

ASEPTIC BIOPROCESS PACKAGE

CROSS-REFERENCE FOR RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Provisional Application Serial No. 62/477,647 filed on March 28, 2017 and U.S. Provisional Application Serial No. 62/640,097 filed March 8, 2018 the contents of which are relied upon and incorporated herein by reference in their entirety as if fully set forth below.

FIELD

[0002] The present disclosure generally relates to bioprocess bags for cell culture and systems employing the same. In particular, the present disclosure relates to bioprocess bags having a channel-forming feature that facilitates removal of fluid and/or other components from the interior compartment of the bioprocess bag.

BACKGROUND

[0003] Bags containing fluids under sterile conditions are used in the bioprocessing industry for the formulation, storage, transfer and transport of fluid while maintaining sterile conditions. Some of the characteristics of the bags to preserve the quality of the products contained within include biocompatibility with the products, sterility, and non-pyrogenicity. The bags are typically disposed of after use and are recognized as efficient means to prepare and store sterile fluids. Generally, these disposable bioprocessing bags are flexible and made from compatible plastic that is sterilized by Gamma radiation. The bags can be used for all bioprocessing applications including, but not limited to, formulating, filling, storing and transporting final product, stocking pharmaceuticals in cold storage or deep freeze and for sampling and analytical purposes. The bags may also provide an environment for cell culture. Additionally, the bags may be used for biological fluids such as serum, buffers, and ultrapure water and also for growing cell cultures to obtain the valuable biopharmaceutical compounds produced by cells.

[0004] For cell culture it is conventional to grow cells on a cell adhering surface since most mammalian cells and certain other cells are anchorage-dependent to be able to grow. In contrast to cell culture on flat surfaces where adherent cells can reach high confluence and thus limit cell expansion via cell-to-cell contact inhibition, spherically-shaped microcarriers

having a high ratio of surface area/volume present an attractive platform for efficient cell culture scale-up or expansion where either harvested cells, cell-based products, or conditioned media can be the desired product. While microcarriers formed from plastic materials have previously been used for cell culture, dissolvable microcarriers, or microcarriers which are enzymatically digested to separate cells from the surface of the microcarrier, are providing certain advantages in cell culture applications.

[0005] Cell culture materials, including microcarriers, are preferably sterile. However, the emphasis on sterility in the bioprocessing industry has given rise to a demand for the ability to aseptically transfer pre-sterilized microcarriers into a bioreactor without compromising sterility and to perform most phases of cell growth in a closed system. As used herein, the term “closed system” refers to a system sealed to ensure sterility of the contents of the system and to limit or prevent the introduction of contaminants from the surrounding atmosphere. Conventionally, microcarriers are sterilized through autoclaving prior to adding the microcarriers to a bioreactor. Gamma sterilization, due to its process efficiency and depth of penetration, may also be a useful method for disinfecting dissolvable microcarriers. However, the presence of water or humidity during gamma sterilization creates undesired free radicals, which can damage cells. It is thus contemplated that dissolvable microcarriers be dried prior to sterilization and then rehydrated after sterilization. Thus, there is also a demand for the ability to rehydrate and wash dissolvable microcarriers and to aseptically transfer the rehydrated dissolvable microcarriers into a bioreactor without compromising sterility.

SUMMARY

[0006] According to an embodiment of the present disclosure, an aseptic bioprocess package is provided. The aseptic bioprocess package includes a 2D flexible container having an interior compartment, a height having an upper half and a lower half, an inlet and an outlet, the inlet and the outlet being disposed on the same half of the 2D flexible container and a channel-forming feature in the interior compartment of the container, the channel-forming feature being configured to maintain a fluid flow path that fluidly connects the interior compartment of the flexible container with the outlet.

[0007] According to an embodiment of the present disclosure, a method for processing dry microcarrier material in an aseptic bioprocess package is provided. The

method includes filling a bioprocess package with dry microcarrier material. The bioprocess package includes a 2D flexible container having an interior compartment, a height having an upper half and a lower half, an inlet and an outlet, the inlet and the outlet being disposed on the same half of the 2D flexible container, and a channel-forming feature in the interior compartment of the container, the channel-forming feature being configured to maintain a fluid flow path that fluidly connects the interior compartment of the flexible container with the outlet. The method further includes sterilizing the dry microcarrier material in the bioprocess package, hydrating the dry microcarrier material in the bioprocess package to form a hydrated microcarrier material, washing the hydrated microcarrier material in the bioprocess package, and aseptically transferring the hydrated microcarrier material from the bioprocess package to a cell culture vessel.

[0008] It is to be understood that both the foregoing general description and the following detailed description are merely exemplary, and are intended to provide an overview or framework to understanding the nature and character of the claims. The accompanying drawings are included to provide a further understanding, and are incorporated in and constitute a part of this specification. The drawings illustrate one or more embodiment(s), and together with the description serve to explain principles and operation of the various embodiments.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] The disclosure will be understood more clearly from the following description and from the accompanying figures, given purely by way of non-limiting example, in which:

[0010] Figure 1 illustrates an exemplary bioprocess bag having a channel-forming feature in accordance with embodiments of the present disclosure;

[0011] Figure 2A is a schematic illustration of a bioprocess bag having a channel-forming feature in accordance with embodiments of the present disclosure;

[0012] Figure 2B is a schematic illustration showing a side view of the bioprocess bag having a channel-forming feature of Figure 2A;

[0013] Figure 2C is a schematic illustration showing an enlarged and exaggerated top view of the bioprocess bag having a channel-forming feature of Figure 2B;

[0014] Figure 3A is a schematic illustration of a bioprocess bag having a channel-forming feature in accordance with embodiments of the present disclosure;

[0015] Figure 3B is a schematic illustration of a port fitment having a channel-forming feature attached thereto in accordance with embodiments of the present disclosure;

[0016] Figure 3C is a cross sectional view of the port fitment of Figure 3B sectioned along line 1-1' of Figure 3B;

[0017] Figure 4A is a schematic illustration of a bioprocess bag having a channel-forming feature in accordance with embodiments of the present disclosure;

[0018] Figure 4B is a schematic illustration showing a side view of a bioprocess bag having a channel-forming feature of Figure 4A;

[0019] Figure 5 illustrates an exemplary port fitment in accordance with embodiments of the present disclosure;

[0020] Figure 6 illustrates a cross section of an exemplary port fitment in accordance with embodiments of the present disclosure;

[0021] Figure 7 illustrates an exemplary channel-forming feature extender in accordance with embodiments of the present disclosure;

[0022] Figure 8 illustrates an exemplary channel-forming feature extender in accordance with embodiments of the present disclosure;

[0023] Figure 9 illustrates an exemplary channel-forming feature extender in accordance with embodiments of the present disclosure;

[0024] Figure 10 is a flow chart illustrating a method in accordance with embodiments of the present disclosure;

[0025] Figure 11A is a schematic illustration of a bioprocess bag having a channel-forming feature in accordance with embodiments of the present disclosure;

[0026] Figure 11B is a schematic illustration showing a side view of a bioprocess bag having a channel-forming feature of Figure 11A; and

[0027] Figure 12 illustrates an exemplary face port in accordance with embodiments of the present disclosure.

DETAILED DESCRIPTION

[0028] Reference will now be made in detail to the present embodiment(s), an example(s) of which is/are illustrated in the accompanying drawings. Whenever possible, the same reference numerals will be used throughout the drawings to refer to the same or like parts.

[0029] The singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. The endpoints of all ranges reciting the same characteristic are independently combinable and inclusive of the recited endpoint. All references are incorporated herein by reference.

[0030] As used herein, "have," "having," "include," "including," "comprise," "comprising" or the like are used in their open ended sense, and generally mean "including, but not limited to."

