed before treatment is started. This may be difficult when patients undergo home dialysis without supervision from a medical professional, since patients cannot be relied on to ensure that the dialysis fluid is completely dissolved and mixed.

Further, when dialysis fluid is provided as a single liquid concentrate, it may suffer from long term storage stability issues.

There is a need for improved dialysis bags that overcome some or all of the problems associated with the prior art.

SUMMARY OF THE INVENTION

The present inventors have surprisingly found that the dialysate bags disclosed herein overcome the problems discussed above. In particular, the dialysate bags disclosed herein contain dialysate concentrates that are storage stable under home conditions, and which may be quickly and easily reconstituted by a patient at home, reliably ensuring full reconstitution and thorough mixing.

Thus, the invention provides the following numbered clauses.

1. A peritoneal dialysate bag comprising:
 - an inlet/outlet port; and
 - an inner chamber comprising a peritoneal dialysate concentrate, the inner chamber being fluidly connected to the inlet/outlet port.

2. The peritoneal dialysate bag according to Clause 1, wherein the dialysate bag comprises a further inlet/outlet port that is fluidly connected to the inner chamber, optionally wherein the inlet/outlet port and/or further inlet/outlet port has an open state and a closed state,
 - when in the open state the inlet/outlet port and/or the further inlet/outlet port fluidly connects the inner chamber to an exterior of the dialysate bag, and
 - when in the closed state the inlet/outlet port and/or the further inlet/outlet port fluidly isolates the inner chamber from the exterior of the dialysate bag.

3. The peritoneal dialysate bag according to Clause 1 or Clause 2, wherein the peritoneal dialysis bag comprises:
 - a first inlet/outlet port;
 - an inner chamber comprising:
 - a first region comprising a first peritoneal dialysate concentrate, the first region being fluidly connected to the first inlet/outlet port;
 - a second region fluidly separate from the first region and comprising a second peritoneal dialysate concentrate; and
 - a breakable barrier separating the first region from the second region,
 - wherein the dialysate bag is configured such that breakage of the breakable barrier results in the first region being fluidly connected to the second region; and
 - where at least one of the following applies:

(a) a maximum volume of the first region is lower than a maximum volume of the second region; and

(b) the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region.

4. The dialysate bag according to Clause 3, wherein the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region.

5. The dialysate bag according to Clause 4, wherein the second inlet/outlet port has an open state and a closed state,

where when in the open state the second inlet/outlet port fluidly connects the second region to an exterior of the dialysate bag, and

when in the closed state the second region is fluidly isolated from the exterior of the dialysate bag.

6. The dialysate bag according to any one of Clauses 3 to 5, wherein a maximum volume of the first region is lower than a maximum volume of the second region.

7. The dialysate bag according to any one of Clauses 3 to 6, wherein the first region comprises less than 40 vol. % (e.g. less than 35 vol. % or less than 30 vol. %) of a total maximum volume of the dialysate bag.

8. The dialysate bag according to any one of Clauses 3 to 7, wherein:

a maximum volume of the first region is lower than a maximum volume of the second region; and

the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region.

9. The dialysate bag according to any one of Clauses 3 to 8, wherein the breakable barrier is configured to break upon inflation of the first region.

10. The dialysate bag according to any one of Clauses 3 to 9, wherein the breakable barrier is configured to break along substantially its entire length (e.g. at least 60% of its length, at least 70% of its length, at least 80% of its length, such as at least 90% of its length),

optionally wherein the breakable barrier comprises a peelable seal and/or a frangible seal.

11. The dialysate bag according to any one of Clauses 3 to 10, wherein the dialysate bag comprises edges, and the breakable barrier extends from a first edge to an opposite edge.
12. The dialysate bag according to any one of Clauses 3 to 11, wherein the first dialysate concentrate and second dialysate concentrate are together suitable for forming a dialysis fluid suitable for direct administration to a patient by mixing with an appropriate volume of physiologically acceptable aqueous liquid (e.g. water for injection).
13. The dialysate bag according to any one of Clauses 3 to 12, wherein:
 - (a) the first concentrate occupies from 10 to 90 vol% (e.g. from 10 to 50 vol%) of a maximum volume of the first region; and/or
 - (b) the second concentrate occupies from 10 to 90 vol% (e.g. from 10 to 50 vol%) of a maximum volume of the second region.
14. The dialysate bag according to any one of Clauses 3 to 13, wherein:

the first and second regions together comprise an amount of first and second dialysate concentrate suitable for preparing n litres of dialysis fluid,

n is from 2 to 15 (e.g. 5 to 13, 7 to 12, such as 8 to 11), and

a maximum volume of the dialysate bag is suitable for administering n litres of dialysis fluid to a patient.
15. The dialysate bag according to any one of Clauses 3 to 14, wherein the first inlet/outlet port has an open state and a closed state,

where when in the open state the first inlet/outlet port fluidly connects the first region to the exterior of the dialysate bag, and

when in the closed state the first region is fluidly isolated from the exterior of the dialysate bag.
16. The dialysate bag according to any one of Clauses 3 to 15, wherein the dialysate bag comprises a tapered region and where the first inlet/outlet port is located on (e.g. at the apex of) the tapered region,

optionally wherein the tapered region forms part of the first region.
17. The dialysate bag according to any one of Clauses 3 to 16, wherein the dialysate bag comprises one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag, optionally wherein:

(a) one of the one or more sparging tubes is attached to the first inlet/outlet port;
or

(b) one of the one or more sparging tubes is attached to the breakable barrier;
and/or

wherein the breakable barrier, in an unbroken state, is configured to prevent the passage of liquid through the sparging tube.

18. The dialysate bag according to any one of Clauses 3 to 17, wherein the dialysate bag comprises:

a third region fluidly separate from the first and second regions and comprising a third dialysate concentrate; and

a second breakable barrier separating the second region from the third region, optionally wherein a maximum volume of the third region is greater than a maximum volume of each of the first and second regions.

19. The dialysate bag according to Clause 18, wherein the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region; and a third inlet/outlet port fluidly connected to the third region, optionally wherein the third inlet/outlet port has an open state and a closed state,

where when in the open state the third inlet/outlet port fluidly connects the third region to an exterior of the dialysate bag, and
when in the closed state the third region is fluidly isolated from the exterior of the dialysate bag.

20. The dialysate bag according to any one of Clauses 1 to 17, wherein the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region; and a third inlet/outlet port fluidly connected to the first region, optionally wherein the third inlet/outlet port has an open state and a closed state,

where when in the open state the third inlet/outlet port fluidly connects the first region to an exterior of the dialysate bag, and
when in the closed state the first region is fluidly isolated from the exterior of the dialysate bag.

21. The dialysate bag according to any one of Clauses 3 to 20, wherein the dialysate bag is suitable for formation of dialysis fluid whilst in a horizontal configuration.

22. The dialysate bag according to any one of Clauses 3 to 21, wherein the dialysate bag is suitable for formation of dialysis fluid whilst in a vertical configuration.

23. The dialysate bag according to any one of Clauses 3 to 22, wherein the first inlet/outlet port comprises two or more (e.g. three or more, four or more or five or more) diverging channels configured to distribute fluid flowing through the first inlet/outlet port in two or more (e.g. three or more, four or more or five or more) directions,

optionally wherein the second and/or third inlet/outlet ports, when present, each comprise two or more (e.g. three or more, four or more or five or more) diverging channels configured to distribute fluid flowing through the second and/or third inlet/outlet ports, respectively, in two or more (e.g. three or more, four or more or five or more) directions.

24. A peritoneal dialysis fluid reconstitution system comprising:

a peritoneal dialysate bag according to any one of Clauses 1 to 22; and

a source of physiologically acceptable aqueous liquid in fluid communication with the dialysate bag.

