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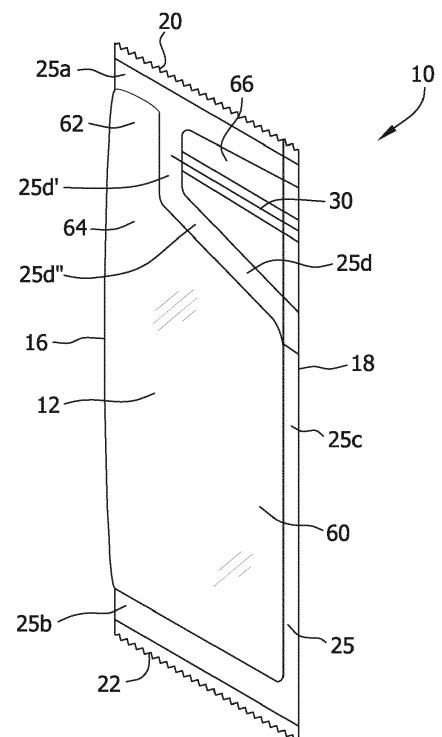
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(54) **Pouch, method of manufacturing a pouch and a method of dispensing a product from a pouch**

(57) A single-use pouch (10) for liquid product has a front panel (12) and a back panel (14). The front and back panels at least in part cooperatively define an interior space (15) of the pouch. The interior space has a total liquid capacity. A volume of liquid product is contained within the interior space. The volume of liquid product is less than about 60% of the total liquid capacity of the pouch.

**FIG. 1**



**Description**

## FIELD OF THE DISCLOSURE

5     **[0001]** The field of this disclosure relates generally to packaging for liquid products and more particularly to a pouch for containing and dispensing aseptically processed low acid concentrated liquid (e.g., human milk fortifier), methods for manufacturing a hermetically sealed pouch, methods for aseptically packaging the human milk fortifier in the pouch, method for testing of seal integrity of the pouch and methods of using the pouch to dispense human milk fortifier.

## 10     BACKGROUND OF THE DISCLOSURE

**[0002]** Human milk is generally recognized as an ideal food source for most infants due to its overall nutritional composition. It is well known and generally accepted that human milk provides infants with unique immunologic and developmental benefits as compared generally to commercially available infant formulas.

15     **[0003]** For some infants, however, especially preterm infants, human milk does not always meet their complete nutritional needs. Although these infants still generally benefit from human milk, it is often desirable to supplement their human milk feedings with additional nutrients. Initially, preterm infants may grow more rapidly than many of their term counterparts, and accelerated growth often requires additional nutrition, which can be made possible by the use of a human milk fortifier in combination with human milk.

20     **[0004]** Human milk fortifiers described in literature and commercially available have been formulated as reconstitutable powders rather than liquids in order to minimize the volume displacement of human milk by the fortifier. Powdered human milk fortifiers, however, are not considered commercially sterile therefore microbes can be present in powdered human milk fortifiers and may grow once dispensed from the package into the human milk.

25     **[0005]** More recently, liquid human milk fortifiers, and specifically highly concentrated human milk fortifier liquids, have received more attention as an alternative to powders. Although these highly concentrated human milk fortifiers do generally displace slightly more volume than powders, the liquids are processed to be commercially sterile, which is not an option for powders.

30     **[0006]** Hydrolyzed proteins are often desirable to utilize in human milk fortifiers as they are generally more easily digested and absorbed into the gut of a preterm infant as compared to substantially intact proteins. Additionally, the hydrolyzed proteins may be hypoallergenic such that they may not predispose the infant to cow's milk allergies later in life. However, as compared to intact proteins, extensively hydrolyzed proteins (i.e., proteins having a degree of hydrolysis of about 20% or more) tend to have poor ability to form long term stable emulsions. Additionally, the presence of high levels of insoluble minerals such as calcium salts may also cause a number of stability issues when used in combination with extensively hydrolyzed proteins. As such, manufacturing long term stable liquid concentrated human milk fortifiers including extensively hydrolyzed proteins have proven difficult.

35     **[0007]** To combat this problem, many liquid human milk fortifiers have been manufactured with stabilizers, such as carrageenan. The stabilizers act to hold the nutrients and insolubles in solution over time and thus improve long term stability of the product. Although stabilizers, such as carrageenan, have generally proven to retard precipitation of many ingredients in the liquid human milk fortifier, these types of stabilizers are not permitted in infant formulas and human milk fortifiers in many countries around the world. When stabilizers cannot be used in highly concentrated human milk fortifiers, it can be very difficult to produce a long term stable highly concentrated human milk fortifier.

40     **[0008]** As such, there is a need for liquid human milk fortifiers that are commercially sterile, do not require refrigeration, and have relatively low acidity. In addition, there is a need for packaging for liquid human milk fortifiers that is sufficiently flexible to allow insitu mixing of the fortifier, and transparent so that a user can visually observe the human milk fortifier to ensure proper mixing has occurred before opening the packaging to dispense the human milk fortifier. Moreover, the packaging should be easy to use and should minimize the amount of residual human milk fortifier remaining in the packaging after dosing.

## BRIEF DESCRIPTION OF THE DISCLOSURE

50     **[0009]** In one aspect, a single-use pouch for liquid product generally comprises a front panel and a back panel. The front and back panels at least in part cooperatively define an interior space of the pouch. The interior space has a total liquid capacity. A volume of liquid product is contained within the interior space. The volume of liquid product is less than about 50% of the total liquid capacity of the pouch.

55     **[0010]** In another aspect, a single-use pouch for liquid product generally comprises a front panel and a back panel. The front and back panels at least in part cooperatively define an interior space of the pouch. The interior space has a total liquid capacity. A volume of liquid product and gas is contained within the interior space. The volume of liquid product and gas is less than about 40% of the total liquid capacity of the pouch.

**[0011]** In yet another aspect, a pouch generally comprises a front panel and a back panel. The front and back panels at least in part cooperatively define an interior space of the pouch. At least one of the front panel and the back panel is made at least in part from a flexible, transparent material. An aseptically processed liquid product is contained within the interior space of the pouch and visually observable through the at least one of the front panel and the back panel.

**[0012]** In still another aspect, a method of packaging an aseptic liquid product into a pouch generally comprises sterilizing both sides of a flexible and transparent web of sheet material with a sterilant. The web is drawn across forming shoulders, around filling tubes, to create longitudinal pouch tubes. Two pouches are formed, one from each lane. Each pouch is filled with an aseptically processed liquid product.

**[0013]** In still yet another aspect, a method of dispensing a liquid product from a pouch generally comprises obtaining a pouch having an aseptically processed liquid product contained therein. At least a portion of the pouch is transparent for allowing visual observation of the liquid product contained therein. The pouch is manually kneaded to mix the liquid product within the pouch. The liquid product is visually observed through the transparent portion of the pouch to determine if the liquid product has been sufficiently mixed. The pouch is opened and the liquid product is poured from the pouch.

**[0014]** In still a further aspect, a single-use pouch for product generally comprises a body having a front panel and a back panel. The front and back panels at least in part cooperatively define an interior space of the pouch for containing the product. A spout is in fluid communication with the interior space. Product is dispensed from the pouch through the spout. The spout has a width and the body has a width wherein the ratio of the width of the body and the width of the spout is between about 3:1 and about 5:1.

**[0015]** In yet a further aspect, a secondary container for holding a plurality of pouches generally comprises a base section and a lid hingely attached to the base section for movement between a closed position and an opened position. A pair of hold downs are disposed adjacent opposite ends of the hinge.

**[0016]** In still another aspect, a secondary container for holding a plurality of pouches generally comprises a base section and a lid hingely attached to the base section for movement between a closed position and an opened position. The base section includes a bottom wall, at least one side wall extending up from the bottom wall, a top wall, and an interior floor. The interior floor is tented along its center line.

#### BRIEF DESCRIPTION OF THE DRAWINGS

##### **[0017]**

Fig. 1 is a perspective of one suitable embodiment of a pouch for containing and dispensing a liquid product, the pouch being illustrated in a closed configuration;

Fig. 2 is a front elevation thereof;

Fig. 3 is a back elevation thereof;

Fig. 4 is a cross-section taken along line 4-4 of Fig. 2;

Fig. 5 is a cross-section taken along line 5-5 of Fig. 2;

Fig. 6 is a front elevation similar to Fig. 2 but illustrating the pouch in an opened configuration;

Fig. 7A is an enlarged fragmentary cross-section taken along line 7-7 of Fig. 3 illustrating one suitable laminate for forming the pouch;

Fig. 7B is an enlarged fragmentary cross-section similar to Fig. 7A but illustrating another suitable laminate for forming the pouch

Fig. 8 is a front elevation of another suitable embodiment of a pouch for containing and dispensing a liquid product, the pouch being illustrated in a closed configuration;

Fig. 9 is a front elevation of another suitable embodiment of a pouch for containing and dispensing a liquid product, the pouch being illustrated in a closed configuration

Fig. 10 is a flow diagram illustrating one suitable embodiment of a process for manufacturing the pouch and filling the pouch with a liquid product;

Figs. 11A - 11C are schematics illustrating sequential aspects of the process for manufacturing and filling the pouch;

Fig. 12 is a perspective of one suitable embodiment of a secondary packaging for containing a plurality of the pouches;

Fig. 13 is a perspective illustrating the pouch in its opened configuration and the liquid product contained therein being dispensed into a nursing bottle containing human milk;

Figs. 14A and 14B are side elevations of pouches similar to the ones illustrated in Figs. 2 and 9 except that the pouches seen herein are opaque;

Figs. 15A and 15B illustrate the pouch of Fig. 14A in the process of being opened and being tilted as if the product contained therein is being dispensed;

Figs. 16A and 16B illustrate another suitable embodiment of a secondary packaging for containing a plurality of the pouches illustrating a lid of the packaging in a closed position and in an opened position;

Fig. 17 is a front perspective view of the secondary packaging of Fig. 12 with the lid closed;

Fig. 18 is another front perspective of the secondary packaging of Fig. 12 with the lid closed;

Fig. 19 is a rear perspective of the secondary packaging of Fig. 12 with the lid closed;

Fig. 20 is a front perspective of the secondary packaging of Fig. 12 with the lid opened;

Fig. 21 is a side elevation of the secondary packaging of Fig. 12 with the lid opened;

Fig. 22 is a schematic illustration of a plastic container including a concentrated liquid human milk fortifier that does not contain any OSA-modified corn starch or low acyl gellan gum;

Fig. 23 is a schematic illustration of a plastic container including a concentrated liquid human milk fortifier that contains OSA-modified corn starch but does not contain low acyl gellan gum;

Fig. 24 is a schematic illustration of a plastic container including a concentrated liquid human milk fortifier that contains low acyl gellan gum but does not contain OSA-modified corn starch; and

Fig. 25 is a schematic illustration of a plastic container including a concentrated liquid human milk fortifier that contains both OSA-modified corn starch and low acyl gellan gum.

**[0018]** Corresponding reference characters indicate corresponding parts throughout the drawings.

## DETAILED DESCRIPTION OF THE DRAWINGS

### Pouch

**[0019]** Figs. 1-5 of the drawings illustrate one embodiment of a pouch, indicated generally at 10, suitable for packaging and dispensing a liquid product, e.g., a liquid product intended for human consumption. As used herein "liquid product" means a product that is a flowable non-solid product including, for example but not limited to, aqueous solutions, solutions having a determinable viscosity, emulsions, colloids, pastes, gels, dispersions and other flowable non-solid products so as to exclude solid products such as bars and particulate products, such as powders.

**[0020]** As seen therein, the illustrated pouch 10 has a front panel 12 and a back panel 14 generally opposed to and sealingly engaged with the front panel to at least in part define an interior space 15 sized and shaped for containing the product. The illustrated pouch 10 comprises two side edges 16, 18, two end edges 20, 22, a longitudinal axis LA, and a transverse axis TA. In the illustrated embodiment, the pouch 10 is formed from a single-piece of sheet material that has been folded about a longitudinal fold line. As seen in Figs. 2-5, the fold line forms one of the side edges 16 of the pouch 10. The front panel 12 of the pouch 10 is joined to the back panel 14 along the other side edge 18 and at the end edges 20, 22 along a plurality of seal lines 25, such as by heat sealing, to seal the interior space 15 of the pouch. It is understood, however, that the front panel 12 and back panel 14 of the pouch 10 may be joined in other ways without departing from the scope of the present invention (e.g., adhesive). It is also understood that the pouch 10 could be

formed from two separate panels that are sealed together along both side edges 16, 18 and the end edges 20, 22. It is also contemplated that the pouch 10 may include sidewalls (not shown) intermediate the front panel 12 and the back panel 14 without departing from the scope of this invention.

**[0021]** With reference to Figs. 2 and 3, the seal lines 25 include end segments 25a, 25b disposed along the margins adjacent the end edges 20, 22 of the pouch 10, respectively, to fluidly seal the ends of the pouch. A side edge segment 25c is disposed adjacent one of the side edges 18 (i.e., opposite the side edge 16 defined by the fold line) and extends the longitudinal length of the pouch 10. The side edge segment 25c intersects (or otherwise contacts) the end segments 25a, 25b to define the interior space 15 of the pouch 10 and to seal the pouch in a fluid-tight manner. As seen in Figs. 2 and 3, the seal lines 25 further comprise an inboard seal segment 25d that connects one of the end segments 25a (the upper seal segment as viewed in Figs. 2 and 3) to the side edge segment 25c. In the illustrated embodiment, the inboard seal segment 25d includes a longitudinal component 25d' extending downward from the end segment 25a and a diagonal component 25d'' extending diagonally from the longitudinal component to the side edge segment 25c. It is understood, however, that the inboard seal segment 25d can have different configurations (e.g., generally L-shaped) without departing from the scope of this invention.

**[0022]** With reference still to Figs. 2 and 3, the pouch 10 includes a body 60, a spout 62, and a transition (or funnel) portion 64 connecting the body to the spout. The body 60 is the portion of the pouch 10 below the lower extent of the diagonal component 25d'' of the inboard seal segment 25d of the seal lines 25. The body 60 has a height H1 and a width W1. In the illustrated embodiment, the height H1 of the body 60 is approximately 75 mm and the width W1 of the body is approximately 36 mm. It is understood that the body 60 can have heights and widths less than or greater than the exemplary heights and widths provided herein. The spout 62 is defined by the end segment 25a and the longitudinal component 25d' of the inboard seal segment 25d of the seal lines 25. As seen in Figs. 2-4, the spout 62 includes the fold line defining one of the side edges 16 of the pouch 10. In use, the fold line acts as a channel and guides the product along the fold line and towards an opening in the spout. The spout 62 has a height H2 and a width W2. In the illustrated embodiment, the height H2 of the spout 62 is approximately 17 mm and the width W1 of the spout is approximately 10 mm. Thus, the illustrated body 60 of the pouch 10 has a width ratio of about 3.6:1 with respect to the width of the spout 62. That is, the body has a width that is about 3.6 times larger than the width of the spout 62. It is understood that the spout 62 can have heights and widths less than or greater than the exemplary heights and widths provided herein. For example, the ratio of the width of the body and the width of the spout may be between about 3:1 and about 5:1, such as, about 4:1.

**[0023]** The transition portion 64 is a portion of the pouch 10 disposed between the spout 62 and body 60, and includes the diagonal component 25d'' of the inboard seal segment 25d of the seal lines 25. In use, the diagonal component 25d'' of the inboard seal segment 25d acts as a funnel-like surface to funnel the product towards the spout. The transition portion 64 has a height H3. In the illustrated embodiment, the height H3 of the transition portion 64 is approximately 17 mm. The width of the transition portion 64 reduces along its height as it extends from the body 60 to the spout 62. It is understood that the transition portion 64 can have heights and widths less than or greater than the exemplary heights and widths provided herein.

**[0024]** In a sealed (broadly, closed) configuration of the pouch 10, as illustrated in Figs. 1-3, the product is sealingly enclosed in the interior space 15 of the pouch. In one suitable embodiment, the product is aseptically processed and sealed within the pouch 10 as described in more detail below. The pouch 10 can be selectively configured from the sealed configuration to an opened configuration as illustrated in Fig. 6 to permit dispensing of the product from the pouch. In one suitable embodiment, the product is a liquid and can be poured from the pouch 10 through the spout 62. It is understood, however, that the product can be any suitable, liquid substance including a gel or a paste.

**[0025]** As illustrated in Figs. 1-3, the pouch 10 has a first line of weakness 30 formed on the front panel 12 of the pouch and a second line of weakness 32 formed on the back panel 14 of the pouch. The lines of weakness 30, 32 provide a path along which the pouch 10 is more readily torn to open the pouch (i.e., configured to the opened configuration). It is understood that the pouch 10 may have a line of weakness 30, 32 disposed on only one of the front and back panels 12, 14, with the other panel being free of a line of weakness and remain within the scope of this invention. While the lines of weakness 30, 32 in the illustrated embodiment are substantially equal in length, the lengths of the lines of weakness 30, 32 can be different without departing from the scope of this invention. Thus, the line of weakness 30 on the front panel 12 of the pouch 10 may be longer or shorter than the line of weakness 32 on the back panel 14 of the pouch.

**[0026]** In the illustrated embodiment, the lines of weakness 30, 32 comprise score lines. The term "line of weakness" is used herein to mean any defined (e.g., intended) structural feature that weakens the pouch 10 along a predetermined path so that the pouch 10 is more readily ruptured, or torn, upon application of a tearing force along the line of weakness and is not limited to score lines. For example, in other embodiments, the lines of weakness 30, 32 may comprise a plurality of separation points, a score line, a breakaway line or areas, a chain stitch, a thinning of the pouch material, a plurality of aligned perforations (e.g., holes, slits, apertures, voids, or the like) or other suitable line of weakness. The lines of weakness 30, 32 may be formed by partial pressure cutting, partial ultrasonic cutting, partial thermal deformation,

mechanical thinning, or other suitable techniques.

**[0027]** As mentioned, the lines of weakness 30, 32 provide a path of low resistance along which the pouch 10 may be torn. However, the level of resistance to tearing provided by the lines of weakness 30, 32 can be altered. Lowering the tear resistance would make the pouch 10 easier to open. As a result, less force is needed to tear the pouch 10 along the lines of weakness 30, 32. However, lowering the tear resistance may increase the risk that the pouch 10 will unintentionally tear apart or otherwise leak. On the other hand, increasing the resistance of the lines of weakness 30, 32, would require a greater force to tear the pouch 10 along the lines of weakness. In addition, the lines of weakness 30, 32 can have varying tear resistance along their length or a portion of their length. In addition, the tear resistance of the line of weakness 30 in the front panel 12 of the pouch 10 may be equal to or different than the tear resistance of the line of weakness 32 in the back panel 14 of the pouch.

**[0028]** In the illustrated embodiment, the lines of weakness 30, 32 begin at the side edge 18 (e.g., the side edge not defined by the fold line), extend through the side edge segment 25c of the seal lines 25 and generally parallel to but spaced from one of the end edges 20, and terminate within the longitudinal component 25d' of the inboard seal segment 25d of the seal lines and generally adjacent the spout 62. Accordingly, the product can be accessed by tearing the pouch 10 along the lines of weakness 30, 32 as illustrated in Fig. 6. The spout 62 is torn approximately in half longitudinally during tearing of the lines of weakness 30, 32. It is understood, however, that more or less of the spout 62 can be torn away.

**[0029]** In the illustrated embodiment, the portion of the pouch 10 above the lines of weakness 30, 32 defines a gripping portion 66 suitable for manually grasping to facilitate opening of the pouch 10 by tearing along the lines of weakness 30, 32. In one suitable embodiment, the gripping portion 66 is removed from the remainder of the pouch 10 when the pouch is opened (i.e., when the pouch is torn along the lines of weakness 30, 32). It is contemplated, however, that the gripping portion 66 can remain connected to the pouch 10 so long as the spout 62 is sufficiently open to allow the product to flow out of the interior space 15 of the pouch.

**[0030]** The pouch 10 may be formed from any suitable material including woven material, non-woven material, films, laminates, or a combination thereof. For example, in one suitable embodiment, the pouch 10 comprises a two layered laminate having an inner layer 50 and an outer layer 52 (Fig. 7A). In one particularly suitable embodiment, the inner layer 50 is formed from a co-extrusion of linear low density polyethylene (LLDPE) and ethylene vinyl alcohol (EVOH), and the outer layer 52 from barrier coated polyethylene terephthalate (PET). In another suitable embodiment, which is illustrated in Fig. 7B, the pouch 10 comprises a three layered laminate having an inner layer 50', an outer layer 52', and an intermediate layer 54' disposed between the inner and outer layers (Fig. 7B). In one particularly suitable embodiment, the inner layer 50' is formed from a co-extrusion of linear low density polyethylene (LLDPE) and ethylene vinyl alcohol (EVOH), and the outer layer 52' from barrier coated polyethylene terephthalate (PET). The intermediate layer 54' is formed from one of aluminum oxide coated PET, a silicon oxide coated PET, or ethylene vinyl alcohol. As explained in more detail below, the pouch 10, in one suitable embodiment, is formed from a non-metallic material. That is, the pouch 10 is substantially free from metal. It is understood, however, that the layers 50, 50', 52, 52', 54' can be formed from any suitable materials without departing from some aspects of this invention.

**[0031]** As seen in Fig. 7A, the layers 50, 52 of the two layer laminate are bonded together using adhesive 51. It is understood, however, that the layers 50, 52 can be bonded together using other suitable techniques. As also seen in Fig. 7A, indicia 53 is printed on an inner surface of the inner layer 50 (i.e., the surface that faces and is bonded to the outer layer 52) using suitable ink. It is understood, however, that the indicia 53 can be printed on either surface of the outer layer 52.

**[0032]** In one suitable embodiment, at least a portion of the pouch 10 is generally transparent to permit visual observation of the product contained therein. In the illustrated embodiment, for example, the entire pouch 10 is generally transparent. In one suitable embodiment, the inner surface of the inner layer 50 of either the front panel 12 or the back panel 14 can be covered with a white ink to render the front/back panel generally transparent. It is understood, however, that less than the entire pouch can be transparent. For example, the front panel 12 could be made from a generally transparent material and the back panel 14 formed from a translucent or opaque material, or vice versa. In another example, the pouch 10 could include a longitudinally extending strip of transparent material (e.g., to form a window) on either one of or both the front and back panels 12, 14 of the pouch while the remainder of the pouch is formed from a generally translucent or opaque material. It is understood, that the pouch 10 can be formed from generally opaque material as seen in Figs. 14A and 14B without departing from some aspects of this invention.

