

PACKAGE SYSTEM AND METHOD FOR INHIBITING MOISTURE ENTRY

[001] This application claims priority from provisional application Serial No. 61/971,003, filed on March 27, 2014, which is incorporated herein in its entirety.

FIELD OF THE INVENTION

5 [002] The present invention is a package system that maintains the physicochemical integrity of its contents, free-flowing characteristics. In particular, the present invention relates to package systems that prevent the caking of salts used in the manufacture of biopharmaceuticals (e.g., in cell culture production).

BACKGROUND OF INVENTION

10 [003] Various salts and buffers are used in the manufacturing operations associated with biopharmaceuticals production (e.g., cell culture production and protein purification). These chemicals are dissolved under sterile conditions to make up a variety of solutions. A common problem with delivering granular solids is that they have a tendency to cake (i.e., joined together to form a mass) due to the presence of moisture in the solid. The moisture
15 can come from two sources, externally and internally. Internal moisture is found on the surface of the salt and it can be released when there are changes in temperature. External moisture enters the package system from the environment exterior to the package system. Caking of solids is a major problem in the industry and attempts to solve this problem include adding anti-caking agents and changing the crystal size. However, none of these
20 attempts have completely solved the problem. The addition of anti-caking agents to

packages containing salts is undesirable because the anti-caking agents frequently include compounds that interfere with the pharmaceutical manufacturing process.

- [004] Salts tend to cake together during storage due to migration of free moisture present on the surface of the salt or due to migration of moisture from the outside environment. The mechanism of caking is the result of the formulation of small salt bridges between the particles due to a partial dissolving of the salt contacted by the free moisture. Over time the bridges become stronger and, when a sufficient amount of moisture is present, the product can turn into a solid unusable mass. Temperature changes in the environment help to release free moisture on the surfaces of these materials and caking increases the more the temperature changes.
- [005] A package system that prevents salts from caking is disclosed in U.S. Patent No. 6,102,198 to Mallinckrodt, which utilizes a moisture permeable bag to allow the moisture to pass from the salts through the bag into the desiccants placed around the bag—either underneath, on top or on the sides of the bag. Any free moisture in the salts or that enters from the outside is trapped (i.e., absorbed) by the desiccants. However, the system has some drawbacks; the drum is expensive and can be difficult for the user to empty. Therefore, there is a need for new package systems that can remove free moisture from its contents and prevent caking until the contents of the package have been completely consumed. The system should maintain free flowing (cake free) material uniformity throughout the drum/package. The location of the desiccant should be selected so that it cannot migrate or break-up and contaminate the product. The package system should also be designed to provide direct dispensing of the product into a reactor/mixing vessel through a port and permit spectroscopic (Raman spectroscopy) analysis of the product without opening the inner bag and risking product contamination. Additionally, the package system should

prevent outside moisture from passing water through the walls of the package into the inside of the package.

SUMMARY OF THE INVENTION

[006] In accordance with the present invention, a package system for inhibiting moisture entry into the contents of the package and continuous removal of any free moisture in the contents is provided. In a preferred embodiment, the package system has a first end and a second end and comprises, consists of or consists essentially of: an inner bag, an outer bag, a discharge port, a pressure equalizing port and at least one desiccant or gas scavenging material. The inner bag is formed from a gas and/or moisture permeable material and has an interior, a first end and a second end. The outer bag is formed from a gas and/or moisture impermeable polymeric material (e.g., HDPE, various LDPEs, and other similar polymeric materials) and has a first end and a second end. The outer bag is also clear to facilitate rapid identification of the package system's contents by Raman spectroscopy (e.g., a handheld Raman spectrometer).

[007] The discharge port has an exterior wall that defines an interior passage that provides access to the interior of the outer bag. The pressure equalizing port vents air from the interior of the inner bag, when it is being filled, and allows filtered or inert gas to enter the interior, when the inner bag is being emptied. The desiccant(s) or gas scavenging material can be a moisture or gas absorbing material that can be used safely with pharmaceutical products.

[008] The inner bag is formed from a layer of a gas and/or moisture permeable material and has a first end, a second end and opposing side edges. The side edges are sealingly attached

to the side wall on the interior of the outer bag from the second end of the outer bag. The first end of the inner bag is attached to the interior of the outer bag at a point intermediate the first and second ends of the outer bag or to the exterior wall of the discharge port to form a second compartment. After the first end of the inner bag is sealingly attached to the exterior wall of the discharge port, the first end of the outer bag sealingly surrounds the first end of the inner bag and the entire exterior wall of the discharge port to form an intermediate space (also referred to herein as a first compartment) between the inner bag and the side wall of the outer bag. The outer bag can be comprised of two layers and preferably can be formed as one continuous layer for increased product strength by extruding the outer bag as a tube or sleeve.