25. The dialysis fluid reconstitution system according to Clause 24, wherein:

the dialysate bag is according to Clause 4 or any one of Clauses 5 to 23 as dependent on Clause 4, and

the second inlet/outlet port is fluidly connected to the first inlet/outlet *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, first region, second region, second inlet/outlet port and external connection.

26. The dialysis fluid reconstitution system according to Clause 24 or 25, wherein:

the dialysate bag is according to Clause 19 or any one of Clauses 20 to 23 as dependent on Clause 19;

the first, second and, when present, third inlet/outlet ports are fluidly connected to each other *via* an external connection so as to form a plurality of circulating fluid flow paths through two or more of the first region, second region and third region.

27. The dialysis fluid reconstitution system according to Clause 24 or 25, wherein:

the dialysate bag is according to Clause 20 or any one of Clauses 21 to 23 as dependent on Clause 20;

the first, second and, when present, third inlet/outlet ports are fluidly connected to each other *via* an external connection so as to form a plurality of circulating fluid flow paths through the first region, or the first and second regions.

28. A method of preparing peritoneal dialysis fluid within a dialysate bag as defined in any one of Claims 1 to 23, comprising:

- (i) providing a dialysate bag as defined in any one of Clauses 1 to 23; and
- (ii) providing a physiologically acceptable aqueous liquid through the inlet/outlet port of the dialysate bag so as to form a dialysis fluid.

29. The method according to Clause 28, where the dialysate bag is as described in any one of Clauses 4 and 5 to 23, as dependent upon Clause 1, wherein step (ii) comprises:

- (iia) providing the physiologically acceptable aqueous liquid through the first inlet/outlet port to the first region of the dialysate bag to form a first intermediate dialysis fluid from the first dialysate concentrate and physiologically acceptable aqueous liquid,
 - where providing the physiologically acceptable aqueous liquid to the first region inflates the first region and breaks the breakable barrier, thereby allowing fluid communication with the second region;
- (iib) providing additional physiologically acceptable aqueous liquid through the first inlet/outlet port to form a second intermediate dialysis fluid from the first intermediate dialysis fluid, additional physiologically acceptable aqueous liquid and the second dialysate concentrate; and
- (iic) mixing the second intermediate dialysis fluid to form a dialysis fluid suitable for direct administration to a patient.

30. The method according to Clause 28, wherein the dialysate bag is as defined in Clause 18, or any one of Clauses 19 to 13 as dependent on Clause 18, and step (ii) comprises:

- (iia2) providing the physiologically acceptable aqueous liquid through the first inlet/outlet port to the first region of the dialysate bag to form a first intermediate dialysis fluid from the first dialysate concentrate and physiologically acceptable aqueous liquid,
 - where providing the physiologically acceptable aqueous liquid to the first region inflates the first region and breaks the breakable barrier, thereby allowing fluid communication with the second region;
- (iib2) providing additional physiologically acceptable aqueous liquid to the second region through the first inlet/outlet port to form a second intermediate dialysis fluid from the first intermediate dialysis fluid, additional physiologically acceptable aqueous liquid and the second dialysate concentrate,
 - where providing the physiologically acceptable aqueous liquid to the second region inflates the second region and breaks the second breakable barrier, thereby allowing fluid communication with the third region;

- (iic2) providing further physiologically acceptable aqueous liquid through the first inlet/outlet port to form a third intermediate dialysis fluid from the second intermediate dialysis fluid, further physiologically acceptable aqueous liquid and the third dialysate concentrate; and
- (iid2) mixing the third intermediate dialysis fluid to form a dialysis fluid suitable for direct administration to a patient.

31. The method according to Clause 29 or Clause 30, wherein step (iic) or (iid2) comprises manual mixing of the second intermediate dialysis fluid.

32. The method according to:

- (i) Clause 29, wherein the dialysate bag comprises a second inlet/outlet port; and step (iic) comprises recirculating the second intermediate dialysis fluid *via* the first and second inlet/outlet ports; or
- (ii) Clause 30, wherein the dialysate bag comprises a third inlet/outlet port; and step (iid2) comprises recirculating the third intermediate dialysis fluid *via* two or more of the first, second and third inlet/outlet ports.

33. A method of treating a patient in need of peritoneal dialysis treatment, said method comprising:

- (A) preparing peritoneal dialysate within a peritoneal dialysate bag according to any one of Clauses 28 to 32; and
- (B) subjecting said patient to a dialysis treatment using the dialysate prepared in step (A).

34. A system for preparing a peritoneal dialysis fluid comprising:

- (i) a source of physiologically acceptable aqueous liquid (e.g. water for injection);
- (ii) a peritoneal dialysate bag comprising one or more dialysate concentrates; and
- (iii) a fluid connection between the source of physiologically acceptable aqueous liquid and dialysate bag,

where the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection together form a fluid flow path consisting of the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection, and wherein:

the fluid connection is connected to a first inlet/outlet port of the dialysate bag; and

the dialysate bag comprises a second inlet/outlet port fluidly connected to the fluid connection *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, dialysate bag, second inlet/outlet port, external connection and fluid connection.

35. The system according to Clause 34, wherein the dialysate bag comprises one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag, optionally wherein one of the one or more sparging tubes is attached to a first inlet/outlet port of the dialysate bag.

36. A method of preparing a peritoneal dialysis fluid comprising the steps:

(a) providing a system comprising:

- (i) a source of physiologically acceptable aqueous liquid (e.g. water for injection);
- (ii) a peritoneal dialysate bag comprising one or more dialysate concentrates; and
- (iii) a fluid connection between the source of physiologically acceptable aqueous liquid and dialysate bag,

where the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection together form a fluid flow path consisting of the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection;

(b) providing physiologically acceptable aqueous liquid from the source of physiologically acceptable aqueous liquid to the dialysate bag and mixing the physiologically acceptable aqueous liquid with the dialysate concentrate to form a dialysis fluid, wherein:

- (1) the fluid connection is connected to a first inlet/outlet port of the dialysate bag; and the dialysate bag comprises a second inlet/outlet port fluidly connected to the fluid connection *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, dialysate bag, second inlet/outlet port, external connection and fluid connection, and where step (b) comprises recirculating the physiologically acceptable aqueous liquid and dialysate concentrate around the circulating fluid flow path to form a dialysis fluid; or
- (2) step (b) comprises mixing the physiologically acceptable aqueous liquid with the dialysate concentrate manually; by using an orbital shaker or vibrating table; or by using a robotic arm.

37. The method of Clause 36, wherein option (1) applies and the recirculating is performed while the dialysate bag is in a vertical configuration.

38. The method of Clause 36 or Clause 37, wherein the dialysate bag comprises one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag, optionally wherein one of the one or more sparging tubes is attached to a first inlet/outlet port of the dialysate bag.

39. The method of Clause 36, wherein step (b) comprises manually mixing the physiologically acceptable aqueous liquid with the dialysate concentrate,

optionally wherein the manual mixing is performed while the dialysate bag is in a horizontal configuration (e.g. while the dialysate bag is on a horizontal surface).

40. The method of Clause 36, wherein step (b) comprises mixing the physiologically acceptable aqueous liquid with the dialysate concentrate using an orbital shaker or vibrating table.

41. The method of Clause 36, wherein step (b) comprises mixing the physiologically acceptable aqueous liquid with the dialysate concentrate using a robotic arm.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows a first dialysis fluid reconstitution system according to the invention, which comprises a first dialysate bag according to the invention.

Figure 2 shows a second dialysis fluid reconstitution system according to the invention, which comprises a second dialysate bag according to the invention.