**[0033]** The pouch 10 illustrated in Figs. 1-6 is suitably configured for containing and dispensing a predetermined target dispensing dosage, such as, approximately 5 ml. It is understood, however, that the pouch 10 can be configured to hold any suitable target dosage. For example, Fig. 8 illustrates a second embodiment of a pouch 110 substantially similar to the pouch 10 of Figs. 1-6 except that the pouch of this second embodiment is smaller and designed to hold a target dosage of approximately 2 ml. More specifically, the pouch 110 has a shorter body 160 than the body 60 of the pouch 10 illustrated in Figs. 1-6. Otherwise, the pouches 10, 110 are substantially the same including, in one embodiment, being of the same width for ease of manufacturing different sized pouches. In another example, Fig. 9 illustrates a third embodiment of a pouch 210 substantially similar to the previous described pouch 10 of Figs. 1-6 except that the pouch

of this embodiment is larger and designed to hold a target dosage of approximately 80 ml. More specifically, the pouch 210 has a longer body 260 than the body 60 of the pouch 10 illustrated in Figs. 1-6. Otherwise, the pouches 10, 210 are substantially the same. Depending on the product and the desired target dosage, it is understood that the pouch may be sized and configured for generally any target dosage.

**[0034]** In one suitable embodiment, each of the pouches 10, 110, 210 is filled with a greater quantity of product as compared to its intended target dispensing dosage to account for residual product that remains within the pouch after use, such as, due to viscosity and stickiness of the product. Testing of the pouch 10 illustrated in Figs. 1-6 determined that approximately 88 percent of the pouch contents are typically dispensed during use. As a result, each of the pouches 10, 110, 210 has an actual fill volume that is approximately 12 percent greater than the target dispensing dosage. Thus, the pouch 110 intended to have a 2 ml dosage (Fig. 8) has a fill volume of approximately 2.27 ml. The pouch 10 intended to have a 5 ml dosage (Figs. 1-7) has a fill volume of approximately 5.69 ml. And the pouch 210 intended to have an 80 ml dosage size (Fig. 9) has a fill volume of approximately 90.91 ml. It is understood that the pouches 10, 110, 210 can have other anticipated residual rates (i.e., besides 88 percent) as a result of viscosity, stickiness or other factors and thus other fill volumes without departing from the scope of this invention.

**[0035]** Moreover, it is anticipated that each of the pouches 10, 110, 210 will have a distribution ratio within  $\pm 4$  percent. That is, the actual amount of product distributed from each of the pouches 10, 110, 210 will be within 4 percent of the target dosage for that pouch. Thus, the pouch 110 intended to have a 2 ml dosage (Fig. 8) will actually dispense a quantity of product between about 1.92 ml and about 2.08 ml. The pouch 10 intended to have a 5 ml dosage (Figs. 1-7) will actually dispense a quantity of product between about 4.8 ml and about 5.2 ml. And the pouch 210 intended to have an 80 ml dosage (Fig. 9) will actually dispense a quantity of product between about 76.8 ml and about 83.2 ml. It is understood that the pouches 10, 110, 210 can have a different distribution ratio (i.e., besides  $\pm 4$  percent) without departing from the scope of this invention.

**[0036]** Each of the pouches 10, 110, 210 is capable (e.g., sufficiently flexible) of being manually kneaded or otherwise manipulated by a user to ready the product within the pouch before opening the pouch. Thus, in one embodiment, the product can be thoroughly mixed within the pouch 10, 110, 210 before the pouch is opened and the product dispensed therefrom. In other embodiments where the product is more gel-like, kneading also, or alternatively, thins the product to render it easier to pour. In one suitable embodiment, the front and back panels 12, 14 of the pouch 10 contact each other during the kneading process under relatively light, manual pressure and the product is able to move freely throughout the interior space 15.

**[0037]** A qualitative kneadability study was performed on pouches designed for a target dispensing dosage of about 5 ml. The pouches had a total (e.g., maximum) liquid capacity of about 20 ml. In Example 1, ten pouches were filled with a various amount of air (broadly, a gas) and manually kneaded. The kneadability of the pouch was rated as being easy, moderate, difficult or extremely difficult. The amount of air and the results of the testing are provided in the following Table. In Example 2, ten pouches were filled with a various amount of liquid and manually kneaded. The kneadability of the pouch was rated as being easy, moderate, difficult or extremely difficult. The amount of liquid and the results of the testing are provided in the following Table. In Example 3, ten pouches were filled with various combinations of liquid and air and manually kneaded. The kneadability of the pouch was rated as being easy, moderate, difficult or extremely difficult. The amount of liquid and air and the results of the testing are provided in the following Table.

| Example 1       |                 |              |                     |
|-----------------|-----------------|--------------|---------------------|
| Air Only Sample | Air Volume (ml) | Total Volume | Ease of Kneading    |
| 1               | 6               | 6            | Easy                |
| 2               | 7               | 7            | Easy                |
| 3               | 8               | 8            | Easy                |
| 4               | 9               | 9            | Easy                |
| 5               | 10              | 10           | Easy                |
| 6               | 11.5            | 11.5         | Moderate            |
| 7               | 16.5            | 16.5         | Moderate            |
| 8               | 19              | 19           | Moderate            |
| 9               | 22              | 22           | Difficult           |
| 10              | 26.5            | 26.5         | Extremely Difficult |

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(continued)

| Example 2                         |                                |              |                     |
|-----------------------------------|--------------------------------|--------------|---------------------|
| Liquid Only Sample                | Liquid Volume (ml)             | Total Volume | Ease of Kneading    |
| 1                                 | 4                              | 4            | Easy                |
| 2                                 | 5                              | 5            | Easy                |
| 3                                 | 6                              | 6            | Easy                |
| 4                                 | 7                              | 7            | Easy                |
| 5                                 | 8                              | 8            | Easy                |
| 6                                 | 9                              | 9            | Easy                |
| 7                                 | 10                             | 10           | Easy                |
| 8                                 | 12                             | 12           | Moderate            |
| 9                                 | 16                             | 16           | Difficult           |
| 10                                | 20                             | 20           | Extremely Difficult |
| Example 3                         |                                |              |                     |
| Liquid + Air Liquid Vol = 5.56 ml | Air Volume (ml) / % Air Volume | Total Volume | Ease of Kneading    |
| 1                                 | 0.6 / 10%                      | 6.2          | Easy                |
| 2                                 | 1.4 / 20%                      | 7.0          | Easy                |
| 3                                 | 2.4 / 30%                      | 7.9          | Easy                |
| 4                                 | 3.7 / 40%                      | 9.3          | Easy                |
| 5                                 | 5.6 / 50%                      | 11.1         | Easy                |
| 6                                 | 8.3 / 60%                      | 13.9         | Moderate            |
| 7                                 | 10.3 / 65%                     | 15.9         | Moderate            |
| 8                                 | 13 / 70%                       | 18.5         | Difficult           |
| 9                                 | 16.7 / 75%                     | 22.2         | Extremely Difficult |
| 10                                | 22.2 / 80%                     | 27.8         | Extremely Difficult |

**[0038]** The intent of the kneadability study was to determine suitable packaged volumes at which kneading of the product/pouch becomes impractical (i.e., difficult or extremely difficult).

**[0039]** As seen above for Example 2, where no air is present the amount of liquid within the pouch should be less than or equal to about 50% of the total liquid capacity of the pouch. When the amount of liquid in the pouch exceeded 50%, the kneadability of the pouch was reduced. In one suitable embodiment, the volume of liquid in the pouch is between about 20% and about 50%, more suitably between about 30% and about 40%, and even more suitably about 35% of the total liquid capacity of the pouch.

**[0040]** As seen above for Example 3, the total volume taken up by liquid and gas (e.g., air) within the pouch should be less than or equal to about 50% of the total liquid capacity of the pouch. When the combined volume of liquid and gas exceeds about 50%, the kneadability of the pouch is reduced. In one suitable embodiment, the combined volume of liquid and gas in the pouch is between about 10% and about 50%, more suitably between about 20% and about 40% of the total liquid capacity of the pouch.

### Human Milk Fortifiers

#### Concentrated Liquid Human Milk Fortifier

**[0041]** In one suitable use, the pouch 10, 110, 210 can contain liquid human milk fortifier capable of being poured directly from the pouch into a container having human milk therein. It is understood, however, that the pouch 10, 110,



210 can contain any suitable product including other products intended for human consumption. One suitable liquid human milk fortifier is a concentrated liquid human milk fortifier comprising protein, fat, carbohydrate OSA-modified starch and low acyl gellan gum. The concentrated liquid human milk fortifier has a solids content of at least about 20%, or even at least about 25%, including from about 25% to about 32%, and further including from about 29% to about 32%.  
 5 The concentrated liquid human milk fortifier has a caloric density of at least about 1.25 kcal/ml (37 kcal/fl oz), including from about 1.4 kcal/ml (42 kcal/fl oz) to about 5 kcal/ml (149 kcal/fl oz), and also including from about 1.5 kcal/ml (44 kcal/fl oz) to about 2.5 kcal/ml (74 kcal/fl oz), and also including from about 1.9 kcal/ml (56 kcal/fl oz) to about 2.0 kcal/ml (59 kcal/fl oz). The concentrated liquid human milk fortifiers is formulated to provide fortified human milk having an osmolality of less than about 400 mOsm/kg water, preferably from about 300 mOsm/kg water to about 400 mOsm/kg water.

### **Extensively Hydrolyzed Casein Protein**

[0042] The concentrated liquid human milk fortifier includes hypoallergenic extensively hydrolyzed casein as a protein source. The term "hypoallergenic" as used herein means that the concentrated liquid human milk fortifier has a decreased tendency to provoke an allergic reaction in a preterm or term infant as compared to non-hypoallergenic fortifiers. Generally,  
 15 the concentrated liquid human milk fortifier includes at least about 35%, including at least about 50%, including at least about 60%, including at least about 75%, including at least about 90% and further including about 100% extensively hydrolyzed casein, by total weight of protein in the concentrated human milk fortifier. In one embodiment, the concentrated liquid human milk fortifier includes 100% extensively hydrolyzed casein, by total weight of the protein in the concentrated  
 20 human milk fortifier. In this embodiment, the concentrated liquid human milk fortifier is hypoallergenic. In some other embodiments, the concentrated liquid human milk fortifier will include from about 35% to 100%, including from about 50% to 100%, further including from about 75% to 100% extensively hydrolyzed casein, by total weight of protein in the concentrated human milk fortifier. The concentrated liquid human milk fortifier may optionally include other hypoallergenic or non-hypoallergenic proteins in addition to the extensively hydrolyzed casein protein.

[0043] Extensively hydrolyzed casein proteins suitable for use in concentrated liquid human milk fortifiers include those having a degree of hydrolysis of from about 20% to about 70%, including from about 30% to about 60%, and further including from about 40% to about 60%. Generally, the extensively hydrolyzed casein has a ratio of total amino nitrogen (AN) to total nitrogen (TN) of from about 0.2 AN to 1.0 TN to about 0.4 AN to about 0.8 TN. Suitable commercially available extensively hydrolyzed caseins will generally have a protein level in the ingredient of from about 50% to about  
 30 95%, including from about 70% to about 90%. One suitable commercially available extensively hydrolyzed casein is Dellac CE90, which is a spray dried powder casein hydrolysate (Friesland Campina Domo, Amersfoort, The Netherlands).

### **Stabilizer System**

[0044] The concentrated liquid human milk fortifier includes a synergistic two component stabilizer system. The first component is an octenyl succinic anhydride (OSA) modified corn starch. The second component is a low acyl gellan gum. These two components act in a synergistic manner to stabilize the concentrated liquid human milk fortifier emulsion and retard the precipitation of nutrients therefrom.

[0045] The OSA-modified corn starch is generally prepared by esterifying a dextrinized, ungelatinized waxy corn starch with 1-octenyl succinic anhydride. Methods of this type are well known in the art. One suitable commercially available  
 40 OSA-modified corn starch is N-CREAMER™ 46 (National Starch Food Innovation, Bridgewater, New Jersey). Without being bound to a particular theory, it is believed that the OSA-modified corn starch adsorbs in the oil and water interface thus preventing the oil droplets from coalescence/aggregation by steric hinderance and charge repulsion. The OSA-modified corn starch is present in the concentrated liquid human milk fortifier in an amount of from about 0.1% to about 3.5%, including from about 0.6% to about 2.0%, including from about 0.8% to about 1.5%, and further including about 1.2% by weight of the concentrated liquid human milk fortifier.

[0046] The low acyl gellan gum (also known as and commonly referred to as deacylated gellan gum) may be a water-soluble polysaccharide produced by fermentation of a pure culture of *Sphingomonas elodea*. As used herein, "low acyl" means that the gellan gum has been treated such that it forms firm, non-elastic, brittle gels, that are heat stable, as  
 50 compared to "high acyl" which forms soft, very elastic, non-brittle gels. Without being bound to a particular theory, it is believed that the low acyl gellan gum creates a three dimensional gelled network of very small microgels that interact with each other to provide a stable suspension. One suitable commercially available low acyl gellan gum is Kelcogel F (CP Kelco U.S. Inc., Atlanta Georgia).

[0047] The low acyl gellan gum is present in the concentrated liquid human milk fortifier in an amount from greater than 125 ppm to about 800 ppm, including from about 150 ppm to about 400 ppm, including from about 200 ppm to about 300 ppm and further including about 200 ppm.

**Macronutrients**

**[0048]** The concentrated liquid human milk fortifier comprises carbohydrate, fat, and protein macronutrients of sufficient types and amounts, that when used in combination with human milk (or other infant feeding formula), they help meet the nutritional needs of infants and especially premature infants. The concentration of these macronutrients includes the ranges described hereinafter. The term "infant" as used herein, refers generally to individuals less than about 1 year of age, actual or corrected. The term "premature infants" are used herein refers to those infants born at less than 37 weeks gestation, have a birth weight of less than 2500 gm, or both.

**Protein**

**[0049]** The concentrated liquid human milk fortifier comprises a protein suitable for use with infants, especially preterm infants, at concentrations ranging from about 5% to about 50%, including from about 20% to about 40%, including from about 5% to about 30%, including from about 10% to about 25%, and also including from about 15% to about 25%, on a dry weight basis. In some embodiments, the protein may be at a concentration of less than 10%, on a dry weight basis. The protein concentration may be from about 7 to about 15 grams, including from about 9 to about 12 grams of protein per 100 grams of final liquid product.

**[0050]** As noted above, the protein component of the concentrated liquid human milk fortifier is at least partially comprised of extensively hydrolyzed casein. In one particularly suitable embodiment, the protein component of the concentrated human milk fortifier is entirely comprised of extensively hydrolyzed casein. In embodiments wherein additional proteins sources (i.e., one or more protein sources in addition to the extensively hydrolyzed protein source) are to be used in the concentrated liquid human milk fortifier in addition to the extensively hydrolyzed casein (i.e., the concentrated human milk fortifier protein component is not 100% extensively hydrolyzed casein), the fortifier may still be made hypoallergenic by including additional hypoallergenic proteins such as soy protein hydrolysate, whey protein hydrolysate, rice protein hydrolysate, potato protein hydrolysate, fish protein hydrolysate, egg albumen hydrolysate, gelatin protein hydrolysate, combinations of animal and vegetable protein hydrolysates, and combinations thereof.

**[0051]** In this context, the terms "protein hydrolysates" or "hydrolyzed protein" are used interchangeably herein and include extensively hydrolyzed proteins, wherein the degree of hydrolysis is most often at least about 20%, including from about 20% to about 80%, and also including from about 30% to about 80%, even more preferably from about 40% to about 60%. The degree of hydrolysis is the extent to which peptide bonds are broken by a hydrolysis method. The degree of protein hydrolysis for purposes of characterizing the extensively hydrolyzed protein component of these embodiments is easily determined by one of ordinary skill in the formulation arts by quantifying the amino nitrogen to total nitrogen ratio (AN/TN) of the protein component of the selected formulation. The amino nitrogen component is quantified by USP titration methods for determining amino nitrogen content, while the total nitrogen component is determined by the Tecator Kjeldahl method, all of which are well known methods to one of ordinary skill in the analytical chemistry art.

**[0052]** In other embodiments, the concentrated liquid human milk fortifier, in addition to the extensively hydrolyzed protein, may include an additional non-hypoallergenic protein source including for example, partially hydrolyzed or non-hydrolyzed (intact) protein, and can be derived from any known or otherwise suitable source such as milk (e.g., casein, whey, lactose-free milk protein isolates), animal (e.g., meat, fish), cereal (e.g., rice, corn), vegetable (e.g., soy), or combinations thereof. The protein can include, or be entirely or partially replaced by, free amino acids known or otherwise suitable for use in nutritional products, non-limiting examples of which include free amino acids including L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-carnitine, L-cystine, L-glutamic acid, L-glutamine, glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-serine, L-taurine, L-threonine, L-tryptophan, L-tyrosine, L-valine, and combinations thereof.

**Carbohydrate**

**[0053]** The concentrated liquid human milk fortifier comprises a carbohydrate suitable for use with infants, especially preterm infants, at concentrations most typically ranging up to about 75% by weight on a dry weight basis, including from about 10% to about 50%, and also including from about 20% to about 40%, by weight on a dry weight basis. Carbohydrates suitable for use in the concentrated liquid human milk fortifier include hydrolyzed or intact, naturally and/or chemically modified, starches sourced from corn, tapioca, rice or potato, in waxy or non-waxy forms. Other non-limiting examples of suitable carbohydrate sources include hydrolyzed cornstarch, maltodextrin (i.e. non-sweet, nutritive polysaccharide having a DE value less than 20), corn maltodextrin, glucose polymers, sucrose, corn syrup, corn syrup solids (i.e., polysaccharide having a DE value greater than 20), glucose, rice syrup, fructose, high fructose corn syrup, indigestible oligosaccharides such as fructooligosaccharides (FOS), galactose, glycerol and combinations thereof. The carbohydrates may comprise lactose or can be substantially free of lactose.

**[0054]** The concentrated liquid human milk fortifier may include a non-reducing carbohydrate component, which may represent from about 10% to 100%, including from about 80% to 100%, and also including 100%, by weight of the total carbohydrate in the concentrated liquid human milk fortifier. The selection of a non-reducing carbohydrate may enhance the product stability and is generally better tolerated by infants, especially premature infants. Non-limiting examples of non-reducing carbohydrates include sucrose or other carbohydrates that do not readily oxidize or react with Tollen's, Benedict's, or Fehling's reagents. The concentrated liquid human milk fortifier may have a carbohydrate component, wherein the carbohydrate component comprises a mono- and/or disaccharide such that at least about 50%, including from about 80% to 100%, and also including 100%, of the mono- and/or disaccharide is a non-reducing carbohydrate.

## **Fat**

**[0055]** The concentrated liquid human milk fortifier comprises a fat component suitable for use with infants, especially preterm infants, at concentrations most typically ranging up to about 40% by weight on a dry weight basis, including from about 10% to about 40%, and also including from about 15% to about 37%, and also including from about 18% to about 30%, by weight on a dry weight basis. Fats suitable for use in the concentrated liquid human milk fortifier include coconut oil, soy oil, corn oil, olive oil, safflower oil, high oleic safflower oil, MCT oil (medium chain triglycerides), sunflower oil, high oleic sunflower oil, structured triglycerides, palm and palm kernel oils, palm olein, canola oil, marine oils, cottonseed oils, and combinations thereof.

**[0056]** Suitable fats for use in the concentrated liquid human milk fortifier include emulsifiers to help the various fortifier components readily disperse when combined with human milk. Non-limiting examples of suitable emulsifiers include soya bean lecithin, or fractions thereof, polyoxyethylene stearate, mono and di-glycerides, and combinations thereof, polyoxyethylene sorbitan monopalmitate, polyoxyethylene sorbitan monostearate, ammonium phosphatides, polyoxyethylene sorbitan monolaurate, citric acid esters of mono and diglycerides of fatty acids, tartaric acid esters of mono and diglycerides of fatty acids, and combinations thereof. Natural soy lecithin is especially useful in this respect. The fat component of the concentrated liquid human milk fortifier may therefore optionally include any emulsifier suitable for use in infant nutritional products. Emulsifier concentrations in these products may range up to about 10%, including from about 1% to about 10%, even more typically from about 1.5% to about 5%, by weight of the total fat component.

**[0057]** The concentrated liquid human milk fortifier also include embodiments that comprise as part of the fat component one or more of arachidonic acid, docosahexaenoic acid, or combinations thereof, alone or in further combination with linoleic acid, linolenic acid, or both.

**[0058]** The weight ratio of fat to protein in the concentrated liquid human milk fortifier is at least about 0.9, including from about 1 to about 5, and also including from about 2 to about 4. These ratios may be helpful in further stabilizing the concentrated liquid human milk fortifier.

## **Vitamins and Minerals**

**[0059]** The concentrated liquid human milk fortifier may further comprise any of a variety of vitamins, non-limiting examples of which include vitamin A, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, pyridoxine, vitamin B 12, niacin, folic acid, pantothenic acid, biotin, vitamin C, choline, inositol, salts and derivatives thereof, and combinations thereof. The concentrated liquid human milk fortifier includes embodiments comprising per 100 kcal of fortifier solids one or more of the following: vitamin A (from about 250 to about 6500 IU), vitamin D (from about 40 to about 1200 IU), vitamin K, vitamin E (at least about 0.3 IU), vitamin C (at least about 8 mg), thiamine, vitamin B12, niacin, folic acid, pantothenic acid, biotin, choline (at least about 7 mg), and inositol (at least about 2 mg).

**[0060]** The concentrated liquid human milk fortifiers may also further comprise any of a variety of minerals known or otherwise suitable for use in infant or other nutritional formulas, non-limiting examples of which include phosphorus, magnesium, calcium as described hereinbefore, zinc, manganese, copper, iodine, sodium, potassium, chloride, selenium, chromium, and combinations thereof. The concentrated liquid human milk fortifier also includes embodiments comprising per 100 kcal of the fortifier solids one or more of the following: calcium (at least about 50 mg), phosphorus (at least about 25 mg), magnesium (at least about 6 mg), iodine, zinc (at least about 0.5 mg), copper, manganese, sodium (from about 20 to about 60 mg), potassium (from about 80 to about 200 mg), chloride (from about 55 to about 150 mg) and selenium (at least about 0.5 mcg).

