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(54) Title: APPARATUS AND METHOD FOR FORMING A BIOPROCESSING BAG

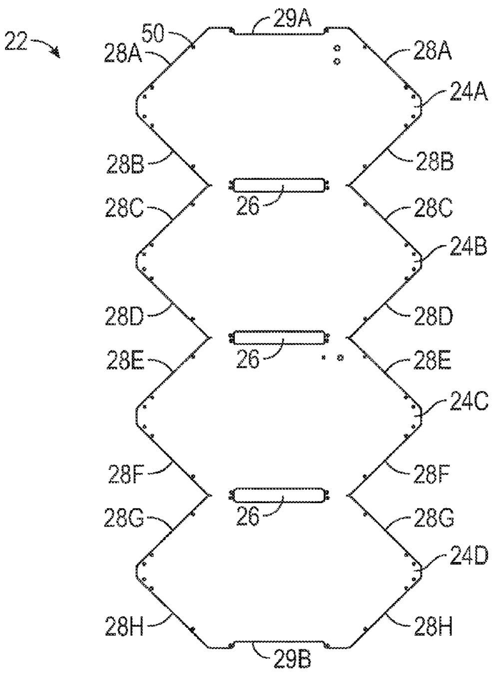

FIG. 3

(57) Abstract: A bioprocessing bag formed from a single sheet of flexible material including connected panels and a method of making is disclosed. In one embodiment, a bioprocessing bag is disclosed. The bioprocessing bag includes a single sheet of flexible material including a plurality of connected panels, wherein each of the panels are folded and sealed to form a sealed bioprocessing bag. In another embodiment, a method of assembling a bioprocessing bag is disclosed. The method includes obtaining a single sheet of flexible material including a plurality of connected panels, folding the panels, and sealing the folded panels to form a sealed bioprocessing bag.

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APPARATUS AND METHOD FOR FORMING A BIOPROCESSING BAG

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Serial No. 63/273,310, filed on October 29, 2021, which is hereby incorporated by reference herein in its entirety.

BACKGROUND

TECHNICAL FIELD

[0002] Embodiments of the invention relate generally to bioprocessing systems and methods and, more particularly, to a bioprocessing bag formed from a single sheet of flexible material having a plurality of individually connected panels and a method of making the bioprocessing bag.

DISCUSSION OF ART

[0003] A variety of vessels, devices, components and unit operations are known for carrying out biochemical and/or biological processes and/or manipulating liquids and other products of such processes. In order to avoid the time, expense, and difficulties associated with sterilizing the vessels used in biopharmaceutical manufacturing processes, single-use or disposable bioreactor bags and single-use mixer bags are used as such vessels. For instance, biological materials (e.g., animal and plant cells) including, for example, mammalian, plant or insect cells and microbial cultures can be processed using disposable or single-use mixers and bioreactors.

[0004] These single use or disposable bioprocessing bags are typically flexible or collapsible plastic bags that are supported by an outer rigid structure such as a stainless steel tank/vessel of a stirred tank reactor or mixer. Use of sterilized disposable bags eliminates the time-consuming step of cleaning of the vessel and reduces the chance of contamination. The bags can vary in size from a few liters up to several thousand liters and include the various ports, tubing, connectors and other components necessary to allow for mixing, sparging, draining, sampling and sensing/measurement of the contents of the bag.

[0005] Flexible, single use bioprocessing bags that take the form of three-dimensional (3-D) structures (e.g., stirred-tank bioreactor and mixer bags) are typically produced from individual, separate sheet/panels of material, e.g., plastic, that are assembled (e.g., sealed/welded together) to form a disposable bioprocessing bag. In applications where such bags are used in generally cylindrical bioreactor vessels, the flexible bags are also cylindrical.

[0006] Such bags are typically manufactured by overlapping the edges of adjoining sheets of material and welding such sheets to one another to form the cylindrical sidewalls of the bag. To close off the bag, multi-seam welds are often utilized, which brings together the upper edges of each sheet of material used in the bag construction.

[0007] In one known bag, four separate individual panels are used to assemble the bag. As will be appreciated, with a plurality of separate panels that need to be conjoined, sometimes there are instances where the wrong panels are sealed together, or film of the individual panels are sealed facing the wrong side. These errors result in defective bioprocessing/mixing bags.

BRIEF DESCRIPTION

[0008] The various embodiments of the present invention provide a solution that addresses the technical problems associated with assembling flexible, single use bioprocessing bags from individual separate panels than can result in defective bags.

[0009] In one embodiment, an apparatus for bioprocessing is provided. The apparatus comprises a single sheet of flexible material. The single sheet of flexible material is shaped such that the sheet includes a plurality of connected panels, wherein each of the panels are folded and sealed to form a sealed bioprocessing bag.

[00010] In another embodiment, a method is disclosed. The method includes obtaining a single sheet of flexible material such that the sheet includes a plurality of connected panels, folding the panels, and sealing the folded panels to form a sealed bioprocessing bag.