Figure 3 shows a third dialysis fluid reconstitution system according to the invention, which comprises a third dialysate bag according to the invention.

Figure 4 shows a fourth dialysis fluid reconstitution system according to the invention, which comprises a fourth dialysate bag according to the invention.

Figure 5 shows a fifth dialysis fluid reconstitution system according to the invention, which comprises a fifth dialysate bag according to the invention.

Figure 6 shows a dialysis fluid reconstitution system according to the, which comprises a dialysate bag and described herein.

Figure 7 shows a dialysis fluid reconstitution system, which comprises a dialysate bags and is described herein.

Figure 8 shows a dialysis fluid reconstitution system, which comprises a dialysate bag and is described herein.

Figure 9 shows a peritoneal dialysis fluid reconstitution system according to the invention, which comprises a peritoneal dialysate bag according to the invention.

Figure 10 shows results of a dialysis fluid reconstitution test for the peritoneal dialysis fluid reconstitution system of **Figure 1**.

Figure 11 shows results of a dialysis fluid reconstitution test for the peritoneal dialysis fluid reconstitution system of **Figure 2**.

Figure 12 shows results of a dialysis fluid reconstitution test for the peritoneal dialysis fluid reconstitution system of **Figure 3**.

Figure 13 shows results of a dialysis fluid reconstitution test for the peritoneal dialysis fluid reconstitution system of **Figure 5**.

Figure 14 shows results of a dialysis fluid reconstitution test for the dialysis fluid reconstitution system of **Figure 6**.

Figure 15 shows results of a dialysis fluid reconstitution test for the dialysis fluid reconstitution system of **Figure 7**.

Figure 16 shows results of a dialysis fluid reconstitution test for the dialysis fluid reconstitution system of **Figure 8**.

Figure 17 shows results of a peritoneal dialysis fluid reconstitution test for the dialysis fluid reconstitution system of **Figure 9**.

Figure 18 shows a peritoneal dialysis fluid reconstitution system according to the invention, which comprises a peritoneal dialysate bag according to the invention.

DETAILED DESCRIPTION OF THE INVENTION

The word “comprising” refers herein may be interpreted as requiring the features mentioned, but not limiting the presence of other features. Alternatively, the word “comprising” may also relate to the situation where only the components/features listed are intended to be present

(e.g. the word “comprising” may be replaced by the phrases “consists of” or “consists essentially of”). It is explicitly contemplated that both the broader and narrower interpretations can be applied to all aspects and embodiments of the present invention. In other words, the word “comprising” and synonyms thereof may be replaced by the phrase “consisting of” or the phrase “consists essentially of” or synonyms thereof and vice versa.

The phrase, “consists essentially of” and its pseudonyms may be interpreted herein to refer to a material where minor impurities may be present. For example, the material may be greater than or equal to 90% pure, such as greater than 95% pure, such as greater than 97% pure, such as greater than 99% pure, such as greater than 99.9% pure, such as greater than 99.99% pure, such as greater than 99.999% pure, such as 100% pure.

As used herein, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to “a composition” includes mixtures of two or more such compositions, reference to “an oxygen carrier” includes mixtures of two or more such oxygen carriers, reference to “the catalyst” includes mixtures of two or more such catalysts, and the like.

In a first aspect of the invention, there is provided a peritoneal dialysate bag comprising:

an inlet/outlet port; and

an inner chamber comprising a peritoneal dialysate concentrate, the inner chamber being fluidly connected to the inlet/outlet port.

In embodiments of this aspect, the peritoneal dialysate bag may comprise a further inlet/outlet port that is fluidly connected to the inner chamber, optionally wherein the inlet/outlet port and/or further inlet/outlet port has an open state and a closed state,

when in the open state the inlet/outlet port and/or the further inlet/outlet port fluidly connects the inner chamber to an exterior of the dialysate bag, and

when in the closed state the inlet/outlet port and/or the further inlet/outlet port fluidly isolates the inner chamber from the exterior of the dialysate bag.

In more particular embodiments of the aspect, the peritoneal dialysate bag may comprise:

a first inlet/outlet port (i.e. corresponding to the inlet/outlet port of the first aspect of the invention);

a first region comprising a first peritoneal dialysate concentrate, the first region being fluidly connected to the first inlet/outlet port;

a second region fluidly separate from the first region and comprising a second peritoneal dialysate concentrate; and

a breakable barrier separating the first region from the second region,

wherein the dialysate bag is configured such that breakage of the breakable barrier results in the first region being fluidly connected to the second region; and

where at least one of the following applies:

(a) a maximum volume of the first region is lower than a maximum volume of the second region; and

(b) the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region.

As used herein, a “peritoneal dialysate bag” refers to a bag containing one or more (e.g. 1, 2, 3, or 4) dialysis fluid concentrates, which concentrates may be reconstituted and combined within the bag to form a ready to use dialysis fluid. Thus, the dialysate fluid may be reconstituted and then used in a dialysis treatment directly from the dialysis bag.

In some embodiments, the peritoneal dialysate bag comprises a first region and a second region. The first and second regions are fluidly separate from each other, and are separated by a breakable barrier. The breakable barrier may be breakable by inflation of the first region of the dialysate bag, such as inflation by providing liquid (e.g. water or saline) to the first region of the dialysate bag. Once the breakable barrier is broken, the first and second regions will be fluidly connected. In other words, once the breakable barrier is broken, the first and second regions will be combined. For example, if the inner volume of a dialysate bag is formed from a first region and a second region, and the breakable barrier is broken, the inner volume will then form a singular region that replaces the previously-existing first and second regions.

As will be appreciated by a person skilled in the art, it may be advantageous for the breakable barrier to be configured to break along substantially its entire length. This will allow for improved mixing of fluid between the first and second regions. As used, herein, substantially the entire length of the breakable barrier means, for example, at least 60% of its length, at least 70% of its length, at least 80% of its length, such as at least 90% of its length. Thus, in some embodiments of the invention that may be mentioned herein, the breakable barrier may comprise a peelable seal and/or a frangible seal.

The peritoneal dialysate bag will be defined by edges. In some embodiments of the invention that may be mentioned herein, the breakable barrier may extend from a first edge to an

opposite edge. When such a breakable barrier breaks, it will allow for easy mixing of fluid between the first and second regions.

The first region, when present, may comprise a first peritoneal dialysate concentrate, and the second region, when present, comprise a second peritoneal dialysate concentrate. This may be advantageous because the first and second concentrates may contain different species and keep them separate until reconstitution for immediate use. This may ensure that the separated peritoneal dialysate concentrates have an improved shelf life as compared to a single combined dialysate concentrate.

The first region comprises a first inlet/outlet port, which may connect the first region to the exterior of the peritoneal dialysate bag, and may be used to allow fluid to enter or leave the dialysate bag. Thus, water may be provided to the dialysate bag to reconstitute dialysis fluid from the dialysate concentrates, and the resulting dialysis fluid may be removed from the bag to be used in a dialysis treatment.

In peritoneal dialysate bags according to embodiments of the invention, a maximum volume of the first region may be lower than a maximum volume of the second region. This may provide for improved (e.g. more reliable, and more complete) breaking of the breakable barrier separating the first region from the second region, when the first region is inflated. For example, the first region may comprise less than 40 vol. % of the maximum volume of the dialysate bag, such as less than 35 vol. % or less than 30 vol. %.