[009] After desiccant(s) and/or gas scavenging material are disposed inside the inner bag (also referred to herein as the second compartment), the second end of the inner bag is sealed closed. The bottom end of the inner bag that contains the desiccant material can be heat sealed or fused along a line that extends horizontally and parallel to the second end of the inner bag. The heat seal is located at least 4 inches above the bottom port, preferably a minimum of 5 inches from the bottom port and most preferably 6 or more inches. The function of this seal is to keep the inner bag containing the desiccant away from the discharge port so that it does not impede the flow of material during emptying operations. After the desiccant material is added to the inner bag, the second ends of the inner and outer bags are sealed closed to isolate the intermediate space from the environment exterior to the package system. The HDPE liner does not include slip agents or block agents; however, an antistatic agent can be added to the HDPE liner to ensure that all of the product is delivered and prevents sticking of the product to the walls due to static buildup.

[010] In a second embodiment, the first end of the inner bag is sealingly attached to the exterior wall of the discharge port and the first end of the outer bag sealingly surrounds the first end of the inner bag and is sealingly attached around the exterior wall of the discharge port to form an intermediate space (also referred to herein as a compartment or the second
5 compartment) between the inner bag and the outer bag. The desiccant(s) and/or gas scavenging material are disposed in the intermediate space and the second end of the inner bag is sealed closed. The function of this seal at the bottom end of the inner bag is to keep the inner bag from falling to the bottom of the package system and impeding the flow of material through the discharge port during emptying operations. The second end of the outer
10 bag is then sealed closed to isolate the intermediate space (i.e., first compartment) from the environment exterior to the package system. HDPE liner does not include slip agent, or block agents, however an antistatic agent is added to the HDPE liner to ensure that all of the product is delivered and prevents sticking of the product to the walls due to static buildup.

[011] The discharge port is used to fill and discharge materials contained in the interior of
15 the inner bag. The first end of the HDPE outer bag forms a seal around the exterior wall of the discharge port. The discharge port is located at the bottom of the packaging system in the HDPE outer bag. The discharge port can have a removable cap for closing and sealing the discharge port. The removable cap isolates the contents of the package system from the outside environment during transportation and storage. The package system can also include
20 a handle attached to the second end of the package system to facilitate the handling of the package system by the user.

[012] The pressure equalizing port is located near the second end of the package system and has a passage that extends between the interior of the inner bag and the environment

exterior to the package system. The passage of the pressure equalizing port contains one or more filter materials that contain at least one desiccant and/or gas scavenging materials, which can selectively prevent moisture or certain gases from entering the interior of the inner bag. The pressure equalizing port can also facilitate the introduction of dry inert gas to
5 blanket the material in the inner bag.

[013] The gas permeable material of the inner bag is preferably formed from continuous and very fine fibers of randomly distributed and non-directional high-density polyethylene. The gas impermeable material of the outer bag preferably includes a low density or a high density polyethylene. The gas impermeable material can include at least three layers with an
10 inner layer formed from a gas barrier material. In a preferred embodiment, the gas barrier material of the inner layer is an ethylene/vinyl alcohol copolymer or polychlorotrifluoroethene.

[014] In another embodiment, the package system has a first end and a second end and comprises, consists of or consists essentially of: a first plastic layer, a second plastic layer, a
15 layer of permeable material disposed between the first and second plastic layers, a discharge port, a pressure equalizing port and at least one desiccant or gas scavenging material. The first and second plastic layers are preferably made of substantially gas impermeable plastic, most preferably from HDPE and/or LLDPE, and at least one of the layers is transparent. The permeable inner layer is preferably made of an ethylene/vinyl alcohol copolymer or
20 polychlorotrifluoroethene. The three layers have substantially the same dimensions and the outer edges are aligned and sealed by a well-known method (e.g., heat stamping or ultrasonic welding) to form a bag with first and second compartments separated by the gas permeable layer.

[015] The first end of the package system is attached to the handle and the pressure equalizing port is located in the first plastic layer near the first end. The discharge port is located in the first plastic layer near the second end. The first compartment is disposed between the first plastic layer and the permeable layer and contains the contents, such as salts used in the manufacture of biopharmaceuticals. The desiccant and/or gas scavenging agent(s) are placed in the second compartment between the second plastic layer and the gas permeable layer. The second compartment is segregated from the first compartment so that the desiccant and/or scavenging agents are isolated from the contents, such that they are not unintentionally poured out with the contents of the first compartment. The pressure equalizing port vents air from the interior of the first compartment, when it is being filled, and allows filtered or inert gas to enter the interior, when the first compartment is being emptied. Optionally, a port can be located in the second plastic layer for adding and removing desiccants and/or gas scavenging agents.