DRAWINGS

[00011] The present invention will be better understood from reading the following description of non-limiting embodiments, with reference to the attached drawings, wherein below:

[00012] FIGS. 1A and 1B are graphical illustrations of single use, flexible 3-D mixer and bioreactor bags, respectively, that are suitable for manufacture utilizing embodiments of the present invention.

[00013] FIG. 2 is a schematic top view of individual panels of flexible material used to assemble a bioprocessing bag according to a known process.

[00014] FIG. 3 is a schematic top view of a single sheet of flexible material having a plurality of connected panels used to assemble a bioprocessing bag according to an embodiment of the present invention.

[00015] FIGS. 4A-4D is a schematic illustrating a method of assembling a bioprocessing bag from a single sheet of flexible material including a plurality of connected panels according to an embodiment of the present invention.

[00016] FIG. 5 is a schematic top view of the single sheet of flexible material of FIG. 3 with annotations to illustrate an assembly method according to an embodiment of the present invention.

DETAILED DESCRIPTION

[00017] Reference will be made below in detail to exemplary embodiments of the invention, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference characters used throughout the drawings refer to the same or like parts.

[00018] As used herein, the term “flexible” or “collapsible” refers to a structure or material that is pliable, or capable of being bent without breaking, and may also refer to a material that is compressible or expandable. An example of a flexible structure is a bag formed of polyethylene film. The terms “rigid” and “semi-rigid” are used herein interchangeably to describe structures that are “non-collapsible,” that is to say structures that do not fold, collapse, or otherwise deform under normal forces to substantially reduce their elongate dimension. Depending on the context, “semi-rigid” can also denote a structure that is more flexible than a “rigid” element, e.g., a bendable tube or conduit, but still one that does not collapse longitudinally under normal conditions and forces.

[00019] A “vessel,” as the term is used herein, means a flexible bag, a flexible container, a semi-rigid container, or a rigid container, as the case may be. The term “vessel” as used herein is intended to encompass bioreactor vessels having a wall or a portion of a wall that is flexible or semi-rigid, single use flexible bags, as well as other containers or conduits commonly used in biological or biochemical processing, including, for example, cell culture/purification systems, mixing systems, media/buffer preparation systems, and filtration/purification systems.

[00020] As used herein, the terms “bag” and “bioprocessing bag” mean a flexible or semi-rigid container or vessel used, for example, as a reactor or mixer for the contents within.

[00021] Although the embodiments of the present invention are described with respect to bioprocessing/mixing bags such as a single-use, flexible bags for use in bioprocessing/mixing operations, it is contemplated that the bags and manufacturing methods disclosed herein may likewise be utilized for flexible bags for use in a variety of industries and end uses.

[00022] Embodiments of the present invention are directed to providing a bioprocessing bag that obviates the issues associated with assembling bioprocessing bags from individual panels than can result in defective bags. In one embodiment, a bioprocessing bag is provided. The bioprocessing bag comprises a single sheet of flexible material such that the sheet includes a plurality of connected panels, wherein each of the panels are folded and sealed to form a sealed bioprocessing bag.

[00023] In another embodiment, a method of assembling a bioprocessing bag is disclosed. The method includes obtaining a single sheet of flexible material such that the sheet includes a plurality of connected panels, folding the panels, and sealing the folded panels to form a sealed bioprocessing bag.

[00024] Turning now to the figures, FIGS. 1A and 1B depict known 3-D flexible, single use bioprocessing bags. In particular, FIG. 1A depicts a mixer bag 10 manufactured from four panels 14 that are welded together at seams/joints 16 where the panels 14 overlap. Similarly, FIG. 1B depicts a stirred tank bioreactor bag 12 that includes a plurality of panels 18 that are joined together at welded seams 16. Such bags are currently manufactured by welding together individual separate panels/sheets.

[00025] More specifically, FIG. 2 depicts individual, separate panels 20 of flexible material that can be used to assemble a bioprocessing bag (e.g., the mixer bag 10 of FIG. 1A) according to a known manufacturing process in which the individual panels 20 are welded together to form seams between adjacent panels. In this example, four separate individual panels 20 are used to assemble a bioprocessing/mixing bag, with each of the four panels 20 forming a side of a bag. As will be appreciated, in having to join a plurality of individual, separate panels, there are instances where the wrong panels are welded/sealed together, or film of the individual panels 20 are sealed facing the wrong side. These errors result in defective bioprocessing bags that are not suitable for use.

[00026] Referring now to FIG. 3, a single sheet of flexible material 22 including a plurality (e.g., four) of connected panels 24A – 24D used to assemble a bag according to an embodiment of the present invention is depicted. The single sheet of flexible material 22 can be formed of a suitable flexible material, such as a homopolymer or a copolymer. The flexible material can be one that is USP Class VI certified, for example, silicone, polycarbonate, polyethylene, and polypropylene.

[00027] Non-limiting examples of flexible materials include polymers such as polyethylene (for example, linear low-density polyethylene and ultra-low density polyethylene), polypropylene, polyvinylchloride, polyvinyldichloride, polyvinylidene chloride, ethylene vinyl acetate, polycarbonate, polymethacrylate, polyvinyl alcohol, nylon, silicone rubber, other synthetic rubbers and/or plastics. In an embodiment, the flexible material may be a multilayer laminate of several different materials. In a specific embodiment, the flexible material is a laminate of ten-layers, including inner and outer layers, as well as multiple interior, gas barrier, and tie layers.

