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(54) **PACKAGE OF SENSITIVE ARTICLES**

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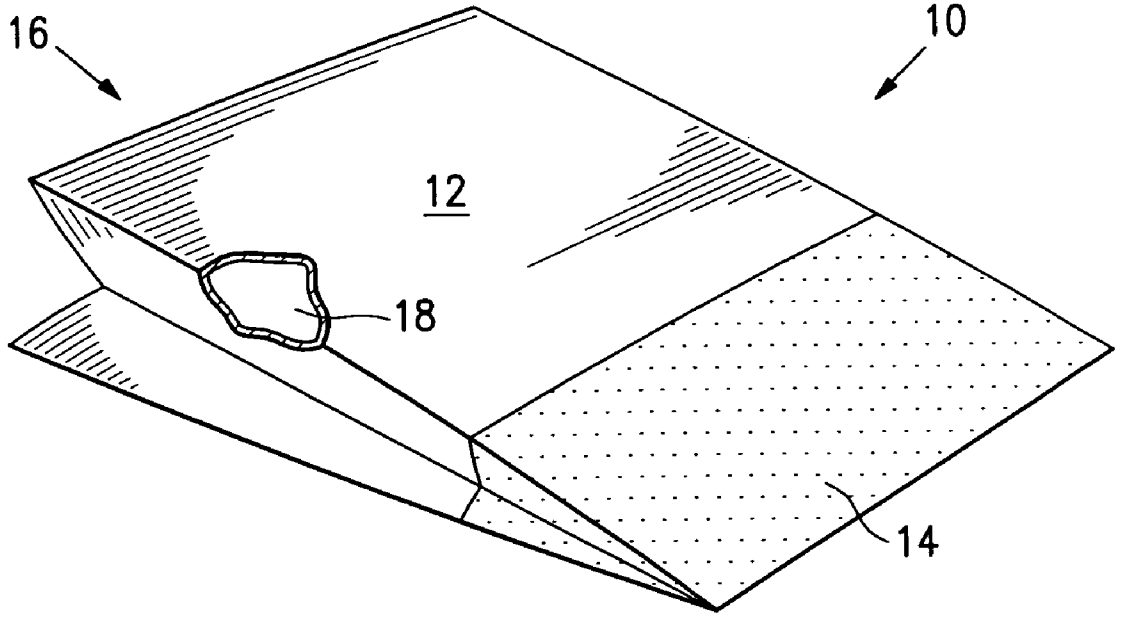
(52) **U.S. Cl.** **53/425**; 422/28; 422/34; 422/37; 206/439

(57) **ABSTRACT**

The invention is directed to the treating, e.g. sterilizing and packaging of medical devices and other articles, particularly such devices and articles which are reactive to oxygen or moisture containing atmospheres. The sterilized package has a container which includes at least one portion which is gas permeable and at least one portion which is gas impermeable and an interior in fluid communication with the gas permeable portion. The container may be sealed by applying an impermeable patch to the permeable portion thereof or by disposing the container in an enclosure formed of impermeable material and sealing the enclosure. After exposing the container to a sterilizing gas, the gas permeable portion may be removed or sealed off from the gas impermeable portion of the container in order to provide a package which is gas impermeable and can protect one or more articles within the interior of the container against environmental gases and moisture.