[016] For long term storage of the package system with product inside the inner bag, an over bag is placed over the primary bag and heat sealed closed. The over bag serves as a moisture barrier and further isolates the product in the package system from moisture. The over bag can be composed of a Mylar®-type material (i.e. a layer of polyester or polyethylene terephthalate (PET) film) that has a very low moisture transmission rate.

BRIEF DESCRIPTION OF THE FIGURES

[017] The preferred embodiments of the package system of the present invention, as well as other objects, features and advantages of this invention, will be apparent from the accompanying drawings wherein:

[018] FIG. 1 is a side view of a first embodiment of the package system of the present invention.

[019] FIG. 2 is a side view of the embodiment of the package system in FIG. 1 showing the outer bag and inner bag.

5 [020] FIG. 3 is a side view of the embodiment of the package system in FIG. 1 showing the inner and outer.

[021] FIG. 4 is a side view of the embodiment of the package system in FIG. 1 showing the outer bag with a transparent panel and window for viewing the contents.

10 [022] FIG. 5 is a perspective view of the pressure equalizing port and filter system of the package system shown in FIG 1.

[023] FIG. 6 is a perspective view of the cap and locking ring for the pressure equalizing port shown in FIG 5.

[024] FIG. 7 is a top view of the locking ring for the pressure equalizing port shown in FIG. 5.

15 [025] FIG. 8 is a side view of the embodiment of the package system in FIG. 1 showing the handle.

[026] FIG. 9 is a side view of a second embodiment of the package system having two compartments separated by a gas permeable layer attached to the discharge port.

[027] FIG. 10 is a front view of the package system shown in FIG. 9 with the handle
20 removed to show the relationship of the three layers that form the package system.

[028] FIG. 11 is a front view of the package system shown in FIG. 9 enclosed in an over bag.

[029] FIG. 12 is a photograph of the package system after testing in a stability chamber.

[030] FIG. 13 is a photograph of a prior art package system after testing in a stability

5 chamber.

DETAILED DESCRIPTION OF THE INVENTION

[031] The present invention is a package system that reduces the caking of products contained in the package system, preferably salts, due to moisture. The package utilizes a moisture barrier film that prevents the migration of outside moisture through the walls of the package and into the inside of the package. Caking is prevented by removing excess water covering all particles even when they are packed in a bulk package. The package system removes excess moisture in the crystals. In one embodiment, the package system includes a gas, vapor, and/or moisture permeable inner bag that contains the product and a moisture and/or gas impermeable outer bag that encloses the inner bag and creates an intermediate space between the inner bag and the outer bag. The key to preventing caking of the product due to moisture is keeping the inner bag at the correct moisture and gas level and capturing any free moisture or gas that may be released by the product (e.g., salts) as a result of temperature changes in the environment. Moisture is uniformly removed from the product by forming the inner bag using a gas permeable material that transmits moisture (i.e., water vapor) through the wall of the bag to the intermediate space. The intermediate space contains materials that absorbs moisture, oxygen and/or selected gasses (e.g., HCl). The space can also be filled with an inert gas.

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[032] As used herein, the term “outer bag” refers to the enclosed structure formed by the impermeable, exterior walls of the package system. The term is used interchangeably with the term “first compartment.”

[033] As used herein, the term “inner bag” refers to the enclosed structure inside the outer bag of the package system that has at least one wall formed by a permeable material and receives the desiccant. The term is used interchangeably with the term “second compartment.”

[034] As used herein, the term “layer” refers to one or more layers of polymeric material that are formed into a single layer structure. The layers can be formed from the same polymer or different polymers. With regard to the permeable layer, the layer or layers can be formed from a polymer or from a woven cloth or synthetic material.

[035] As used herein, the term “impermeable” refers to a material through which substances, such as liquids or gases, cannot pass or can only pass in very small amounts.

[036] As used herein, the term “permeable” refers to a material through which substances, such as liquids or gases, can pass freely but substantially prevents the passage of solid materials.

[037] As used herein, the term “desiccant” refers to a hygroscopic substance that induces or sustains a state of dryness (desiccation) in its vicinity. The desiccants are preferably pre-packaged solids that adsorb water. In preferred embodiments, the desiccant material is clay, molecular sieves, or silica.

[038] As used herein, the term “unit” refers to a quantity of desiccant, which will absorb a set percentage of its weight at certain levels of humidity. For this disclosure, one “unit” is approximately equal to one ounce.

[039] As used herein, the term “fused” or “fusion” refers to a method of sealing two or more layers of polymeric materials together by applying heat at a temperature above the highest melting point of the two or more polymeric materials. Ultrasonic welding is one method of fusion. When the two or more layers of polymeric materials cool, they are sealed together in the areas where the heat was applied.