[00028] In one embodiment, the single sheet of flexible material 22 with the connected panels 24A – 24D can be folded and sealed to form a sealed bioprocessing bag. As shown in FIG. 3, the plurality of connected panels 24A – 24D can comprise a linear arrangement. Each of the panels 24A – 24D can have a polygonal-like shape. Further, each of the panels 24A – 24D can be distinguished from an adjacent panel by a cutout 26 formed in the single sheet of flexible material 22. The cutouts 26 facilitate folding of the material 22 as well as the insertion of components such as tubing fixtures or an impeller that involve access to the interior of the bag. As such, the cutouts 26 may be sized and shaped to accommodate the insertion of a bioreactor/mixer impeller

via a human hand. In one embodiment, an accordion-style folding technique can be applied about each of the cutouts 26 to facilitate the folding and sealing of the connected panels 24A – 24D.

[00029] The panels 24A-24D may further include alignment apertures 50 which are configured to receive alignment pins 52 (FIG. 4C) of the seam welding machine. As will be appreciated, in such embodiments, the alignment holes of panels to be joined are aligned/stacked and placed on the alignment pins 52 prior to welding. This ensures the correct placement of each linear seam.

[00030] Referring to FIGS. 3 and 5, in an embodiment, at an initial step 1, edge 29A of panel 24A is joined with edge 29B of panel 28H and sealed at the depicted dashed weld line. The weld is created via stacking the corresponding alignment apertures 50 of each panel on the alignment pins 52 of the machine. At step 2, panels 24A and 24B are joined at a seam (represented again by a dashed weld line) that closes off the cutout 26 between said panels. At step 3, panels 24B and 24C are joined at the depicted dashed weld line that again closes off cutout 26. Similarly, at step 4, panels 24C and 24D are joined at the depicted dashed weld line that closes off cutout 26.

[00031] Once the panels 24A – 24D are joined about the cutouts 26, as described above, the edges (28A – 28H) of adjacent sheets are joined together. For example, the edges 28B of panel 24A are joined (e.g., edge overlaps are welded together) to edges 28C of panel 24B. Edges 28D of panel 24B are joined with edges 28E of panel 24C. Edge 28F of panel 24C is joined to edge 28G of panel 24D and edges 28A and 28H are joined. In embodiments, the distal tips of the edges 28A – 29H may then be joined with a single weld. Optionally, the extra panel material 55 (FIG. 4D) that is generated when creating the welds that close off the cutouts 26 may be removed via a cutting process.

[00032] The single sheet of flexible material 22 with the connected panels 24A – 24D illustrated in FIG. 3 is representative of one configuration and is not meant to be limiting. For example, it is contemplated that the connected panels 24A-24D can be arranged in other patterns instead of a linear arrangement. In addition, it is contemplated that the connected panels 24A-24D can take the form of other shapes in addition to polygonal-like shapes. Also, it is envisioned that the cutouts 16 depicted in FIG. 3 may be placed in other locations and/or have different shapes in addition to the elongated shaped cutouts depicted in FIG. 3. Further, it is understood that other folding techniques are possible, and thus, the accordion folding technique is not meant to limit the embodiments described herein.

[00033] FIGS. 4A-4D illustrate a method 30 of assembling a bioprocessing bag 40 from a single sheet of flexible material 22 having a plurality of connected panels 24A – 24D as depicted in FIG. 3, according to an embodiment of the present invention. As shown in FIG. 4A, the method 18 begins by obtaining a single sheet of flexible material 22 that includes a plurality of connected panels 24A-24D. In FIG. 4B, the panels 24A-24D of the single sheet of flexible material 12 are then folded.

[00034] The folded panels are sealed in FIG. 4C using conventional sealing equipment 32 to form the sealed bioprocessing bag 40 depicted in FIG.4D. In an embodiment, the user will manually align the seals using the alignment holes 50 in the panels 24A-24D. The alignment holes 50 of panels to be joined are stacked and placed on alignment pins 52 of the seam welding machine. The welding machine will then apply heat to weld the seam together. In one embodiment, the bioprocessing bag 40 formed from the method depicted in FIGS. 4A-4D is a 3-D bioprocessing bag.

[00035] While, for purposes of simplicity of explanation, the operations shown in FIGS. 4A-4D and 5 are described as a series of acts. It is to be understood and appreciated that the subject innovation associated with FIGS. 4A-4D and 5 is not limited by the order of acts, as some acts may, in accordance therewith, occur in a different order and/or concurrently with other acts from that shown and described herein.

[00036] For example, those skilled in the art will understand and appreciate that a methodology or operations depicted in FIGS. 4A-4D and 5 could alternatively be represented as a series of interrelated states or events. Moreover, not all illustrated acts may be required to implement a methodology in accordance with the innovation. Furthermore, two or more of the disclosed example methods can be implemented in combination with each other, to accomplish one or more features or advantages described herein.