[0031] All scientific and technical terms used herein have meanings commonly used in the art unless otherwise specified. The definitions provided herein are to facilitate understanding of certain terms used frequently herein and are not meant to limit the scope of the present disclosure.

[0032] The present disclosure is described below, at first generally, then in detail on the basis of several exemplary embodiments. The features shown in combination with one another in the individual exemplary embodiments do not all have to be realized. In particular, individual features may also be omitted or combined in some other way with other features shown of the same exemplary embodiment or else of other exemplary embodiments.

[0033] Embodiments of the present disclosure relate to bioprocess bags. The bioprocess bags described herein are 2D bags formed from flexible materials. As used herein, the term "2D bag" refers to a flat, rectangular, "pillow-style" bag formed by seaming together two flexible sheets. Bioprocess bags in accordance with embodiments of the present disclosure are formed from disposable materials and may be discarded after a single use, thereby eliminating washing/sterilizing operations as well as maintenance associated with

conventional cell culture vessels. The bioprocess bags described herein advantageously allow for one or more of sterilizing microcarrier material, transporting the sterilized microcarrier material, hydrating the sterilized microcarrier material, washing the sterilized microcarrier material and aseptically transferring the microcarrier material from the bag to a cell culture vessel, such as, for example, a bioreactor. With the bioprocess bags described herein, such actions can be taken without exposing the microcarrier material to the surrounding atmosphere.

[0034] Figure 1 illustrates a bioprocess bag in accordance with embodiments of the present disclosure. As shown, the bioprocess bag **100, 1100** includes at least two sheets **102, 104** formed from films or laminates. The sheets **102, 104** are hermetically sealed (for example by welding or by an adhesive) along the edges of the sheets to form a pillow-shaped bag having an interior compartment for receiving fluid. The bioprocess bag **100, 1100** preferably provides a closed system for use in all phases of processing fluid and/or other components. Figure 1 illustrates an exemplary configuration of a bioprocess bag formed from two sheets **102, 104** that are longer than they are wide and, when attached along their edges, form a bioprocess bag **100, 1100** having two sides, a top and a bottom where the two sides are longer than the top and the bottom are wide. It should be understood that this is just an exemplary configuration, and that the bioprocess bag as described herein may have a top, a bottom and two sides having equal lengths. The bioprocess bag **100, 1100** is described herein as having two sides, a top and a bottom. However, it should be understood that the terms “top”, “bottom”, “side” and the like are used herein for descriptive purposes and not necessarily for describing permanent relative positions. It should be understood that the terms so used are interchangeable under appropriate circumstances such that embodiments of the present disclosure are, for example, capable of operation in other orientations than those illustrated or otherwise described herein.

[0035] As used herein, the term “fluid” refers to any substance capable of flowing, such as liquids, liquid suspensions, gases, gaseous suspensions, or the like, without limitation. The term “fluid and/or other components” is used throughout the present disclosure to refer to fluid which may include cell culture media having nutrients for cell growth, cells, byproducts of the cell culture process, and any other biological materials or components that may conventionally be added or formed in a bioprocess system. Bioprocess bags and other vessels described herein may include one or more cells or reagents. The bags may also

include buffers. Additionally, the bags may include cell culture media. Cell culture media may be for example, but is not limited to, sugars, salts, amino acids, serum (e.g., fetal bovine serum), antibiotics, growth factors, differentiation factors, colorant, or other desired factors. Common culture media that may be provided in the bag includes Dulbecco's Modified Eagle Medium (DMEM), Ham's F12 Nutrient Mixture, Minimum Essential Media (MEM), RPMI Medium, and the like. Any type of cultured cell may be included in the bag including, but not limited to, immortalized cells, primary culture cells, cancer cells, stem cells (e.g., embryonic or induced pluripotent), etc. The cells may be mammalian cells, avian cells, piscine cells, etc. The cells may be of any tissue type including, but not limited to, kidney, fibroblast, breast, skin, brain, ovary, lung, bone, nerve, muscle, cardiac, colorectal, pancreas, immune (e.g., B cell), blood, etc. The cells may be in any cultured form in the bag including disperse (e.g., freshly seeded), confluent, 2-dimensional, 3-dimensional, spheroid, etc. In some embodiments, cells are present without media (e.g., freeze-dried, in preservative, frozen, etc.). As will be described in further detail below, bioprocess bags and other vessels described herein may also include microcarrier material.

[0036] Each of the sheets **102, 104** of the bioprocess bag **100, 1100** may be formed from one or more of the same or different materials. Such materials are those conventionally associated with disposable products for bioprocess applications. Any or all of the sheets **102, 104** of the bioprocess bag **100, 1100** may be formed from a film or laminate that includes at least one plastic material from the following group: polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polystyrene (PS), polycarbonate (PC), polymethylpentene (PMP), polyetheretherketone (PEEK) polytetrafluoroethylene (PTFE), polyfluoroalkoxy (PFA), polychlorotrifluoroethylene (PCTFE) , ethylene vinyl acetate (EVA), and derivatives thereof.

[0037] It should be understood that the dimensions of the bioprocess bag **100, 1100** including both relative and absolute dimensions can be varied. For example, the bags may be configured to hold a volume of fluid and/or other components of about 1.0 mL, or about 5.0 mL, or about 10 mL, or about 25 mL, or about 50 mL, or about 100 mL, or about or about 250 mL, or about 500 mL, or about 1.0 L, or 5.0 L, or about 10 L, or about 50 L, or about 100 L, or about 150 L or even about 200 L, as well as all volumes therein between.

[0038] Total thickness of the film or laminate may be selected, for example, based on the desired gas permeability of the bioprocess bag **100, 1100** or based on the desired rigidity

or flexibility of the bag **100, 1100**. For example, the thickness of sheets **102, 104** may be between about 0.002 inches and about 1.5 inches. As described herein, the thickness of sheet **102** and sheet **104** may be the same or different.

[0039] The bioprocess bag **100, 1100** is hermetically sealed and may have one or more openings for introducing or recovering fluid and/or other components. Where the bioprocess bag **100, 1100** includes one or more openings, the one or more openings may include seals that in a first configuration expose the one or more openings to aseptic fluid communication between an external container and the interior compartment of the bag through the opening. In a second configuration, the seals close the one or more openings and prevent or reduce fluid communication between the outside of the bag and the interior compartment of the bag through the opening. The seals may take any desired form, including, but not limited to, a clamp, tape, a cap, a tube portion having a welded end, a zipper, a slide zipper, interlocking or coupling structures, aseptic connectors and the like.

[0040] Bioprocess bags **100, 1100** as described herein include at least one connection apparatus which includes an internal fluid passage that permits the flow of fluids and/or other components into or out of the interior compartment of the bioprocess bag **100, 1100**. With further reference to Figure 1, the at least one connection apparatus may be at least one connector **140** which includes an internal fluid passage that permits the flow of fluids and/or other components into or out of the interior compartment of the bioprocess bag **100**. The at least one connector **140** includes a proximal end and a distal end and extends through an opening formed in a portion of the sealed edge of the bioprocess bag **100**. The proximal end of the at least one connector **140** may extend through the opening and into the interior compartment of the bioprocess bag **100**. Alternatively, without extending into the interior compartment of the bioprocess bag **100**, the proximal end of the at least one connector **140** may be positioned in the opening such that flow of fluids and/or other components into or out of the interior compartment of the bioprocess bag **100** is permitted. At least a portion of the film or laminate of the sheets **102, 104** is heat sealed, or otherwise adhered, around the at least one connector **140** such that the bioprocess bag **100** is hermetically sealed.