[040] The package system must also protect the product and maintain the integrity of the product, e.g., keeping the product sterile, dry, and clump free. Additionally, some materials are sensitive to oxygen and need to be maintained in an inert oxygen free environment. Another feature of the package system is that the product can be dispensed directly into the reactor system without contacting the outside environment and affecting the integrity of the product. This is preferably accomplished using a discharge port on one end of the package system, preferably about 4-inches in diameter, and a pressure equalizing port located at the other end of the package system. The pressure equalizing port allows filtered air or an inert gas to enter the package system as the product is removed to prevent a vacuum from forming and to ensure continuous flow of the product.

[041] In a preferred embodiment, the package system has an inner bag surrounded by an outer bag. The inner bag has a first end that is connected to a discharge port and an inner wall formed from a gas permeable material that extends from the discharge port to a sealed second end. The first end of the outer bag is joined to the first end of the inner bag around

the discharge port and a surrounding outer wall extends co-extensively with the inner wall to form an intermediate space around the inner bag. A desiccant or other moisture absorbing material (gas or oxygen absorbing materials may also be added) is placed in the intermediate space and then the second end of the outer bag is sealed over the second end of the inner
5 bag. The second end of the package system (i.e., the second ends of the inner and outer bags) can be attached to a handle that can be used for transporting, hanging or securing the package system and its contents during use or storage.

[042] A pressure equalizing port can be located near the second end of the package system to provide a passage between the interior of the inner bag and the outside environment. The
10 pressure equalizing port can be connected to an inert gas source, such as nitrogen, at a low pressure to maintain an “inert gas blanket” between the contents of the inner bag and the outside environment. Alternatively, the pressure equalizing port can be connected to a filter system that allows the interior of the inner bag to “breathe” the air from the outside environment. The filter system can be formed by a cylindrical tube and can contain one or
15 more filters that filter out moisture, oxygen and/or other gasses that could potentially contaminate the product in the package system. Preferably, the filter material includes at least one desiccant or gas scavenging material. The end of the filter opposite the pressure equalizing port can be sealed with a locking cap, which is used when the package system is being shipped or stored. When the contents of the package system are being removed
20 through the discharge port, the cap on the filter system is removed so that outside air can enter the filter system and pass through the pressure equalizing port to facilitate the delivery of the package system contents.

[043] The package system includes an inner bag formed from a moisture permeable, porous material layer, such as a cloth or Tyvek®, and an outer bag formed from a non-porous layer, e.g., any one of several different polyethylenes. The porous material layer allows water vapor to pass in order to prevent moisture build-up in the inner bag that contains the product.

5 The cloth is typically produced by weaving or knitting textile fibers, such as wool, cotton or a similar fiber or threads made from polymeric materials. Tyvek® is the preferred material for the porous layer and it is manufactured by E. I. Du Pont De Nemours and Company, Wilmington Delaware. Tyvek® is formed using continuous and very fine fibers of high-density polyethylene, preferably 100 percent high-density polyethylene, that are randomly
10 distributed and non-directional. These fibers are first flash spun, then laid as a web on a moving bed before being bonded together by heat and pressure - without the use of binders, sizings or fillers. By varying both the lay-down speed and the bonding conditions, the flashspun layer can be engineered to form either soft-structure or hard-structure Tyvek®.

[044] A portion of the inner bag wall can be transparent so that the contents of the inner
15 bag can be viewed through the wall of the transparent or semi-transparent outer bag. The transparent portion of the inner bag wall does not have to be gas permeable and can be formed by a panel or by a window. Such windows or panels are commonly used in the packaging industry so that the contents can be viewed and one of ordinary skill in the art would be familiar with the methods used to form such transparent portions.

20 [045] The package system has an outer bag with an outer bag structure, also referred to herein as the exterior film structure. In particular, the present invention relates to exterior films structures made of copolymers of polyethylene; although polypropylene films can also be used. For the purposes of this disclosure, the terms “polyethylene film” or “polyethylene

layer” are intended to include any one of the types of polyethylene that are disclosed below, as well as multi-layer films that contain two or more types of polyethylene, e.g., a layer of high density polyethylene and a layer of low density polyethylene.

- [046] Polyethylene is the name for a polymer whose basic structure is characterized by the chain $-\text{CH}_2\text{CH}_2)_n$. Polyethylene homopolymer is generally described as being a solid, which has a partially amorphous phase and partially crystalline phase with a density of between 0.915 to 0.970 g/cm³. The relative crystallinity of polyethylene is known to affect its physical properties. The amorphous phase imparts flexibility and high impact strength while the crystalline phase imparts a high softening temperature and rigidity.
- [047] Unsubstituted polyethylene is generally referred to as high density homopolymer and has a crystallinity of 70 to 90 percent with a density between about 0.96 to 0.97 g/cm³. Most commercially utilized polyethylenes are not unsubstituted homopolymer but instead have C₂-C₈ alkyl groups attached to the basic chain. These substituted polyethylenes are also known as branched chain polyethylenes. Also, commercially available polyethylenes frequently include other substituent groups produced by copolymerization. Branching with alkyl groups generally reduces crystallinity, density and melting point. The density of polyethylene is recognized as being closely connected to the crystallinity. The physical properties of commercially available polyethylenes are also affected by average molecular weight and molecular weight distribution, branching length and type of substituents.
- [048] People skilled in the art generally refer to several broad categories of polymers and copolymers as “polyethylene.” Placement of a particular polymer into one of these categories of “polyethylene” is frequently based upon the density of the “polyethylene” and