[00037] It should be apparent from the embodiments described herein that the bioprocessing bag formed from a single sheet of flexible material having a plurality of connected panels will obviate the defects in bags that oftentimes result from assembling from a plurality of separate individual panels. Other advantages of the various embodiments include, but are not limited to, minimal material handling of panels (e.g., four panels vs one panel), use of poka yoke sealing to seal the interconnected panels, reduced need to staple panels together, higher equipment uptime, and applicability to multiple different sized bags.

[00038] As used herein, an element or step recited in the singular and proceeded with the word “a” or “an” should be understood as not excluding plural of said elements or steps, unless such exclusion is explicitly stated. Furthermore, references to “one embodiment” of the present invention are not intended to be interpreted as excluding the existence of additional embodiments that also incorporate the recited features. Moreover, unless explicitly stated to the contrary, embodiments “comprising,” “including,” or “having” an element or a plurality of elements having a particular property may include additional such elements not having that property.

[00039] This written description uses examples to disclose several embodiments of the invention, including the best mode, and also to enable one of ordinary skill in the art to practice the embodiments of invention, including making and using any devices or systems and performing any incorporated methods. The patentable scope of the invention is defined by the claims, and may include other examples that occur to one of ordinary skill in the art. Such other examples are intended to be within the scope of the claims if they have structural elements that do not differ from the literal language of the claims, or if they include equivalent structural elements with insubstantial differences from the literal languages of the claims.

What is claimed is:

1. An apparatus for forming a bioprocessing bag, comprising:

a single sheet of flexible material including a plurality of connected panels; and

wherein each of the panels may be folded and sealed to form a sealed bioprocessing bag.

2. The apparatus of claim 1, wherein the plurality of panels comprises a linear arrangement of connected panels.

3. The apparatus of claim 1, wherein each of the panels are distinguished from an adjacent panel by a cutout formed in the single sheet of flexible material.

4 The apparatus of claim 3, wherein the single sheet of flexible material is folded about each of the cutouts.

5. The apparatus of claim 4, wherein the folds about each of the cutouts comprises an accordion fold.

6. The apparatus of claim 1, wherein each of the plurality of panels comprises a polygonal-like shape.

7. The apparatus of claim 1, wherein the sealed bioprocessing bag comprises a three-dimensional (3-D) bioprocessing bag.

8. The apparatus of claim 1, wherein the plurality of connected panels is four connected panels.

9. The apparatus of claim 1, wherein the panels are sealed via thermal welding.

10. A method, comprising:

obtaining a single sheet of flexible material including a plurality of connected panels;

folding the panels; and

sealing the folded panels to form a sealed bioprocessing bag.

11. The method of claim 10, wherein the plurality of panels comprises a linear arrangement of connected panels.

12. The method of claim 10, wherein each of the panels are distinguished from an adjacent panel by a cutout formed in the single sheet of flexible material.