## **Other Optional Ingredients**

**[0061]** The concentrated liquid human milk fortifier may further optionally comprise other ingredients that may modify the physical, chemical, aesthetic or processing characteristics of the formulas or serve as pharmaceutical or additional nutritional components when used in the targeted population. Many such optional ingredients are known for use in food and nutritional products, including infant formulas, and may also be used in the concentrated liquid human milk fortifiers,

provided that such optional materials are compatible with the essential materials described herein, are safe and effective for their intended use, and do not otherwise unduly impair the performance of the concentrated liquid human milk fortifier. Non-limiting examples of such optional ingredients include preservatives, anti-oxidants, various pharmaceuticals, buffers, carotenoids, colorants, flavors, nucleotides and nucleosides, thickening agents, prebiotics, probiotics, sialic acid-containing materials, and other excipients or processing aids.

### Examples

#### Examples 1-4

**[0062]** The ingredients for the concentrated liquid human milk fortifiers of Examples 1-4 are shown in the following table.

| Ingredient (Per 1000 Kg)    | Example 1 | Example 2 | Example 3 | Example 4 |
|-----------------------------|-----------|-----------|-----------|-----------|
| Water                       | Q.S.      | Q.S.      | Q.S.      | Q.S.      |
| Casein Hydrolysate          | 108 Kg    | 108 Kg    | 125 Kg    | 150 Kg    |
| Maltodextrin                | 104 Kg    | 104 Kg    | 104 Kg    | 104 Kg    |
| MCT Oil                     | 17.3 Kg   | 17.3 Kg   | 17.3 Kg   | 17.3 Kg   |
| Tricalcium Phosphate        | 16.0 Kg   | 16.0 Kg   | 16.0 Kg   | 16.0 Kg   |
| Soy Oil                     | 10.4 Kg   | 10.4 Kg   | 10.4 Kg   | 10.4 Kg   |
| OSA-Modified Corn Starch    | 12.0 Kg   | 10.0 Kg   | 35.0 Kg   | 6.0 Kg    |
| Coconut Oil                 | 6.3 Kg    | 6.3 Kg    | 6.3 Kg    | 6.3 Kg    |
| Potassium Citrate           | 6.9 Kg    | 6.9 Kg    | 6.9 Kg    | 6.9 Kg    |
| Ascorbic Acid               | 2.9 Kg    | 2.9 Kg    | 2.9 Kg    | 2.9 Kg    |
| Magnesium Chloride          | 4.0 Kg    | 4.0 Kg    | 4.0 Kg    | 4.0 Kg    |
| M. Alpina Oil (ARA)         | 2.6 Kg    | 2.6 Kg    | 2.6 Kg    | 2.6 Kg    |
| Leucine                     | 1.8 Kg    | 1.8 Kg    | 1.8 Kg    | 1.8 Kg    |
| C. Cohnii Oil (DHA)         | 2.1 Kg    | 2.1 Kg    | 2.1 Kg    | 2.1 Kg    |
| Potassium Chloride          | 1.1 Kg    | 1.1 Kg    | 1.1 Kg    | 1.1 Kg    |
| Tyrosine                    | 1.4 Kg    | 1.4 Kg    | 1.4 Kg    | 1.4 Kg    |
| Distilled Monoglycerides    | 800 g     | 800 g     | 800 g     | 800 g     |
| Mixed Carotenoid Premix     | 551 g     | 551 g     | 551 g     | 551 g     |
| M-Inositol                  | 529 g     | 529 g     | 529 g     | 529 g     |
| Sodium Chloride             | 861 g     | 861 g     | 861 g     | 861 g     |
| L-Carnitine                 | 221 g     | 221 g     | 221 g     | 221 g     |
| Tryptophan                  | 331 g     | 331 g     | 331 g     | 331 g     |
| Zinc Sulfate                | 309 g     | 309 g     | 309 g     | 309 g     |
| Niacinamide                 | 320 g     | 320 g     | 320 g     | 320 g     |
| dl-Alpha-Tocopheryl Acetate | 364 g     | 364 g     | 364 g     | 364 g     |
| Gellan Gum                  | 200 g     | 300 g     | 400 g     | 600 g     |
| Ferrous Sulfate             | 106 g     | 106 g     | 106 g     | 106 g     |
| Choline Chloride            | 353 g     | 353 g     | 353 g     | 353 g     |
| Calcium Pantothenate        | 132 g     | 132 g     | 132 g     | 132 g     |
| Vitamin A Palmitate         | 77 g      | 77 g      | 77 g      | 77 g      |

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(continued)

| Ingredient (Per 1000 Kg) | Example 1 | Example 2 | Example 3 | Example 4 |
|--------------------------|-----------|-----------|-----------|-----------|
| Riboflavin               | 33 g      | 33 g      | 33 g      | 33 g      |
| Vitamin D3               | 13 g      | 13 g      | 13 g      | 13 g      |
| Copper Sulfate           | 18 g      | 18 g      | 18 g      | 18 g      |
| Pyridoxine Hydrochloride | 20 g      | 20 g      | 20 g      | 20 g      |
| Thiamin Hydrochloride    | 24 g      | 24 g      | 24 g      | 24 g      |
| Folic Acid               | 3.3 g     | 3.3 g     | 3.3 g     | 3.3 g     |
| Biotin                   | 2.5 g     | 2.5 g     | 2.5 g     | 2.5 g     |
| Manganese Sulfate        | 1.8 g     | 1.8 g     | 1.8 g     | 1.8 g     |
| Phylloquinone            | 880 mg    | 880 mg    | 880 mg    | 880 mg    |
| Sodium Selenate          | 90 mg     | 90 mg     | 90 mg     | 90 mg     |
| Cyanocobalamin           | 88 mg     | 88 mg     | 88 mg     | 88 mg     |
| Potassium Hydroxide      | Q.S.      | Q.S.      | Q.S.      | Q.S.      |

**[0063]** The concentrated liquid human milk fortifier is prepared by solubilizing and combining/mixing ingredients into a homogeneous aqueous mixture which is subjected to a sufficient thermal treatment and aseptic filling to achieve long term physical and microbial shelf stability. The term "shelf stability" as used herein means that the concentrated liquid human milk fortifier is resistant to separation and precipitation for time period after manufacture of at least three months, and preferably at least six months.

**[0064]** To begin the manufacturing process, macronutrients (carbohydrate, protein, fat, and minerals) are combined in several slurries together and with water. This blend is subjected to an initial heat treatment and then tested to verify proper nutrient levels. An intermediate aqueous carbohydrate-mineral (CHO-MIN) slurry is prepared by heating appropriate amount of water to 140-160°F. With agitation, the following soluble ingredients are added: maltodextrin, potassium citrate, magnesium chloride, potassium chloride, sodium chloride, and choline chloride. The carbohydrate-mineral slurry is held at 130-150 °F under agitation until added to the blend.

**[0065]** An intermediate oil slurry is prepared by heating MCT oil and coconut oil to 150 to 170°C and then adding distilled monoglycerides with agitation for a minimum of 10 minutes in order to the ingredient to dissolve. Soy oil, vitamin A palmitate, vitamin D<sub>3</sub>, di-alpha-tocopheryl-acetate, phylloquinone, ARA-containing oil, DHA-containing oil, and carotenoid premix are then added with agitation to the oil blend. Insoluble mineral calcium source, and ultra micronized tricalcium phosphate is added to the oil. Gellan gum and OSA-modified starch are then added to the oil blend with proper agitation. The oil blend slurry is maintained at 130-150 °F under agitation until added to the blend.

**[0066]** The blend is prepared by combining the ingredient water, casein hydrolysate, all of the CHO-MIN slurry and whole oil blend slurry. The blend is maintained at 120 °F for a period of time not to exceed two hours before further processing.

**[0067]** The blend is then homogenized using one or more in-line homogenizers at pressures from 1000-4000 psig with or without a second stage homogenization from 100-500 psig followed by heat treatment using a UHTST (ultra-high temperature short time, 292-297 °F for 5-15 seconds) process. After the appropriate heat treatment, the batch is cooled in a plate cooler to 33-45 °F and then transferred to a refrigerated holding tank, where it is subjected to analytical testing.

**[0068]** The next step in the manufacturing process involves adding vitamins, trace minerals, other ingredients, and water in order to reach the final target total solids and vitamin/mineral contents. The final batch is filled into a suitable container under aseptic conditions or treated with a terminal sterilization process so the product will be stable at room temperature for an extended shelf-life. Additional detail on this process is provided in the following paragraphs.

**[0069]** A trace mineral/vitamin/nutrient solution (STD1) is prepared by heating water to 80-100°F and adding the following ingredients with agitation: potassium citrate, ferrous sulfate, zinc sulfate, copper sulfate, manganese sulfate, sodium selenate, pyridoxine hydrochloride, riboflavin, thiamine hydrochloride, cyanocobalamin, folic acid, calcium pantothenate, niacinamide, biotin, m-inositol, nucleotide/choline premix, L-carnitine, L-Leucine, and L-tyrosine.

**[0070]** A vitamin C solution (STD2) is prepared by adding ascorbic acid to a water solution with agitation.

**[0071]** All STD1 and STD2 solutions are then added to the refrigerated batch, with agitation. The appropriate amount of ingredient dilution water is then added to the batch to achieve a target total solids level of 29.0- 32.0%. The final batch

is then subjected to appropriate thermal treatment and filled into a suitable container (e.g., pouches 10, 110, 120) under aseptic packaging conditions and processes. The term "aseptic packaging" as used herein, unless otherwise specified, refers to the manufacture of a packaged product without reliance upon "retort packaging", wherein the nutritional liquid and package are sterilized separately prior to filling, and then are combined under sterilized or aseptic processing conditions to form a sterilized, aseptically packaged, nutritional liquid product. The term "retort packaging" as used herein, and unless otherwise specified, refers to the common practice of filling a container, most typically a metal can or other similar package, with a nutritional liquid and then subjecting the liquid-filled package to the necessary heat sterilization step, to form a sterilized, retort packaged, nutritional liquid product.

#### **Example 5**

**[0072]** In Example 5, four separate concentrated liquid human milk fortifiers were prepared and the overall stability in terms of amount of phase separation (emulsion stability), sediment at the bottom of the container, and creaming at the top of the liquid, of each was evaluated at 24 hours after manufacture. Each of the four tested concentrated liquid human milk fortifiers was based on the concentrated liquid human milk fortifier of Example 2 above.

**[0073]** The first concentrated liquid human milk fortifier was identical to that of Example 2 except that it did not contain any OSA-modified corn starch and did not contain any low acyl gellan gum. The second fortifier was identical to that of Example 2 except that it did not contain any low acyl gellan gum. The third fortifier was identical to that of Example 2 except that it did not contain any OSA-modified corn starch. The fourth fortifier was identical to that of Example 2. Each of the four fortifiers was prepared in accordance with the manufacturing process of Examples 1-4.

**[0074]** Upon evaluation, the first fortifier (no OSA-modified corn starch and no low acyl gellan gum) showed nearly complete phase separation of the oil and water phases, and showed both heavy creaming at the top of the liquid and heavy sediment at the bottom of the container. See Figure 22.

**[0075]** Upon evaluation, the second fortifier (no low acyl gellan gum) showed both heavy creaming at the top of the liquid and heavy sediment at the bottom of the container. See Figure 23.

**[0076]** Upon evaluation, the third fortifier (no OSA-modified corn starch) showed nearly complete phase separation of the oil phase and the water phase. See Figure 24.

**[0077]** Upon evaluation, the fourth fortifier (containing both OSA-modified corn starch and low acyl gellan gum) showed no phase separation, no creaming, and no sediment. See Figure 25. The stabilizing system of a combination of OSA-modified corn starch and low acyl gellan gum showed a synergistic interaction and allowed for the manufacture of physically stable concentrated liquid human milk fortifier containing extensively hydrolyzed casein and a high level of insoluble calcium salts without causing defects in emulsion stability and sediment fall out.

#### **Gelled Human Milk Fortifier**

**[0078]** Another suitable human milk fortifier suitable for packaging in the pouches 10, 110, 210 is a gelled human milk fortifier. The gelled human milk fortifier generally comprises protein, fat, and carbohydrate in a stable, concentrated gel that is shear thinning and stabilizer-free. The term "gelled human milk fortifier" as used herein means a human milk fortifier that is in the form of a colloid in which the dispersed phase has combined with the dispersion medium to produce a semisolid material, such as a jelly, pudding or yogurt. A "gelled human milk fortifier" has a viscosity at room temperature of greater than 800, 900 or even 1000 cps as measured using a Brookfield Viscometer (spindle 61, 60 rpm, after 10 seconds of rotation). The term "shear thinning" as used herein means an effect where viscosity decreases with increasing rate of shear stress.

**[0079]** Various embodiments of the gelled human milk fortifiers can be substantially free of any optional or selected essential ingredient or feature described herein, provided that the remaining gelled human milk fortifier still contains all of the required ingredients or features as described herein. In this context, and unless otherwise specified, the term "substantially free" means that the selected gelled human milk fortifier contains less than a functional amount of the optional ingredient, typically less than 0.1% by weight, and also including zero percent by weight of such optional or selected essential ingredient. The gelled human milk fortifiers can comprise, consist of, or consist essentially of the essential elements, as well as any additional or optional ingredients, components, or limitations described herein or otherwise useful in the gelled human milk fortifier.

#### **Product Form**

**[0080]** The gelled human milk fortifier is shear thinning such that they can easily be converted from the gelled form to a liquid form by shaking and/or kneading prior to being poured from the pouch 10, 110, 210. Generally, the gelled human milk fortifier has a viscosity of greater than 1000 cps at room temperature as measured using a Brookfield Viscometer Model DVII (spindle 61, 60 rpm, after 10 seconds rotation). The gelled human milk fortifier has a shaken viscosity, as

defined herein, of from about 20 cps to about 200 cps, or even from about 20 cps to about 150 cps, or even from about 20 cps to about 100 cps, or even from about 20 cps to about 80 cps, or even from about 50 cps to about 95 cps. Generally, as the gelled human milk fortifier ages, the shaken viscosity will increase slightly.

**[0081]** The gelled human milk fortifier has a gel strength, as defined herein, of from about 25 grams to about 200 grams, or even from about 50 grams to about 200 grams, or even from about 75 grams to about 150 grams. The gelled human milk fortifier has a shaken gel strength of less than 10, or even less than 5 or even zero. In one suitable embodiment, the shaken gel strength is zero.

**[0082]** The gelled human milk fortifiers can be stabilizer free. That is, they may be formulated to not include any stabilization agent for keeping precipitation and/or settling from occurring in the fortifier. By formulating the gelled human milk fortifier to be stabilizer free, it becomes more acceptable worldwide. Specifically, the gelled human milk fortifier can be formulated to be carrageenan-free.

**[0083]** The gelled human milk fortifier is generally formulated to have a caloric density of at least about 1.25 kcal/ml (37 kcal/fl oz), including from about 1.4 kcal/ml (42 kcal/fl oz) to about 5 kcal/ml (149 kcal/fl oz), and also including from about 1.5 kcal/ml (44 kcal/fl oz) to about 2.5 kcal/ml (74 kcal/fl oz), and also including from about 1.9 kcal/ml (56 kcal/fl oz) to about 2.0 kcal/ml (59 kcal/fl oz). The gelled human milk fortifier is preferably formulated to provide fortified human milk having an osmolality of less than about 400 mOsm/kg water, preferably from about 300 mOsm/kg water to about 400 mOsm/kg water.

## **Macronutrients**

**[0084]** The gelled human milk fortifiers of the present disclosure comprise carbohydrate, fat, and protein macronutrients of sufficient types and amounts, that when used in combination with human milk or other infant feeding formula, they help meet the nutritional needs of the infant, especially the premature infant. The concentration of these macronutrients in the various embodiments of the present disclosure includes the ranges described hereinafter.

## **Protein**

**[0085]** The gelled human milk fortifier comprises a protein suitable for use with infants, especially preterm infants, at concentrations ranging from about 10% to about 30%, including from about 10% to about 25%, and also including from about 15% to about 25%, on a dry weight basis. In some embodiments, the protein may be at a concentration of less than 10%.

**[0086]** In one suitable embodiment, the gelled human milk fortifier is prepared by aseptic processing, which comprise the requisite protein concentrations with a specific blend of casein and whey protein. The blend includes from about 40% to about 80% by weight of whey protein, including from about 50% to about 70% by weight whey protein, including from about 55% to about 70% by weight whey protein, and including from about 60% to about 70% by weight whey protein, in combination with from about 20% to about 60% by weight of casein protein, including from about 30% to about 50% by weight of casein protein, including from about 20% to about 50% by weight casein protein, including from about 20% to about 45% by weight casein protein, including from about 20% to about 40% by weight casein protein, including from about 20% to about 30% casein protein. It has been found that these particular blends of whey protein and casein protein provide for a suitable gelled human milk fortifier that can be prepared by aseptic processing.

**[0087]** In some embodiments, in addition to the whey protein and casein protein outlined above, the gelled human milk fortifier may contain additional protein. Suitable additional protein may include soy protein hydrolysate, casein protein hydrolysate, whey protein hydrolysate, rice protein hydrolysate, potato protein hydrolysate, fish protein hydrolysate, egg albumen hydrolysate, gelatin protein hydrolysate, combinations of animal and vegetable protein hydrolysates, and combinations thereof.

**[0088]** Proteins suitable for use in the gelled human milk fortifier may include intact or hydrolyzed proteins, free amino acids, or combinations thereof. Non-limiting examples of suitable proteins include hydrolyzed, partially hydrolyzed or non-hydrolyzed protein, and can be derived from any known or otherwise suitable source such as milk (e.g., casein, whey, lactose-free milk protein isolates), animal (e.g., meat, fish), cereal (e.g., rice, corn), vegetable (e.g., soy), or combinations thereof. The protein can include, or be entirely or partially replaced by, free amino acids known or otherwise suitable for use in nutritional products, non-limiting examples include L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-carnitine, L-cystine, L-glutamic acid, L-glutamine, glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-serine, L-taurine, L-threonine, L-tryptophan, L-tyrosine, L-valine, and combinations thereof.

## **Carbohydrate**

**[0089]** The gelled human milk fortifiers comprises a carbohydrate suitable for use with infants, especially preterm

infants, at concentrations most typically ranging up to about 75% by weight on a dry weight basis, including from about 10% to about 50%, and also including from about 20% to about 40%, by weight on a dry weight basis. Carbohydrates suitable for use in the gelled human milk fortifiers include hydrolyzed or intact, naturally and/or chemically modified, starches sourced from corn, tapioca, rice or potato, in waxy or non-waxy forms. Other non-limiting examples of suitable carbohydrate sources include hydrolyzed cornstarch, maltodextrin (i.e. non-sweet, nutritive polysaccharide having a DE value less than 20), corn maltodextrin, glucose polymers, sucrose, corn syrup, corn syrup solids (i.e., polysaccharide having a DE value greater than 20), glucose, rice syrup, fructose, high fructose corn syrup, indigestible oligosaccharides such as fructooligosaccharides (FOS), and combinations thereof. The carbohydrates may comprise lactose or can be substantially free of lactose.

**[0090]** One embodiment of the gelled human milk fortifier includes a non-reducing carbohydrate component, which may represent from about 10% to 100%, including from about 80% to 100%, and also including 100%, by weight of the total carbohydrate. The selection of a non-reducing carbohydrate may enhance the product stability and is generally better tolerated by infants, especially premature infants. Non-limiting examples of non-reducing carbohydrates include sucrose or other carbohydrates that do not readily oxidize or react with Tollen's, Benedict's, or Fehling's reagents. The gelled human milk fortifier therefore includes embodiments comprising a carbohydrate component, wherein the carbohydrate component comprises a mono- and/or disaccharide such that at least about 50%, including from about 80% to 100%, and also including 100%, of the mono- and/or disaccharide is a non-reducing carbohydrate.

### **Fat**

**[0091]** The gelled human milk fortifiers also comprises a fat component suitable for use with infants, especially preterm infants, at concentrations most typically ranging up to about 40% by weight on a dry weight basis, including from about 10% to about 40%, and also including from about 15% to about 37%, and also including from about 18% to about 30%, by weight on a dry weight basis. Fats suitable for use in the gelled human milk fortifier may include coconut oil, soy oil, corn oil, olive oil, safflower oil, high oleic safflower oil, MCT oil (medium chain triglycerides), sunflower oil, high oleic sunflower oil, structured triglycerides, palm and palm kernel oils, palm olein, canola oil, marine oils, cottonseed oils, and combinations thereof.

**[0092]** Suitable fats for use in the gelled human milk fortifier include emulsifiers to help the various fortifier components readily disperse when combined with human milk. Non-limiting examples of suitable emulsifiers include soya bean lecithin, polyoxyethylene stearate, polyoxyethylene sorbitan mono-oleate, polyoxyethylene sorbitan monopalmitate, polyoxyethylene sorbitan monostearate, ammonium phosphatides, polyoxyethylene sorbitan monolaurate, citric acid esters of mono and diglycerides of fatty acids, tartaric acid esters of mono and diglycerides of fatty acids, and combinations thereof. Natural soy lecithin is especially useful in this respect. The fat component of the gelled human milk fortifier may therefore optionally include any emulsifier suitable for use in infant nutritional products. Emulsifier concentrations in these products may range up to about 10%, including from about 1% to about 10%, even more typically from about 1.5% to about 5%, by weight of the total fat component. The weight ratio of fat to protein (fat:protein, by weight) in the human milk fortifier is at least about 0.9, including from about 1 to about 5, and also including from about 2 to about 4. These ratios may be helpful in further stabilizing the gelled human milk fortifier.

**[0093]** The gelled human milk fortifier also include embodiments that comprise, as part of the fat component, one or more of arachidonic acid, docosahexaenoic acid, or combinations thereof, alone or in further combination with linoleic acid, linolenic acid, or both.

### **Vitamins and Minerals**

**[0094]** The gelled human milk fortifier may further comprise any of a variety of vitamins, non-limiting examples of which include vitamin A, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, pyridoxine, vitamin B 12, niacin, folic acid, pantothenic acid, biotin, vitamin C, choline, inositol, salts and derivatives thereof, and combinations thereof. The gelled human milk fortifier includes embodiments comprising per 100 kcal of fortifier solids one or more of the following: vitamin A (from about 250 to about 750 IU), vitamin D (from about 40 to about 100 IU), vitamin K, vitamin E (at least about 0.3 IU), vitamin C (at least about 8 mg), thiamine, vitamin B12, niacin, folic acid, pantothenic acid, biotin, choline (at least about 7 mg), and inositol (at least about 2 mg).