often by additional reference to the process by which it was made since the process often determines the degree of branching, crystallinity and density. In general, the nomenclature used is nonspecific to a compound but refers instead to a range of compositions. This range often includes both homopolymers and copolymers.

5 [049] For example, “high density” polyethylene (HDPE) is ordinarily used in the art to refer to both (a) homopolymers of densities between about 0.960 to 0.970 g/cm³ and (b) copolymers of ethylene and an alpha-olefin (usually 1-butene or 1-hexene), which have densities between 0.940 and 0.958 g/cm³. HDPE includes polymers made with Ziegler or Phillips type catalysts and is also said to include high molecular weight “polyethylenes.” In
10 contrast to HDPE, whose polymer chain has some branching, are “ultra high molecular weight polyethylenes” which are essentially unbranched specialty polymers having a much higher molecular weight than the high molecular weight HDPE.

[050] Hereinafter, the term “polyethylene” will be used (unless indicated otherwise) to refer to ethylene homopolymers as well as copolymers of ethylene with alpha-olefins and the
15 term will be used without regard to the presence or absence of substituent branch groups.

[051] Another broad grouping of polyethylene is “high pressure, low density polyethylene” (LDPE). The polyethylene industry began in the 1930s as a result of the discovery of a commercial process for producing LDPE by Imperial Chemical Industries, Ltd. researchers. LDPE is used to denominate branched homopolymers having densities between 0.915 and
20 0.930 g/cm³ as well as copolymers containing polar groups resulting from copolymerization, e.g. with vinyl acetate or ethyl acrylate. LDPEs typically contain long branches off the main chain (often termed “backbone”) with alkyl substituents of 2 to 8 carbon atoms.

[052] In the 1970s, a new grouping of polyethylene was commercialized--Linear Low Density Polyethylene (LLDPE). Only copolymers of ethylene with alpha-olefins are in this group, LLDPEs are presently recognized by those skilled in the art as having densities from 0.915 to .940 g/cm³. The alpha-olefin utilized is usually 1-butene, 1-hexene, or 1-octene and
5 Ziegler-type catalysts are usually employed (although Phillips catalysts are also used to produce LLDPE having densities at the higher end of the range).

[053] In the 1980s, yet another grouping of polyethylene came into prominence--Very Low Density Polyethylene (VLDPE), which is also called "Ultra Low Density Polyethylene" (ULDPE). This grouping like LLDPEs comprise only copolymers of ethylene with alpha-
10 olefins, usually 1-butene, 1-hexene or 1-octene and are recognized by those skilled in the art as having a high degree of linearity of structure with short branching rather than the long side branches characteristic of LDPE. However, VLDPEs have lower densities than LLDPEs. The densities of VLDPEs are recognized by those skilled in the art to range between 0.860 and 0.915 g/cm³.

15 [054] Various types of polyethylene resins have long been used to produce films having different properties. These polyethylenes have been used alone, in blends and with copolymers in both monolayer and multi-layer films for packaging applications for such food products. In the food industry, greater use of centralized processing of foods in conjunction with increased handling and long distance transportation have increased the
20 demand for packaging films having superior properties.

[055] In the packaging industry, films are known to use coextruded, extrusion coated or laminated films which utilize such compositions as LLDPE, nylon, polyester, copolymer of vinylidene chloride (PVDC), ethylene-vinyl acetate copolymer (EVA) and ionomers.

[056] It is generally known that selection of films for packaging pharmaceutical products includes consideration of one or more criteria such as puncture resistance, cost, sealability, stiffness, strength, printability, durability, barrier properties, machinability, optical properties such as haze and gloss, flex-crack resistance and government approval for contact with pharmaceutical products. The type of polyethylene selected for use in the present invention and the thickness of the film (or layer for a multi-layer film) will depend on these considerations, as well as the size of the inner and outer bags and the estimated weight of the product.