The peritoneal dialysate bag may comprise a second inlet/outlet port fluidly connected to the second region. This may enable easy mixing of the peritoneal dialysate concentrates with water during reconstitution, because water may be provided to the first region, inflating the first region and breaking the breakable barrier. This results in mixing of the dialysate concentrates with the water, and reconstitution of dialysis fluid. To ensure full mixing and dissolution of the dialysate concentrates, the mixture may be recirculated around a fluid flow path comprising the first inlet/outlet port, the interior of the dialysate bag (i.e. the space formed from the first and second regions once the breakable barrier is broken), the second inlet/outlet port, and external tubing connecting the first and second inlet/outlet ports. This recirculation of fluid may quickly, easily and reliably provide a fully mixed and reconstituted dialysis fluid, eliminating user error.

The inlet/outlet ports (e.g. the first and/or second inlet/outlet ports, or a third inlet/outlet port as discussed below) may have an open state and a closed state. When in the open state, the

inlet/outlet ports may fluidly connect the inside and exterior of the peritoneal dialysate bag, and when in the closed state the inside and exterior of the dialysate bag may be fluidly isolated. The closed state may be useful, for example, during storage of the dialysate bags, while the open state may be useful during reconstitution of dialysis fluid.

The inlet/outlet ports (e.g. the first and/or second inlet/outlet ports, or a third inlet/outlet port as discussed below) may comprise two or more (e.g. three or more, four or more or five or more) diverging channels configured to distribute fluid flowing through the respective inlet/outlet port in two or more (e.g. three or more, four or more or five or more) directions.

During use of the peritoneal dialysate bag, water (or an appropriate aqueous solution, e.g. saline) may be provided to the dialysate bag (e.g. to the first region). This will reconstitute the first dialysate concentrate, inflate the first region and break the breakable barrier (when present), thus also reconstituting the second dialysate concentrate. In some embodiments of the invention that may be mentioned herein, the first dialysate concentrate and second dialysate concentrate may together be suitable for forming a peritoneal dialysis fluid suitable for direct administration to a patient, when they are mixed with an appropriate volume of physiologically acceptable aqueous liquid (e.g. water for injection). In other words, a dialysis fluid may be easily prepared simply by providing an appropriate aqueous liquid to the dialysate bag.

The peritoneal dialysate concentrates may occupy any suitable proportion of the first and second regions. Preferably, this proportion is less than 90 vol% of the regions, to minimise the risk of the dialysate bag bursting or breaking during storage or transport. Thus, in some embodiments of the invention that may be mentioned herein:

- (a) the first concentrate may occupy from 10 to 90 vol% (e.g. from 10 to 50 vol%) of a maximum volume of the first region; and/or
- (b) the second concentrate may occupy from 10 to 90 vol% (e.g. from 10 to 50 vol%) of a maximum volume of the second region. It will be appreciated that the proportion of space mentioned herein may also apply to the first aspect of the invention, which may have a single region (i.e. the inner chamber).

The peritoneal dialysis bags of the invention may be used to prepare any suitable amount of dialysis fluid, e.g. from 2 to 15 litres. In other words, in some embodiments of the invention that may be mentioned herein:

the first and second regions may together comprise an amount of first and second dialysate concentrate suitable for preparing n litres of dialysis fluid, wherein:

n is from 2 to 15 (e.g. 5 to 13, 7 to 12, such as 8 to 11), and a maximum volume of the dialysate bag is suitable for administering n litres of peritoneal dialysis fluid to a patient.

In some embodiments of the invention that may be mentioned herein, the peritoneal dialysate bags may have a tapered region (which may form part of the first region), and the first inlet/outlet port may be located on (e.g. at the apex of) the tapered region. This may be advantageous to ensure that liquid is dispersed through the entirety of the first region during inflation of the bag. More specifically, when dialysis fluid is reconstituted in a dialysate bag that is hanging from a stand, the dialysate bag will be in a “vertical” configuration. Dialysis concentrate is dense and so will collect at the bottom of the bag that is hanging vertically. During reconstitution, water may be provided to the dialysate bag from the bottom of the bag, preferably at an apex located at the bottom of the bag. This ensures that the water will mix with the entirety of the concentrate, improving mixing and reconstitution.

Distribution of liquid in the first and/or second regions may also be improved by the use of one or more sparging tubes. Thus, in some embodiments of the invention that may be mentioned herein, the peritoneal dialysate bag may comprise one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag. The sparging tubes may be attached to the first inlet/outlet port to distribute liquid around the first region, or may be attached to the breakable barrier to distribute liquid around the second region upon breakage of the breakable barrier. In the latter case, the breakable barrier, in an unbroken state, may be configured to prevent the passage of liquid through the sparging tube.

The peritoneal dialysate bag may comprise a third region fluidly separate from the first and second regions and comprising a third dialysate concentrate; and a second breakable barrier separating the second region from the third region. This may be advantageous if it is desired to include a third dialysate concentrate separate from the first and second dialysate concentrates. In some embodiments, the maximum volume of the third region may be greater than a maximum volume of each of the first and second regions. The dialysate bag may comprise a second inlet/outlet port fluidly connected to the second region; and a third inlet/outlet port fluidly connected to the third region, such that all regions are connected to an inlet/outlet port, which may each have an open state and a closed state.

Alternatively, a third inlet/outlet port may be connected to the first region. Together with the first inlet/outlet port, this would allow recirculation of fluid through the first region without

breaking the breakable barrier, which may be advantageous to fully reconstitute the first dialysate concentrate before breaking the breakable barrier.

The dialysate bags of the invention may be used in any appropriate conformation, such as horizontal or vertical.

As discussed herein, the peritoneal dialysate bags comprise one or more dialysate concentrates. The dialysate concentrates may have any appropriate composition such that, when reconstituted together, they form a dialysate fluid/dialysate. Examples of dialysates that may be prepared using the present invention include those listed in Table 1 below. As will be appreciated by a person skilled in the art, different patients may require dialysate having different concentrations of electrolytes, and the invention may be implemented using dialysis bags suitable for preparing dialysate having different compositions to those listed in Table 1.

Table 1: Exemplary final peritoneal dialysate compositions

Dialysate		Concentration					
Number	Description	Glucose % w/v	Sodium mEq/L	Calcium mEq/L	Magnesium mEq/L	Chloride mEq/L	Lactate mEq/L
1	1.5% Glucose Low Calcium	1.5 ± 10%	132 ± 10%	2.5 ± 15%	0.5 ± 20%	95 ± 10%	40 ± 10%
2	2.5% Glucose Low Calcium	2.5 ± 10%	132 ± 10%	2.5 ± 15%	0.5 ± 20%	95 ± 10%	40 ± 10%
3	4.25% Glucose Low Calcium	4.25 ± 10%	132 ± 10%	2.5 ± 15%	0.5 ± 20%	95 ± 10%	40 ± 10%
4	1.5% Glucose Standard Calcium	1.5 ± 10%	132 ± 10%	3.5 ± 15%	0.5 ± 20%	96 ± 10%	40 ± 10%
5	2.5% Glucose Standard Calcium	2.5 ± 10%	132 ± 10%	3.5 ± 15%	0.5 ± 20%	96 ± 10%	40 ± 10%

Dialysate		Concentration					
Number	Description	Glucose % w/v	Sodium mEq/L	Calcium mEq/L	Magnesium mEq/L	Chloride mEq/L	Lactate mEq/L
6	4.25% Glucose Standard Calcium	4.25 ± 10%	132 ± 10%	3.5 ± 15%	0.5 ± 20%	96 ± 10%	40 ± 10%

Suitable peritoneal dialysate compositions may be prepared from concentrates as set out below.