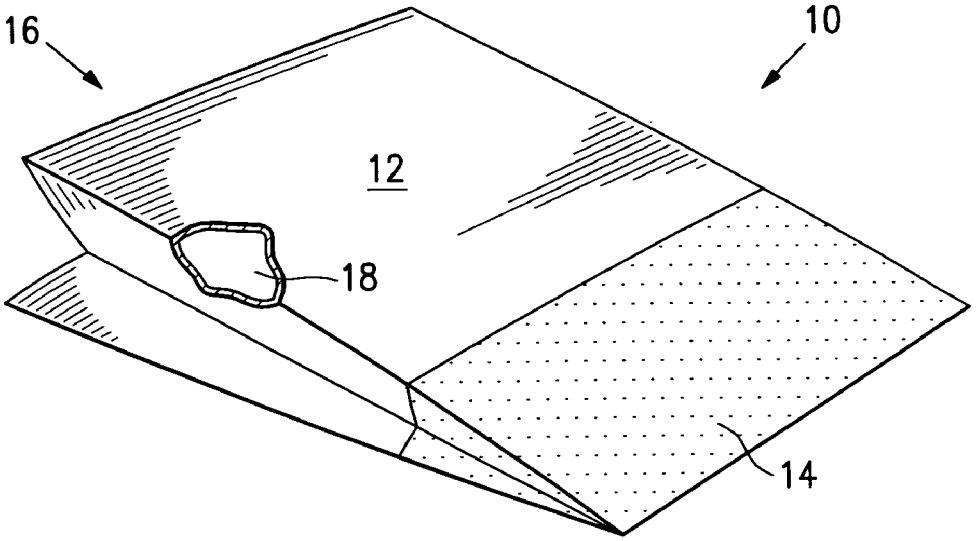


FIG. 1

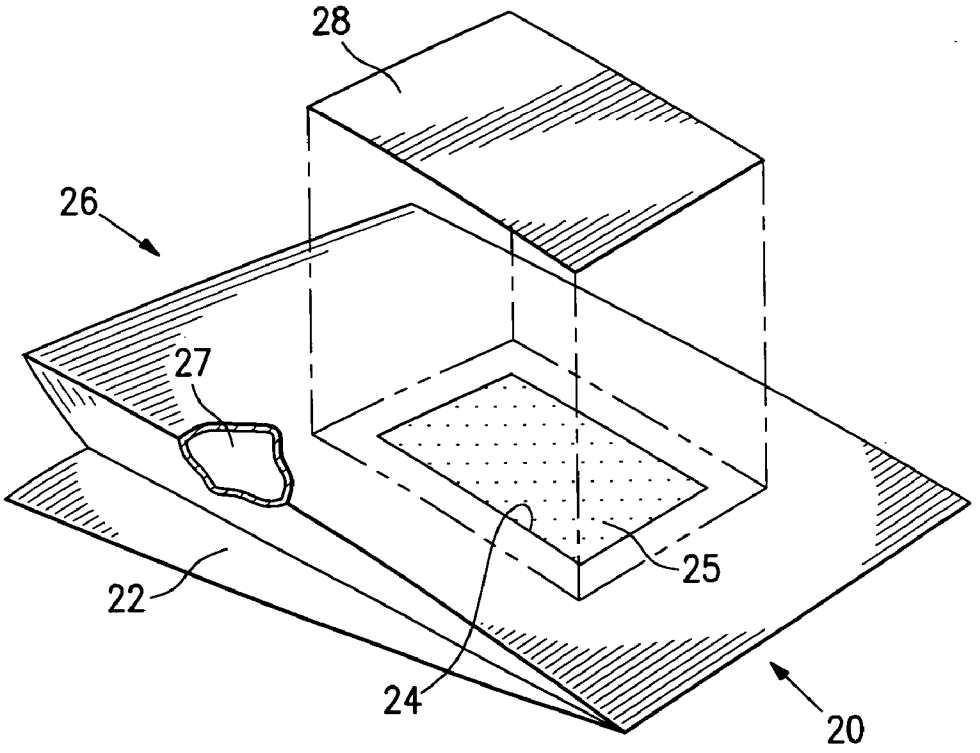


FIG. 2

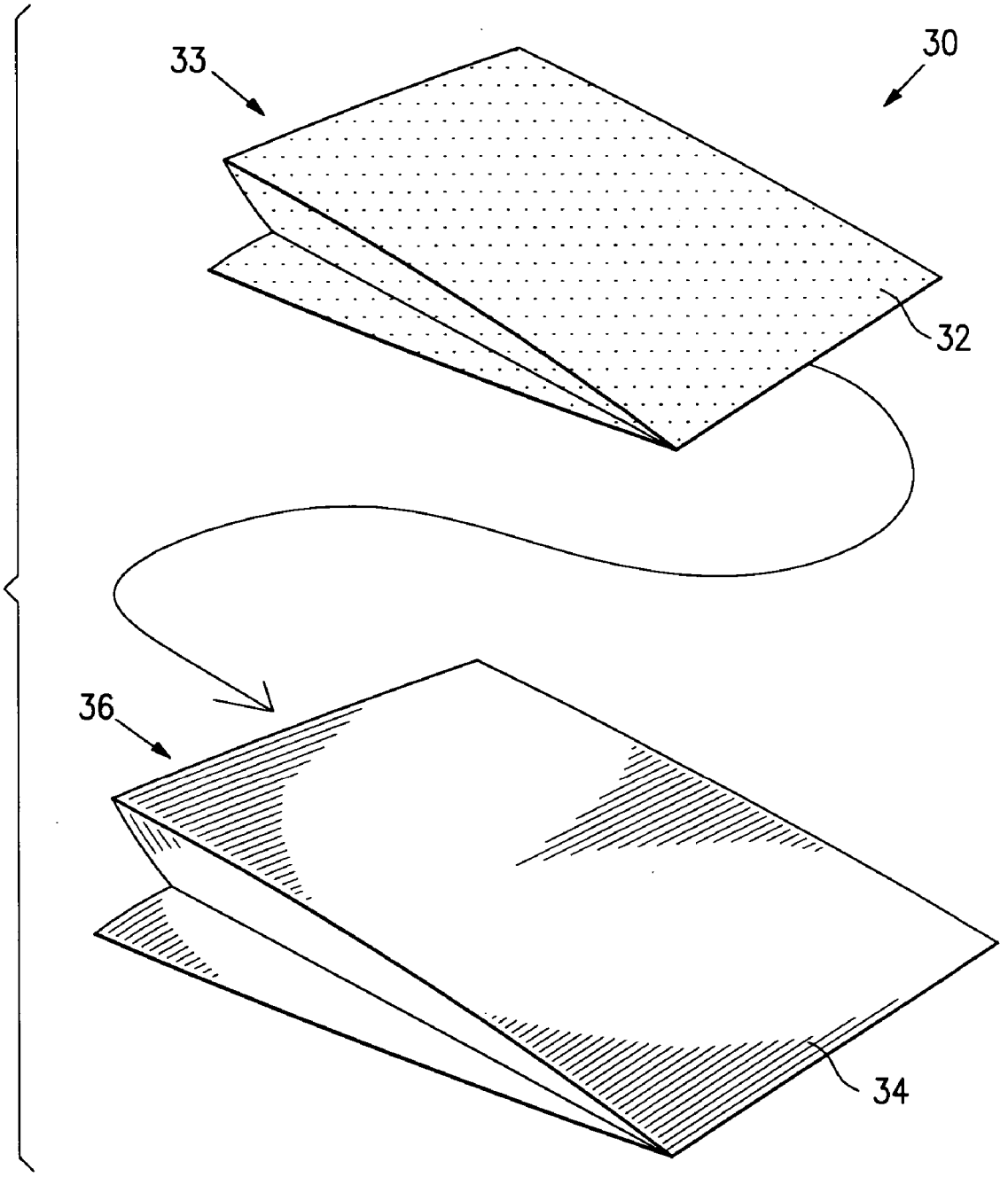


FIG. 3

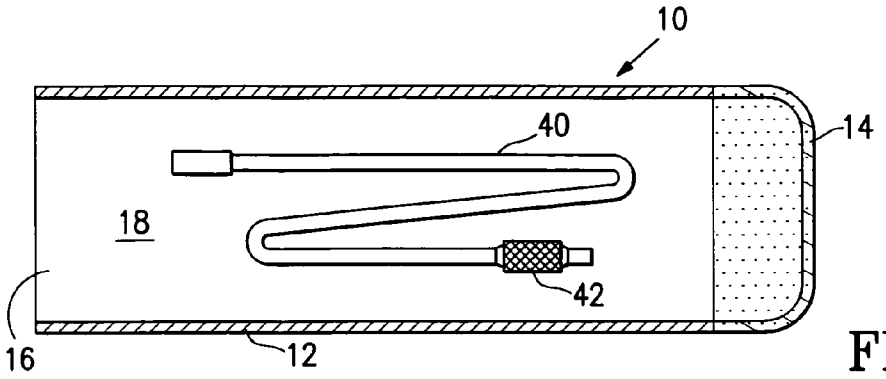


FIG. 4A

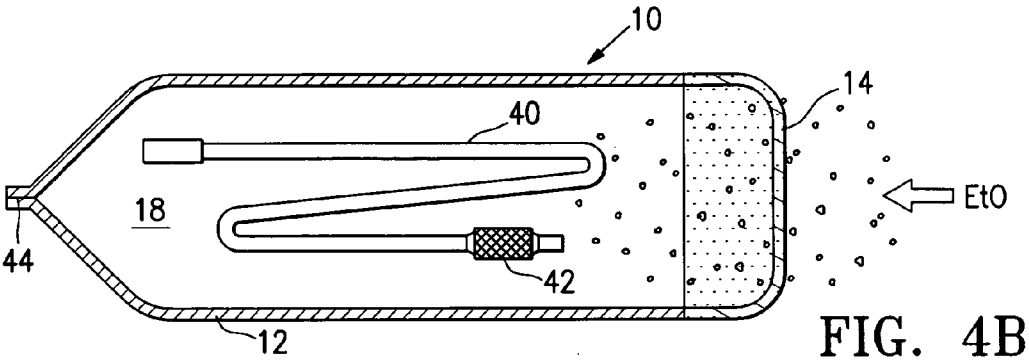


FIG. 4B

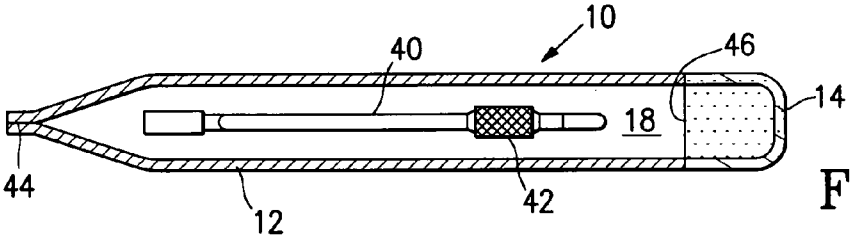


FIG. 4C

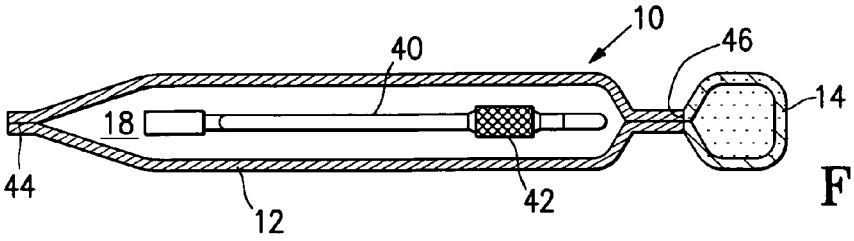


FIG. 4D

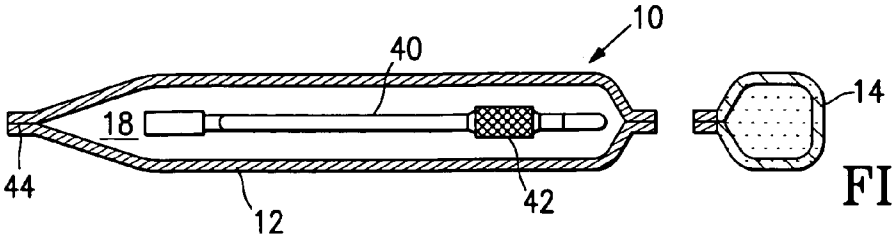


FIG. 4E

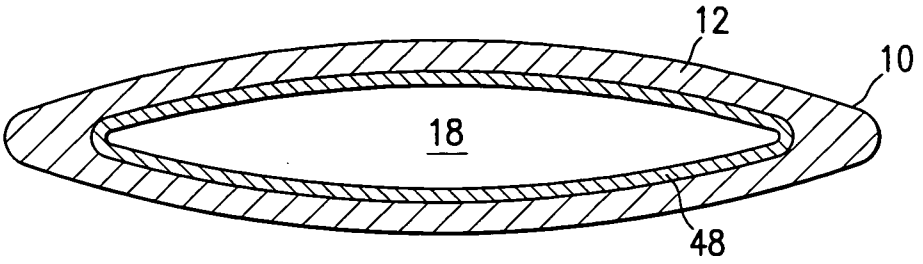


FIG. 5

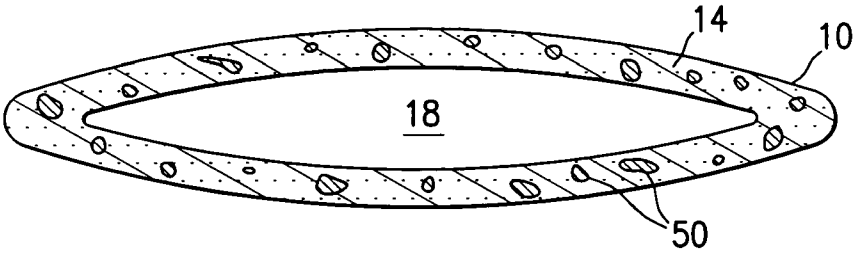


FIG. 6A

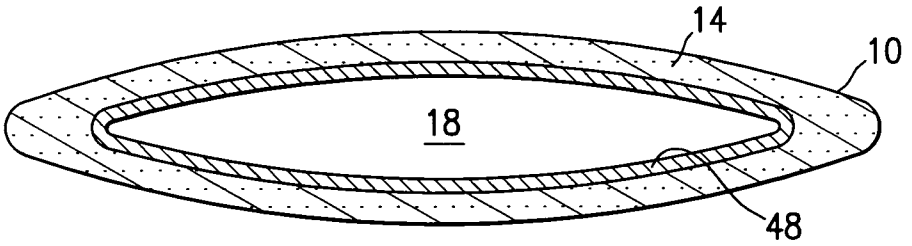


FIG. 6B

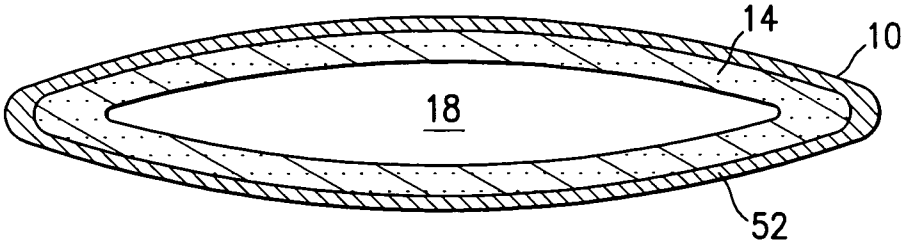


FIG. 6C

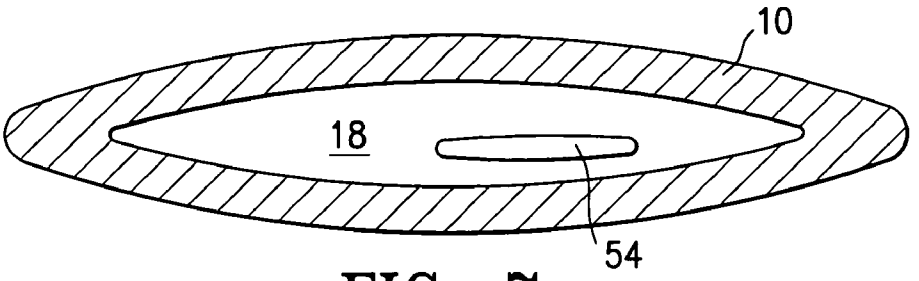


FIG. 7

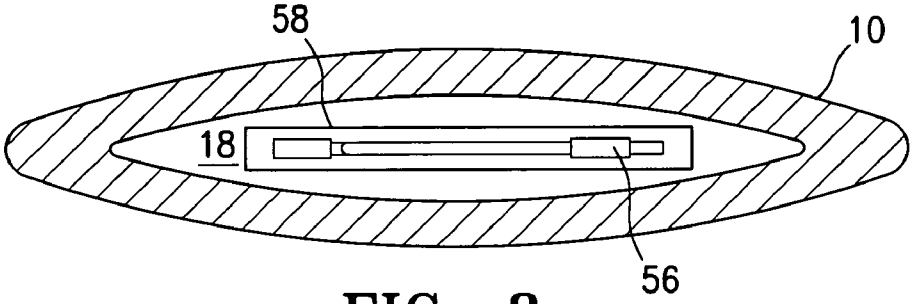


FIG. 8

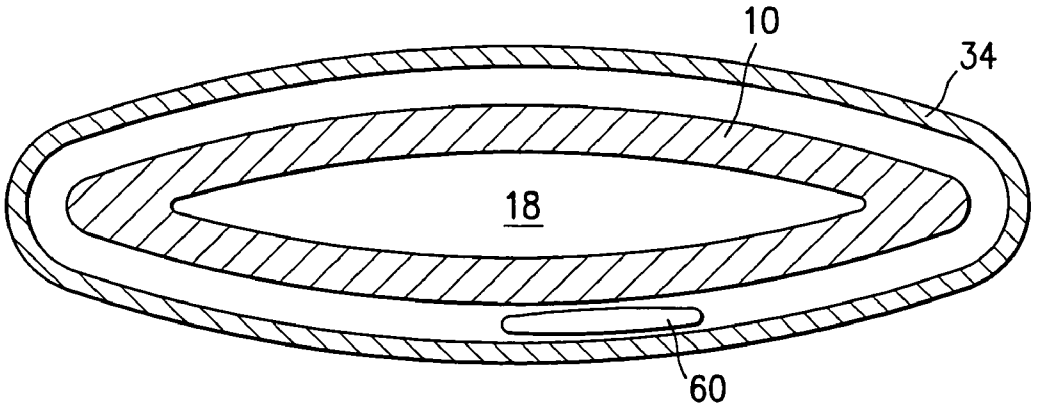


FIG. 9

PACKAGE OF SENSITIVE ARTICLES

RELATED APPLICATIONS

[0001] This application is based upon and claims priority to Provisional Application Ser. No. 60/537,972, filed on Jan. 20, 2004 and Provisional Application Ser. No. 60/540,828, filed on Jan. 29, 2004. Both applications are incorporated herein by reference in their entireties.