[0041] With reference to Figures 11A and 11B, the at least one connection apparatus may be at least one outwardly facing face port **1140** which includes an internal fluid passage that permits the flow of fluids and/or other components into or out of the interior compartment of the bioprocess bag **1100**. The outwardly facing face port **1140** may be

formed in a face of at least one of sheets **102**, **104**. As shown in Figure 12, the at least one face port **1140** may include a base flange **1150** having a top surface **1152** and a bottom surface **1154**. At least a portion of the film or laminate of one of sheet **102** and sheet **104** is welded, heat sealed, or otherwise adhered to the base flange **1150** of at least one face port **1140** such that the bioprocess bag **1100** is hermetically sealed. The at least one face port **1140** further includes an extension **1144** that extends a predetermined length from the base flange **1150** and is configured to engage an open end of a length of tubing. The extension **1144** may include a coupler, such as a barb **1160**, at one end to facilitate engagement with an open end of tubing. According to embodiments of the present disclosure, the at least one face port **1140** is configured such that the extension **1144** extends to an external side of the bioprocess bag **1100** and not into the interior compartment of the bioprocess bag **1100**. One of sheet **102** and sheet **104** may be welded, heat sealed, or otherwise adhered to the top surface **1152** of the base flange **1150**. Alternatively, one of sheet **102** and sheet **104** may be welded, heat sealed, or otherwise adhered to the bottom surface **1154** of the base flange **1150**. As used herein, the term “face port” refers to a port that is located on the face of at least one of sheet **102** and sheet **104** rather than on an edge or seam of the bioprocess bag **100**, **1100**. Also as used herein, the term “outwardly facing face port” refers to a face port having an extension which extends from a sheet to an external side of the bioprocess bag and not into the interior compartment of the bioprocess bag. In contrast, as used herein, the term “inwardly facing face port” refers to a face port having an extension which extends from a sheet to into the interior compartment of the bioprocess bag.

[0042] The at least one connector **140** or the at least one face port **1140** may be a relatively rigid plastic component formed from, for example, but not limited to, high density polypropylene (HDPP), polypropylene, high density polyethylene (HDPE), polyethylene, EVA, LDPE and LLDPE. Optionally, the at least one connector **140** may be flexible plastic tubing. Where the at least one connector **140** is a relatively rigid plastic component, the distal end of the at least one connector **140** is configured to engage an open end of a length of tubing which aseptically fluidly connects the at least one connector **140** to a separate length of tubing (i.e., through an aseptic connector) or to a connection apparatus of an external container. Similarly, where the at least one face port **1140** is a relatively rigid plastic component, the extension **1144** is configured to engage an open end of a length of tubing which aseptically fluidly connects the at least one face port **1140** to a separate length of tubing (i.e., through an aseptic connector) or to a connection apparatus of an external

container. Where the at least one connector **140** is flexible plastic tubing, the at least one connector **140** may be aseptically fluidly connected to a separate length of tubing (i.e., through an aseptic connector) or to a connection apparatus of an external container. The seals described above may interact with, or be connected to, the at least one connector **140**, the extension **1144** and/or the separate length of tubing to selectively permit or prevent fluid communication between the interior compartment of the bag **100**, **1100** and an external container.

[0043] The bioprocess bag **100** may include a plurality of connectors **140**, such as connectors **140a**, **140b** and **140c** shown, for example, in Figure 1. The dimensions of the plurality of connectors **140** may be equal, or the dimensions of each of the plurality of connectors **140** may vary. It is also contemplated that the dimensions of at least two of the plurality of connectors **140** may be equal and at least one other of the plurality of connectors **140** differs from the dimensions of the at least two of the plurality of connectors **140**. Where the at least one connector **140** is a relatively rigid plastic connector, the at least one connector **140** may include a coupler configured to hold the at least one connector **140** in the bioprocess bag **100**. The coupler may be a portion having any shape that extends from an outer wall of the at least one connector **140** around which portions of the film or laminate of sheets **102**, **104** may be heat sealed. The coupler may be, for example, a barb, a plastic ring, or a plastic flange. The coupler may be integrally formed with the at least one connector **140** or may be separately formed and attached to the at least one connector **140**. Where the bioprocess bag **100** includes a plurality of connectors **140a**, **140b**, **140c** with a first of the connectors **140** being an inlet and a second of the connectors **140** being an outlet, the inlet and the outlet are arranged on the same side of the bioprocess bag **100** (i.e., at the top of the bag). Optionally, a bioprocess bag **100** having more than two connectors **140** may include any number of connectors **140** arranged on any side of the bioprocess bag **100** so long as two of the connectors **140** are located on the same side of the bag with a first of the two connectors **140** being an inlet and a second of the two connectors **140** being an outlet. Referring once again to Figure 1 as an example, connector **140a** may be an inlet and connector **140c** may be an outlet.

[0044] The bioprocess bag **1100** may include a plurality of face ports **1140**, such as face ports **1140a**, **1140b** and **1140c** shown, for example, in Figures 11A and 11B. The dimensions of the plurality of face ports **1140** may be equal, or the dimensions of each of the

plurality of face ports **1140** may vary. It is also contemplated that the dimensions of at least two of the plurality of face ports **1140** may be equal and at least one other of the plurality of face ports **1140** differs from the dimensions of the at least two of the plurality of face ports **1140**. Where the bioprocess bag **1100** includes a plurality of face ports **1140a**, **1140b**, **1140c** with a first of the face ports **1140** being an inlet and a second of the face ports **1140** being an outlet, the inlet and the outlet are arranged on the same half of the height of the bioprocess bag **1100** (i.e., an upper half of a sheet **102**, **103** of the bag). Optionally, a bioprocess bag **1100** having more than two face ports **1140** may include any number of face ports **1140** arranged on any side of the bioprocess bag **1100** so long as two of the face ports **1140** are located on the same side of the bag with a first of the two face ports **1140** being an inlet and a second of the two face ports **1140** being an outlet. Referring once again to Figures 11A and 11B as an example, face port **1140a** may be an inlet and face port **1140b** may be an outlet.

[0045] According to embodiments of the present disclosure, the at least one connection apparatus may be a port fitment **40**, such as the port fitment **40** shown in Figure 5, having at least one port **42** that permits the flow of fluids and/or other components into or out of an interior compartment of the bioprocess bag **100**. As shown in Figure 6, the at least one port **42** is in fluid communication with an interior passage of an extension **44** that extends a predetermined length from an opening of the at least one port **42** and is configured to engage an open end of a length of tubing. The extension **44** may include a coupler, such as a barb, at one end to facilitate engagement with an open end of tubing. The port fitment **40** may include a plurality of ports **42**. The dimensions of the plurality of ports **42** may be equal for each of the plurality of ports **42**, or the dimensions of each of the plurality of ports **42** may vary. It is also contemplated that the dimensions of at least two of the plurality of ports **42** may be equal and at least one other of the plurality of ports **42** differs from the dimensions of the at least two of the plurality of ports **42**. According to embodiments of the present disclosure, the port fitment **40** may be any shape. The exemplary port fitment **40** illustrated in the figures is a boat shaped port fitment, but the port fitment **42** disclosed herein is not so limited. The port fitment **40** may be a plastic port fitment formed from, for example, but not limited to, high density polypropylene (HDPP), polypropylene, high density polyethylene (HDPE), polyethylene, EVA, LDPE and LLDPE.

[0046] Connection is formed between a polymer layer of the film or laminate of the sheets **102**, **104** and the port fitment **40** to form a hermetic seal between the bag **100** and the

port fitment **40**. As shown in Figure 6, the port fitment **40** includes an exterior surface **54** and an interior surface **52**. Connection between the bioprocess bag **100** and the port fitment **40** may be along any one of the exterior surface **54** and the interior surface **52**. The connection may be made by welding or any other type of attachment, such that, with the exception of the at least one port **42**, a fluid-impervious seal is formed between the port fitment **40** and the bioprocess bag **100**.