Table 2A: Exemplary single peritoneal dialysate concentrate compositions

Low Calcium Concentrate: composition g/100mL					
	NaCl	CaCl ₂ ·2H ₂ O	MgCl ₂ ·6H ₂ O	Glucose monohydrate	Sodium Lactate
Glucose 1.5%	8.69±5%	0.30±14%	0.08±20%	24.23±5%	7.24±6%
Glucose 2.5%	8.69±5%	0.30±14%	0.08±20%	40.38±5%	7.24±6%
Glucose 4.25%	8.69±5%	0.30±14%	0.08±20%	68.65±5%	7.24±6%

Table 2B: Exemplary single peritoneal dialysate concentrate compositions

Standard Calcium Concentrate: composition g/100mL					
	NaCl	CaCl ₂ ·2H ₂ O	MgCl ₂ ·6H ₂ O	Glucose monohydrate	Sodium Lactate
Glucose 1.5%	8.69±5%	0.42±14%	0.08±20%	24.23±5%	7.24±6%
Glucose 2.5%	8.69±5%	0.42±14%	0.08±20%	40.38±5%	7.24±6%
Glucose 4.25%	8.69±5%	0.42±14%	0.08±20%	68.65±5%	7.24±6%

Icodextrin Concentrate: composition g/100mL					
	NaCl	CaCl ₂ ·2H ₂ O	MgCl ₂ ·6H ₂ O	Icodextrin	Sodium Lactate
Icodextrin 7.50%	3.59±5%	0.17±14%	0.03±20%	50.00±5%	2.99±6%

Without being bound by theory, it is believed that providing the peritoneal dialysate concentrate (such as the dialysate concentrates listed above) in the form of two or three separate concentrates, will advantageously improve the stability, shelf life and longevity of the concentrate.

In some embodiments of the invention, the dialysate concentrate is provided as two separate concentrates, with a first concentrate present in a first region of a dialysate bag, and a second concentrate present in a second region. In such embodiments, the concentrates may comprise the following components.

Table 3A: Exemplary dual peritoneal dialysate concentrate compositions (low calcium)

Low Calcium					
Solution 1: composition g/100mL				Solution 2: composition g/100mL	
	CaCl ₂ ·2H ₂ O	MgCl ₂ ·6H ₂ O	Glucose monohydrate	NaCl	Sodium Lactate
Glucose 1.5%	0.74±14%	0.20±20%	60.00±5%	19.20±5%	16.01±6%
Glucose 2.5%	0.74±14%	0.20±20%	100.00±5%	19.20±5%	16.01±6%
Glucose 4.25%	0.74±14%	0.20±20%	170.00±5%	19.20±5%	16.01±6%

Table 3B: Exemplary dual peritoneal dialysate concentrate compositions (low calcium)

Standard Calcium					
Solution 1: composition g/100mL				Solution 2: composition g/100mL	
	CaCl ₂ ·2H ₂ O	MgCl ₂ ·6H ₂ O	Glucose monohydrate	NaCl	Sodium Lactate
Glucose 1.5%	1.04±14%	0.20±20%	60.00±5%	19.20±5%	16.01±6%
Glucose 2.5%	1.04±14%	0.20±20%	100.00±5%	19.20±5%	16.01±6%
Glucose 4.25%	1.04±14%	0.20±20%	170.00±5%	19.20±5%	16.01±6%

In some embodiments of the invention, the peritoneal dialysate concentrate is provided as three separate concentrates, with a first concentrate present in a first region of a dialysate bag, a second concentrate present in a second region, and a third concentrate present in a third region. These concentrates may be formed from any suitable components, for example by splitting the above two-part concentrates into three separate concentrates (e.g. by providing the sugar as a separate concentrate).

The invention further provides a peritoneal dialysis fluid reconstitution system comprising:

a peritoneal dialysate bag as defined herein; and

a source of physiologically acceptable aqueous liquid in fluid communication with the dialysate bag.

Such a peritoneal dialysis fluid reconstitution system may be used to reconstitute peritoneal dialysis fluid within the peritoneal dialysis bag. When the dialysate bag comprises a second fluid inlet/outlet port, the second inlet/outlet port may be fluidly connected to the first inlet/outlet *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, first region, second region, second inlet/outlet port and external connection. This allows for recirculation of fluid through the first and second regions, which may be advantageous to fully reconstitute the first and second dialysate concentrates to ensure effective mixing. As will be appreciated by a person skilled in the art, a similar configuration may be used when the dialysate bag comprises three fluid inlet/outlet ports. In such cases, the first, second and/or third inlet/outlet ports may be fluidly connected to each other *via* an external connection so as to form one or more circulating fluid flow paths through the first region, second region and/or

third region. For example, if the dialysate bag comprises three regions each being fluidly connected to an inlet/outlet port, these inlet/outlet ports may be fluidly connected *via* an external connection to form fluid flow paths through the first and second; first and third; second and third; and first, second and third inlet/outlet ports. This will allow for selective recirculation through different regions of the dialysate bag during reconstitution of dialysis fluid. As explained herein, the dialysate bag may also comprise two fluid inlet/outlet ports fluidly connected to the same region (e.g. the first region), and these may be connected *via* an external connection to recirculate liquid within a single region during reconstitution

The invention also provides a method of preparing peritoneal dialysis fluid within a peritoneal dialysate bag defined herein, said method comprising:

- (i) providing a peritoneal dialysate bag as defined herein; and
- (ii) providing a physiologically acceptable aqueous liquid through the first inlet/outlet port of the dialysate bag so as to form a dialysis fluid.

In this method, when the dialysate bag comprises two regions each containing a dialysate concentrate, step (ii) may comprise:

- (iia) providing the physiologically acceptable aqueous liquid through the first inlet/outlet port to the first region of the dialysate bag to form a first intermediate dialysis fluid from the first dialysate concentrate and physiologically acceptable aqueous liquid,
 - where providing the physiologically acceptable aqueous liquid to the first region inflates the first region and breaks the breakable barrier, thereby allowing fluid communication with the second region;
- (iib) providing additional physiologically acceptable aqueous liquid through the first inlet/outlet port to form a second intermediate dialysis fluid from the first intermediate dialysis fluid, additional physiologically acceptable aqueous liquid and the second dialysate concentrate; and
- (iic) mixing the second intermediate dialysis fluid to form a dialysis fluid suitable for direct administration to a patient.

In such cases, the dialysate bag may comprises a second inlet/outlet port; and step (iic) may comprise recirculating the second intermediate dialysis fluid *via* the first and second inlet/outlet ports.

When the dialysate bag comprises three regions as disclosed herein, and each of the three regions contains a dialysate concentrate, step (ii) may comprise:

- (iia2) providing the physiologically acceptable aqueous liquid through the first inlet/outlet port to the first region of the dialysate bag to form a first intermediate dialysis fluid from the first dialysate concentrate and physiologically acceptable aqueous liquid,
 - where providing the physiologically acceptable aqueous liquid to the first region inflates the first region and breaks the breakable barrier, thereby allowing fluid communication with the second region;
- (iib2) providing additional physiologically acceptable aqueous liquid to the second region through the first inlet/outlet port to form a second intermediate dialysis fluid from the first intermediate dialysis fluid, additional physiologically acceptable aqueous liquid and the second dialysate concentrate,
 - where providing the physiologically acceptable aqueous liquid to the second region inflates the second region and breaks the second breakable barrier, thereby allowing fluid communication with the third region;
- (iic2) providing further physiologically acceptable aqueous liquid through the first inlet/outlet port to form a third intermediate dialysis fluid from the second intermediate dialysis fluid, further physiologically acceptable aqueous liquid and the third dialysate concentrate; and
- (iid2) mixing the third intermediate dialysis fluid to form a dialysis fluid suitable for direct administration to a patient.

In such cases, the dialysate bag may comprise a third inlet/outlet port; and step (iid2) may comprise recirculating the third intermediate dialysis fluid *via* two or more of the first, second and third inlet/outlet ports.