BACKGROUND OF THE INVENTION

[0002] The present invention relates generally to sterilized medical devices and packaging for sterilized medical devices. In particular, the present invention relates to the packaging of sterilized environmentally sensitive medical devices, such as drug-coated stents.

[0003] Most, if not all, disposable medical devices require sterilization prior to or concurrent with packaging. The packaging, which may be in the form of a pouch, bag, tube, box, or other sealed container, will maintain the sterility of the product until it is withdrawn from the packaging for use. A particularly successful system and method for sterile packaging of medical devices relies on use of high-density polyethylene (HDPE) pouches which are used to contain the medical device or other product. The device may be placed in the package prior to sterilization. Sterilization is then effected by placing the package in an environment including a sterilant gas, such as ethylene oxide (EtO), ethylene oxide with nitrogen, various blends of ethylene oxide and carbon dioxide, ethylene oxide with chlorofluorocarbon diluent(s), Oxyfume 2000 series of sterilant, ozone, hydrogen peroxide, chlorine dioxide, or others. The spun HDPE material, such as Tyvek® which is available from Medical Packaging Division of E. I. DuPont de Nemours and Company (DuPont), permits passage of the small molecule sterilant gas while remaining a barrier to bacteria, viruses, and other larger substances which might compromise sterility. It also acts as a barrier to water and other fluids which might detrimentally affect the sterilized contents.

[0004] While this packaging system has been highly successful for conventional medical devices, such as catheters, stents, surgical instruments, probes, and the like, it is frequently not suitable for "hybrid" devices which contain coatings or components which are subject to oxygen degradation. For example, the use of drug-eluting stents is promising to revolutionize interventional cardiology. The stents are coated with drug at a central fabrication facility and must be distributed to the end user in sterile packaging. While at least some drugs presently contemplated for use will remain stable during ethylene oxide sterilization, exposure to oxygen during lengthy distribution and storage periods can adversely affect the drug.

[0005] For these reasons, it would be desirable to provide improved methods and systems for sterilizing and packaging medical devices.

SUMMARY OF THE INVENTION

[0006] The present invention is directed to packages of articles such as medical devices, methods of packaging such articles and is particularly directed to packaging articles which are labile when exposed to ambient oxygen concentrations or oxygen containing materials over prolonged periods of time. The present invention provides convenient, effective, and economical approaches for such packaging. The method of packaging, the packages and the packaging systems are particularly suitable for drug-device combinations, such as drug-eluting stents and other drug-coated medical articles. The packaging, the system and method may be utilized for sterilizing articles such as medical devices which are reactive to an ambient environment.