[0047] According to embodiments of the present disclosure, the bioprocess bag **100**, **1100** includes a channel-forming feature. A problem encountered when dispensing the contents of flexible bags is that portions of the sheets of the bags can collapse into contact with each other to form sealed pockets as the volume of the bag shrinks. The channel-forming feature described herein prevents the sheets **102**, **104** of the bioprocess bag **100**, **1100** from sealing off portions of the bag **100**, **1100** and/or from isolating the fluid and/or other components in the bag **100**, **1100** from reaching an outlet. The channel-forming feature prevents the bag **100**, **1100** from closing on itself, thus providing a fluid flow path for the contents of the bag **100**, **1100** to reach an outlet.

[0048] As shown in Figures 2A-2C, the channel-forming feature as described herein may be a solid extruded plastic component **120** that extends from a first end **171** to a second end, **172** the second end **172** being disposed in the interior compartment of the bioprocess bag **100**. The first end **171** of the solid extruded plastic component **120** may be welded into a seam of the bioprocess bag **100**, for example, into the top seam of the bioprocess bag **100**. Alternatively, the first end **171** of the solid extruded plastic component **120** may be disposed in one of the plurality of connectors **140**. Similarly, where the at least one connection apparatus is a port fitment **40** as described herein, the first end **171** of the solid extruded plastic component **120** may be disposed within one of the plurality of ports **42**. The solid extruded plastic component **120** extends into the interior compartment of the bioprocess bag **100** a distance sufficient to prevent the sheets **102**, **104** of the bioprocess bag **100** from sealing off portions of the bag **100** and/or from isolating the fluid and/or other components in the bag **100** from reaching an outlet. According to embodiments of the present disclosure, the solid extruded plastic component **120** may have a length such that it spans at least about half the distance between the top of the bioprocess bag **100** and the bottom of the bioprocess bag **100**. In other words, the solid extruded plastic component **120** may have a length that is at least about half the length of the sheets **102**, **104** of the bioprocess bag **100**, but preferably

less than the full length of the sheets **102, 104** of the bioprocess bag **100**. For example, where the length of the sheets **102, 104** is represented by “L”, the solid extruded plastic component **120** may have a length that is between about 0.5L and about 0.95L, or between about 0.5L and about 0.85L, or even between about 0.5L and about 0.75L. The solid extruded plastic component **120** may have any cross-sectional shape such as round, square or rectangular. The solid extruded plastic component **120** may also have a shape that advantageously provides additional channels through which fluid may flow. For example, the solid extruded plastic component **120** may have a star-shaped cross-section.

[0049] As shown in Figures 3A-3C, the channel-forming feature as described herein may be a tubular plastic component **122** (such as a portion of tubing) that extends from a first end **173** to a second end **174**, the second end **174** being disposed in the interior compartment of the bioprocess bag **100**. The first end **173** of the tubular plastic component **122** may be welded into a seam of the bioprocess bag **100**, for example, into the top seam of the bioprocess bag **100**. Alternatively, as shown in Figure 3A, the first end **173** of the tubular plastic component **122** may be attached to, or disposed in, one of the plurality of connectors **140**. Similarly, as shown in Figures 3B and 3C, where the at least one connection apparatus is a port fitment **40** as described herein, the first end **173** of the tubular plastic component may be attached to, or disposed within, one of the plurality of ports **42**. Such arrangement also allows the channel-forming feature to form a conduit which cannot be closed off by exertion of a pressure on sheets **102, 104** as the bioprocess bag **100** collapses. The second end **174** of the tubular plastic component **122** may be a closed end, or may include a plug inserted in the end of the tubular plastic component **122** to isolate the interior of the tubular plastic component **122** from the contents of the interior compartment of the bioprocess bag **100**. The tubular plastic component **122** extends into the interior compartment of the bioprocess bag **100** a distance sufficient to prevent the sheets **102, 104** of the bioprocess bag **100** from sealing off portions of the bag **100** and/or from isolating the fluid and/or other components in the bag **100** from reaching an outlet. According to embodiments of the present disclosure, the tubular plastic component **122** may have a length such that it spans at least about half the distance between the top of the bioprocess bag **100** and the bottom of the bioprocess bag **100**. In other words, the tubular plastic component **122** may have a length that is at least about half the length of the sheets **102, 104** of the bioprocess bag **100**, but preferably less than the full length of the sheets **102, 104** of the bioprocess bag **100**. For example, where the length of the sheets **102, 104** is represented by “L”, the tubular plastic

component **122** may have a length that is between about 0.5L and about 0.95L, or between about 0.5L and about 0.85L, or even between about 0.5L and about 0.75L.

[0050] As shown in Figures 4A and 4B, the channel-forming feature as described herein may be a raised portion **124** which extends from an interior face of at least one of sheet **102** and sheet **104** into the interior compartment of the bioprocess bag **100**. The raised portion **124** may be a textured portion of the interior face of at least one of sheet **102** and sheet **104**. As used herein, the term “textured” refers to surface deformations (relative to a planar untextured sheet) as well as multiple surface regions or faces produced by uniaxial or biaxial folding, shaping, or the like that are intentionally imparted to the surface rather than merely the texture that is inherently present on the surface due to the natural topography of the surface, surface contamination, and the like. Alternatively, the raised portion **124** may be a plastic component attached, using an adhesive or via heat sealing, to the interior face of the sheet **102**, **104** which is more rigid than the film or laminate of sheets **102**, **104**. Such plastic component may be formed from, for example, but not limited to, high density polypropylene (HDPP), polypropylene, high density polyethylene (HDPE), polyethylene, EVA, LDPE and LLDPE. While these materials do have some inherent flexibility when used to form relatively thin components or when a moderate amount of bending force is applied thereto, the raised portion **124** is distinguished from the flexible portions of the bioprocess bag **100** in that the raised portion **124** generally maintains its shape when a force is applied to dispense the contents of the bioprocess bag **100**.

[0051] As shown in Figure 4A and 4B, The raised portion **124** may extend along any portion of the interior face of at least one of sheet **102** and sheet **104** a distance sufficient to prevent the sheets **102**, **104** of the bioprocess bag **100** from sealing off portions of the bag **100** and/or from isolating the fluid and/or other components in the bag **100** from reaching an outlet. The raised portion **124** shown in Figures 4A and 4B extends from a first end **175** to a second end **176** along the interior face of at least one of sheet **102** and sheet **104** from approximately the top of the bioprocess bag **100** and to at least about half the distance between the top of the bioprocess bag **100** and the bottom of the bioprocess bag **100**. The raised portion **124** shown in Figures 4A and 4B extends from approximately the top of the bioprocess bag **100** along the interior face of at least one of sheet **102** and sheet **104** and is substantially straight. However, the raised portion **124** is not so limited. The raised portion **124** as describe herein may have any shape, or may follow any path extending from

approximately the top of the bioprocess bag **100** along the interior face of at least one of sheet **102** and sheet **104**. For example, the raised portion **124** may extend in a curved or circuitous path from approximately the top of the bioprocess bag **100**. Additionally, while the bioprocess bag **100** shown in Figures 4A and 4B includes one raised portion **124**, bioprocess bags **100** as described herein may include any number of a plurality of raised portions **124** having any dimensions. Also, as a non-limiting example, the interior face of at least one of sheet **102** and sheet **104** may include a plurality of individual and distinct raised portions **124** of the same or varying dimensions which form a pattern on the interior face of at least one of sheet **102** and sheet **104**. Such pattern may generally extend from approximately the top of the bioprocess bag **100**.