Alternatively, the mixing steps above (e.g. steps (iic) or (iicd)) may comprise manual mixing (e.g. by hand). This may be done by gently pressing on the dialysate bag with a person's hands to mix the liquid until the concentrates are fully dissolved and the liquid is fully mixed. Such manual mixing may be performed when the dialysate bag is placed in a horizontal position, such as on a horizontal surface.

The invention also provides a method of treating a patient in need of peritoneal dialysis treatment, said method comprising:

- (A) preparing peritoneal dialysate within a peritoneal dialysate bag as disclosed herein; and
- (B) subjecting said patient to a peritoneal dialysis treatment using the dialysate prepared in step (A).

The invention also provides a system for preparing a peritoneal dialysis fluid comprising:

- (i) a source of physiologically acceptable aqueous liquid (e.g. water for injection);
- (ii) a peritoneal dialysate bag comprising one or more dialysate concentrates; and
- (iii) a fluid connection between the source of physiologically acceptable aqueous liquid and dialysate bag,

where the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection together form a fluid flow path consisting of the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection, and wherein:

the fluid connection is connected to a first inlet/outlet port of the dialysate bag; and

the dialysate bag comprises a second inlet/outlet port fluidly connected to the fluid connection *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, dialysate bag, second inlet/outlet port, external connection and fluid connection.

In some embodiments of the above system, the dialysate bag comprises one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag. One of the one or more sparging tubes may be attached to a first inlet/outlet port of the dialysate bag.

The invention also provides a method of preparing a peritoneal dialysis fluid comprising the steps:

- (a) providing a system comprising:

- (i) a source of physiologically acceptable aqueous liquid (e.g. water for injection);
- (ii) a peritoneal dialysate bag comprising one or more dialysate concentrates; and
- (iii) a fluid connection between the source of physiologically acceptable aqueous liquid and dialysate bag,

where the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection together form a fluid flow path consisting of the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection;

- (b) providing physiologically acceptable aqueous liquid from the source of physiologically acceptable aqueous liquid to the dialysate bag and mixing the physiologically acceptable aqueous liquid with the dialysate concentrate to form a dialysis fluid, wherein:

- (1) the fluid connection is connected to a first inlet/outlet port of the dialysate bag; and the dialysate bag comprises a second inlet/outlet port fluidly connected to the fluid connection *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, dialysate bag, second inlet/outlet port, external connection and fluid connection, and where step (b) comprises

- recirculating the physiologically acceptable aqueous liquid and dialysate concentrate around the circulating fluid flow path to form a dialysis fluid; or
- (2) step (b) comprises mixing the physiologically acceptable aqueous liquid with the dialysate concentrate manually; by using an orbital shaker or vibrating table; or by using a robotic arm.

In some embodiments that may be mentioned herein, option (1) applies and the recirculating may be performed while the dialysate bag is in a vertical configuration.

The peritoneal dialysate bag may comprise one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag, one of the one or more sparging tubes may be attached to a first inlet/outlet port of the dialysate bag.

Step (b) may be performed in a number of ways. For example, step (b) may comprise:

- manually mixing the physiologically acceptable aqueous liquid with the dialysate concentrate; or
- mixing the physiologically acceptable aqueous liquid with the dialysate concentrate using an orbital shaker or vibrating table; or
- mixing the physiologically acceptable aqueous liquid with the dialysate concentrate using a robotic arm.

The invention is described in more detail below with reference to the Figures.

Figure 1 shows a dialysis system comprising a peritoneal dialysate bag **100** that comprises a first region **101** comprising a first peritoneal dialysate concentrate, and a second region **102** comprising a second peritoneal dialysate concentrate. The first and second regions are fluidly separated by a breakable barrier **103**. During use, water may be provided to the peritoneal dialysate bag by a water source **104** along connection **1001** and to the first fluid inlet/outlet port **105**. Inflation of the first region **101** will result in breakage of the breakable barrier **103**, and mixing of the water and peritoneal dialysate concentrates. Full mixing may be achieved by recirculating water using connection **1002**, the second inlet/outlet port **106**, the peritoneal dialysate bag and connection **1001**. The direction of water flow may be controlled by unit **1003**. While shown as operating in this mode, it is possible for the dialysis system to be operated in reverse.

Variants of the design of **Figure 1** are shown in **Figures 2 to 4**.

Figure 2 shows a variant of the design in which the peritoneal dialysate bag has a tapered region **107** and the first fluid inlet/outlet port **105** is located at an apex of the tapered region.

Figure 3 shows a variant of the design in which the first **101** and second **102** regions each comprise a sparging tube **107**, **108** configured to increase distribution of fluid flowing through the dialysate bag.

Figure 4 shows a variant of the design which comprises a third inlet/outlet port **107**. This may allow selective recirculation of fluid in the first region **101**, before breakage of the breakable barrier **103**. It may also allow for improved mixing of the peritoneal dialysate concentrates and water, by recirculation through all three of the inlet/outlet ports **105**, **106** and **107**.

Figure 5 shows a peritoneal dialysis system comprising a dialysate bag **500** that comprises a first region **501** comprising a first peritoneal dialysate concentrate, and a second region **502** comprising a second peritoneal dialysate concentrate. The first and second regions are fluidly separated by a breakable barrier **503**. During use, water may be provided to the dialysate bag by a water source **504** along connection **5001** and to the first fluid inlet/outlet port **505**. Inflation of the first region **501** will result in breakage of the breakable barrier **503**, and mixing of the water and dialysate concentrates. Full mixing may be achieved by manually manipulating the bag, for example by gently pressing on the edges or corners of the bag. Water flow may be controlled by unit **503**.

Figure 6 shows a dialysis system comprising a dialysis bag **600**, which comprises a first region **601** and a second region **602** each containing a dialysis concentrate. The first **601** and second **602** regions are separated by a permanent barrier, that includes a fluid port **603** which allows fluid to flow from the first region **601** to the second region **602**. Water may be provided to the bag **600** from water source **604** along connection **6001** and through fluid inlet/outlet port **605**, and recirculated *via* fluid inlet/outlet port **606** and connection **6002**. Water flow may be controlled by unit **6003**.

Figure 7 shows a dialysis system comprising a first dialysis bag **701** and a second dialysis bag **702** arranged in series. The first bag **701** comprises a first dialysate concentrate and the second bag **702** comprises a second dialysate concentrate. The second bag **702** comprises a sparging tube **707** configured to increase distribution of fluid flowing through the second bag **702**. Water may be provided to the first bag **701** and mixed with the first dialysate concentrate, after which it flows to the second bag **702** and is mixed with the second dialysate concentrate.

Water may be provided from water source **704** along connections **7001a** and **7001b**. Water may be recirculated *via* connection **7002**. Water flow may be controlled by unit **7003**.

Figure 8 shows a variant of the design of **Figure 7**, which includes only one dialysis bag **801** containing a single dialysate concentrate. The dialysis bag **801** comprises a sparging tube **807** configured to increase distribution of fluid flowing through the dialysis bag **801**. Water may be provided to the dialysis bag **801** and mixed with the dialysate concentrate. Water may be provided from water source **804** along connection **8001**. Water may be recirculated *via* connection **8002**. Water flow may be controlled by unit **8003**.

Figure 9 shows a peritoneal dialysis system comprising a peritoneal dialysis bag **901** comprising a peritoneal dialysate concentrate. Water may be provided to the peritoneal dialysis bag **901** and mixed with the dialysate concentrate. Water may be provided from water source **904** along connection **9001**. Water may be recirculated *via* connection **9002**. Water flow may be controlled by unit **9003**.