[0007] The sterilized packaging embodying features of the invention generally includes a container which has a wall defining at least part of an interior configured to receive one or more articles or products for sterilization. The container has a portion, such as part of a wall forming the container, which is permeable to sterilizing gas, e.g. EtO, ethylene oxide with nitrogen, various blends of ethylene oxide and carbon dioxide, ethylene oxide with chlorofluorocarbon diluent(s), Oxyfume 2000 series of sterilant (from Honeywell Chemicals, Morristown, N.J.), ozone, hydrogen peroxide, chlorine dioxide, or others. The permeable portion allows the article or articles to be placed in the interior, the container sealed, a vacuum applied to the container interior and an environment of sterilizing gas in contact with the permeable portion of the container under conditions which drives the sterilizing gas through the gas permeable portion into the inner chamber to sterilize the one or more products disposed within the chamber.

[0008] The container interior is evacuated to about 15 psia to about 0.1 psia preferably 7 psia to about 0.5 psia for the purpose of aspirating the sterilizing gas through the permeable portion of the container. During this time, the container interior can be partially or totally evacuated of oxygen and replaced totally or partially with a non-reactive gas such as nitrogen. This is followed by a steam injection slightly increasing the vacuum to about 0.1 psia to about 5 psia higher than the container interior, preferably to about 1 psia to about 3 psia higher than the container interior. Sterilizing gas maintained about the exterior of the permeable portion of the container is drawn into the container interior through the permeable portion thereof. The pressure of the sterilizing gas within the container interior for effective sterilization is about 20 psia to about 2 psia, preferably about 15 psia to about 5 psia. The dwell time of the sterilizing gas within the container interior at that pressure is about 1 to about 24 hours preferably about 6 to about 18 hours.

[0009] After the sterilization, essentially all of the sterilizing gas is removed from the container interior, either by exposing the interior to a vacuum, by flushing or purging the container interior with air or a non reactive gas such as nitrogen, or some combination thereof or both. Usually, after the sterilizing gas is removed from the container interior, the sterilized package is left at room temperature for several days to ensure that the interior is essentially free of sterilizing gas, i.e. less than about 150 ppm, preferably about 10 to about 50 ppm, and typically about 25 ppm.

[0010] At this point, at least the permeable portion of the container is sealed to prevent permeation of undesirable gas into the container interior while the one or more articles remain within the interior. The sealing of the container may comprise, for example, sealing the permeable portion of the container with a impermeable patch or partitioning the container to isolate or seal off the portion of the container interior which contains the article(s) from the portion of the

container interior in fluid communication with the gas permeable portion of the container. Optionally, the gas permeable portion of the container may be separated, e.g. severed, from the non-gas permeable portion. Another approach is to place the sterilized container inside a impermeable enclosure in order to prevent subsequent gas permeation into the container interior containing the sterilized article(s) through the permeable portion of the container. In the latter instance, any atmosphere within the impermeable enclosure would have to be non-detrimental to the articles disposed in the interior of the container within the enclosure. It would of course also be possible to combine two or more of these approaches, although that will usually not be necessary.

[0011] The gas permeable portion of the container will typically be composed of a material which is permeable to the sterilizing gas and impermeable to liquids. Suitable gas permeable materials include high-density polyethylene (HDPE), typically a spun HDPE or other spun olefin. Commercially available materials such as Tyvek® (2FS, 1059B, 1073B or others) are specifically designed for packaging medical devices. Typically, the available materials are coated partially or totally with an adhesive for the purpose of sealing the material to itself or to adjacent materials.

[0012] The permeability required for the sterilizing gas to permeate into the interior of the container and contact the one or more articles therein, can vary depending upon the pressure differential, the temperature and the time available for permeation of the sterilizing gas into the interior.

[0013] In one embodiment, the container has both a gas permeable portion, as described above, and a gas impermeable portion, typically formed from a metal or polymer film or a metal-polymer composite which is impermeable to gases. By "impermeable to gases," it is meant that the permeation of oxygen is below about 30 $cm^3/100\ in^2$/day-atm, preferably below about 2 $cm^3/100\ in^2$/day-atm. Exemplary suitable material for the gas impermeable portion include metal foils such as aluminum; polymer films such as polyethylene, polyester, polyester (PET)/modified low density polyethylene (LDPE) laminated film; or any combination thereof (e.g., metalized PET).