13. The method of claim 12, wherein the folding of the panels comprises folding the panels about each of the cutouts.

14. The method of claim 10, wherein the folding of the panels comprises an accordion fold.

15. The method of claim 10, wherein the plurality of connected panels is four connected panels.

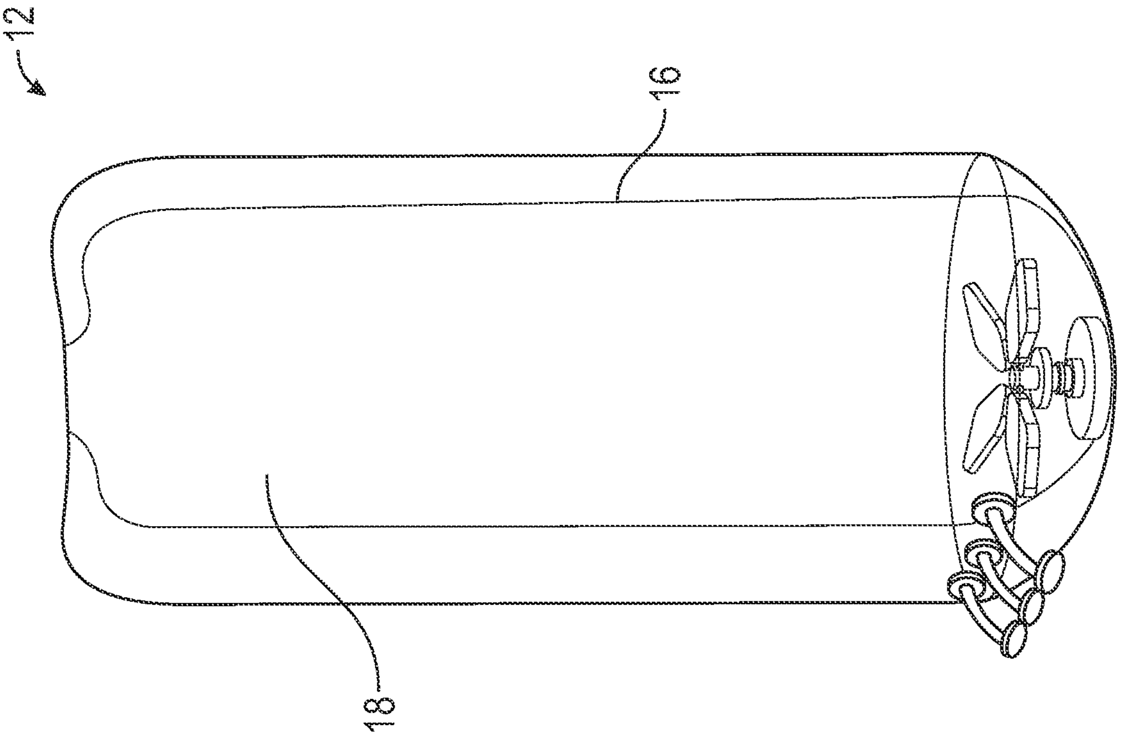

FIG. 1B

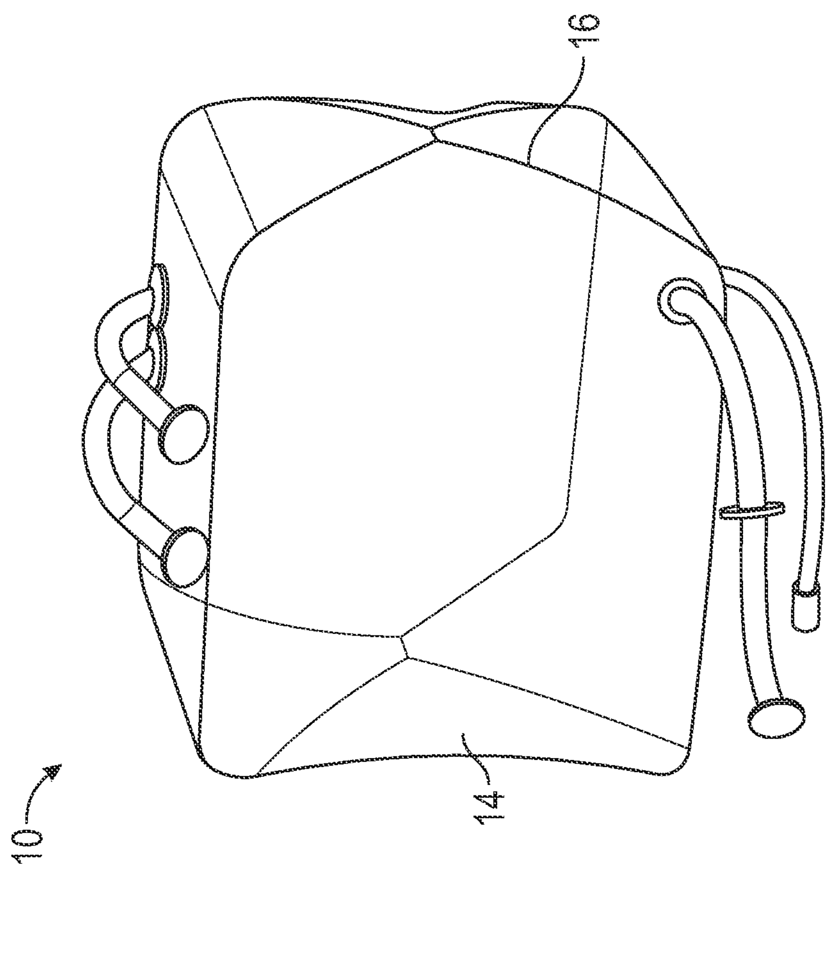

FIG. 1A

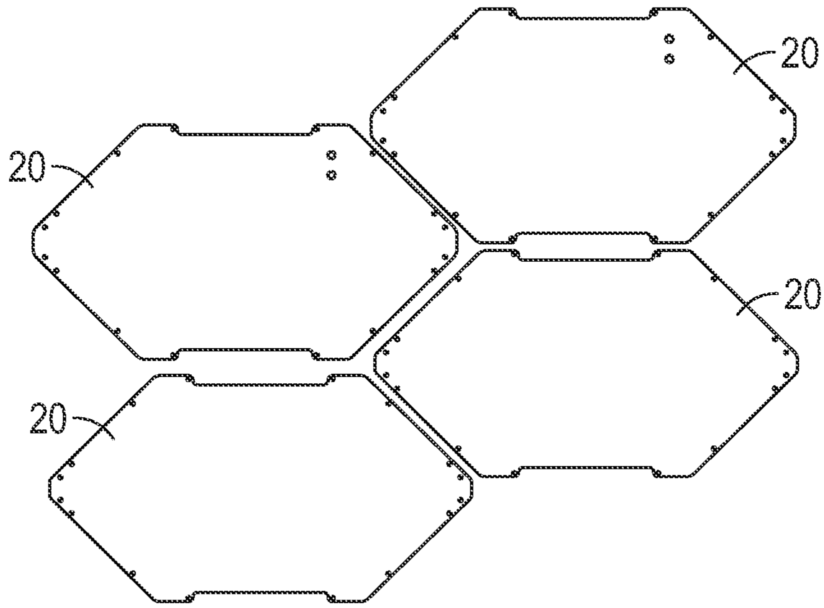
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FIG. 2