**[0095]** The gelled human milk fortifier may also further comprise any of a variety of minerals known or otherwise suitable for use in infant or other nutritional formulas, non-limiting examples of which include phosphorus, magnesium, calcium as described hereinbefore, zinc, manganese, copper, iodine, sodium, potassium, chloride, selenium, and combinations thereof. The gelled human milk fortifier also include embodiments comprising per 100 kcal of the fortifier solids one or more of the following: calcium (at least about 50 mg), phosphorus (at least about 25 mg), magnesium (at least about 6 mg), iodine, zinc (at least about 0.5 mg), copper, manganese, sodium (from about 20 to about 60 mg), potassium (from about 80 to about 200 mg), chloride (from about 55 to about 150 mg) and selenium (at least about 0.5 mcg).



**Other Optional Ingredients**

**[0096]** The gelled human milk fortifier may further optionally comprise other ingredients that may modify the physical, chemical, aesthetic or processing characteristics of the formulas or serve as pharmaceutical or additional nutritional components when used in the targeted population. Many such optional ingredients are known for use in food and nutritional products, including infant formulas, and may also be used in the gelled human milk fortifiers of the present disclosure, provided that such optional materials are compatible with the essential materials described herein, are safe and effective for their intended use, and do not otherwise unduly impair product performance. Non-limiting examples of such optional ingredients include preservatives, anti-oxidants, various pharmaceuticals, buffers, carotenoids, colorants, flavors, nucleotides and nucleosides, thickening agents, prebiotics, probiotics, sialic acid-containing materials, and other excipients or processing aids.

**Examples**

**[0097]** The following examples illustrate specific embodiments and/or features of the gelled human milk fortifier. The examples are given solely for the purpose of illustration as many variations thereof are possible. All exemplified amounts are weight percentages based upon the total weight of the formulation, unless otherwise specified.

**Example 1**

**[0098]** In this Example, a gelled human milk fortifier is prepared with the ingredients shown in the following table.

| Ingredients                | Qty. per | 32000 | lb |
|----------------------------|----------|-------|----|
| Water                      | Q.S.     |       |    |
| Condensed Skim Milk        | 5250     | Kg    |    |
| Non-Fat Milk Solids        | 1365     | Kg    |    |
| Corn Maltodextrin          | 1450     | Kg    |    |
| Corn Syrup Solids          | 1388     | Kg    |    |
| Medium Chain triglycerides | 694      | Kg    |    |
| Whey Protein Concentrate   | 634      | Kg    |    |
| Calcium Phosphate          | 271      | Kg    |    |
| Ascorbic Acid              | 152      | Kg    |    |
| Magnesium Chloride         | 38.0     | Kg    |    |
| Potassium Citrate          | 12.2     | Kg    |    |
| Sodium Chloride            | 12.1     | Kg    |    |
| Soy Lecithin               | 8.84     | Kg    |    |
| M-Inositol                 | 7.98     | Kg    |    |
| Magnesium Phosphate        | 5.55     | Kg    |    |
| M. Alpina Oil              | 5.35     | Kg    |    |
| Niacinamide                | 4.35     | Kg    |    |
| Alpha-Tocopheryl Acetate   | 4.21     | Kg    |    |
| Zinc Sulfate               | 3.51     | Kg    |    |
| C. Cohnii Oil              | 3.45     | Kg    |    |
| Choline Chloride           | 2.90     | Kg    |    |
| Calcium Pantothenate       | 1.89     | Kg    |    |
| Potassium Phosphate        | 1.62     | Kg    |    |
| Ferrous Sulfate            | 1.64     | Kg    |    |

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(continued)

| Ingredients              | Qty. per  | 32000 | lb |
|--------------------------|-----------|-------|----|
| Vitamin A Palmitate      | 900       | g     |    |
| Cupric Sulfate           | 678       | g     |    |
| Riboflavin               | 572       | g     |    |
| Thiamine Hydrochloride   | 373       | g     |    |
| Pyridoxine Hydrochloride | 232       | g     |    |
| Vitamin D3               | 152       | g     |    |
| Folic Acid               | 47.9      | g     |    |
| Biotin                   | 34.1      | g     |    |
| Manganese Sulfate        | 23.2      | g     |    |
| Phylloquinone            | 11.6      | g     |    |
| Cyanocobalamin           | 1.60      | g     |    |
| Sodium Selenate          | 0.798     | g     |    |
| Calcium Carbonate        | as needed |       |    |
| Sodium Citrate           | as needed |       |    |
| Potassium Hydroxide      | as needed |       |    |

**[0099]** The gelled human milk fortifier is prepared by solubilizing and combining ingredients into a homogeneous aqueous mixture which is subjected to an adequate heat treatment to achieve long term shelf stability. To begin the manufacturing process, the ingredients that supply the macronutrients (carbohydrate, protein, fat and minerals) are combined in multiple slurries together and with water. This blend is subjected to an initial heat treatment and then tested to verify proper nutrient levels. Additional detail on this process is provided in the following paragraphs.

**[0100]** An intermediate aqueous carbohydrate-mineral slurry is prepared by heating water to 60-66 °C. With agitation, the following soluble minerals are added: magnesium chloride, potassium citrate, sodium chloride, monopotassium phosphate and magnesium phosphate. Once fully dissolved, corn maltodextrin and corn syrup solids are added to the mineral solution. The carbohydrate-mineral slurry is held at 54°C under low agitation until added to the blend.

**[0101]** An intermediate oil and protein slurry is prepared by heating MCT oil to 32-43 °C and then adding DHA oil and AA oil, with agitation. A soy lecithin emulsifier (8.84 kg) is added with agitation to the heated oils and allowed to dissolve. Vitamin A, vitamin D, and vitamin K, and natural vitamin E are then added with agitation to the oil blend. Whey protein concentrate and tricalcium phosphate are added to the oil. The oil and protein slurry is maintained at 38 °C under low agitation until added to the blend.

**[0102]** An intermediate aqueous protein slurry is prepared by heating ingredient water to 49-54 °C, and then adding whey protein concentrate with moderate agitation. The aqueous protein slurry is held at 52 °C under low agitation until added to the blend.

**[0103]** The blend is prepared by combining the carbohydrate-mineral slurry with condensed skim milk and non-fat milk solids and then adding the oil and protein slurry and the aqueous protein slurry. After no less than five minutes, the blend pH is adjusted to 6.8-7.0 using a 1N KOH solution, and thereafter maintained at 52-60 °C, for a period of time not to exceed two hours before further processing.

**[0104]** The pH adjusted blend is then homogenized using one or more in-line homogenizers at pressures from 1000-4000 psig with or without a second stage homogenization from 100-500 psig followed by heat treatment using a HTST (high temperature short time, 74 °C for 16 seconds). After the appropriate heat treatment, the batch is cooled in a plate cooler to 1.0-5.0 °C and then transferred to a refrigerated holding tank, where it is subjected to analytical testing.

**[0105]** The next step in the manufacturing process involves adding vitamins, trace minerals and water to the target total solids. The final batch is sterilized and filled into a suitable container under aseptic conditions or treated with a terminal sterilization process so the product will be stable at room temperature for an extended shelf life. Additional detail on this process is provided in the following paragraphs.

**[0106]** A trace mineral solution is prepared by heating water to 27-38 °C and adding the following minerals with agitation: potassium citrate, ferrous sulfate, zinc sulfate, cupric sulfate, manganese sulfate, sodium selenate.

**[0107]** A water-soluble vitamin solution is prepared by heating water to 27-38 °C. The following vitamins are added to

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the water with agitation: choline chloride, niacinamide, riboflavin, calcium pantothenate, pyridoxine hydrochloride, thiamine hydrochloride, m-inositol, biotin, folic acid, and cyanocobalamin.

[0108] A vitamin C solution is prepared by adding ascorbic acid to 1N KOH solution with agitation.

[0109] All three vitamin or mineral solutions are then added to the refrigerated batch, with agitation. The appropriate amount of ingredient dilution water is then added to the batch to achieve a target total solids level of 32%, and the pH is adjusted to 7.0 with a 1N KOH solution.

### Example 2

[0110] In this Example, the unshaken viscosity, shaken viscosity, unshaken gel strength and shaken gel strength of the human milk fortifier prepared in Example 1 is tested at a sample aged three months and a sample aged six months.

[0111] The viscosities were measured using a Brookfield Viscometer Model DV11+ (spindle 61, 60 rpm, after 10 second of rotation). The gel strengths were measure using a Stable Micro Systems TA.XT plus Texture Analyzer (1 inch ball probe, 20 mm depth). For the shaken samples, each sample was shaken vigorously by hand for five seconds prior to testing.

[0112] The results of the viscosity measurements and gel strengths are shown in the following Table.

|              | Sample A<br>(aged 3 months) |        | Sample B<br>(aged 6 months) |        |
|--------------|-----------------------------|--------|-----------------------------|--------|
|              | Unshaken                    | Shaken | Unshaken                    | Shaken |
| Viscosity    | > 1000 cps                  | 56 cps | > 1000 cps                  | 95 cps |
| Gel Strength | 78 g                        | 0g     | 133 g                       | 0g     |

[0113] As can be seen from the data in the Table, the unshaken viscosities for both samples are greater than 1000 cps, while the viscosities of both shaken samples are substantially less (56 cps for 3 months and 95 cps for 6 months). This indicates that in unshaken form, a gel is present whereas after shear is applied (by shaking) the gel easily breaks for forms a liquid of relatively low viscosity that could easily be poured from one of the pouches 10, 110,210.

[0114] Additionally as can be seen from the data in the Table, the unshaken gel strength for both samples is relatively high (78 grams at 3 months and 133 grams at 6 months), while the gel strengths after shaking for both samples is zero grams. This indicates that after shaking, the gel has transformed into a liquid that could easily be poured from one of the pouches 10, 110,210.

### Dose Pouches

[0115] The concentrated liquid human milk fortifier and the gel human milk fortifier can be packaged in suitable unit dose pouches (e.g., pouches 10, 110, 210). The term "unit dose" as used herein refers to individual, single-use, pouches of concentrated human milk fortifier containing a predetermined amount of human milk fortifier that can be used in a preparation of a predetermined amount of human milk. The unit dose pouches 10, 110, 210 are single use containers that alone, or in combination with other unit dose pouches, provide sufficient human milk fortifier to supplement human milk for immediate use, e.g., preferably within 8-24 hours, more preferably within 0-3 hours, of mixing with human milk.

[0116] The amount or volume of concentrated liquid human milk fortifier or gel human milk fortifier in each unit dose pouch 10, 110, 210 includes those embodiments in which the package contains an amount suitable to prepare an infant's feeding. In one suitable embodiment, the unit dose pouches 10, 110, 210 typically contain sufficient fortifier to provide from about 0.5 g to about 10 g of fortifier solids, more typically from about 0.8 g to about 5.0 g of fortifier solids, and even more typically from about 0.85 g to about 2.0 g, of fortifier solids. The terms "fortifier solids" or "total solids", unless otherwise specified, are used interchangeably herein and refer to all material components of the compositions of the present disclosure, less water.

[0117] The amount of fortified human milk prepared for a premature infant, for example, typically ranges from 25 ml to 150 ml a day. Consequently, in one suitable embodiment, a single unit dose is the appropriate amount of fortifier solids to fortify a 25 ml preparation. Multiple pouches 10, 110, 210 can be used to prepare larger feeding volumes, especially for term infants.

### Aseptic Packaging

[0118] The concentrated liquid human milk fortifier and the gel human milk fortifier can be sterilized and aseptically

packaged into the pouches 10, 110, 210. The aseptic packaging can be accomplished using any of a variety of techniques well known to those of ordinary skill in the formulation art, so long as the technique is sufficient to achieve long term shelf stability of the fortifier. Fig. 10 is a flow diagram of one suitable process for manufacturing a plurality of aseptically sterilized pouches 10, 110, 210 suitable for containing the concentrated liquid human milk fortifier, the gel human milk fortifier, or any other suitable aseptic product. While the following description of the aseptic packaging process is provided with respect to the pouch 10 illustrated in Figs. 1-6, it is understood that the pouches 110, 210 of Figs. 8 and 9 can be processed in substantially the same manner.

**[0119]** In this embodiment, a web of plastic sheeting (e.g., the two layered laminate illustrated in Fig. 7A) is fed from a suitable web feeding device 80 (e.g., unwound from a roll) to a web alignment device 82 as indicated in the flow chart in Fig. 10. In one suitable embodiment, the web has a width sufficient to make four pairs of pouches 10 in side-by-side relationship (Fig 11A-C). It is understood, however, that the width of the web can be sufficient to make more or fewer pairs of pouches 10 in side-by-side relationship. From the web alignment device 82 and as indicated in Fig. 10, the web is directed to a coding station 84 wherein the web is laser coded (or otherwise printed) with indicia, e.g., batch number, expiration date, current time and date. It is contemplated that other indicia can be printed on the pouch 10 including, for example, the manufacturer's name, the trade name of the product, the generic name of the product, direction of use, nutritional information of the product, and/or quantity of the product. The web is then fed to a laser scoring station 86 wherein the web is scored along three longitudinal lines (Figs. 10 and 11A) to delineate the four separate pairs of pouches.

**[0120]** The web next enters a sterilization station 88 wherein the web passes through a peroxide bath, thereby sterilizing the entire web, as both sides of the web are brought into direct contact with a peroxide solution. It is contemplated that other sterilants (e.g., oxonia) or forms of sterilization (e.g., UV light, electron beam) can be used. Once the web has passed through the peroxide bath, the web is dried by blowing sterile air thereon at a drying station 90. While still in a sterile environment, the web is directed to a web separation station 92 and a web folding station 94. More specifically, the web is separated into four lanes at the web separation station 92 as it is pulled across respective forming collars. Each of the four lanes is defined by segments of the web. Each of the web segments are folded by the respective forming collar. Thus, in the described embodiment, the four forming collars both separate the web into segments and fold the segments. In other words, the four forming collars collectively define both the web separation station 92 and the web folding station 94. It is understood, however, that the web separation station 92 and the web folding station 94 can be separate, discrete stations. It is also understood that the forming collars can be any suitable device(s) capable of dividing the web into a plurality of web segments and folding each of the web segments.

**[0121]** As illustrated in Fig. 11B, the respective forming collar folds each of the side edges of the respective web segment inward (i.e., in the direction of the arrows of Fig. 11B) toward the longitudinal center line of the web segment at the folding station 94. As seen in Fig. 11B, each of the web segments are folded about a fill pipe. After the web segment is folded longitudinally, each of the web segments are longitudinally heat sealed at a longitudinal seal station 96 wherein the overlying portion of the web segment is bonded to the underlying portion of the web segment along each of the side edges to form the side edge segments 25c of the seal lines 25.

**[0122]** Next, each of the web segments is perforated along a longitudinal perforation line located between the tubes of each of the web segments at a longitudinal perforation station 97 (Figures 10 and 11B). Once each of the web segments move past a fill nozzle disposed on the respective fill pipe, the web segments are directed to a horizontal sealing station 99 wherein each of the web segments are heat sealed to sealingly bond the overlying portion to the underlying portion of the blank to form one of the end segments 25a and the inboard seal segment 25d of the seal lines 25. As seen in Fig. 11C, two pouches 10, which are separated by the perforated center line, are formed from each of the web segments and the respective fill nozzle is disposed within the interior space of the pouch. The pouches 10 are then filled at a filling station 98 wherein both of the pouches of each of the four web segments are filled with a predetermined amount of sterilized product. Next, each of the pouches 10 is moved past the respective fill nozzle and is heat sealed shut, which forms the other end segment 25b of the seal lines 25, at the horizontal sealing station 99. The lines of weakness 30, 32 for each of the pouches 10 are formed at a tear notch and cutting station 302.

**[0123]** After the pouches 10 are filled with product and sealed, they are transferred to weight and leak inspection stations 304 wherein each of the pouches 10 are weighed and checked for leakage. Pouches 10 that pass inspection are incubated at an incubation station 305 and tested for spoilage at a spoilage inspection station 306. Then, pouches are packaged in pluralities into suitable secondary packaging, e.g., opaque cardboard box 500, 500' as illustrated in Figs. 12, 16A and 16B at a secondary packaging station 307. Figs. 12, 16A and 16B illustrate different embodiments of suitable secondary packaging 500, 500' for the pouches 10. Pouches 10 that fail inspection are discarded.

**[0124]** When the product is a liquid human milk fortifier (e.g., the concentrated liquid human milk fortifier or the gelled human milk fortifier described above), the product can be sterilized by heat treatment via a high temperature short time (HTST) process or an ultra high temperature (UHT) process to sufficiently reduce the bioburden before the pouches 10 are filled. The above described packaging process of a sterile product, allows some products (e.g., some embodiments of the concentrated liquid human milk fortifier and the gelled human milk fortifier described above) to maintain commercially sterility over an extended shelf-life without the need for refrigeration even if the product is low acid (i.e., has a pH

greater than 4.6) and has water activity greater than 0.85.

**[0125]** In one embodiment, the liquid human milk fortifier is photosensitive. That is, the vitamins in liquid human milk fortifier will degrade more slowly when not exposed to light, and conversely, will degrade more rapidly when exposed to light. When the liquid human milk fortifier is photosensitive, the opaque cardboard box 500 inhibits the pouches 10 container therein from being exposed to light and thereby extends the shelf life of the liquid human milk fortifier.

### **Leak Detection Inspection System**

**[0126]** In one suitable inspection station 304, each of the pouches 10 are transferred through an in-line checkweigher where it is weighed. Any pouch 10 having a weight outside an acceptable weight range is rejected. The pouches 10 that pass the inline checkweigher are aligned and conveyed into a high voltage leak detection (HVLD) inspection system. In this system, the seal integrity of each of the pouches 10 is non-destructively inspected by applying high voltage to the sealed liquid-filled pouch. The system is designed to conduct electric current through the pouch 10 and measure the amount of current that passes through the pouch. A pouch 10 with a leak (i.e., a faulty seal) will transfer more current to a ground electric than a pouch having a seal with good integrity. The seals of the pouch 10 act as an insulator to the liquid inside. Any pouch 10 that does not pass inspection (i.e., has a current above an acceptable range) is automatically rejected.

**[0127]** More specifically, once the pouches 10 enter the high voltage leak detection inspection system, they pass to a press that applies a compression force to each of the pouches. The compression force pushes liquid into any weak areas of the pouch body and/or pouch seal. While compressed, each of the pouches 10 is conveyed past a series of rollers and metal electrode brushes in the inspection station wherein high voltage power is applied the pouches. In one suitable configuration, the voltage is transferred from an upper electrode positioned above the pouch through the pouch 10 to ground electrode positioned beneath the pouch. In other words, the pouch 10 completes the circuit between the upper electrode and the ground electrode, which provides a measurable volume of electric current through the pouch.

**[0128]** A pouch 10 with good seal integrity will provide a lower voltage output as compared to a pouch with poor seal integrity, which provides a higher voltage output. Thus, the high voltage leak detection inspection machine determined if each of the pouches 10 is "good" or "bad" based on the measured voltage relative to a voltage threshold, which is a pre-determined set point. If the measured voltage is below the threshold, the pouch will be transferred to an outfeed conveyor for subsequent secondary packaging. If the measured voltage is above the threshold, the pouch 10 will be transferred to a reject bin.

### **Secondary Container**

**[0129]** In one suitable embodiment, the cardboard box 500 (broadly, the secondary container) includes a generally rectangular base section 502 and a lid 501 hingely attached to the base (Figs. 12 and 17-21). The base section 502 and lid 501 are indicated generally by their respective reference numbers. The base section 502 includes a bottom wall 504, four side walls 506 extending up from the bottom wall, and a top wall 508. As seen in Fig. 21, the top wall 508 of the base section 502 extends along only a portion of a length of the box 500. For example, in the illustrated embodiment, the box 500 has a length L of about 12 cm and the top wall 508 has a length L' of 2.5 cm. It is understood that the box 500 and top wall 508 can have different lengths. It is also understood that the ratio between the length of the box 500 and the length of the top wall 508 can be different. It is further understood that the box 500 can be shaped other than rectangular and be constructed from other suitable materials (e.g., plastic).

**[0130]** The lid 501, which is formed integrally with the base section 502, has an upper wall 510 and a pair of tapered sidewalls 503 extending downward from the upper wall. An end wall 505 extends downward from the upper wall 510 and between the sidewalls 503. The lid 501 is pivotally about a living hinge 507 between a closed position (Figs. 17-19) and an opened position (Figs. 12, 20 and 21). The living hinge 507 is located between the top wall 508 of the base section 502 and the upper wall 510 of the lid 501. In one suitable embodiment, the weight of the lid 501 is sufficient to bias the lid about the living hinge toward to the closed position. The end wall 505 of the lid 501 includes a tab 511 adapted for insertion into a slot 513 in one of the side walls (i.e., a front wall) of the box 500 for holding the lid 501 in the closed position. The tab 511 can be seen inserted into the slot 513 in Fig. 17. It is understood that the lid 501 can be hingely attached to the base section 502 in other suitable manners besides the illustrated living hinge 507. It is further understood that the lid 501 can be formed separate from the base section 502 and attached thereto.

**[0131]** A pair of hold-downs 509 are located adjacent the ends of the living hinge 507 to provide rigidity and support to the box 500 about the living hinge. In the illustrated embodiment, each of the hold-downs 509 are flaps that extend outward from the top wall of the base section 502. Each of the flaps are folded about a pair of fold-lines and inserted into an associated slot in one of the sidewalls of the base section (Fig. 21). One of the fold-lines is adjacent the top wall 508 of the base section 502 and the other is adjacent the slot in the respective sidewall. Each of the flaps includes a head portion (not shown) to inhibit the flap from being pulled (or otherwise withdrawn) from the associated slot.

[0132] As seen in Figs. 12 and 20, an interior floor 521 of the box 500 is tented or peaked along its center line 533. That is, the interior floor 521 is highest at its center and slopes downward toward each of its sides. In one suitable embodiment, the interior floor 521 of the box 500 is defined by an insert that is formed separate from the other components of the box and rest on top of the bottom wall of the base section. It is, understood, however, that the interior floor 521 can be formed integrally with another component of the box 500, such as, the bottom wall of the base section.

### **Method of Use**

[0133] In use, a user removes a pair of the joined pouches 10 from the cardboard box 500 of Fig. 12 (or the cardboard box 500' of Figs. 16A and 16B) and separates them by tearing along the perforated center line that divides the two, joined pouches. Once the pouches 10 are separated, the user inspects the contents of one of the pouches through the transparent front and back panels to determine if the product has separated or spoiled. If the product has separated (or mixing is otherwise desired), the user can manually knead (or otherwise manipulate) the product within the pouch 10 as described above to thoroughly mix the product insitu. Once the user observes that the product is thoroughly mixed, the user manually grips the pouch 10 by its grip portion 66 and tears the grip portion along the lines of weakness 30, 32 to completely remove the grip portion from the pouch 10. In doing so, the user opens the pouch 10 by tearing through the spout 62 to form the spout opening 63 (Figs. 6 and 15).