[0014] In one embodiment, the impermeable portions of the container may be incorporated with suitable oxygen scavenger materials or have adjacent thereto a partial or complete film of suitable oxygen absorbers or scavengers, such as ethylene-cyclohexenylmethyl acrylate copolymer (ECHA) and ethylene-methylacrylate-cyclohexeneylmethyl acrylate terpolymer (EMCM) described in Ching et al. (2001), referenced above. Other oxygen scavengers include ethylenically unsaturated polymer, ferrous oxide (partially oxygenated iron), titanium oxide, activated carbon with sodium ascorbate, diethylhydroxylamine (DEHA), carbohydrazide, combination of above, or other chemicals which are readily reactive or combine with oxygen gas. When suitable oxygen scavenger materials are incorporated or lie adjacent to the impermeable portion, oxygen within the interior of the container can be removed to very low levels. Suitable oxygen levels in the container interior in most instances will be below 5% oxygen, preferably below 1%, more preferably below 0.1%.

[0015] The permeable portion or portions of the container may be incorporated with suitable oxygen scavenger materials or may be positioned adjacent to a partial or complete film of suitable oxygen scavengers. Not only oxygen is removed from the package, oxygen gas trying to permeate through the permeable portion will be limited from entering the package.

[0016] Oxygen scavengers can be placed inside the package, such as inside a permeable packet that is placed within the interior of the container or within the interior of an enclosure surrounding the container. Oxygen scavengers can be embedded in a protective sheath over or adjacent to the article within the inner chamber. The sheath can be a polymer incorporated with suitable oxygen scavenger, or it can be formed of a polymer fully or partially coated with a suitable oxygen scavenger, or it can be made from suitable oxygen scavenger.

[0017] Another approach for sealing the gas permeable enclosure is to place a patch, cover, or other gas impermeable barrier over that portion of the enclosure which is initially gas permeable. For example, a window or other area of the enclosure, typically a portion of a pouch, may be formed from gas permeable Tyvek or other material, while the remaining portion of the pouch or other enclosure is formed from a gas impermeable foil, polymer, or other material. A patch sized to cover the gas permeable window may be provided to be sealed over the window after the initial sterilization has been completed.

[0018] Another approach for sealing the gas permeable enclosure is to place the enclosure inside of a separate gas impermeable enclosure after the initial sterilization has been performed.

[0019] Preferred gas impermeable materials will also be non-transmissive for light, UV radiation, heat, and the like. The gas impermeable materials will also be impermeable to moisture.

[0020] In some cases, it will be further desirable to provide desiccant materials in or over a portion of the impermeable enclosure in order to sequester any moisture which may remain within the pouch after final sealing. The desiccant may be coated over or laminated within the polymer or metal film which comprises the gas impermeable enclosure. Alternatively, a small inserter canister of the desiccant material may be provided within the enclosure, similar to the desiccant placed in conventional pharmaceutical packaging.

[0021] These and other advantages of the invention will become more apparent from the following detailed description of the invention when taken in conjunction with the accompanying exemplary drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] **FIG. 1** schematically illustrates a container embodying features of the present invention which includes both gas permeable and gas impermeable portions.

[0023] **FIG. 2** schematically illustrates an alternate design of a container embodying features of the present invention which includes a gas impermeable portions, a gas permeable portion or window and a separate impermeable patch or cover for sealing the window.

[0024] **FIG. 3** schematically illustrates an alternate design of a container having features of the present invention which

includes gas permeable portions and a gas impermeable outer pouch or enclosure to seal the container.

[0025] **FIGS. 4A-4E** schematically illustrate use of the container shown in **FIG. 1** for packaging and sterilizing an article in a manner embodying features of the present invention.

[0026] **FIG. 5** schematically illustrates one embodiment of the container constructed with an impermeable portion having a film adjacent thereto, the film comprising oxygen absorber or scavenger (in pure, composite, or matrix form).

[0027] **FIGS. 6A-6C** schematically illustrate use of one embodiment of a container constructed with a permeable portion incorporated with or has a film adjacent to made from oxygen scavenger material.

[0028] **FIG. 7** schematically illustrates use of one embodiment of a container with an oxygen scavenger packet or material.

[0029] **FIG. 8** schematically illustrates use of one embodiment of a container with a sheath made from oxygen scavenger material.

[0030] **FIG. 9** schematically illustrates use of one embodiment of a container within another enclosure that also contains oxygen scavenger material.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

[0031] Referring now to **FIG. 1**, a container **10** embodying features of the invention has a portion **12** which is not permeable to gas and a portion **14** which is permeable to gas, particularly to sterilizing gas such as EtO, ethylene oxide with nitrogen, various blends of ethylene oxide and carbon dioxide, ethylene oxide with chlorofluorocarbon diluent(s), Oxyfume 2000 series of sterilant, ozone, hydrogen peroxide gas plasma, chlorine dioxide, or others. The container **10** typically has an open end **16** disposed at one end of the impermeable portion, while the permeable portion **14** is formed about another end of the portion **12**. As will be described further with reference to **FIGS. 4A-4E** below, the container **10** is utilized by placing the article to be sterilized into the container interior **18** through the open end **16**, sealing the open end **16**, so that the article is fully contained within the gas permeable but otherwise impermeable structure of the container prior to sterilization.