[057] The outer bag is made from a plastic film that can be transparent or semi-transparent and can have one or more layers formed by well-known extrusion, co-extrusion and/or lamination processes. Preferably, at least one of the film layers is a structural layer and includes polyethylene, most preferably high or low density polyethylene. The structural layer(s) are intended to provide strength and impact resistance, to support the articles in the inner bag and to prevent the outer bag from rupturing. When the film includes multiple layers, it can have a gas barrier layer that prevents oxygen from passing through the film. The preferred construction for a multiple layer film includes a gas barrier layer disposed between two structural layers of polyethylene. The gas barrier layer can be made from ethylene/vinyl alcohol copolymer (EVOH) and polychlorotrifluoroethene (PCTFE or PTFCE). Other materials used in gas barrier layers of films for the food industry can also be used and are well known to one skilled in the art.

[058] The multi-layer films can also have one or more ethylene polymer-based adhesive layers disposed between the gas barrier layer and the outer structural layers. In addition, the outer bag structure can have an outer heat seal layer that includes an ethylene copolymer, such as ethylene vinyl acetate copolymer, for bonding the opposite sides of the outer bag together and for bonding the inner bag to the outer bag.

[059] The inner and outer bags are bonded together along the edges on at least three sides by a fusion bond. The fusion bond can be formed by ultrasonic welding of the layers to another at their registered edges, using a Branson ultrasonic welder (Branson Products, Inc., Danbury, Conn.) or other suitable ultrasonic welding tool. The bonded layers of the inner bag and the outer bag are joined at their edges on three sides to define an enclosed interior volume inside the inner bag for containment of a product article therein, e.g., a pharmaceutical and an intermediate space between the inner bag and the outer bag and an open side. The intermediate space can contain a desiccant for the absorption of moisture or other materials for absorbing oxygen, carbon dioxide or other gases that may be discharged by the product contained in the inner bag.

[060] After the inner and outer bags are formed with the first ends connected to the discharge port and the inner and outer bags defining an intermediate space, a desiccant or oxygen scavenging agent, such as sodium sulfite (Na_2SO_3), can be placed in the intermediate space. The inner and outer bags are then sealed on the second ends to isolate the intermediate space from the outside environment. However, the gas permeable wall of the inner bag allows gasses and water vapor to pass from the interior of the inner bag to the intermediate space. Thus, the intermediate space is isolated from gasses in the outside environment but is accessible to any gasses that may form in the interior of the inner bag.

[061] The package system is now described with reference to the accompanying drawings, FIGs. 1-8, to further describe the features. FIG. 1 shows the package system 10 that includes: an inner bag 12, an outer bag 14 with a compartment or intermediate space 13 therebetween, a discharge port 16 with cap 18 and locking ring 20 and a handle 22. A
5 desiccant 24 is disposed in the intermediate space 13 between the inner and outer bags 12, 14. Also shown is a pressure equalizing port 26 connected to a filter system 28 with a cap 30 and locking ring 32.

[0621] FIG. 2 shows a side view of the package system 10 in which the bottom of the inner bag 12 is attached to the interior surface of the outer bag 14 intermediate the first and second
10 ends of the outer bag 14. Preferably the point where the bottom of the inner bag 12 attaches to the interior surface of the outer bag 14 is at least 4 inches from the discharge port 16, more preferably 5 inches and most preferably 6 or more inches. FIG. 3 shows the inner bag 12 with the bottom end attached to the interior of the outer bag 14 and the other end open. In between the inner and outer bags 12, 14 is the intermediate space 13 that receives
15 the desiccant 24 (FIG. 1) and any gas scavenging materials. FIG. 4 is similar to FIG. 3 and it shows an embodiment in which the inner bag 12 formed by a section 12a of gas permeable material, a panel 12b and a window 12c. Typically, the gas permeable material that forms the inner bag 12 is non-transparent and prevents the contents from being viewed through the transparent outer bag 14. The panel 12b and the window 12c are transparent and can be
20 formed from materials that are not gas permeable. The methods for forming transparent openings in otherwise non-transparent plastic bags are well known to those skilled in the art.

[063] FIG. 5 shows the pressure equalizing port 26 and filter system 28. The filter system 28 can include one or more desiccants and or gas scavenging filter materials 34, 36,

38 that filter moisture and undesired gases to prevent them from entering the interior of the inner bag 12. The cap 30 and locking ring 32 as shown in FIGs. 6 and 7 are secured to the filter system 28 when the package system 10 is transported or stored. FIG. 8 shows the handle that is attached to the package system 10 opposite the discharge port 16 (FIG. 1).

5 [064] FIGs. 9 and 10 show a second embodiment of the package system 110 that includes: a first outer plastic layer 112 and a second outer plastic layer 114 disposed on either side of a gas and moisture permeable layer 115 to form a first compartment 111 and a second compartment 115. A handle 122 is attached to the first end and a discharge port 116 is located near the second end. One or more desiccant packets 124 are disposed in the second
10 compartment 113 between the gas permeable layer 115 and the second plastic layer 114. Also shown is a pressure equalizing port 126 connected to a filter system 128. The gas permeable layer 115 separates the desiccant 124 from the product 125 in the package system 110 but allows moisture and gasses to pass through.