[0134] The product can be poured or squeezed from the pouch 10. In one embodiment, the product is a consumable product that can be consumed directly from the pouch 10. In another embodiment, the product is a consumable product intended to be mixed with another product. For example, if the product is a human milk fortifier (e.g., the concentrated liquid human milk fortifier or the gelled human milk fortifier described above), the human milk fortifier can be dispensed directly into a container (e.g., infant bottle B) containing human milk M (or other suitable infant formula) as illustrated in Fig. 13. In such an embodiment, the resulting fortified human milk or fortified infant formula is suitable for oral feeding to an infant, including a premature infant.

### **General**

[0135] All percentages, parts and ratios as used herein, are by weight of the total composition, unless otherwise specified. All such weights as they pertain to listed ingredients are based on the active level and, therefore, do not include solvents or byproducts that may be included in commercially available materials, unless otherwise specified.

[0136] Numerical ranges as used herein are intended to include every number and subset of numbers within that range, whether specifically disclosed or not. Further, these numerical ranges should be construed as providing support for a claim directed to any number or subset of numbers in that range. For example, a disclosure of from 1 to 10 should be construed as supporting a range of from 2 to 8, from 3 to 7, from 5 to 6, from 1 to 9, from 3.6 to 4.6, from 3.5 to 9.9, and so forth.

[0137] All references to singular characteristics or limitations of the present disclosure shall include the corresponding plural characteristic or limitation, and vice versa, unless otherwise specified or clearly implied to the contrary by the context in which the reference is made.

[0138] All combinations of method or process steps as used herein can be performed in any order, unless otherwise specified or clearly implied to the contrary by the context in which the referenced combination is made.

[0139] When introducing elements of the present invention or the preferred embodiment(s) thereof, the articles "a", "an", "the" and "said" are intended to mean that there are one or more of the elements. The terms "comprising", "including" and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements.

[0140] As various changes could be made in the above constructions without departing from the scope of the invention, it is intended that all matter contained in the above description or shown in the accompanying drawings shall be interpreted as illustrative and not in a limiting sense.

[0141] Thus, in summary, according to first aspect of the present invention there is provided a single-use pouch for liquid product, the pouch comprising: a front panel and a back panel, the front and back panels at least in part cooperatively defining an interior space of the pouch, the interior space having a total liquid capacity; and a volume of liquid product contained within the interior space, the volume of liquid product being less than about 60% of the total liquid capacity of the pouch.

[0142] Advantageously the volume of the liquid product is between about 20% and about 60% of the total liquid capacity of the pouch. Preferably the volume of the liquid product is between about 30% and about 50% of the total liquid capacity of the pouch. Preferably the volume of the liquid product is about 35% of the total liquid capacity of the pouch.

[0143] Advantageously the volume of the liquid product in the pouch is greater than a volume of a predetermined target delivery dosage of the liquid product. Preferably the volume of the liquid product in the pouch is up to about 12 percent greater than the predetermined target delivery dosage of the liquid product. Preferably the pouch has a product distribution ratio within  $\pm 4$  percent of the dose size.

[0144] Advantageously the pouch further comprises a spout through which the product is dispensed from the pouch.

[0145] Advantageously the front panel is disposed in face-to-face engaging relationship with the back panel, the back panel being sealingly engaged with the front panel to define the interior space.

[0146] According to a further aspect of the present invention there is provided a single-use pouch for liquid product, the pouch comprising: a front panel and a back panel, the front and back panels at least in part cooperatively defining an interior space of the pouch, the interior space having a total liquid capacity; and a volume of liquid product and gas contained within the interior space, the volume of liquid product and gas being less than about 40% of the total liquid capacity of the pouch.

[0147] According to a further aspect of the present invention there is provided a pouch comprising: a front panel and a back panel, the front and back panels at least in part cooperatively defining an interior space of the pouch, at least one of the front panel and the back panel being made at least in part from a flexible, transparent material; and an aseptically processed liquid product contained within the interior space of the pouch, the product being visually observable through the at least one of the front panel and the back panel.

[0148] According to a further aspect of the present invention there is provided a method of packaging an aseptic liquid product into a pouch, the method comprising: sterilizing both sides of a web of sheet material with a sterilant; the web being flexible and transparent; dividing the web into a plurality of web segments; forming at least one pouch from each of the web segments; and filling the at least one pouch with an aseptically processed liquid product.

[0149] According to a further aspect of the present invention there is provided a method of dispensing a liquid product from a pouch, the method comprising: obtaining a pouch having an aseptically processed liquid product contained therein, at least a portion of the pouch being transparent for allowing visual observation of the liquid product contained therein; manually kneading the pouch to mix the liquid product within the pouch; visually observing the liquid product through the transparent portion of the pouch to determine if the liquid product has been sufficiently mixed; opening the pouch; and pouring the liquid product from the pouch.

[0150] According to a further aspect of the present invention there is provided a single-use pouch for product, the pouch comprising: a body having a front panel and a back panel, the front and back panels at least in part cooperatively defining an interior space of the pouch for containing the product, and a spout in fluid communication with the interior space and through which the product is dispensed from the pouch, the spout having a width and the body having a width wherein the ratio of the width of the body and the width of the spout is between about 3:1 and about 5:1.

[0151] According to a further aspect of the present invention there is provided a secondary container for holding a plurality of pouches, the container comprising a base section and a lid hingedly attached to the base section for movement between a closed position and an opened position, the base section including a bottom wall, at least one side wall extending up from the bottom wall, a top wall, and an interior floor, the interior floor being tented along its center line.

## Claims

### 1. A single-use pouch comprising:

a web folded to form a pouch having a front panel, a back panel, a top edge, a bottom edge, and two side edges, wherein the top edge, the bottom edge and one of the two side edges are sealed, the other of the two side edges is a fold line, and the front panel and the back panel define an interior space; and a liquid product contained in the interior space;

wherein the interior space includes a body and a spout, one side of the spout defined by the fold line, and the spout in fluid communication with the body and through which the product is dispensed from the pouch.

2. The single-use pouch of claim 1 wherein the fold line acts as a channel to guide liquid product from the body towards an opening at the end of the spout.

3. The single-use pouch of claim 1 wherein a width of the pouch is at least three times a width of the spout.

4. The single-use pouch of claim 1 wherein the interior space includes a transition portion connecting the spout and the body, wherein the transition portion defines a travel path for the liquid product, and the travel path is at an angle to the fold line.

5. The single-use pouch of claim 1 wherein at least one of the front panel and the rear panel includes a line of weakness positioned between the top edge and the body, and in a path transverse to the spout.

6. The single-use pouch of claim 1 further comprising a gripping portion positioned between the top edge and the body.

7. The single-use pouch of claim 6 wherein the gripping portion includes a portion of the front panel sealed to a portion of the back panel.
8. The single-use pouch of claim 7 wherein at least one of the front panel and the rear panel includes a line of weakness positioned entirely within the gripping portion.
9. The single-use pouch of claim 6 wherein the gripping portion defines a side of the spout opposite the fold line.
10. The single-use pouch of claim 1 wherein the liquid product is aseptically processed.
11. The single-use pouch of claim 1 wherein the liquid product is a human milk fortifier.
12. The single-use pouch of claim 1 wherein the liquid product is manually kneadable within the interior space.
13. The single-use pouch of claim 1 wherein the liquid product is visible through at least one of the front panel and the back panel.
14. The single-use pouch of claim 13 wherein indicia is printed on the front panel and the back panel, and at least the majority of at least one of the front panel and the back panel is transparent.
15. The single-use pouch of claim 1 wherein the web is a multi-layer plastic laminate.