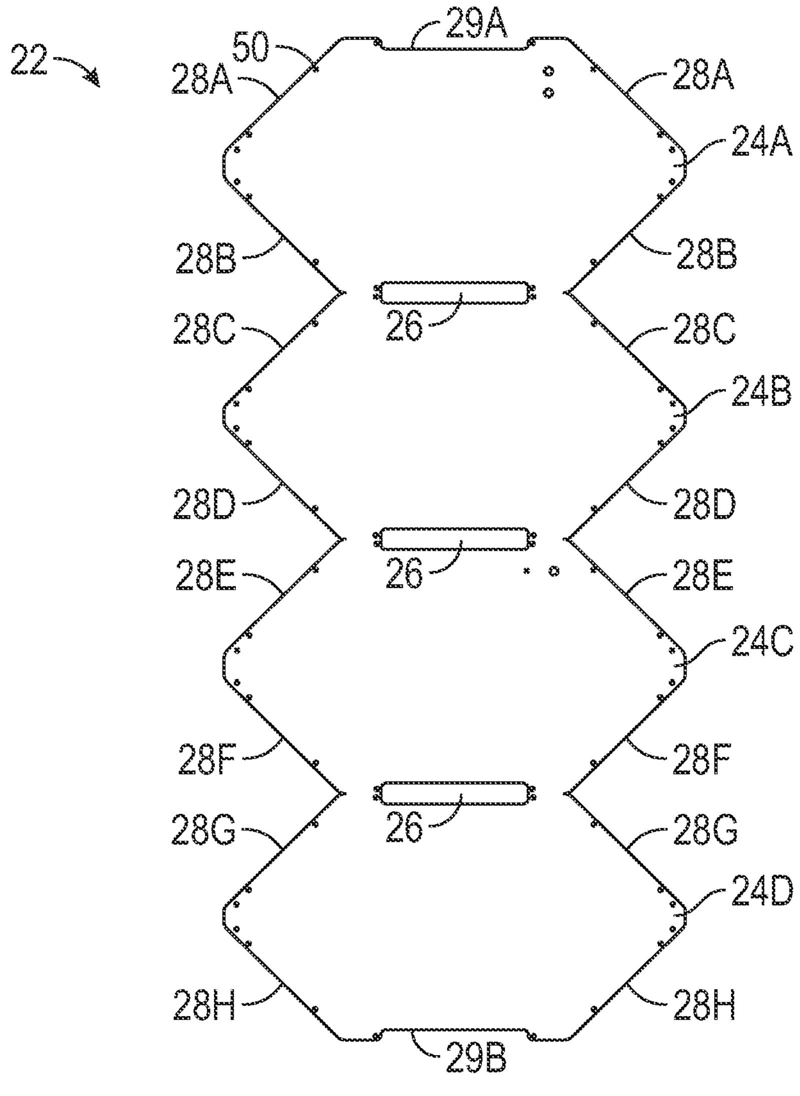
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FIG. 3