[065] FIG. 11 shows an embodiment similar to the second embodiment shown in FIGs. 9
15 and 10 wherein the bag system 110 includes an over bag 150. The outer bag 112 is placed inside the over bag 150 for additional protection from gas and/or moisture contaminating the contents of the outer bag 112 and for physical protection from damage that may occur during transportation. The over bag 150 can be made from Mylar® or a polymer material such as LDPE or HDPE. A seal 152 at the top of the over bag 150 isolates the contents from the
20 exterior environment.

EXAMPLES

Example 1

[066] A model test bag was produced by heat sealing a multi-layer bag, which included an interior layer made of Tyvek® that provides a vapor transmission wall disposed between two outer layers made of substantially gas and moisture impermeable HDPE. The top edges of the three layers were aligned in registration and the interior Tyvek® layer extended to a point intermediate the first and second ends of the two outer layers. The bottom and two side perimetrical edges of the outer layers of HDPE were sealed together to form a first compartment and the perimetrical edges on the bottom and two sides of the Tyvek ® layer were sealed to the first outer HDPE layer to form a second compartment. One kg of the test salt was placed in the first compartment from the top end of the bag on one side of the Tyvek® layer and the desiccant material was placed on the other side (five 1/6 clay type desiccants from Desicare) of the Tyvek® layer in the second compartment. The perimetrical edges of the three layers on top side of the bag were sealed to close the system and isolate the product on one side of the Tyvek® wall from the desiccant on the other side so that the test salt was in contact with the vapor transmission wall. Model salts such as sodium acetate trihydrate, sodium chloride, potassium nitrate, dextrose and mannitol were placed in individual bags. The bags were monitored and after 90 days it was determined that the package system prevents the test salts from caking.

Example 2

[067] A lab study was carried out to demonstrate the ability of the package system to maintain materials in the free-flowing state. In addition, tests were performed to compare the package system to a prior art single use bag. The new package system bag was filled

with 11.3 kg of free-flowing sodium chloride and the end cap, clamp and clip were placed on the bag. Another standard single use bag without the compartment for the desiccant (i.e., the Flowmor™ technology) was filled with same amount of free-flowing sodium chloride and sealed in the same manner. Both bags were placed side by side in a stability chamber at
5 40°C and 75% RH. Both bags were tested after 32 days; the sodium chloride in the package system (see the photograph in FIG. 12) was free flowing and cake free. The material in the prior art bag (see the photograph in FIG. 13) was caked and not free-flowing.

Example 3

[068] Studies were carried out under high moisture conditions (40°C, 90% RH) on the
10 bags, to study moisture infusion rates into the wall of the bag. A bag was placed in the stability chamber with a weighed eight units of desiccant (approximately 8 ounces); the cap and clip were placed on the bag and sealed. The desiccant, after 96 hours, gained 6.5 grams of water, which showed that the desiccant would be used up in 30 days at this water vapor transmission rate. The bag was then placed in a Mylar® bag (or any suitable bag with low
15 moisture vapor transmission rate) and heat sealed. The vapor transmission rate was significantly increased and the test results showed an expected shelf life of over 400 days.

Example 4

[069] The purpose of this study was to test the ability of the bags to deliver a cohesive powder that has poor flow characteristics in small quantities. The first test material was L-
20 Glutamine; 240.0 g of the material was added to the bag. The bag was sealed with an end cap, clamp, and clip. The powder was then delivered to a weighted container. The amount delivered was 238.0 g, giving a 99% recovery of the material. The study was repeated with a large quantity of material 9.1 kg of sodium chloride, recovered 9.1 kg near 100% recovery.

[070] Thus, while there have been described the preferred embodiments of the present invention, those skilled in the art will realize that other embodiments can be made without departing from the spirit of the invention, and it is intended to include all such further modifications and changes as come within the true scope of the claims set forth herein.

Claims :

1. A package system for maintaining the physicochemical integrity of the contents of the package system, the package system having a first end and a second end and comprising:
 - an outer bag having a first compartment and formed from a gas and/or moisture impermeable polymer material and having an interior, a side wall, a first end and a second end;
 - a discharge port having an exterior wall that defines an interior passage, wherein the interior passage provides access to the interior of the outer bag;
 - a removable cap for closing the discharge port and sealingly isolating the interior of the outer bag from the exterior environment;
 - an inner bag formed from a layer of a gas and/or moisture permeable material and having a first end, a second end and opposing side edges, wherein the side edges are sealingly attached to the side wall on the interior of the outer bag from the second end of the outer bag, and wherein the first end of the inner bag is attached to the interior of the outer bag at a point intermediate the first and second ends of the outer bag or to the exterior wall of the discharge port to form a second compartment; and
 - at least one desiccant or gas scavenging material,wherein the first end of the outer bag is sealingly attached around the exterior wall of the discharge port, wherein the at least one desiccant or gas scavenging material is disposed in the inner bag and the second end of the inner bag is sealed closed, and wherein the second end of the outer bag is sealed closed to isolate the interior from an environment exterior to the package system.
2. The package system according to claim 1 further comprising a pressure equalizing port located near the second end of the package system having a passage extending between the interior of the outer bag and the environment exterior to the package system.