FIG. 1

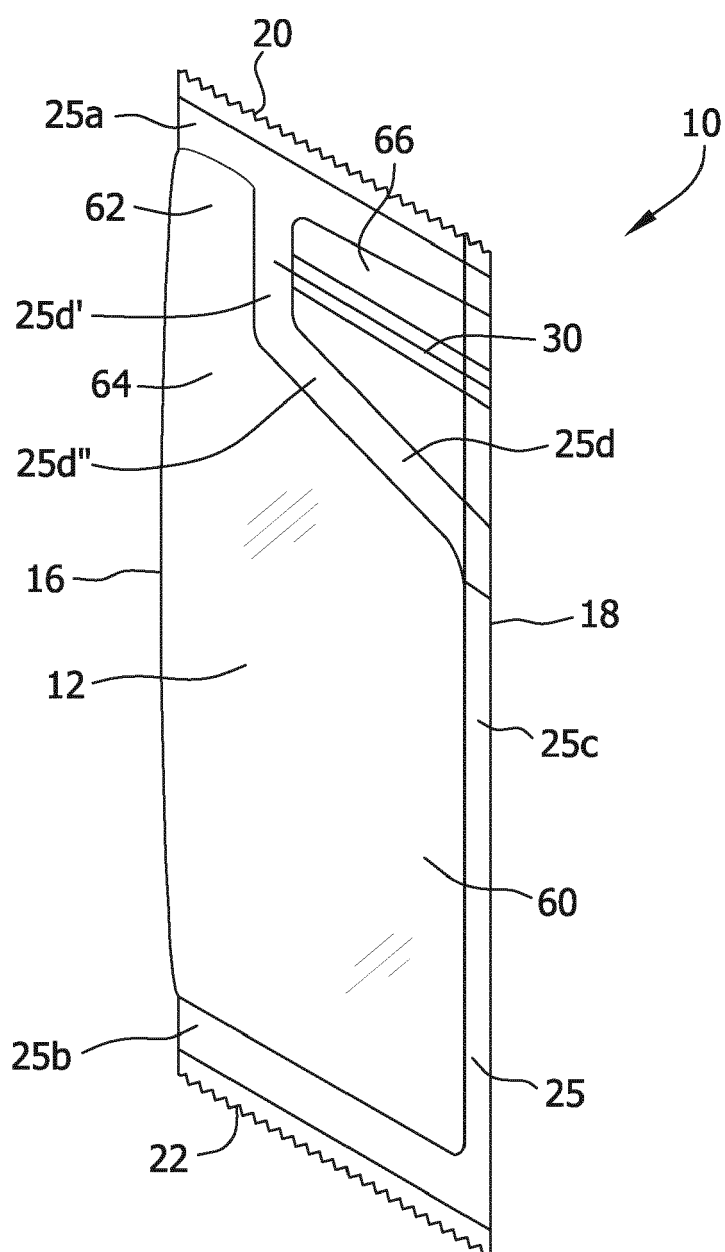


FIG. 2

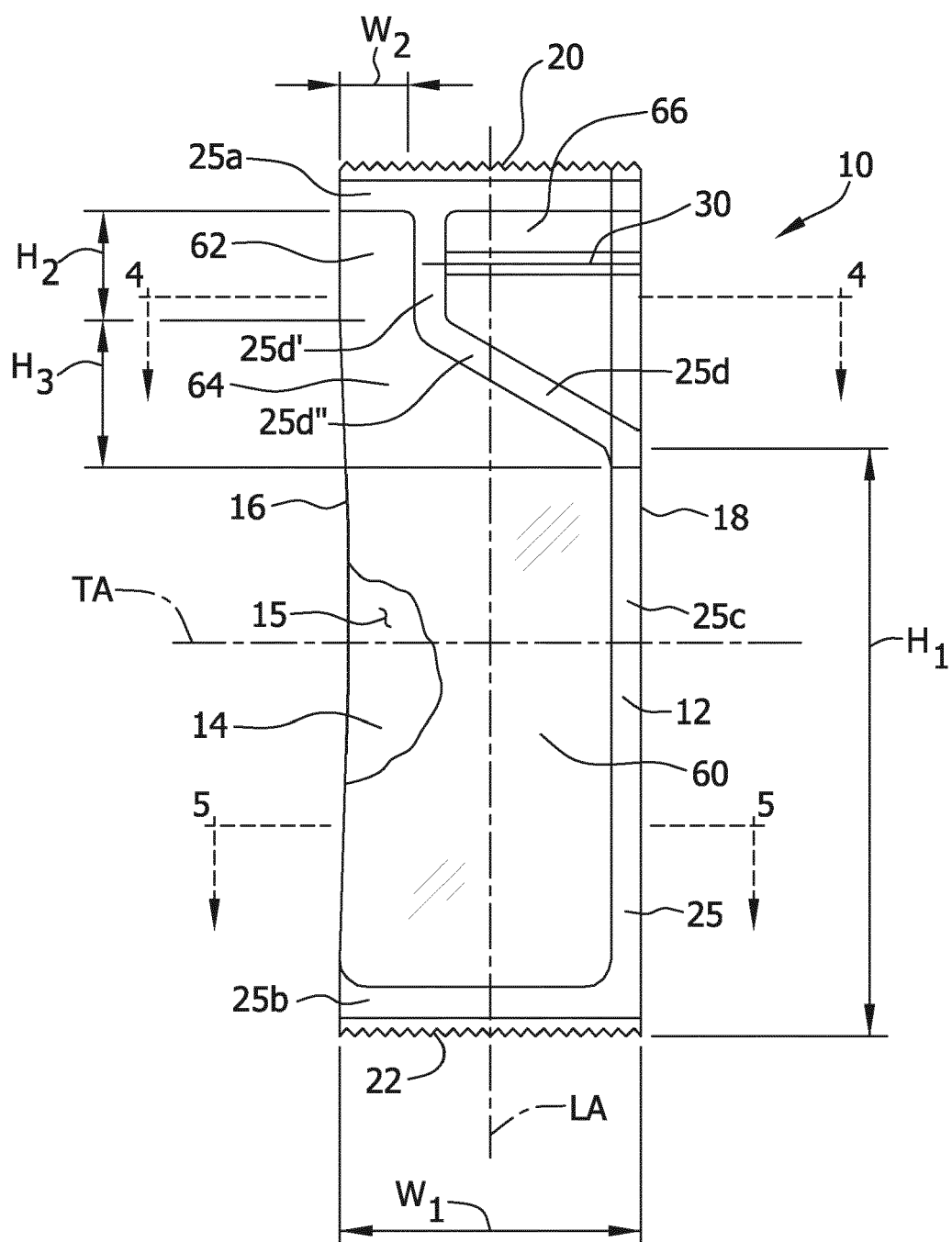


FIG. 3

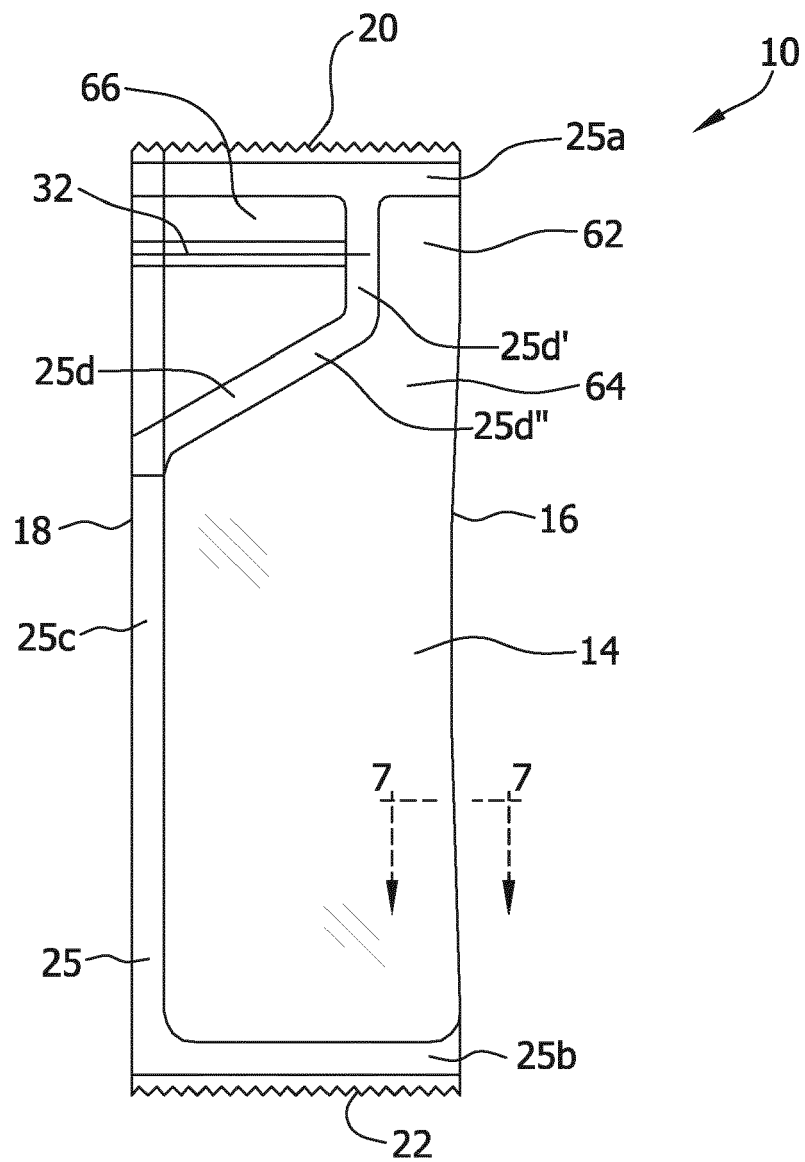


FIG. 4

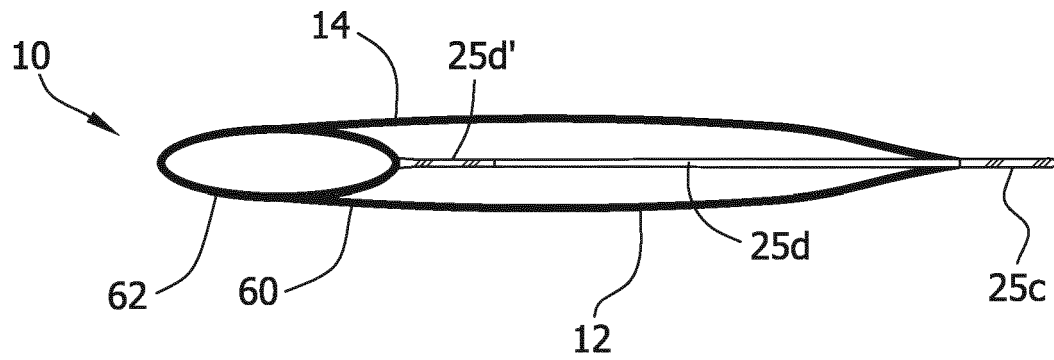


FIG. 5

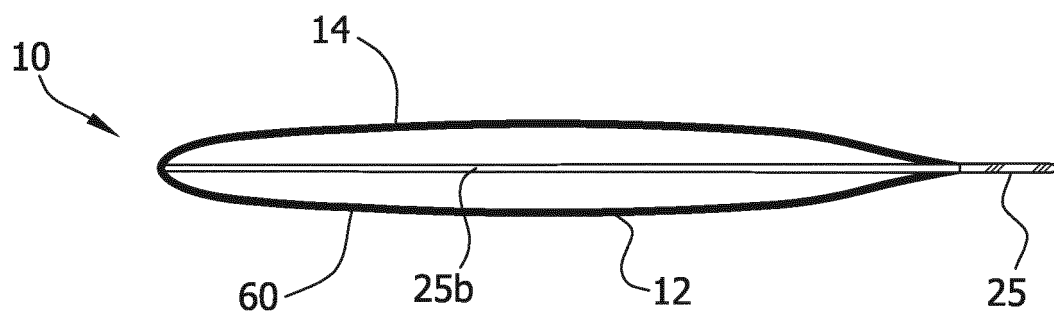


FIG. 6

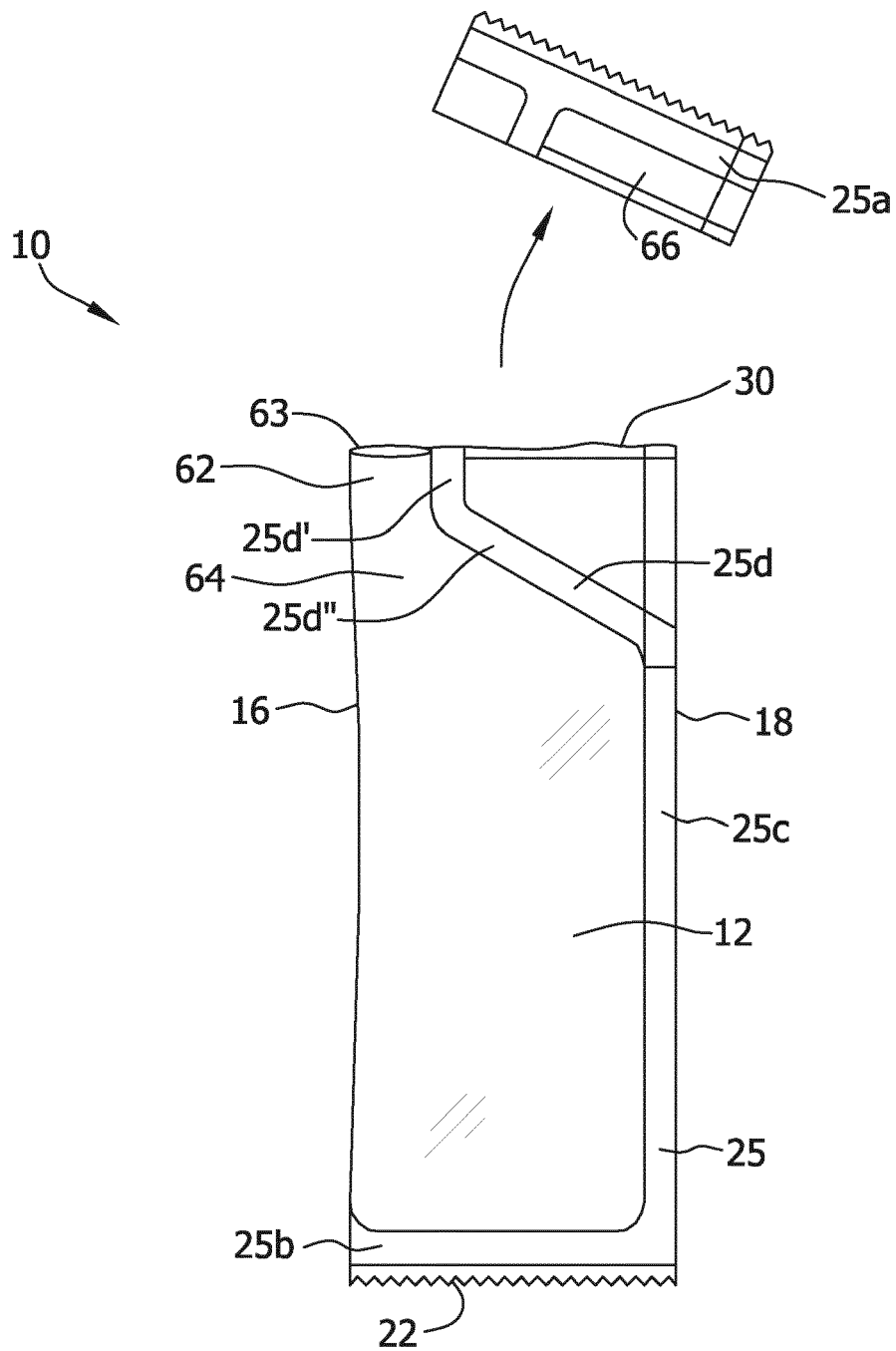


FIG. 7A

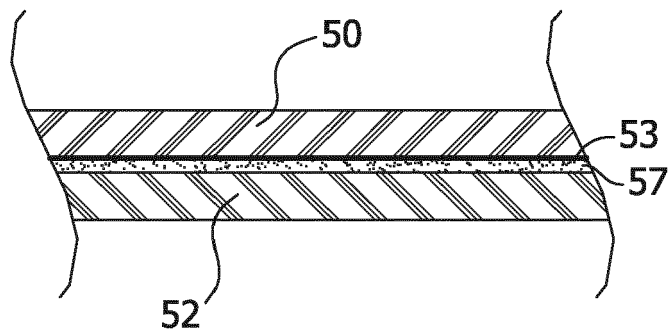


FIG. 7B

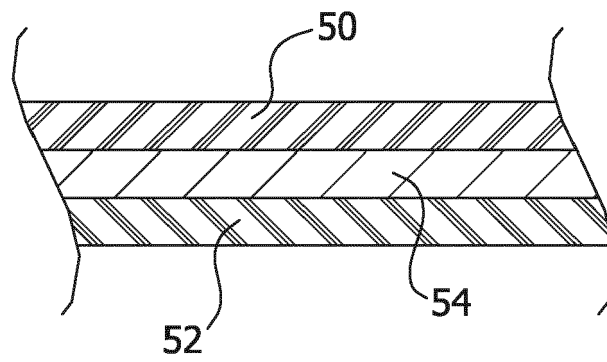


FIG. 8

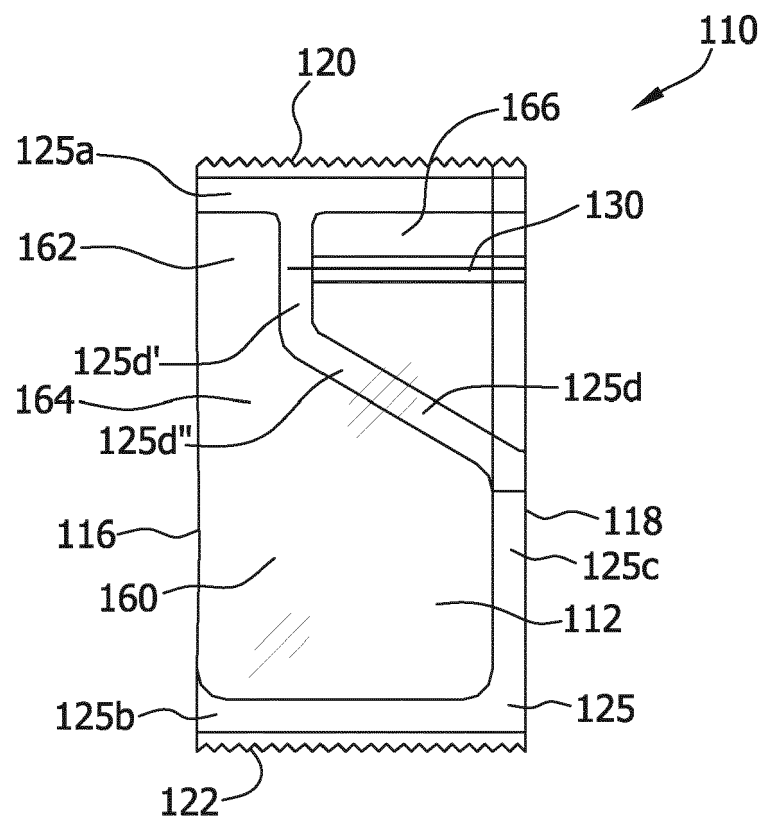
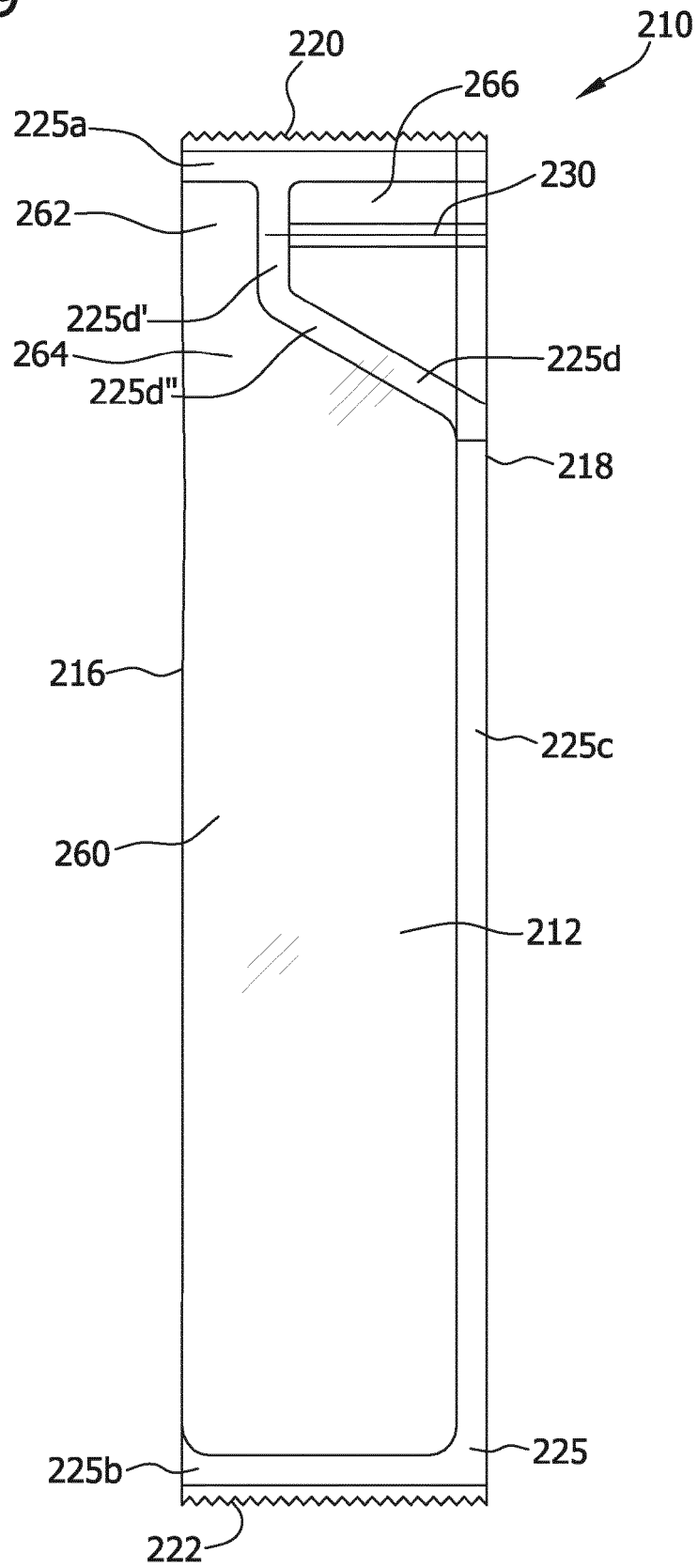