Figure 18 shows a peritoneal dialysis system comprising a peritoneal dialysis bag **1801** comprising first, second and third peritoneal dialysate concentrates in first (**18011**), second (**18012**) and third (**18013**) regions. Water may be provided to the peritoneal dialysis bag **1801** and mixed with the dialysate concentrate. Water may be provided from water source **1804** along connection **18020** to one of inlet/outlet ports **18021**, **18022**, or **18023**, the selection may be controlled through the use of valves. As such, water may be directed to whichever of the first to third regions is desired to be filled first (the selection of the region to be filled may be controlled by the use of any suitable control system, e.g. the use of valves). For example, the third region **18013** (e.g. containing a concentrate comprising 4.25% glu) may be filled first, once this region is filled, the breakable seal **1831** may break and allow the second region **18012** (e.g. containing a concentrate comprising 2.5% glu) to be filled, and the breakable seal **1832** may break leading to the filling of the first region **18011** (e.g. containing a concentrate comprising 1.5% glu). As depicted, the third region **18013** may be have the same volume or be smaller than the second region **18012** and both may be smaller in volume than the first region **18011**. As will be appreciated, the user may select any suitable filing method depending on their preference or the instructions provided to them by the manufacturer.

Specific aspects and embodiments of the invention are described in the below non-limiting Examples.

EXAMPLES

Example 1

Peritoneal dialysis fluid reconstitution was tested for peritoneal dialysate bag designs described herein and depicted in Figures 1-3 and 5-9.

Dialysate was reconstituted by first filling dialysate bags having a maximum volume of 15 L with water at a defined flow rate to a fill level of 10L, followed by recirculation at a defined flow rate. The respective conditions are listed in Table 6 below. The level/completeness of the mixing of the reconstituted dialysis fluid was assessed by measuring the conductivity of the recirculating dialysis fluid over time using an IBP conductivity meter (HDU-CDTP (High Precision Conductivity/Temperature Sensor)) on the recirculation line. The reconstituted dialysis fluid was deemed to be fully mixed once the conductivity readings plateaued.

For the dialysate bags comprising different concentrates present in each of the first and second regions, 300 mL of each concentrate was used (Figures 1, 2, 3, 4, 5, and 6). The concentrates had the following composition (Tables 2A and 2B below). Concentrates 1 and 2, when used together, are suitable for preparing 13 litres of dialysate.

Table 4A: Concentrate 1 for Figures 1-6

Concentrate 1	Mass (g)
CaCl ₂ · 2H ₂ O	2.39
MgCl ₂ · 6H ₂ O	0.66
Anhydrous dextrose	177.28
Water	325

Table 4B: Concentrate 2 for Figures 1-6

Concentrate 2	Mass (g)
NaCl	69.89
Sodium lactate (60%)	97.12
Water	365

For the bags comprising only a single dialysate concentrate, 600 mL of the following concentrate (Table 5) was used (Figures 7, 8 and 9). The concentrate is suitable for preparing 13 litres of dialysate.

Table 5: Concentrate for Figures 7-9

Single Concentrate	Mass (g)
NaCl	69.89
CaCl ₂ · 2H ₂ O	2.39
MgCl ₂ · 6H ₂ O	0.66
Anhydrous dextrose	177.28
Sodium lactate (60%)	97.12
Water	800

Table 6

Example	Bag Design	Fill Conditions	Time required for mixing	Conductivity Measurement Graph
1	Figure 1	Fill rate 500 mL/min, Recirculation rate 250 mL/min	7 minutes	Figure 10
2	Figure 2	Fill rate 1000 mL/min, Recirculation rate 250 mL/min	2 minutes	Figure 11
3	Figure 3	Fill rate 500 mL/min, Recirculation rate 250 mL/min in alternate directions	12 minutes	Figure 12
4	Figure 5	Fill rate 500 mL/min, Manual mixing of the fluid within the bag and no recirculation *It was not feasible to measure conductivity during manual mixing of the fluid within the bag, the conductivity graph in Figure 13 was obtained by draining the bag contents through a conductivity meter flowcell to demonstrate that bag contents were homogenous.	10 seconds (8 L); 15 seconds (9 L); 20 seconds (10 L); Incomplete mixing (12 L)	Figure 13*

Example	Bag Design	Fill Conditions	Time required for mixing	Conductivity Measurement Graph
5	Figure 6	Fill rate 450 mL/min or 250 mL/min, Recirculation rate 250 mL/min	8 minutes	Figure 14
6	Figure 7	Fill rate 500 mL/min, Recirculation rate 250 mL/min	20 minutes (long sparger, 55 cm); 35 minutes (short sparger, 30 cm)	Figure 15
7	Figure 8	Fill rate 500 mL/min, Recirculation rate 250 mL/min	Less than 5 minutes	Figure 16
8	Figure 9	Fill rate 500 mL/min, Recirculation rate 250 mL/min	10 minutes	Figure 17

The results demonstrate that when dialysis fluid is reconstituted in a dialysate bags, recirculation of the fluid and/or manual mixing is required in order for the fluid to become fully mixed. In general, recirculation is appropriate when a bag is arranged in a vertical position, such as hanging from a stand. Manual mixing may be appropriate when a bag is arranged horizontally, such as resting on a flat surface.

The results demonstrate that various means may be used to improve mixing of the fluid, such as recirculation, manual mixing, sparging tubes, and providing fluid from the bottom apex of a hanging bag having a taper.

CLAIMS

1. A peritoneal dialysate bag comprising:
 - an inlet/outlet port; and
 - an inner chamber comprising a peritoneal dialysate concentrate, the inner chamber being fluidly connected to the inlet/outlet port.

2. The peritoneal dialysate bag according to Claim 1, wherein the dialysate bag comprises a further inlet/outlet port that is fluidly connected to the inner chamber, optionally wherein the inlet/outlet port and/or further inlet/outlet port has an open state and a closed state,
 - when in the open state the inlet/outlet port and/or the further inlet/outlet port fluidly connects the inner chamber to an exterior of the dialysate bag, and
 - when in the closed state the inlet/outlet port and/or the further inlet/outlet port fluidly isolates the inner chamber from the exterior of the dialysate bag.

3. The peritoneal dialysate bag according to Claim 1 or Claim 2, wherein the peritoneal dialysis bag comprises:
 - a first inlet/outlet port;
 - an inner chamber comprising:
 - a first region comprising a first peritoneal dialysate concentrate, the first region being fluidly connected to the first inlet/outlet port;
 - a second region fluidly separate from the first region and comprising a second peritoneal dialysate concentrate; and
 - a breakable barrier separating the first region from the second region,
 - wherein the dialysate bag is configured such that breakage of the breakable barrier results in the first region being fluidly connected to the second region; and
 - where at least one of the following applies:
 - (a) a maximum volume of the first region is lower than a maximum volume of the second region; and
 - (b) the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region.

4. The dialysate bag according to Claim 3, wherein the dialysate bag comprises a second inlet/outlet port fluidly connected to the second region.

5. The dialysate bag according to Claim 4, wherein the second inlet/outlet port has an open state and a closed state,

where when in the open state the second inlet/outlet port fluidly connects the second region to an exterior of the dialysate bag, and

when in the closed state the second region is fluidly isolated from the exterior of the dialysate bag.

6. The dialysate bag according to any one of Claims 3 to 5, wherein a maximum volume of the first region is lower than a maximum volume of the second region, optionally wherein the first region comprises less than 40 vol. % (e.g. less than 35 vol. % or less than 30 vol. %) of a total maximum volume of the dialysate bag.