3. The package system according to claim 2, wherein the passage of the pressure equalizing port contains one or more filter materials that comprise at least one desiccant or gas scavenging material.
4. The package system according to claim 1 further comprising a handle attached to the second end of the package system.
5. The package system according to claim 1, wherein the layer of gas and/or moisture permeable material is formed from continuous and very fine fibers of randomly distributed and non-directional high-density polyethylene.
6. The package system according to claim 1, wherein the gas and/or moisture impermeable material of the outer bag comprises a low density or a high density polyethylene.
7. The package system according to claim 6, wherein the gas impermeable material comprises at least three layers with a middle layer formed from a gas barrier material.
8. The package system according to claim 7, wherein the gas barrier material of the middle layer is an ethylene/vinyl alcohol copolymer or polychlorotrifluoroethene.
9. The package system according to claim 1, wherein the side edges of the inner fused to the side wall on the interior of the outer bag.

10. The package system according to claim 1 further comprising an over bag having an outer wall comprising a gas and/or moisture impermeable material, an open first end, a sealed second end and an interior, wherein the outer bag is placed inside the over bag through the first end and the first end of the over bag is sealingly closed.

11. The package system according to claim 10, wherein the over bag comprises two or more layers and one of the two or more layers is a gas and/or moisture barrier layer.

12. The package system according to claim 1, wherein the inner bag has a perimetrical edge extending along the first end, the second end and two or more sides that are contiguous to the first and second ends, wherein the outer bag has a perimetrical edge extending along the first end, the second end and two or more sides that are contiguous to the first and second ends, wherein the perimetrical edge along at least one of the first or second ends or one of the contiguous sides of the inner bag is fused to the perimetrical edge along at least one of the first or second ends or one of the contiguous sides of the outer bag.

13. The package system according to claim 1, wherein the desiccant clay, molecular sieves or silica, and wherein the ratio of desiccant to package system contents is at least 0.4 units desiccant per kilogram contents.

14. The package system according to claim 1, wherein the inner bag is made from a cloth or a layer formed using continuous and very fine fibers of high-density polyethylene that are randomly distributed and non-directional.

15. The package system according to claim 1, wherein the packed material includes inorganic salts, organic compounds, amino acids and buffer materials.

16. A package system for maintaining the physicochemical integrity of the contents of the package system, the package system having a first end and a second end and comprising:

an outer bag having an interior and a side wall comprising a layer of gas and/or moisture impermeable polymeric materials in the form of a tube or first and second sheets, wherein the tube has a continuous outer side wall, wherein the first and second sheets have perimetrical edges, wherein the perimetrical edges are in registration and sealingly attached and wherein the outer bag has first and second ends and interior and exterior surfaces;

a discharge port having an exterior surface, wherein the discharge port is located near the second end of the package system and has an interior passage, wherein the interior passage provides access to the interior of the outer bag;

a removable cap for closing the discharge port and sealingly isolating the interior of the outer bag from the exterior environment;

an inner bag comprising a gas and/or moisture permeable layer disposed in the outer bag, wherein the permeable layer has first and second ends, first and second sides, a perimetrical edge and inner and outer surfaces, wherein the first end of the permeable layer is aligned with the first end of the outer bag, wherein the sides edges of the permeable layer are sealingly attached to the interior surface of the outer bag, and wherein the second end of the permeable layer is sealingly attached to the exterior wall of the discharge port or the interior surface of the outer bag intermediate the first and second ends to form a compartment;

a pressure equalizing port located near the first end of the package system and connected to a filter system having a passage extending between the interior of the outer bag and an environment exterior to the package system; and

at least one desiccant or gas scavenging material disposed in the compartment, wherein the second end of the outer bag is sealingly attached around the exterior surface of the discharge port, and wherein the desiccant or gas scavenging material is separated from the first compartment by the gas and/or moisture permeable layer and the interior of the outer bag and the compartment are isolated from the environment exterior to the package system.

17. The package system according to claim 16, wherein the side wall comprises multiple layers of polymeric material.
18. The package system according to claim 17, wherein at least one layer of the multiple layers is a moisture barrier layer.
19. The package system according to claim 16, wherein the side wall comprises a low density or a high density polyethylene and the gas and/or moisture permeable layer is formed from continuous and very fine fibers of randomly distributed and non-directional high-density polyethylene or cloth.