FIG. 9



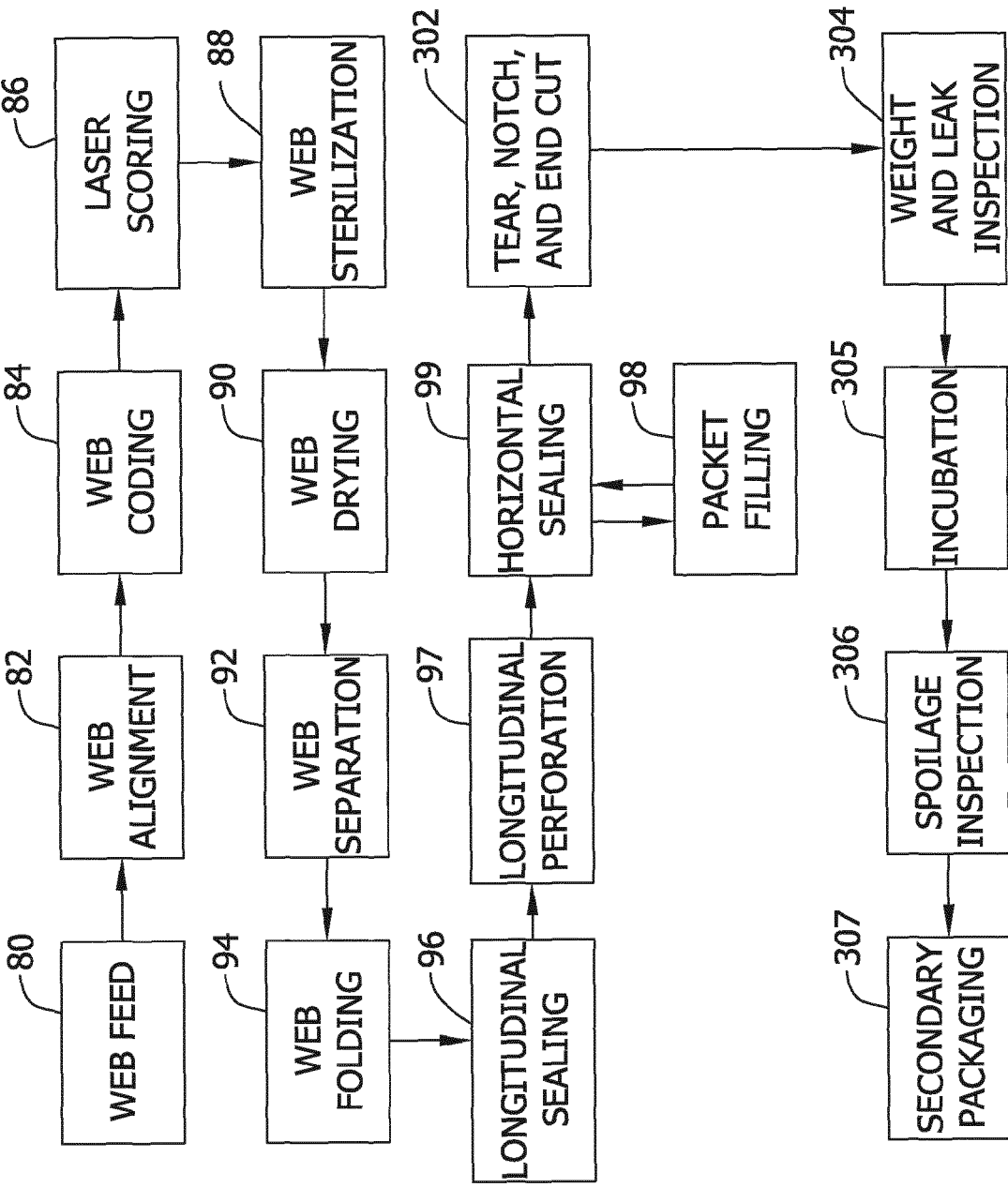


FIG. 11A

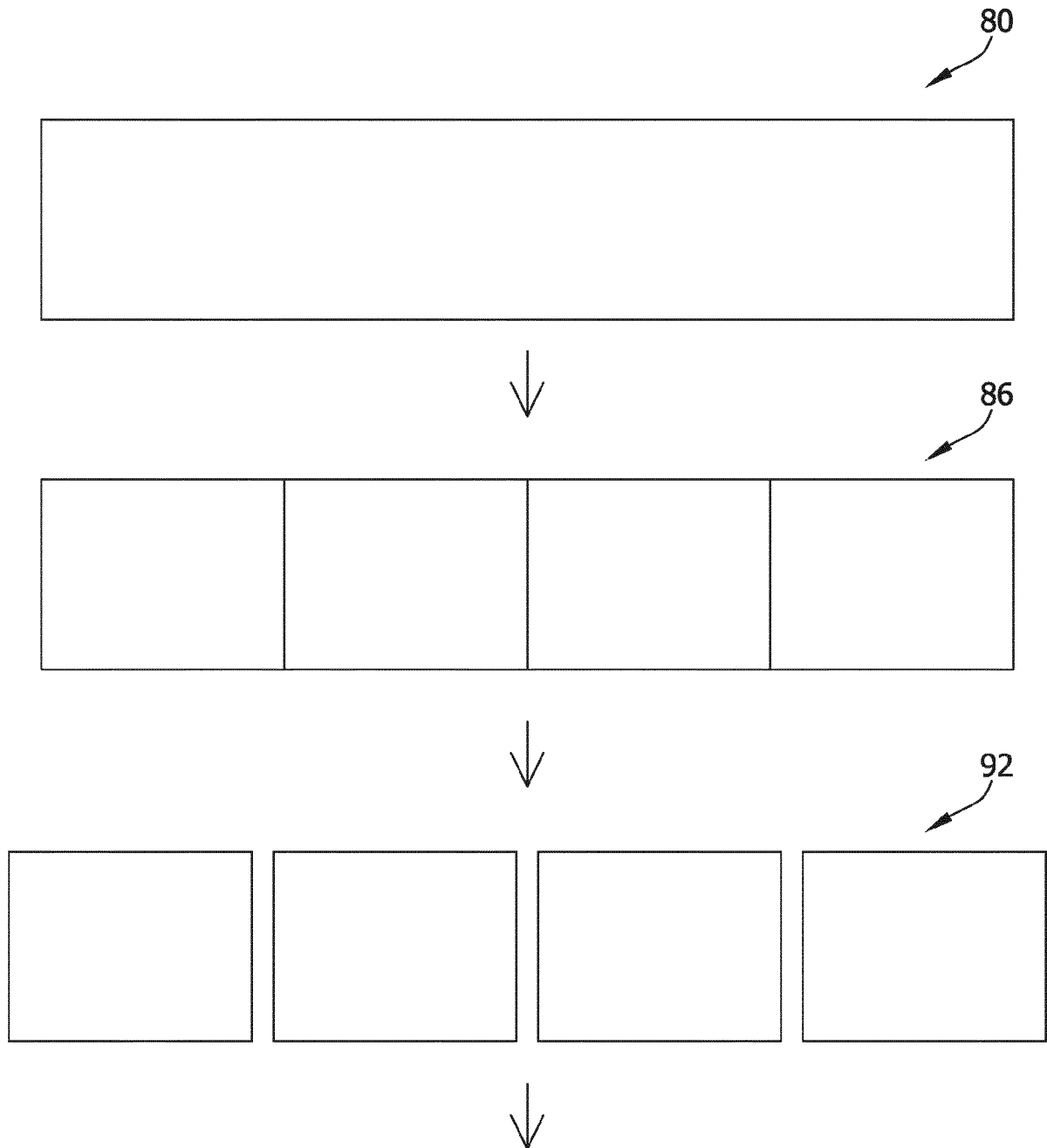


FIG. 11B

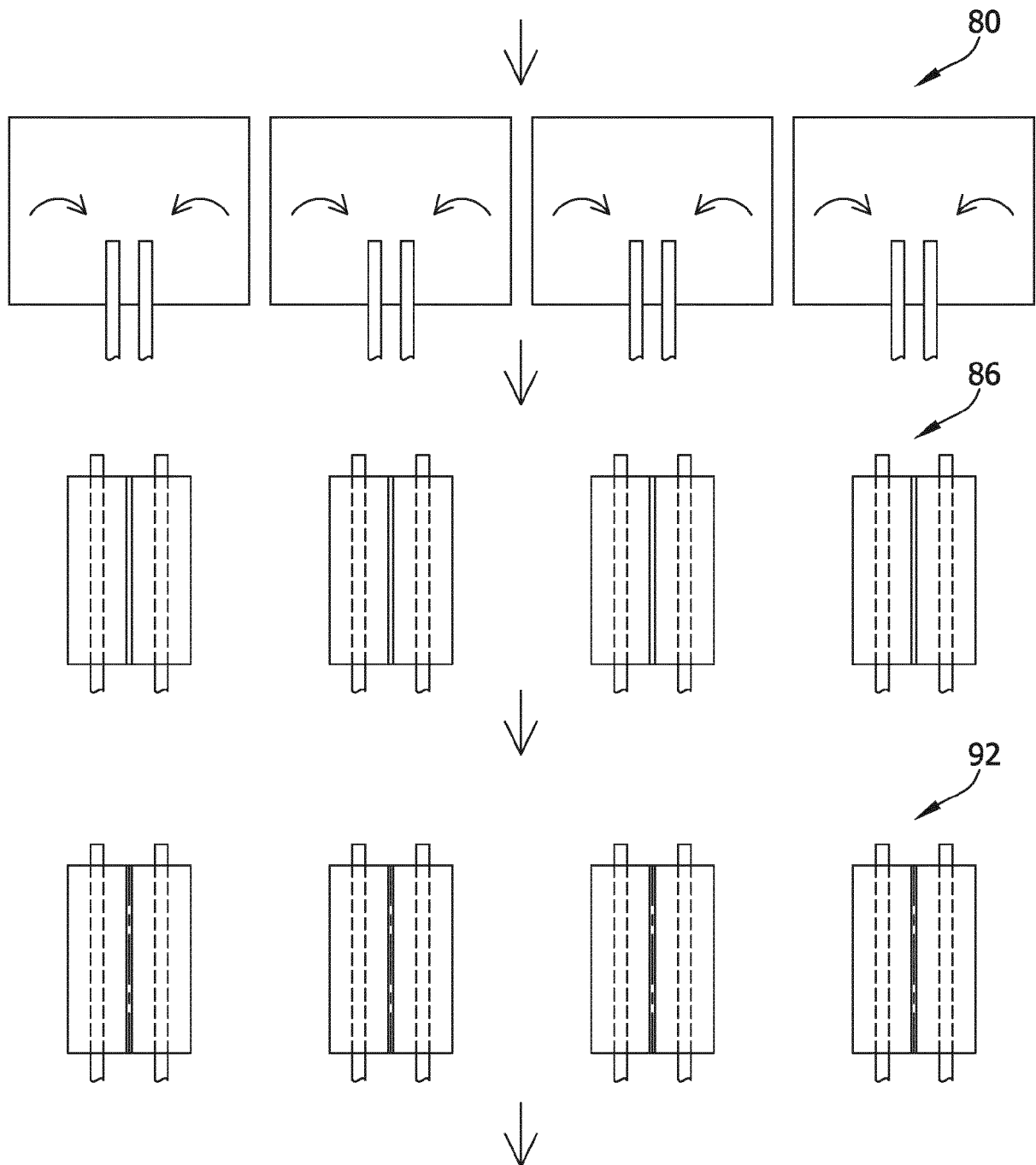


FIG. 11C

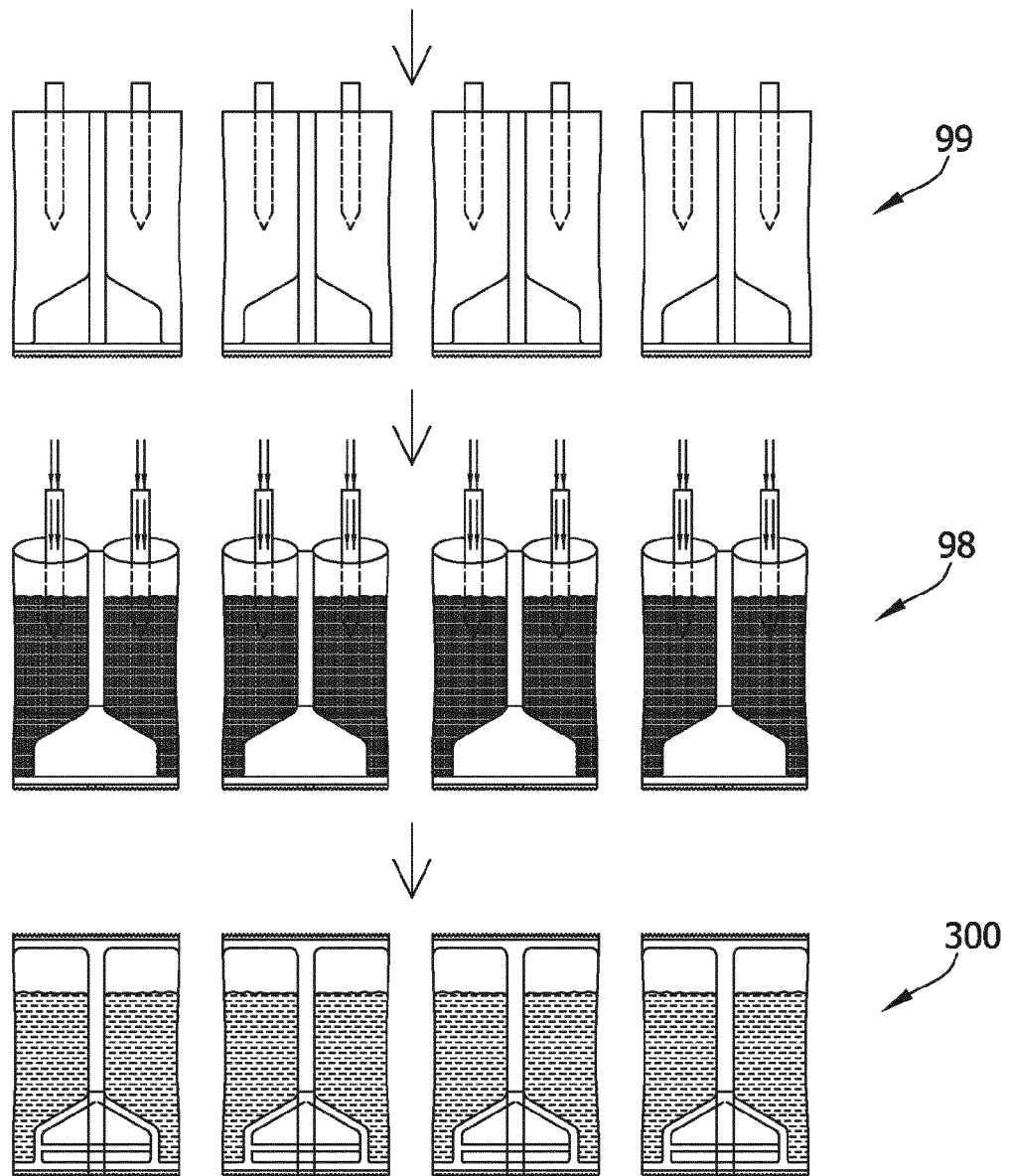


FIG. 12

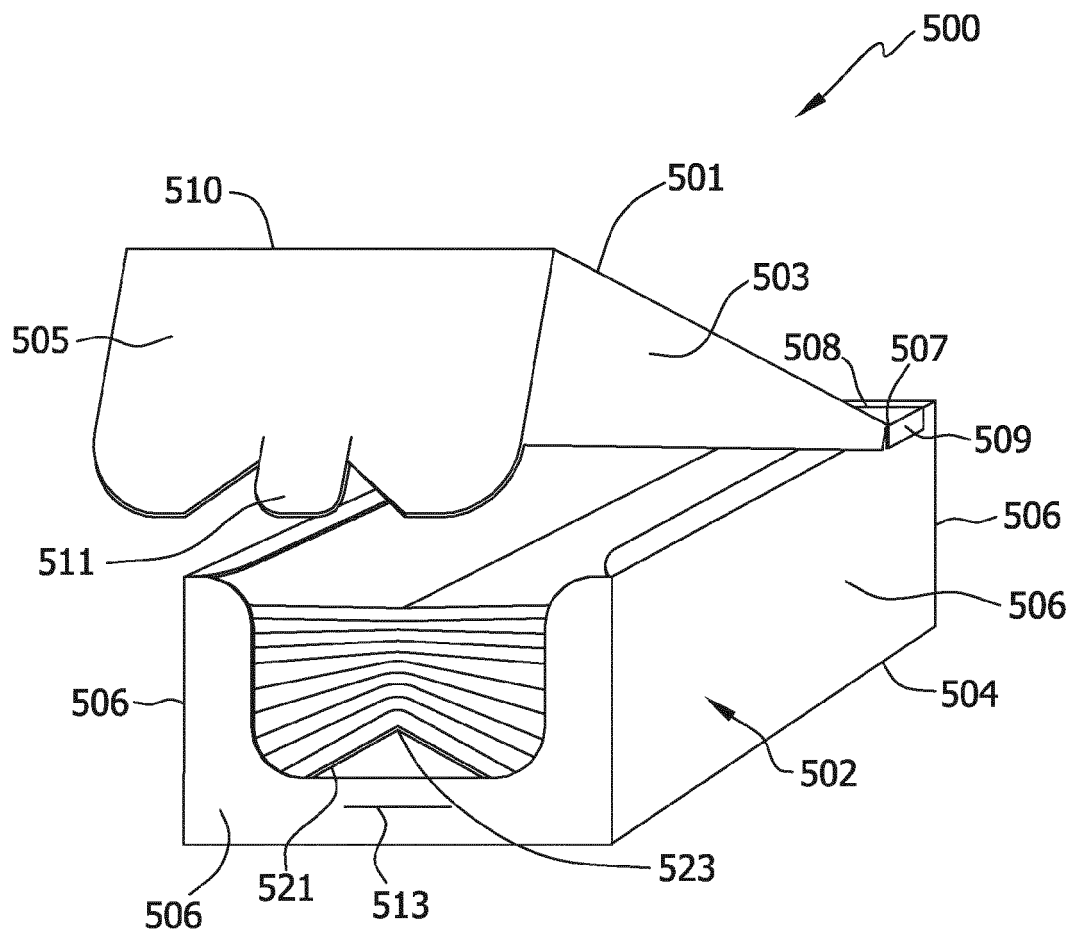


FIG. 13

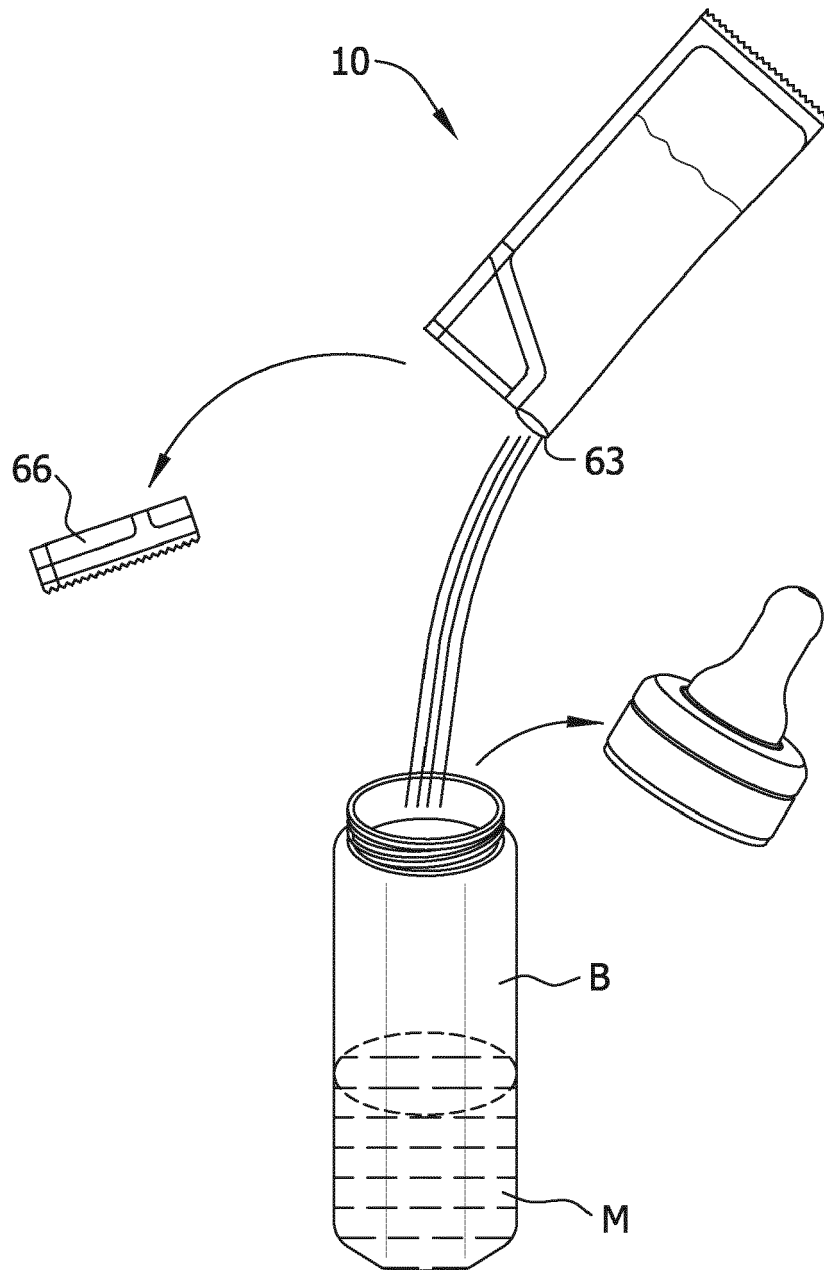


FIG. 14B

210

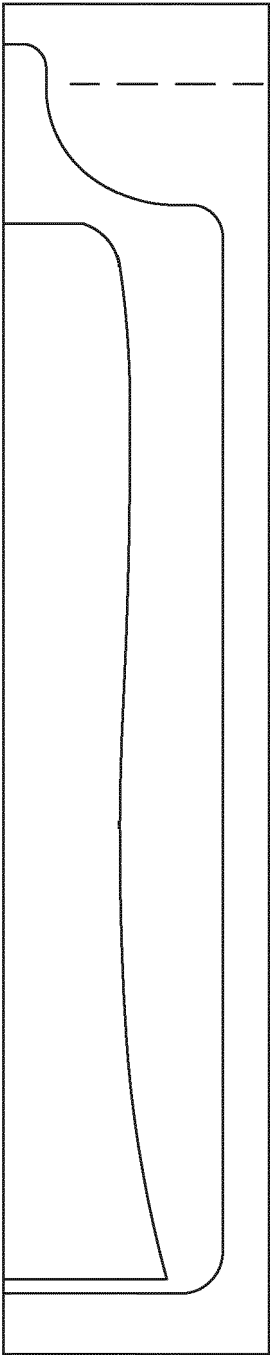


FIG. 14A

10

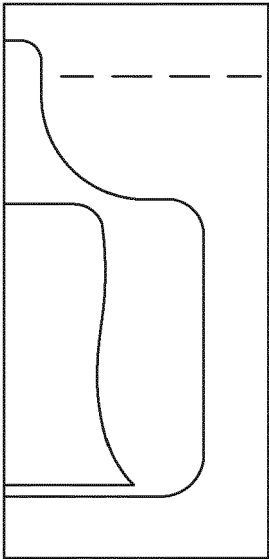




FIG. 15A

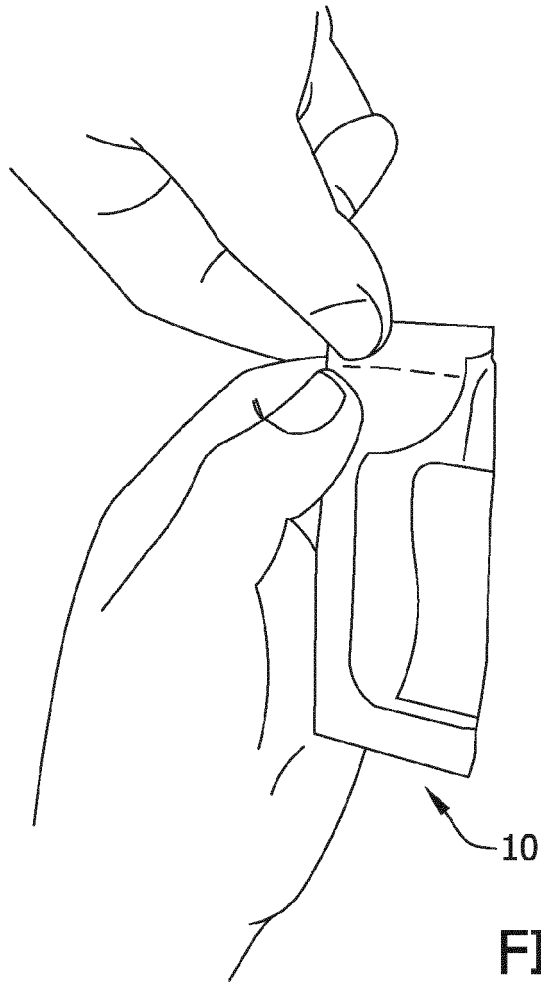


FIG. 15B

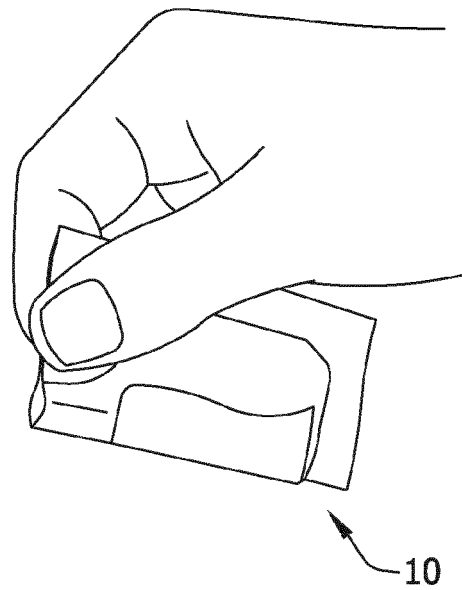