[0052] As shown in Figures 11A and 11B, the channel-forming feature as described herein may be a tubular plastic component **1120** (such as a portion of tubing) that extends from a first end **1171** to a second end **1172**. The bioprocess bag **1100** may include a plurality of inwardly facing face ports **1180**, such as face ports **1180a** and **1180b** shown, for example, in Figures 11A and 11B. Figure 11B illustrates the bioprocess bag **1100** without the tubular plastic component **1120** to more clearly show the inwardly facing face ports **1180**. The inwardly facing face ports **1180** have all of the same features as the outwardly facing face ports **1140** such as illustrated in Figure 12. In contrast to outwardly facing face ports **1140**, inwardly facing face ports **1180** provide an extension **1144** into the interior compartment of the bioprocess bag **1100**, but do not permit the flow of fluids and/or other components into or out of the interior compartment of the bioprocess bag **1100**. Optionally, one of sheet **102** and sheet **104** may be welded, heat sealed, or otherwise adhered to the bottom surface **1154** of the base flange **1150** such that the internal fluid passage of the face ports **1180** is closed to the external side of the bioprocess bag **1100**. Figure 11A illustrates the bioprocess bag **1100** with the tubular plastic component **1120** and, as shown, the first end **1171** of the tubular plastic component **1120** may be attached to, or disposed in, an extension **1144** of one of the face ports **1180a** and the second end **1172** of the tubular plastic component **1120** may be attached to, or disposed in, an extension **1144** of another of the face ports **1180b**. Optionally, the first end **1171** of the tubular plastic component **1120** may be welded or sealed to the extension **1144** of one of the face ports **1180** and the second end **1172** of the tubular plastic component **1120** may be welded or sealed to the extension **1144** of another of the face ports **1180**.

[0053] As shown in Figures 11A and 11B, at least two of the outwardly facing face ports **1140** are disposed between the inwardly facing face ports **1180**. In Figure 11A, outwardly facing face ports **1140a**, **1140b**, are disposed on substantially the same line with the inwardly facing face ports **1180a**, **1180b**, but it should be appreciated that such a configuration is not required. The outwardly facing face ports **1140a**, **1140b** may be disposed anywhere along the height of the bioprocess bag **1100** that is between face port **1180a** and face port **1180b** so long as the channel-forming feature can form a conduit which cannot be closed off by exertion of a pressure on sheets **102**, **104** as the bioprocess bag **1100** collapses. The distance between face port **1180a** and face port **1180b** is sufficient to prevent the sheets **102**, **104** of the bioprocess bag **1100** from sealing off portions of the bag **1100** and/or from isolating the fluid and/or other components in the bag **1100** from reaching an outlet. According to embodiments of the present disclosure, the distance between face port **1180a** and face port **1180b** may be at least about half the height of the bioprocess bag **1100**. In other words, the distance between face port **1180a** and face port **1180b** may be at least about half the length of the sheets **102**, **104** of the bioprocess bag **1100**, but preferably less than the full length of the sheets **102**, **104** of the bioprocess bag **1100**. For example, where the length of the sheets **102**, **104** is represented by “L”, the distance between face port **1180a** and face port **1180b** may be between about 0.5L and about 0.95L, or between about 0.5L and about 0.85L, or even between about 0.5L and about 0.75L.

[0054] Figures 7-9 illustrate exemplary channel-forming feature extenders which are configured to receive, or be otherwise associated with, a channel-forming feature as described herein. Each of the channel-forming feature extenders shown in Figures 7-9 are plastic components which extend from a first end to a second end, the second end being disposed in the interior compartment of the bioprocess bag **100**. The first end of extender **500**, **600**, **700** is configured to be attached to, or disposed in, at least one of the plurality of connectors **140** or attached to, or disposed in, at least one of the plurality of ports **42** of a port fitment **40**. Each of extenders **500**, **600**, **700** includes an opening **510**, **610**, **710** disposed between the first end and the second end of the channel-forming feature **500**, **600**, **700**. Each of extenders **500**, **600**, **700** also includes a lower extension **520**, **620**, **720** which extends between the opening **510**, **610**, **710** and the second end. As will be described in greater detail below, the lower extension **520**, **620**, **720** is configured to receive, or be otherwise associated with, a channel-forming feature such as solid extruded plastic component **120** shown in Figures 1 and 2A-2C, or tubular plastic component **122** shown in Figures 3A-3C. Each of extenders **500**, **600**, **700**

also includes an upper extension **530, 630, 730** which extends between the opening **510, 610, 710** and the first end and which has an interior channel which fluidly connects the opening **510, 610, 710** to the at least one connection apparatus of the bioprocess bag **100**. Extenders **600, 700** also include side extensions **640, 740** which include interior channels that fluidly connect the opening **610, 710** and the interior channel of the upper extension **630, 730**. Generally, the extenders as described herein further facilitate providing a fluid flow path for the contents of the bioprocess bag **100** to reach an outlet.

[0055] The channel-forming feature extender **500** shown in Figure 7 is a straight component that includes an opening **510** formed in a sidewall. The opening **510** is positioned between the lower extension **520** and the upper extension **530**. The upper extension **530** includes an interior channel which fluidly connects the opening **510** to the at least one connection apparatus of the bioprocess bag **100**. The lower extension **520** may be a solid portion of the channel-forming feature **500**, or may also include an interior channel. A channel-forming feature, such as tubular plastic component **122**, may be attached to the lower extension **520**. Where the lower extension **520** includes an interior channel, the end of the lower extension **520** remote from the opening **510** may be a closed end, or may include a plug inserted in the end to prevent fluid and/or other components from flowing into the interior channel. Optionally, a channel-forming feature, such as solid extruded plastic component **120** may be disposed in the interior channel of the lower extension **520**.

[0056] The channel-forming feature extender **600** shown in Figure 8 is a Y-component where one of the legs of the Y is the lower extension **620** and the other leg of the Y is the side extension **640**. The side extension **640** may be shorter in length than the lower extension **620** and includes opening **610** formed in the end of side extension **640**. The upper extension **630** includes an interior channel which fluidly connects the opening **610** via the interior channel of the side extension **640** to the at least one connection apparatus of the bioprocess bag **100**. The lower extension **620** may be a solid portion of the channel-forming feature **600**, or may also include an interior channel. A channel-forming feature, such as tubular plastic component **122**, may be attached to the lower extension **620**. Where the lower extension **620** includes an interior channel, the end of the lower extension **620** remote from the intersection of extensions **620, 630, 640** may be a closed end, or may include a plug inserted in the end to prevent fluid and/or other components from flowing into the interior

channel. Optionally, a channel-forming feature, such as solid extruded plastic component **120** may be disposed in the interior channel of the lower extension **620**.

[0057] The channel-forming feature extender **700** shown in Figure 9 is a Tee-component having a side extension **740** extending at a 90 degree angle from the lower extension **720** and the upper extension **730** which together form a straight portion of the feature **700**. The side extension **740** includes opening **710** formed in the end of side extension **740**. The upper extension **730** includes an interior channel which fluidly connects the opening **710** via the interior channel of the side extension **740** to the at least one connection apparatus of the bioprocess bag **100**. The lower extension **720** may be a solid portion of the channel-forming feature **700**, or may also include an interior channel. A channel-forming feature, such as tubular plastic component **122**, may be attached to the lower extension **720**. Where the lower extension **720** includes an interior channel, the end of the lower extension **720** remote from the intersection of the various extensions may be a closed end, or may include a plug inserted in the end to prevent fluid and/or other components from flowing into the interior channel. Optionally, a channel-forming feature, such as solid extruded plastic component **120** may be disposed in the interior channel of the lower extension **720**.