7. The dialysate bag according to any one of Claims 3 to 8, wherein: (a) the breakable barrier is configured to break upon inflation of the first region; and/or
(b) the breakable barrier is configured to break along substantially its entire length (e.g. at least 60% of its length, at least 70% of its length, at least 80% of its length, such as at least 90% of its length),
optionally wherein the breakable barrier comprises a peelable seal and/or a frangible seal.

8. The dialysate bag according to any one of Claims 3 to 7, wherein the dialysate bag comprises edges, and the breakable barrier extends from a first edge to an opposite edge.

9. The dialysate bag according to any one of Claims 3 to 8, wherein the first dialysate concentrate and second dialysate concentrate are together suitable for forming a dialysis fluid suitable for direct administration to a patient by mixing with an appropriate volume of physiologically acceptable aqueous liquid (e.g. water for injection).

10. The dialysate bag according to any one of Claims 3 to 9, wherein:
(a) the first concentrate occupies from 10 to 90 vol% (e.g. from 10 to 50 vol%) of a maximum volume of the first region; and/or
(b) the second concentrate occupies from 10 to 90 vol% (e.g. from 10 to 50 vol%) of a maximum volume of the second region.

11. The dialysate bag according to any one of Claims 3 to 10, wherein:
the first and second regions together comprise an amount of first and second dialysate concentrate suitable for preparing n litres of dialysis fluid,
n is from 2 to 15 (e.g. 5 to 13, 7 to 12, such as 8 to 11), and

a maximum volume of the dialysate bag is suitable for administering n litres of dialysis fluid to a patient.

12. The dialysate bag according to any one of Claims 3 to 11, wherein the dialysate bag comprises a tapered region and where the first inlet/outlet port is located on (e.g. at the apex of) the tapered region,

optionally wherein the tapered region forms part of the first region.

13. The dialysate bag according to any one of Claims 3 to 12, wherein the dialysate bag comprises one or more (e.g. one) sparging tubes configured to increase distribution of fluid flowing through the dialysate bag, optionally wherein:

(a) one of the one or more sparging tubes is attached to the first inlet/outlet port;

or

(b) one of the one or more sparging tubes is attached to the breakable barrier;

and/or

wherein the breakable barrier, in an unbroken state, is configured to prevent the passage of liquid through the sparging tube.

14. The dialysate bag according to any one of Claims 3 to 13, wherein the dialysate bag comprises:

a third region fluidly separate from the first and second regions and comprising a third dialysate concentrate; and

a second breakable barrier separating the second region from the third region, optionally wherein a maximum volume of the third region is greater than a maximum volume of each of the first and second regions.

15. The dialysate bag according to any one of Claims 3 to 14, wherein the first inlet/outlet port comprises two or more (e.g. three or more, four or more or five or more) diverging channels configured to distribute fluid flowing through the first inlet/outlet port in two or more (e.g. three or more, four or more or five or more) directions,

optionally wherein the second and/or third inlet/outlet ports, when present, each comprise two or more (e.g. three or more, four or more or five or more) diverging channels configured to distribute fluid flowing through the second and/or third inlet/outlet ports, respectively, in two or more (e.g. three or more, four or more or five or more) directions.

16. A peritoneal dialysis fluid reconstitution system comprising:

a peritoneal dialysate bag according to any one of Claims 1 to 15; and

a source of physiologically acceptable aqueous liquid in fluid communication with the dialysate bag.

17. A method of preparing peritoneal dialysis fluid within a dialysate bag as defined in any one of Claims 1 to 15, comprising:

- (i) providing a peritoneal dialysate bag as defined in any one of Claims 1 to 15; and
- (ii) providing a physiologically acceptable aqueous liquid through the inlet/outlet port of the dialysate bag so as to form a dialysis fluid.

18. The method according to Claim 17, wherein:

(A) when the dialysate bag is as described in any one of Claims 4 and 5 to 15, as dependent upon Claim 4, then step (ii) comprises: (iia) providing the physiologically acceptable aqueous liquid through the first inlet/outlet port to the first region of the dialysate bag to form a first intermediate dialysis fluid from the first dialysate concentrate and physiologically acceptable aqueous liquid,

where providing the physiologically acceptable aqueous liquid to the first region inflates the first region and breaks the breakable barrier, thereby allowing fluid communication with the second region;

(iib) providing additional physiologically acceptable aqueous liquid through the first inlet/outlet port to form a second intermediate dialysis fluid from the first intermediate dialysis fluid, additional physiologically acceptable aqueous liquid and the second dialysate concentrate; and

(iic) mixing the second intermediate dialysis fluid to form a dialysis fluid suitable for direct administration to a patient or;

(B) when the dialysate bag is as described in Claim 14 or Claim 15, as dependent upon Claim 14, then step (ii) comprises:

(iia2) providing the physiologically acceptable aqueous liquid through the first inlet/outlet port to the first region of the dialysate bag to form a first intermediate dialysis fluid from the first dialysate concentrate and physiologically acceptable aqueous liquid,

where providing the physiologically acceptable aqueous liquid to the first region inflates the first region and breaks the breakable barrier, thereby allowing fluid communication with the second region;

(iib2) providing additional physiologically acceptable aqueous liquid to the second region through the first inlet/outlet port to form a second intermediate dialysis fluid from the first intermediate dialysis fluid, additional physiologically acceptable aqueous liquid and the second dialysate concentrate,

where providing the physiologically acceptable aqueous liquid to the second region inflates the second region and breaks the second breakable barrier, thereby allowing fluid communication with the third region;

- (iic2) providing further physiologically acceptable aqueous liquid through the first inlet/outlet port to form a third intermediate dialysis fluid from the second intermediate dialysis fluid, further physiologically acceptable aqueous liquid and the third dialysate concentrate; and
- (iid2) mixing the third intermediate dialysis fluid to form a dialysis fluid suitable for direct administration to a patient.

19. A system for preparing a peritoneal dialysis fluid comprising:

- (i) a source of physiologically acceptable aqueous liquid (e.g. water for injection);
- (ii) a dialysate bag comprising one or more dialysate concentrates; and
- (iii) a fluid connection between the source of physiologically acceptable aqueous liquid and dialysate bag,

where the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection together form a fluid flow path consisting of the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection, and wherein:

the fluid connection is connected to a first inlet/outlet port of the dialysate bag; and

the dialysate bag comprises a second inlet/outlet port fluidly connected to the fluid connection *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, dialysate bag, second inlet/outlet port, external connection and fluid connection.

20. A method of preparing a peritoneal dialysis fluid comprising the steps:

- (a) providing a system comprising:
 - (i) a source of physiologically acceptable aqueous liquid (e.g. water for injection);
 - (ii) a dialysate bag comprising one or more dialysate concentrates; and
 - (iii) a fluid connection between the source of physiologically acceptable aqueous liquid and dialysate bag,

where the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection together form a fluid flow path consisting of the source of physiologically acceptable aqueous liquid, dialysate bag and fluid connection;

- (b) providing physiologically acceptable aqueous liquid from the source of physiologically acceptable aqueous liquid to the dialysate bag and mixing the physiologically acceptable aqueous liquid with the dialysate concentrate to form a dialysis fluid, wherein:

- (1) the fluid connection is connected to a first inlet/outlet port of the dialysate bag; and the dialysate bag comprises a second inlet/outlet port fluidly connected to the fluid connection *via* an external connection so as to form a circulating fluid flow path through the first inlet/outlet port, dialysate bag, second inlet/outlet port, external connection and fluid connection, and where step (b) comprises recirculating the physiologically acceptable aqueous liquid and dialysate concentrate around the circulating fluid flow path to form a dialysis fluid; or
- (2) step (b) comprises mixing the physiologically acceptable aqueous liquid with the dialysate concentrate manually; by using an orbital shaker or vibrating table; or by using a robotic arm.