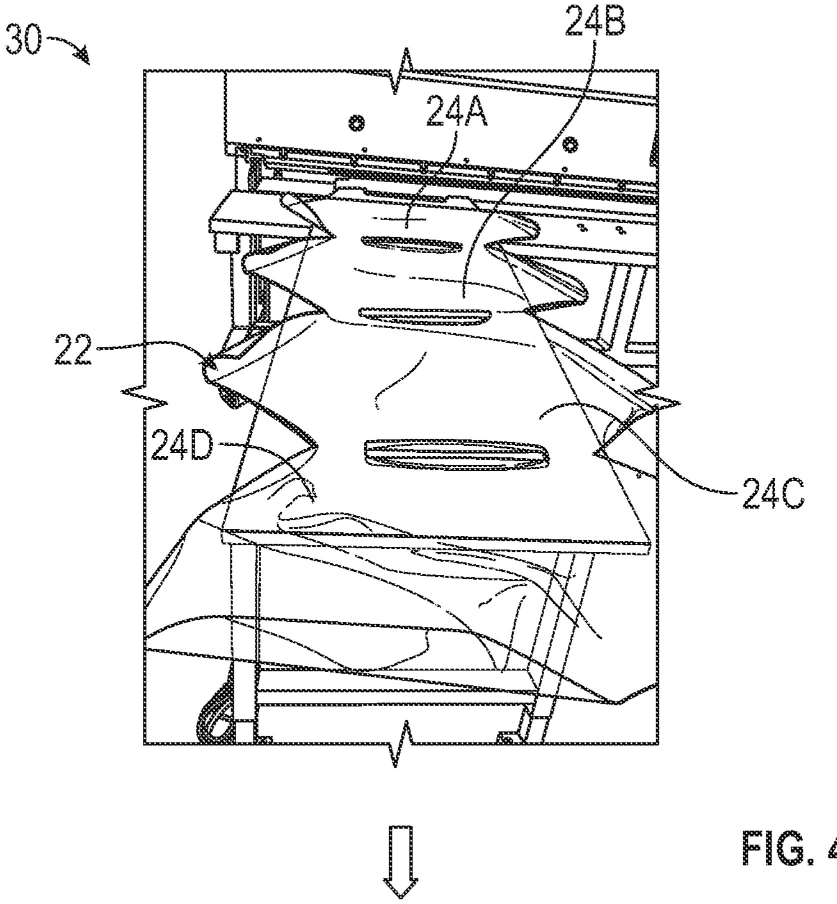

FIG. 4A

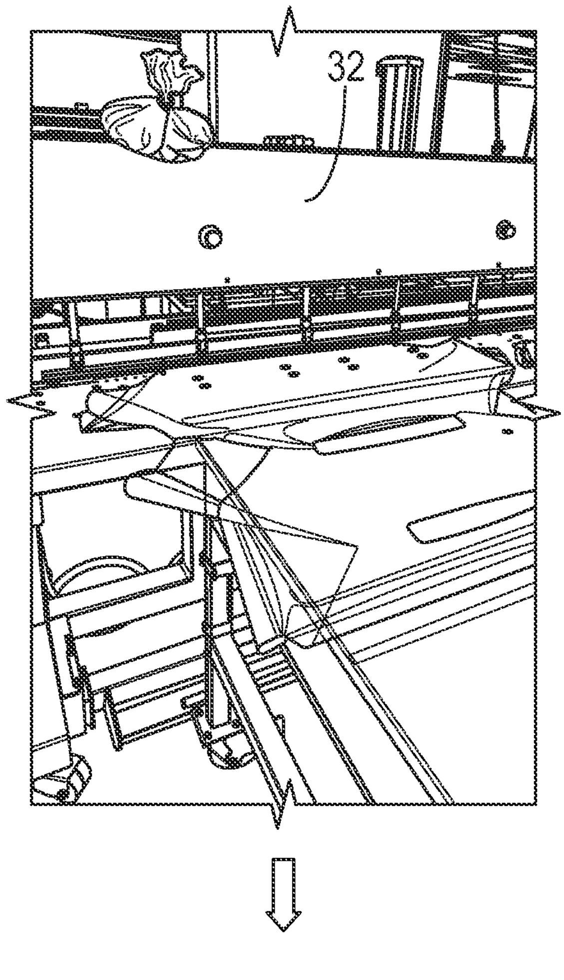

FIG. 4B

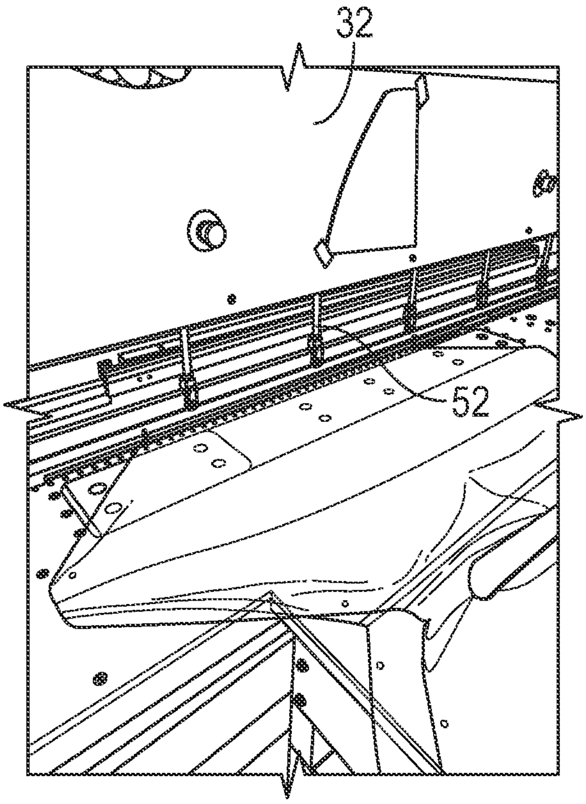

FIG. 4C

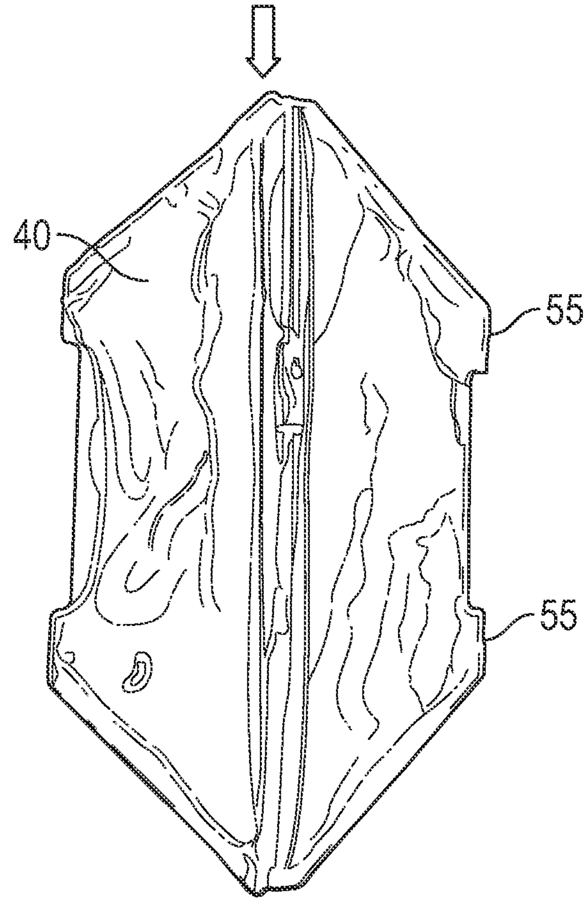

FIG. 4D

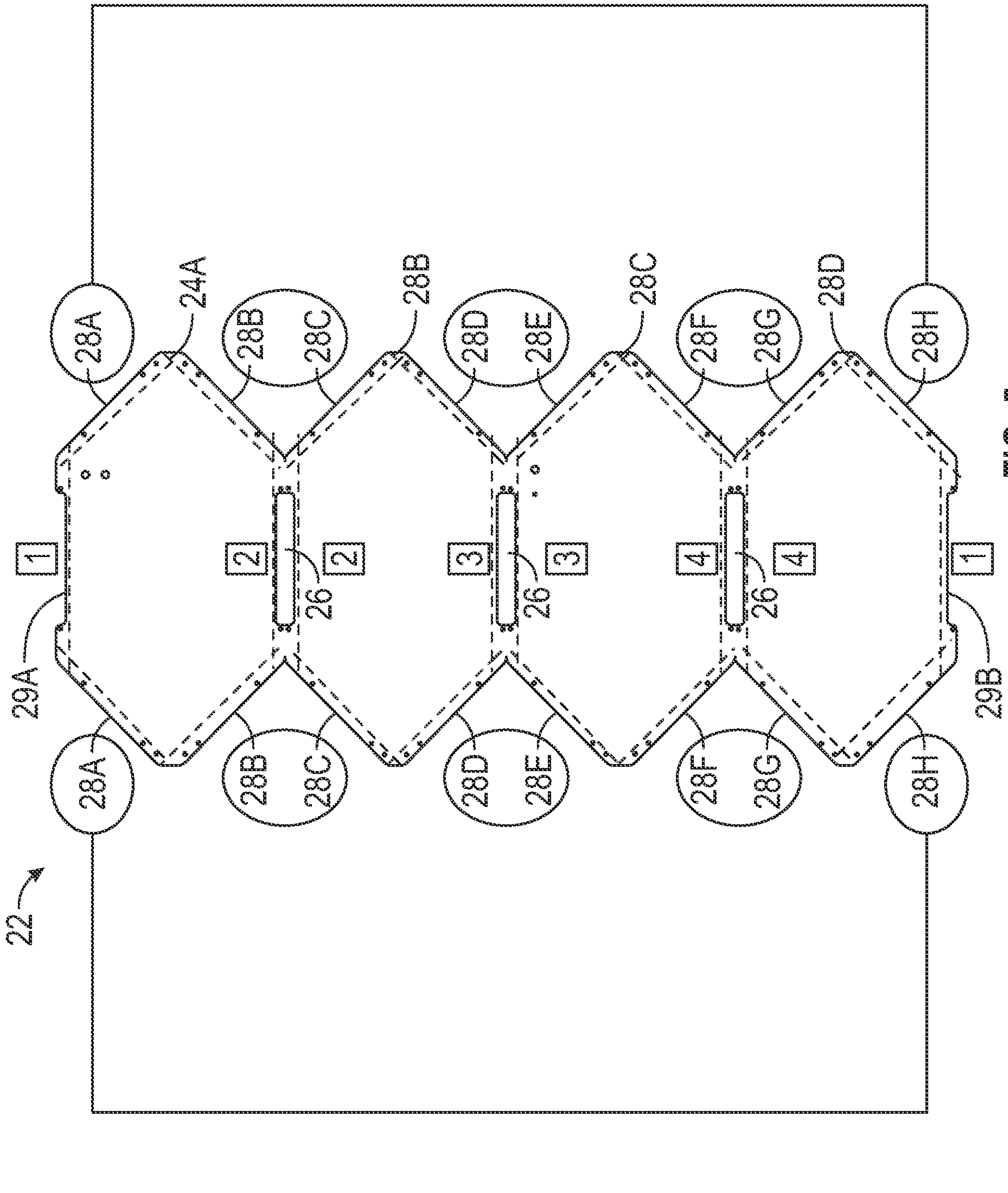
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FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2022/048204

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12M1/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12M B65D A61J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/086324 A1 (GE HEALTHCARE BIO SCIENCES CORP [US] ET AL.) 9 May 2019 (2019-05-09) paragraph [0046]; claim 1; figure 5 -----	1-15
A	US 2016/325873 A1 (SMITH DANIEL T [US] ET AL) 10 November 2016 (2016-11-10) claim 1 -----	1-15
A	CN 109 982 678 A (SARTORIUS STEDIM FMT SAS) 5 July 2019 (2019-07-05) claim 1 -----	1-15

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
23 February 2023	03/03/2023

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Jones, Laura

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2022/048204

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