[0058] According to embodiments of the present disclosure, the channel-forming feature is arranged in the bioprocess bag **100**, **1100** to allow for the fluid flow path provided by the channel-forming feature to be in fluid communication with the outlet. Referring again to Figure 2A as one example, the connector **140c** nearest the channel-forming feature, in this case a solid extruded plastic component **120**, is preferably an outlet and any of the other of the plurality of the connectors **140a**, **140b** may be an inlet. Where two or more of the plurality of the connectors **140** are located a similar distance from the channel-forming feature, any of the plurality of the connectors **140** which the channel-forming feature can be maintain in fluid connection with the interior compartment of bioprocess bag **100** may be an outlet. As will be understood from the discussion herein, it should be appreciated that a similar arrangement applies when the channel-forming feature is any of solid extruded plastic component **120**, a tubular plastic component **122**, a raised portion **124**, or any other feature that prevents the bioprocess bag **100** from closing on itself, thus providing a fluid flow path for the contents of the bag **100** to reach the outlet. As exemplified in Figure 2B, as the bioprocess bag **100** collapses, the channel-forming feature forms a conduit which cannot be

closed off by exertion of a pressure on sheets **102**, **104** of the bioprocess bag **100**. Thus, the entire interior compartment of the bioprocess bag **100** remains in fluid communication with the outlet at all times. Similarly, with reference to Figures 3A and 3B, where the at least one connection apparatus is a port fitment **40** as described herein, at least one of a plurality of ports **42** includes the channel-forming feature attached to, or disposed within, the port **42**. Such arrangement also allows the channel-forming feature to form a conduit which cannot be closed off by exertion of a pressure on sheets **102**, **104** as the bioprocess bag **100** collapses. Figure 2C is a schematic illustration showing a top view of the bioprocess bag having a channel-forming feature such as is shown in Figures 2A and 2B. Figure 2C illustrates that the channel-forming feature, in this illustration the extruded plastic component **120**, prevents sheets **102**, **104** from collapsing to a point where the entire face of one sheet **102** is contacted by the other sheet **104** which prevents the sheets **102**, **104** from sealing off portions of the bag **100** and/or from isolating the fluid and/or other components in the bag **100** from reaching an outlet. As is clearly shown in Figure 2C, a fluid flow path around the outside of the channel-forming feature is always maintained.

[0059] The bioprocess bag **100**, **1100** also includes at least one hole **150** punched in the top welded edge of the bioprocess bag **100**, **1100** and at least one hole **150** punched in the bottom welded edge of the bioprocess bag **100**, **1100**. The holes **150** allow for the bioprocess bag **100**, **1100** to be mounted in a hanging position from either the top or the bottom of the bag **100**, **1100** as will be described further below. Optionally, the bioprocess bag **100**, **1100** may include at least one rigid rod (not shown) sealed within the top welded edge of the bioprocess bag **100**, **1100** and at least one rigid rod (not shown) sealed within the bottom welded edge of the bioprocess bag **100**, **1100**. Similar to the holes **150**, the rigid rods allow for the bioprocess bag **100**, **1100** to be mounted in a hanging position from either the top or the bottom of the bag **100**, **1100**.

[0060] According to embodiments of the present disclosure, the bioprocess bag **100** may include dry microcarrier material in the interior compartment of the bag **100**. As used herein, the term “dry microcarrier material” refers to microcarrier material having a water content of at most 10 wt.% (e.g., at most 1, 2, 4, 5 or 10 wt.% including ranges between any of the foregoing values). The dry microcarrier material may be digestible material such as, but not limited to: pectic acid; pectinic acid; polysaccharides such as dextran, substituted cellulose derivatives, alginic acid, starches, glycogen, arabinoxylans, agarose;

glycosaminoglycans such as hyaluronic acid and chondroitin sulfate; various proteins such as elastin, fibrin, silk fibroin, collagen and their derivatives can be also used. Hydrated microcarrier material formed by adding a hydrating fluid to the dry microcarrier material, may be sphere-shaped and may have diameters of about 125 microns to about 300 microns. A hydrating fluid may be for example, but is not limited to, deionized water, a buffer solution, a polyethylene glycol containing solution, and a dilute media. The microcarriers may be coated with proteins, peptides, or charged molecules.

[0061] According to embodiments of the present disclosure, the bioprocess bag **100**, **1100** may also include a sealable opening **160** which can be used to fill the bag **100**, **1100** with dry microcarrier material. As shown, for example in Figure 2A, the sealable opening **160** may be formed in a face of at least one of sheets **102**, **104**. The sealable opening **160** may be in the form of a port having a collar which can be sealed and unsealed by a sealing cap. The sealable opening **160** may be fabricated using sealing techniques which are known to persons skilled in the art. The sealing cap may be a threaded screw cap having internal threads that engage external threads of the collar to twist the cap into the collar. A gasket may also be provided in order to provide a fluid-tight seal between the collar and the cap.

[0062] Provided are also methods for processing dry microcarrier material in bioprocess bags as described herein. Figure 10 is a flow chart illustrating a method **800** as described herein. The method may include a step **810** of filling the bioprocess bag **100**, **1100** with dry microcarrier material. Filling the bioprocess bag **100**, **1100** may include unsealing the sealable opening **160** and adding dry microcarrier material through the opening **160** and into the interior compartment of the bioprocess bag **100**, **1100**. Once dry microcarrier material has been added and the sealable opening **160** is resealed, the method may further include a step **820** of sterilizing the dry microcarrier material in the bioprocess bag **100**, **1100**. Such sterilizing may be completed using autoclaving, gamma sterilization or any other known sterilization process. Alternatively, the dry microcarrier material and the bioprocess bag **100**, **1100** may be sterilized separately prior to filling the bioprocess bag **100**, **1100** with the dry microcarrier material. Where the dry microcarrier material is sterilized separately, the method preferably includes aseptically filling the bioprocess bag **100**, **1100** using protocols known to persons skilled in the art such as, for example, filling in a clean hood, or otherwise sterile atmosphere, having a HEPA filter. Once filled, the bioprocess bag **100**, **1100** may be

aseptically stored or transported to a location near a cell culture vessel such as, for example, a bioreactor.

[0063] The method may further include a step **830** of hydrating the dry microcarrier material in the bioprocess bag **100, 1100** to form a hydrated microcarrier material. Hydrating the dry microcarrier material may include adding a hydrating fluid into the bioprocess bag **100, 1100** through at least one of the connection apparatuses to contact the hydrating fluid with the dry microcarrier material. Contact with the hydrating fluid results in swelling of the microcarrier material to form hydrated microcarrier material which includes sphere-shaped microcarriers having diameters of about 125 microns to about 300 microns. Once contacted with hydrating fluid, the density of the resulting hydrated microcarrier material allows for settling of the hydrated microcarrier material and formation of at least two separate phases, with the lowest of the at least two separate phases containing the hydrated microcarrier material. After a sufficient amount of settling has occurred, hydrating the dry microcarrier material may further include dispensing the less dense upper phases through the at least one of the connection apparatuses. As used herein, the term “a sufficient amount of settling” refers to a period of time after which an upper liquid phase free of microcarrier material is formed. Dispensing the less dense upper phases includes using a peristaltic pump to pump the less dense upper phases out of the bioprocess bag **100, 1100** to an external container that is aseptically connected to the bioprocess bag **100, 1100**. Alternatively, dispensing the less dense upper phases includes applying a pressure to the outside of the bioprocess bag **100, 1100** to push the less dense upper phases out of the bioprocess bag **100, 1100**. Optionally, adding a hydrating fluid and dispensing the less dense upper phases may be performed any number of times.