FIG. 16A

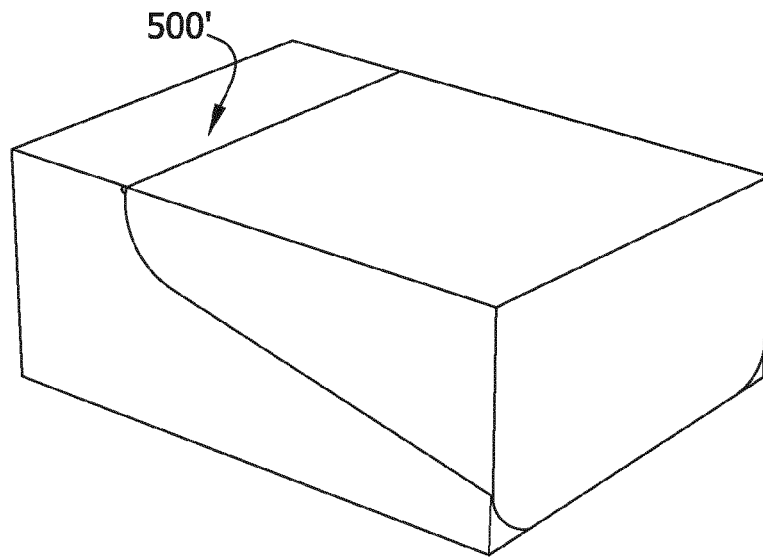


FIG. 16B

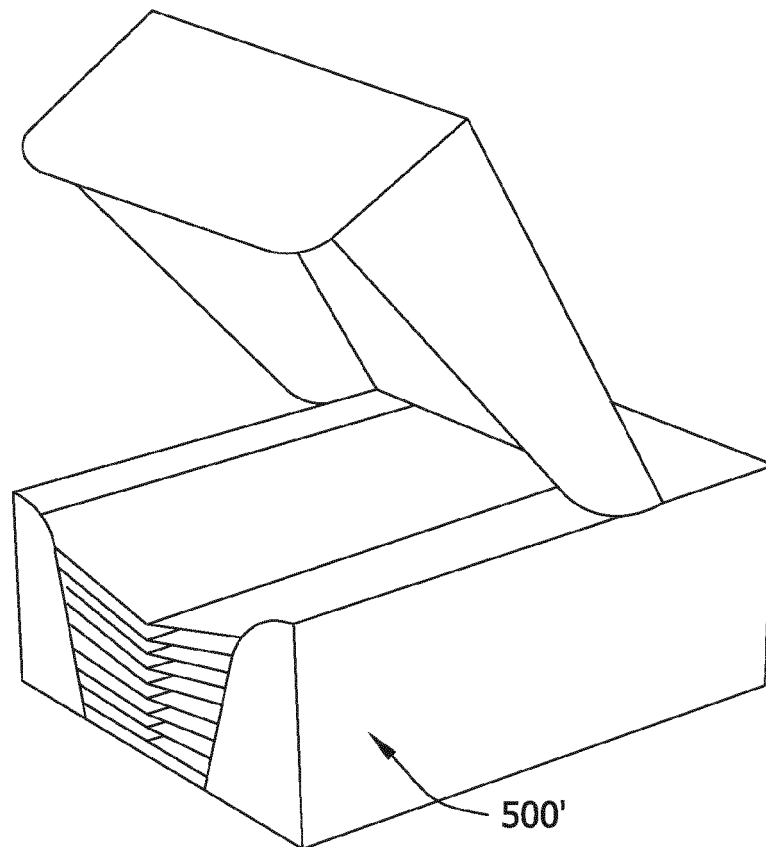


FIG. 17

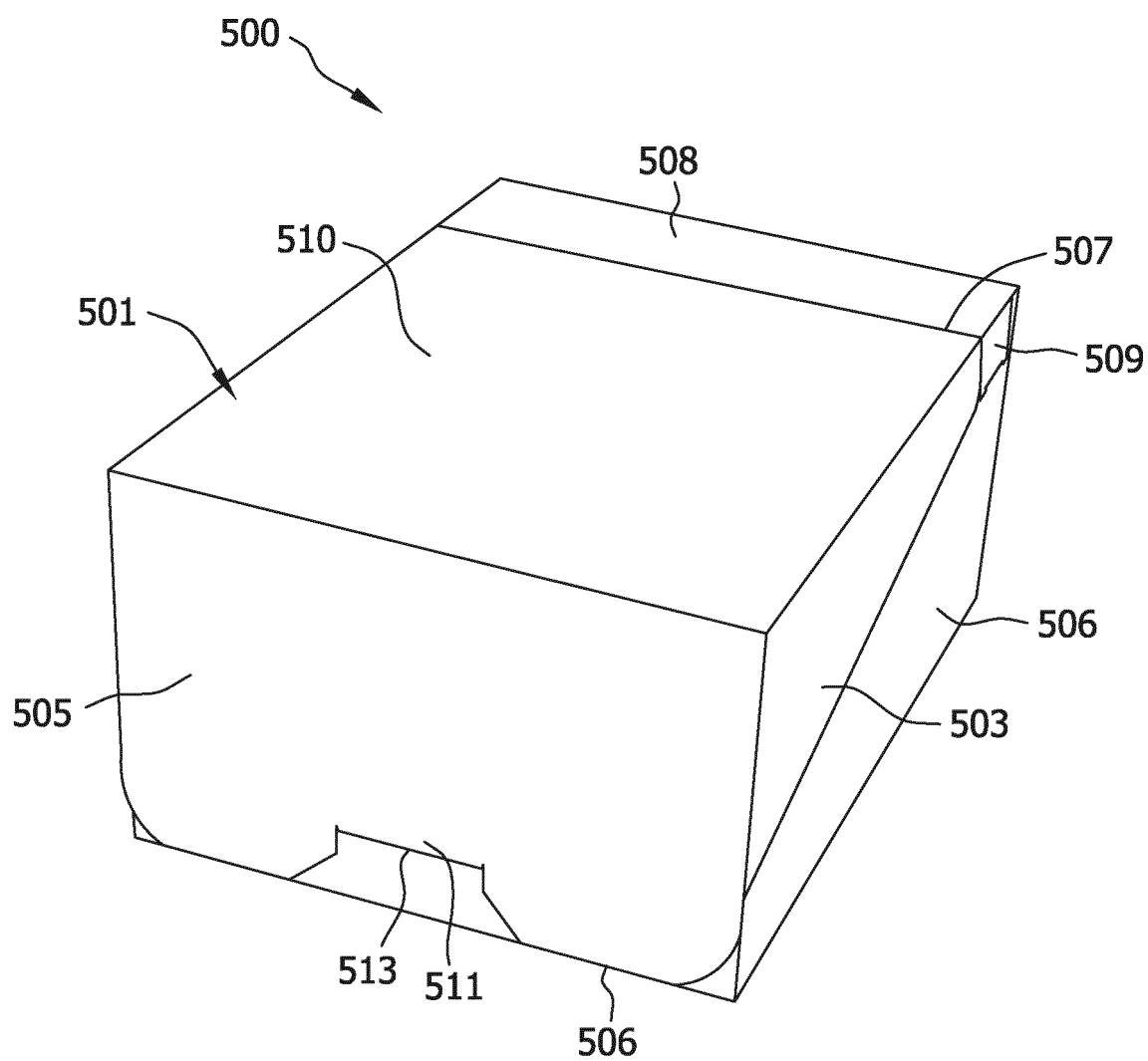


FIG. 18

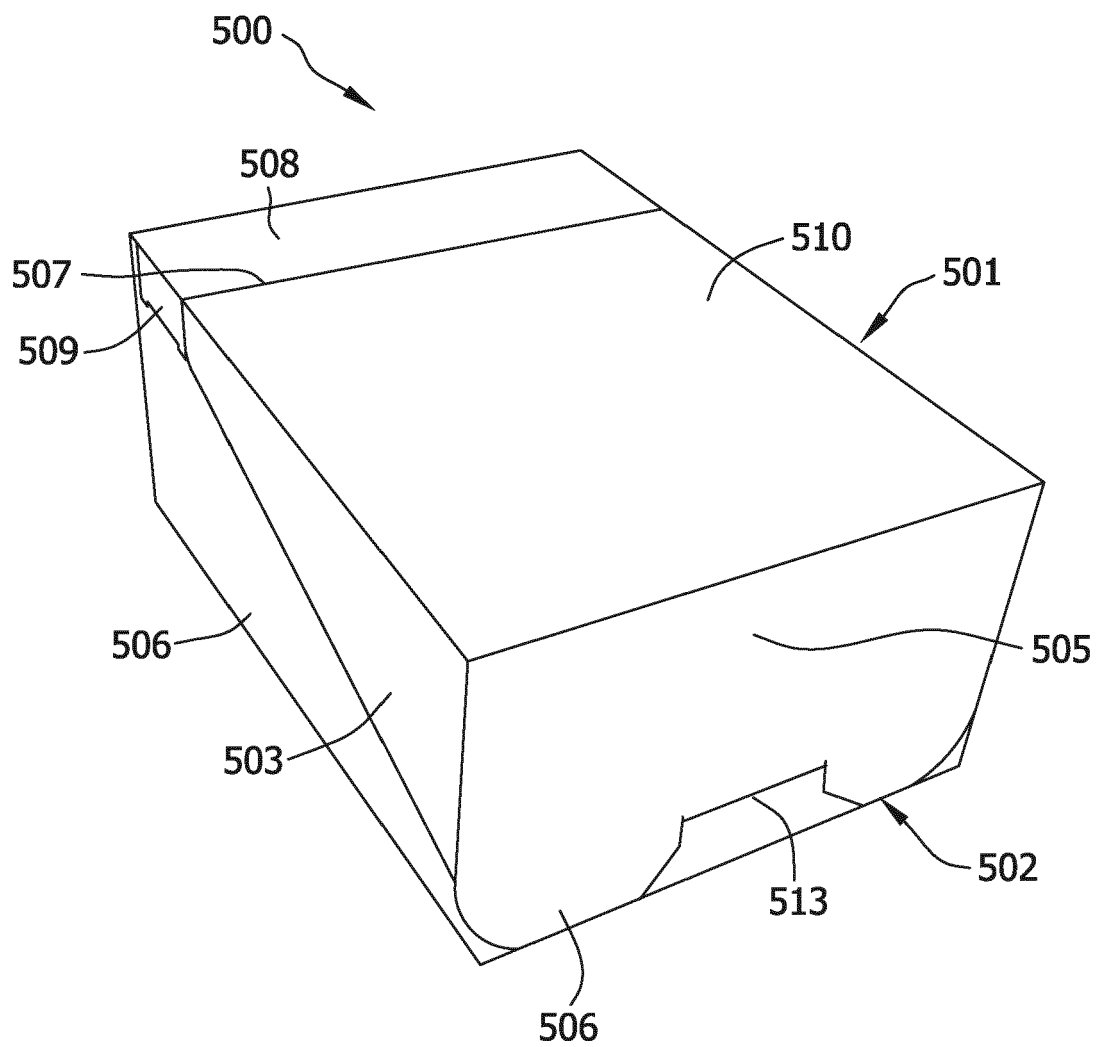


FIG. 19

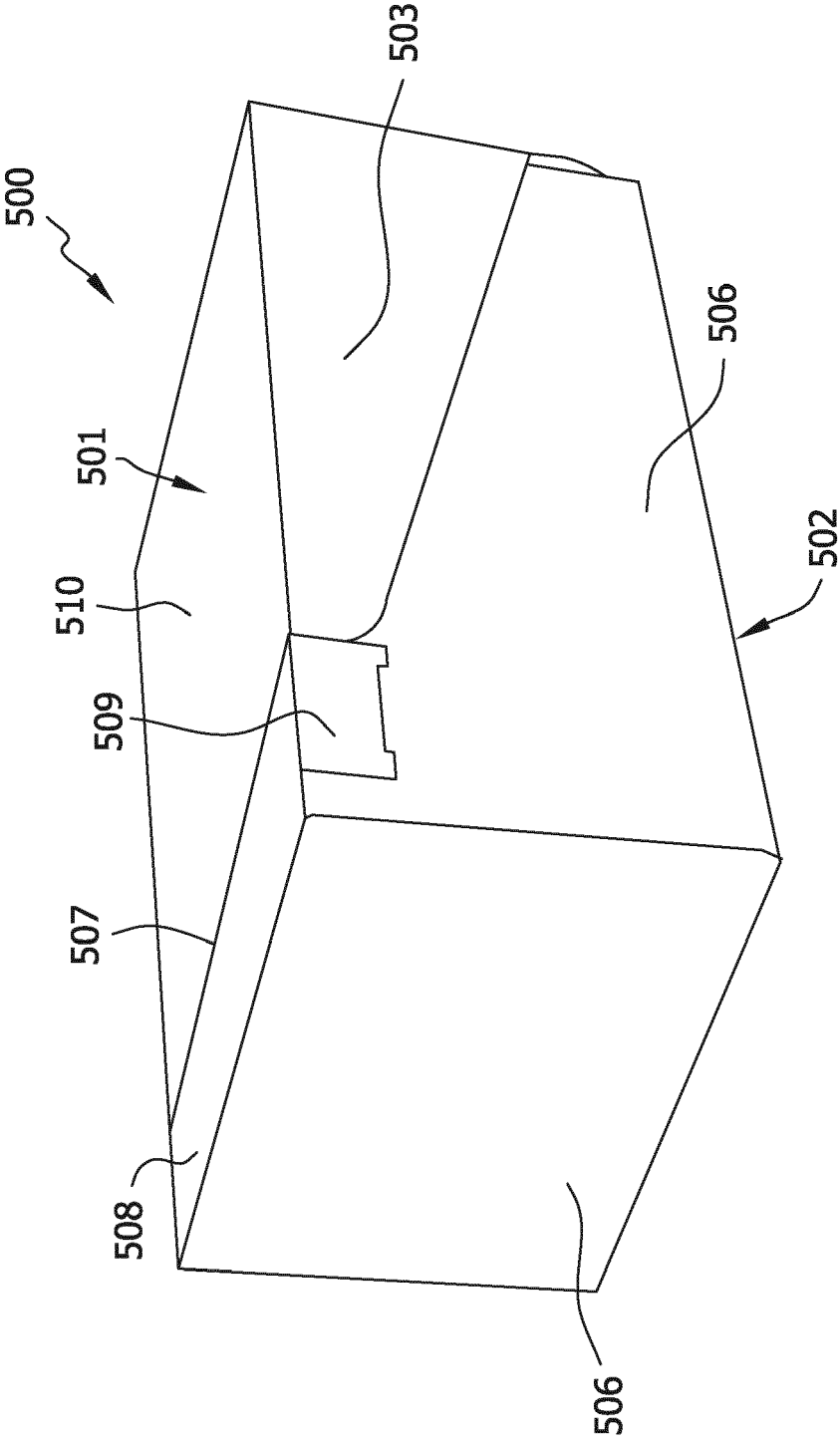


FIG. 20

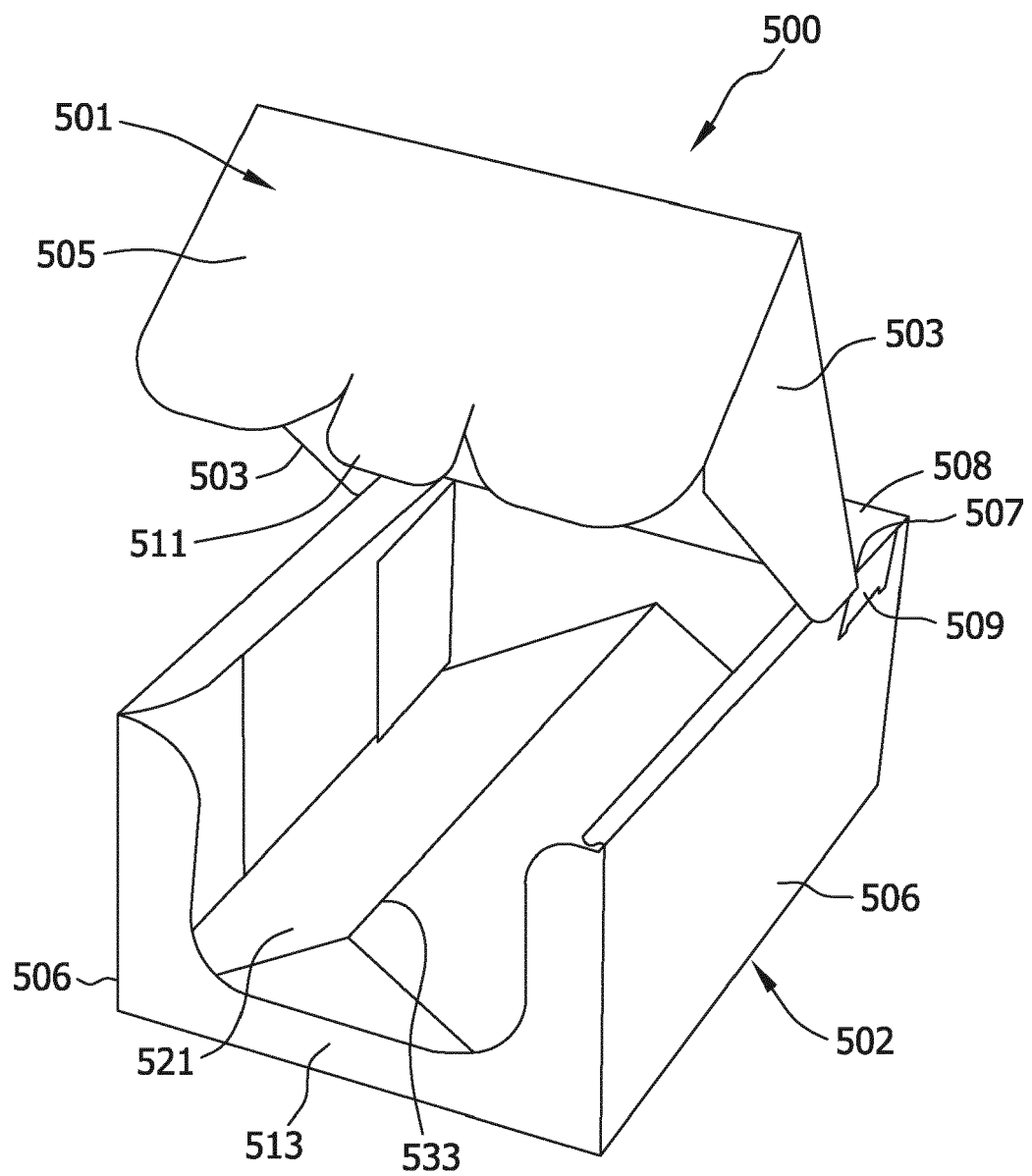


FIG. 21

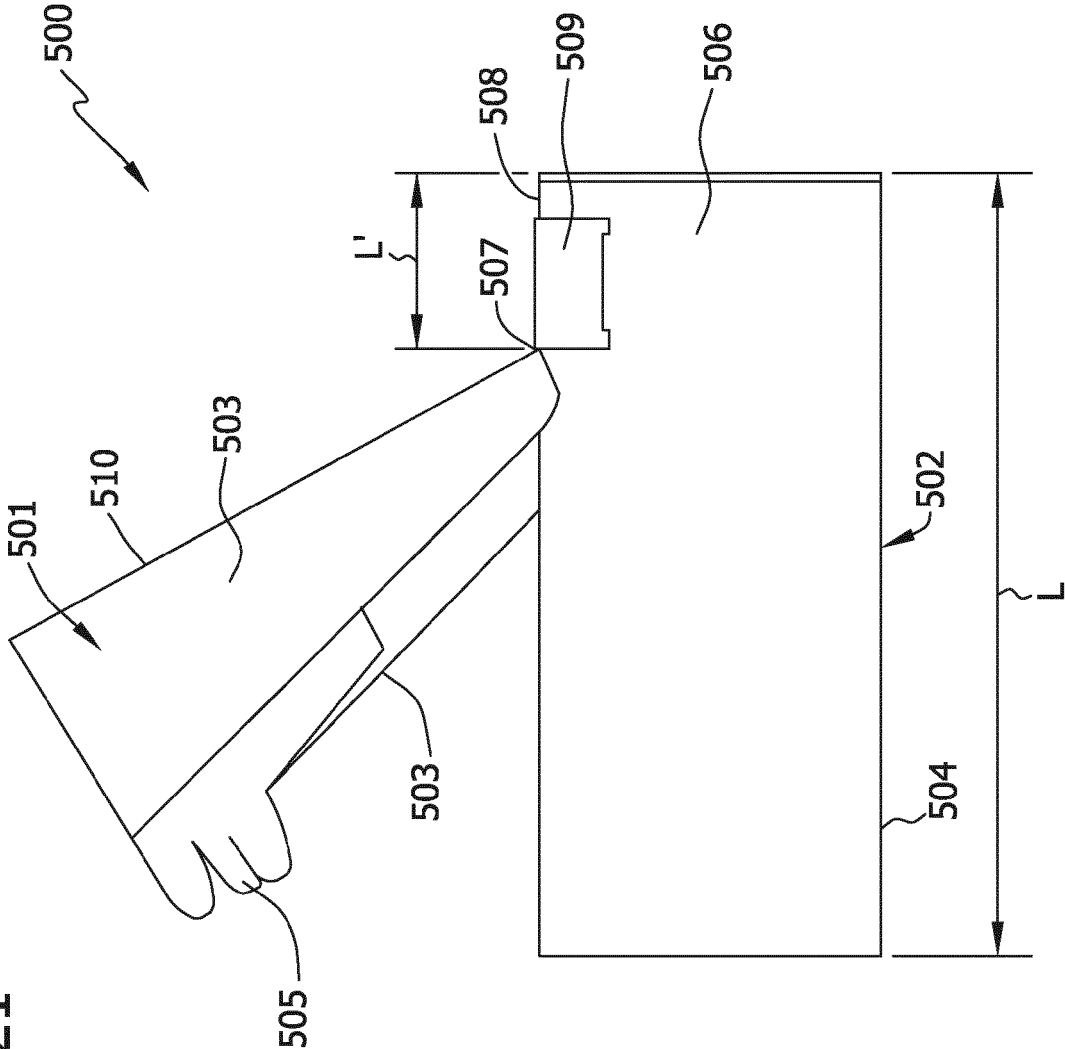


FIG. 22

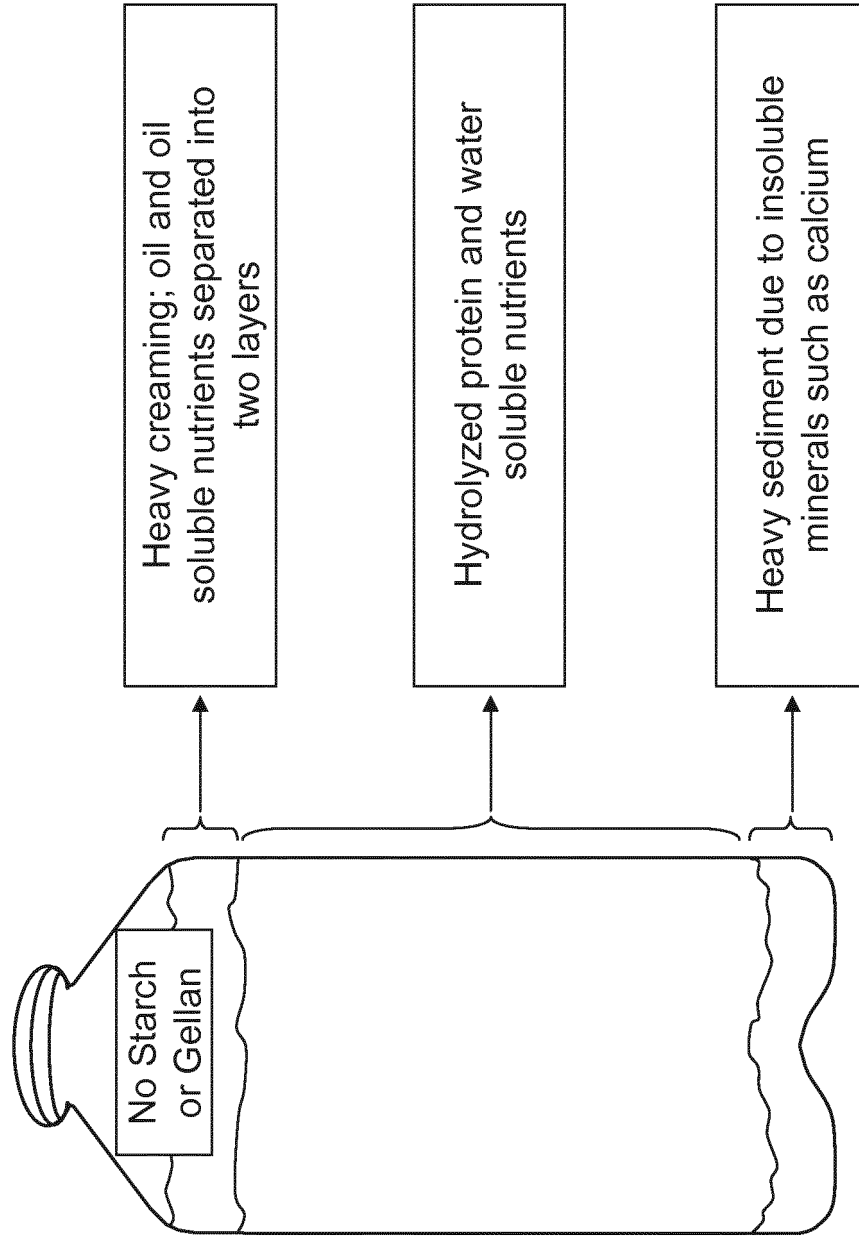




FIG. 23

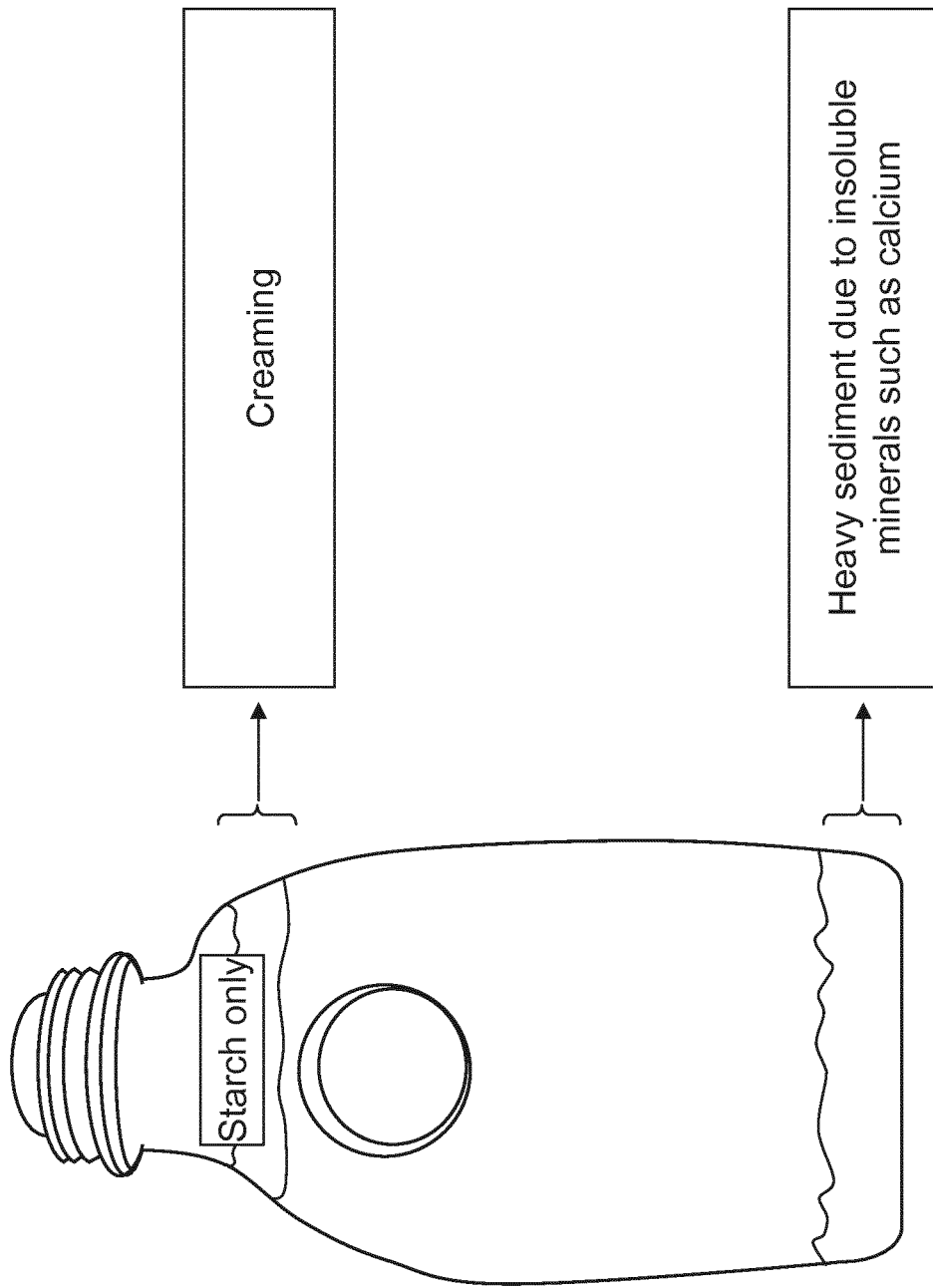


FIG. 24

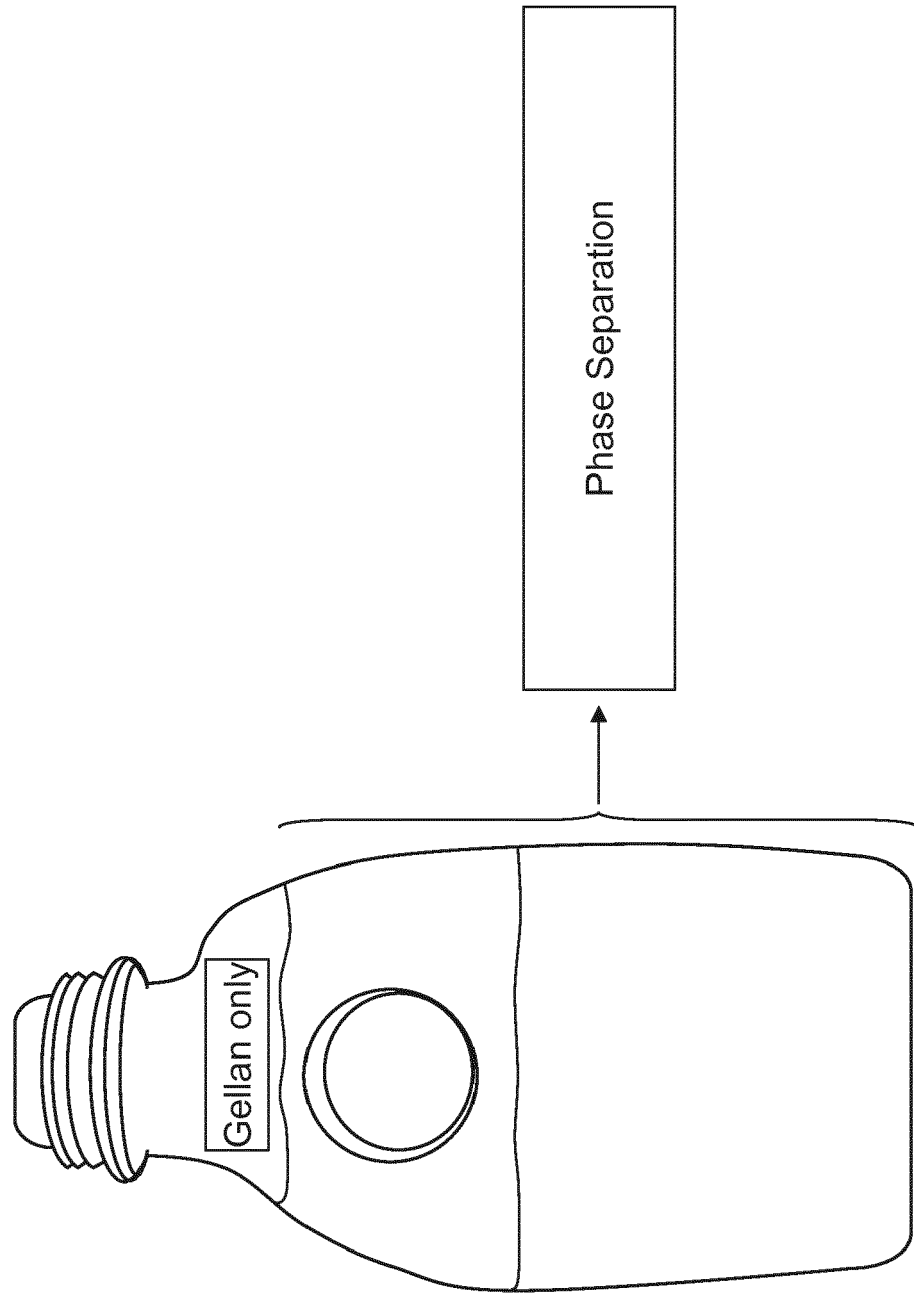


FIG. 25