[0064] The method may further include a step **840** of washing the hydrated microcarrier material in the bioprocess bag **100, 1100**. Washing the hydrated microcarrier material removes excess hydrating fluid from the hydrated microcarrier material and from the bag **100, 1100**. Washing the hydrated microcarrier material may include adding fluid and/or other components into the bioprocess bag **100, 1100** through at least one of the connection apparatuses to contact the fluid and/or other components with the hydrated microcarrier material. Once contacted with fluid and/or other components, the density of the resulting hydrated microcarrier material allows for settling of the hydrated microcarrier material and formation of at least two separate phases, with the lowest of the at least two separate phases

containing the hydrated microcarrier material. After a sufficient amount of settling has occurred, washing the hydrated microcarrier material may further include dispensing the less dense upper phases through the at least one of the connection apparatuses. Dispensing the less dense upper phases includes using a peristaltic pump to pump the less dense upper phases out of the bioprocess bag **100, 1100**. Alternatively, dispensing the less dense upper phases includes applying a pressure to the outside of the bioprocess bag **100, 1100** to push the less dense upper phases out of the bioprocess bag **100, 1100**. Optionally, adding fluid and/or other components and dispensing the less dense upper phases may be performed any number of times.

[0065] The method may further include a step **850** of aseptically transferring the microcarrier material from the bioprocess bag **100, 1100** to a cell culture vessel such as, for example, a bioreactor. Aseptically transferring the microcarrier material includes inverting the bioprocess bag **100, 1100** such that the half of the bioprocessing bag **100, 1100** having the connector **140** that is an inlet and the connector **140** that is an outlet, or the face port **1140** that is an inlet and the face port **1140** that is an outlet, is positioned at the bottom of the bioprocess bag **100, 1100** such that gravity may be used to facilitate removal of the microcarrier material from the bioprocess bag **100, 1100**. Inverting the bioprocess bag **100, 1100** is facilitated, for example, by the holes **150** and/or the at least one rigid rod included on both the top and the bottom of the bioprocess bag **100, 1100**. The at least one connection apparatus may be fluidly connected to, for example through tubing and an aseptic connector known to persons skilled in the art, to an inlet of a cell culture vessel.

[0066] According to an aspect (1) of the present disclosure, an aseptic bioprocess package is provided. The aseptic bioprocess package comprises a 2D flexible container comprising an interior compartment, a height having an upper half and a lower half, an inlet and an outlet, the inlet and the outlet being disposed on the same half of the 2D flexible container and a channel-forming feature in the interior compartment of the container, the channel-forming feature being configured to maintain a fluid flow path that fluidly connects the interior compartment of the flexible container with the outlet.

[0067] According an aspect (2) of the present disclosure, the aseptic bioprocess package of aspect (1) is provided, wherein the 2D flexible container comprises two sheets hermetically sealed along edges of the two sheets to form the interior compartment.

[0068] According an aspect (3) of the present disclosure, the aseptic bioprocess package of aspect (2) is provided, wherein the two sheets comprise a film or laminate comprising a polymeric material selected from a group consisting of polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polystyrene (PS), polycarbonate (PC), polymethylpentene (PMP), polyetheretherketone (PEEK) polytetrafluoroethylene (PTFE), polyfluoroalkoxy (PFA), polychlorotrifluoroethylene (PCTFE), ethylene vinyl acetate (EVA), and derivatives thereof.

[0069] According an aspect (4) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(3) is provided, wherein the inlet and the outlet comprise connectors having an internal fluid passage that permits the flow of fluids and/or other components into or out of the interior compartment of the flexible container.

[0070] According an aspect (5) of the present disclosure, the aseptic bioprocess package of aspect (4) is provided, wherein the connectors comprise rigid plastic.

[0071] According an aspect (6) of the present disclosure, the aseptic bioprocess package of aspect (4) is provided, wherein the connectors comprise flexible plastic tubing.

[0072] According an aspect (7) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(6) is provided, wherein the connectors comprise a face port.

[0073] According an aspect (8) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(3) is provided comprising a port fitment having at least two ports, wherein one of the at least two ports is the inlet and another of the at least two ports is the outlet.

[0074] According an aspect (9) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(8) is provided, wherein the channel-forming feature comprises a solid extruded plastic component.

[0075] According an aspect (10) of the present disclosure, the aseptic bioprocess package of aspect (9) is provided, wherein the solid extruded plastic component is welded into a seam of the flexible container.

[0076] According an aspect (11) of the present disclosure, the aseptic bioprocess package of aspect (9) is provided comprising a plurality of connectors, wherein a first of the

plurality of connectors is the inlet, a second of the plurality of connectors is the outlet and the solid extruded plastic component is disposed within a third of the plurality of connectors.

[0077] According an aspect (12) of the present disclosure, the aseptic bioprocess package of aspect (9) is provided comprising a port fitment having at least two ports, wherein a first of the at least two ports is the inlet, a second of the at least two ports is the outlet, and the solid extruded plastic component is disposed in a third of the plurality of ports.

[0078] According an aspect (13) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(8) is provided, wherein the channel-forming feature comprises a tubular plastic component.

[0079] According an aspect (14) of the present disclosure, the aseptic bioprocess package of aspect (13) is provided, wherein the tubular plastic component is welded into a seam of the flexible container.

[0080] According an aspect (15) of the present disclosure, the aseptic bioprocess package of aspect (13) is provided further comprising at least two inwardly facing face ports, wherein a first end of the tubular plastic component is attached to one of the at least two inwardly facing face ports and a second end of the tubular plastic component is attached to another of the at least two inwardly facing face ports.

[0081] According an aspect (16) of the present disclosure, the aseptic bioprocess package of aspect (13) is provided comprising a plurality of connectors, wherein a first of the plurality of connectors is the inlet, a second of the plurality of connectors is the outlet and the tubular plastic component is disposed within a third of the plurality of connectors.

[0082] According an aspect (17) of the present disclosure, the aseptic bioprocess package of aspect (13) is provided comprising a port fitment having at least two ports, wherein a first of the at least two ports is the inlet, a second of the at least two ports is the outlet, and the tubular plastic component is disposed in a third of the plurality of ports.

[0083] According an aspect (18) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(8) is provided, wherein the channel-forming feature comprises a raised portion which extends from an interior face of at least one of the two sheets.

[0084] According an aspect (19) of the present disclosure, the aseptic bioprocess package of aspect (18) is provided, wherein the raised portion comprises a plastic component attached to the interior face of the at least one of the two sheets.

[0085] According an aspect (20) of the present disclosure, the aseptic bioprocess package of aspect (18) is provided, wherein the raised portion comprises a textured portion of the interior face of the at least one of the two sheets.

[0086] According an aspect (21) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(7) is provided further comprising a channel-forming feature extender having an opening disposed between a lower extension and an upper extension.

[0087] According an aspect (22) of the present disclosure, the aseptic bioprocess package of aspect (21) is provided, wherein the upper extension comprises an interior channel fluidly connecting the opening to the outlet.

[0088] According an aspect (23) of the present disclosure, the aseptic bioprocess package of any of aspects (21)-(22) is provided further comprising a side extension comprising an interior channel fluidly connecting the opening to the interior channel of the upper extension.

[0089] According an aspect (24) of the present disclosure, the aseptic bioprocess package of aspect (23) is provided, wherein the angle between the side extension and the upper extension is about 90 degrees.

[0090] According an aspect (25) of the present disclosure, the aseptic bioprocess package of aspect (23) is provided, wherein the angle between the side extension and the upper extension is greater than about 90 degrees.

[0091] According an aspect (26) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(25) is provided further comprising at least one hanging hole in the top welded edge of the container and at least one hanging hole in the bottom welded edge of the container.

[0092] According an aspect (27) of the present disclosure, the aseptic bioprocess package of any of aspects (1)-(25) is provided further comprising a sealable opening in a face of at least one of two sheets of the flexible container.

[0093] According an aspect (28) of the present disclosure, the aseptic bioprocess package of aspect (27) is provided, wherein the sealable opening comprises a collar and a sealing cap.

[0094] According to an aspect (29) of the present disclosure, a method for processing dry microcarrier material in a microcarrier bioprocess package is provided. The method comprises filling a bioprocess package with dry microcarrier material, the bioprocess package comprising: a 2D flexible container comprising an interior compartment, a height having an upper half and a lower half, an inlet and an outlet, the inlet and the outlet being disposed on the same half of the 2D flexible container; and a channel-forming feature in the interior compartment of the container, the channel-forming feature being configured to maintain a fluid flow path that fluidly connects the interior compartment of the flexible container with the outlet. The method further comprises sterilizing the dry microcarrier material in the bioprocess package, hydrating the dry microcarrier material in the bioprocess package to form a hydrated microcarrier material, washing the hydrated microcarrier material in the bioprocess package, and aseptically transferring the hydrated microcarrier material from the bioprocess package to a cell culture vessel.

[0095] According an aspect (30) of the present disclosure, the method of aspect (29) is provided, wherein filling a bioprocess package with dry microcarrier material comprises adding dry microcarrier material to the interior compartment of the bioprocess package.

[0096] According an aspect (31) of the present disclosure, the method of aspect (29) is provided, wherein hydrating the dry microcarrier material in the bioprocess package comprises adding a hydrating fluid to the bioprocess package to contact the dry microcarrier material with the hydrating fluid.

[0097] According an aspect (32) of the present disclosure, the method of aspect (31) is provided, wherein hydrating the dry microcarrier material in the bioprocess package further comprises forming at least two liquid phases having different densities and dispensing the less dense upper liquid phases from the bioprocess package.

[0098] According an aspect (33) of the present disclosure, the method of aspect (29) is provided, wherein washing the hydrated microcarrier material comprises adding fluid

and/or other components to the bioprocess package to contact the hydrated microcarrier material with the fluid and/or other components.

[0099] According an aspect (34) of the present disclosure, the method of aspect (33) is provided, wherein washing the hydrated microcarrier material further comprises forming at least two liquid phases having different densities and dispensing the less dense upper liquid phases from the bioprocess package.

[00100] According an aspect (35) of the present disclosure, the method of aspect (29) is provided, wherein aseptically transferring the hydrated microcarrier material comprises inverting the bioprocess package such that the half of the bioprocess package comprising the inlet and the outlet is positioned at the bottom of the bioprocess package such that gravity facilitates removal of the hydrated microcarrier material from the bioprocess package.

[00101] According an aspect (36) of the present disclosure, the method of aspect (29) is provided, wherein aseptically transferring the hydrated microcarrier material comprises fluidly connecting the bioprocess package to the cell culture vessel through an aseptic connector.

[00102] While the present disclosure includes a limited number of embodiments, those skilled in the art, having benefit of this disclosure, will appreciate that other embodiments can be devised which do not depart from the scope of the present disclosure

What Is Claimed Is:

1. An aseptic bioprocess package comprising:

a 2D flexible container comprising an interior compartment, a height having an upper half and a lower half, an inlet and an outlet, the inlet and the outlet being disposed on the same half of the 2D flexible container; and

a channel-forming feature in the interior compartment of the container, the channel-forming feature being configured to maintain a fluid flow path that fluidly connects the interior compartment of the flexible container with the outlet.

2. The aseptic bioprocess package of claim 1, wherein the 2D flexible container comprises two sheets hermetically sealed along edges of the two sheets to form the interior compartment.

3. The aseptic bioprocess package of claim 2, wherein the two sheets comprise a film or laminate comprising a polymeric material selected from a group consisting of polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polystyrene (PS), polycarbonate (PC), polymethylpentene (PMP), polyetheretherketone (PEEK), polytetrafluoroethylene (PTFE), polyfluoroalkoxy (PFA), polychlorotrifluoroethylene (PCTFE), ethylene vinyl acetate (EVA), and derivatives thereof.

4. The aseptic bioprocess package of any of the preceding claims wherein the inlet and the outlet comprise connectors having an internal fluid passage that permits the flow of fluids and/or other components into or out of the interior compartment of the flexible container.

5. The aseptic bioprocess package of claim 4, wherein the connectors comprise rigid plastic.

6. The aseptic bioprocess package of claim 4, wherein the connectors comprise flexible plastic tubing.

7. The aseptic bioprocess package of any of the preceding claims wherein the connectors comprise a face port.

8. The aseptic bioprocess package of any of claims 1-3 comprising a port fitment having at least two ports, wherein one of the at least two ports is the inlet and another of the at least two ports is the outlet.
9. The aseptic bioprocess package of any of the preceding claims wherein the channel-forming feature comprises a solid extruded plastic component.
10. The aseptic bioprocess package of claim 9, wherein the solid extruded plastic component is welded into a seam of the flexible container.
11. The aseptic bioprocess package of claim 9 comprising a plurality of connectors, wherein a first of the plurality of connectors is the inlet, a second of the plurality of connectors is the outlet and the solid extruded plastic component is disposed within a third of the plurality of connectors.
12. The aseptic bioprocess package of claim 9 comprising a port fitment having at least two ports, wherein a first of the at least two ports is the inlet, a second of the at least two ports is the outlet, and the solid extruded plastic component is disposed in a third of the plurality of ports.
13. The aseptic bioprocess package of any of claims 1-8, wherein the channel-forming feature comprises a tubular plastic component.
14. The aseptic bioprocess package of claim 13, wherein the tubular plastic component is welded into a seam of the flexible container.
15. The aseptic bioprocess package of claim 13 further comprising at least two inwardly facing face ports, wherein a first end of the tubular plastic component is attached to one of the at least two inwardly facing face ports and a second end of the tubular plastic component is attached to another of the at least two inwardly facing face ports.
16. The aseptic bioprocess package of claim 13 comprising a plurality of connectors, wherein a first of the plurality of connectors is the inlet, a second of the plurality of connectors is the outlet and the tubular plastic component is disposed within a third of the plurality of connectors.

17. The aseptic bioprocess package of claim 13 comprising a port fitment having at least two ports, wherein a first of the at least two ports is the inlet, a second of the at least two ports is the outlet, and the tubular plastic component is disposed in a third of the plurality of ports.
18. The aseptic bioprocess package of any of claim 1-8, wherein the channel-forming feature comprises a raised portion which extends from an interior face of at least one of the two sheets.
19. The aseptic bioprocess package of claim 18, wherein the raised portion comprises a plastic component attached to the interior face of the at least one of the two sheets.
20. The aseptic bioprocess package of claim 18, wherein the raised portion comprises a textured portion of the interior face of the at least one of the two sheets.
21. The aseptic bioprocess package of any of claims 1-7, further comprising a channel-forming feature extender having an opening disposed between a lower extension and an upper extension.
22. The aseptic bioprocess package of claim 21, wherein the upper extension comprises an interior channel fluidly connecting the opening to the outlet.
23. The aseptic bioprocess package of any of claims 21-22, further comprising a side extension comprising an interior channel fluidly connecting the opening to the interior channel of the upper extension.
24. The aseptic bioprocess package of claim 23, wherein the angle between the side extension and the upper extension is about 90 degrees.
25. The aseptic bioprocess package of claim 23, wherein the angle between the side extension and the upper extension is greater than about 90 degrees.
26. The aseptic bioprocess package of any of the preceding claims further comprising at least one hanging hole in the top welded edge of the container and at least one hanging hole in the bottom welded edge of the container.
27. The aseptic bioprocess package of any of the preceding claims further comprising a sealable opening in a face of at least one of two sheets of the flexible container.

28. The aseptic bioprocess package of claim 27 wherein the sealable opening comprises a collar and a sealing cap.