[0032] An alternative container **20** is depicted in **FIG. 2** which has an impermeable portion **22** having a opening **24** covered by a gas permeable layer or wall **25**. The article to be sterilized and packaged may be placed through open-end **26** of the container **20** into the container interior **27** prior to the sealing of the open end. The open end **26** sealed and then sterilization performed by evacuating the interior **27** while maintaining a sterilizing gas at the gas permeable layer **25**. After sterilization, a impermeable sealing patch **28** is placed over the opening **24** as indicated by the dotted lines in order to seal the gas permeable layer **25** against subsequent gas permeation.

[0033] **FIG. 3**, illustrates a third exemplary system **30** for sterilizing and packaging articles according to the present invention. The system **30** includes an inner container **32**, at least a portion of which is formed from a gas permeable material, and an outer enclosure or pouch **34** which is at least substantially formed from a gas impermeable material. The one or more articles to be packaged and sterilized are placed within the interior of container **32** through the open end **33**, the open end **33** sealed, and the sealed container sterilized using a sterilizing gas which passes through the permeable portion of the container. Residual sterilizing gas within the pouch may be removed as previously described. After the sterilization is complete, the container **32** may be placed into the open end **36** of the outer enclosure **34**, and the open end **36** sealed in order to prevent subsequent gas permeation into the interior of the outer enclosure **34** and ultimately into the interior of the container **32**.

[0034] **FIGS. 4A-4E** illustrate the use of the container **10** for packaging and sterilizing a catheter **40** which carries a drug eluting stent **42** (or any other environmentally sensitive medical or non-medical article). The catheter **40** is first placed through the open end **16** of the container **10** so that it is positioned within the interior **18** thereof. The container **10** is open at this point so that the gas impermeable portion **12** generally surrounds the catheter **40** and the gas permeable portion **14** is disposed to one side of the catheter, as shown in **FIG. 4A**.

[0035] Open end **16** is sealed, typically by heat sealing, adhesive sealing, lamination, or the like, along a sealing line **44**, as shown in **FIG. 4B**, and the EtO is introduced through the gas permeable portion **14**, typically by placing the sealed container **10** within a conventional gas sterilizer. Other conditions of sterilization will be chosen to be compatible with the nature of the device and/or drug or other potentially labile component on the device. After the sterilization is complete, the EtO will be removed from the interior of container, typically by vacuum and/or by purging with air, nitrogen, or other inactive gas. Optionally, as discussed above, a desiccant may be placed within the interior of the container and/or a portion of the container, typically the impermeable portion, may contain or be formed of a laminated or otherwise coupled oxygen absorbers or scavenger and/or moisture desiccants.

[0036] As shown in **FIG. 4C**, after the sterilizing gas has been removed from the interior **18** of the container **10**, the container may be flattened so that the catheter **40** remains in the impermeable portion **12**, which is isolated from the permeable portion **14** along a partition line **46**. The partition line **46** may then be flattened and sealed, as shown in **FIG. 4D**, by conventional methods including heat sealing, adhesive bonding, ultrasonic welding, and the like. Preferably, the permeable portion **14** is then severed from the impermeable portion **12**, as shown in **FIG. 4E**. The impermeable portion **12** is then ready for transportation and storage prior to use. The impermeable portion **12** itself may be placed in further packaging, such as boxes, trays, or the like.

[0037] Referring to **FIG. 5**, the impermeable portion **12** of the container **10** can be made from a material with oxygen absorbers or scavengers incorporated therein as well as being coated, including lamination or layer **48** partially or completely with suitable oxygen absorbers or scavengers. The presence of the oxygen absorbers or scavengers can remove oxygen gas as it permeates into the container interior **18** containing the sterilized articles (not shown) during processing and during storage.

[0038] Referring to **FIGS. 6A, 6B**, and 6C, the permeable portion **14** of container **10** can be made from a material

incorporated with oxygen absorbers or scavengers **50** as well as being coated partially or fully on the interior or exterior surface with a layer (or matrix of oxygen absorbers, scavenger, and/or permeable polymers) **50** or **52** of suitable oxygen absorbers or scavengers. The presence of the oxygen absorbers or scavengers can remove oxygen gas within the interior **18** as the gas permeates into the interior during sterilization and during storage. Even if the permeable portion of the enclosure is not eliminated from the path between outside and the drug device, oxygen can be limited from entering the interior **18**.

[**0039**] Referring to **FIG. 7**, the container **10** contains oxygen absorbers or scavengers within the interior **18** that may be packaged in its own packet **54** made from oxygen permeable material such as silicone rubber, polystyrene or any polymer that has an oxygen permeability coefficient greater than about 30 $cm^3/100\ in^2/day\text{-}atm$, matrix into a oxygen permeable polymer, or in its original form with or without a oxygen permeable coating. The oxygen absorbers or scavengers inside the packet **54** absorbs any oxygen gas that may enter the interior **18** during sterilization and storage.

[**0040**] Referring to **FIG. 8**, the container **10** contains a protective sheath **56** made from suitable oxygen absorbers or scavengers that is adjacent to the drug coated device **58**. The sheath **56** can be made directly from suitable oxygen absorbers or scavengers such as ferrous oxide or ethylene-cyclohexenylmethyl acrylate copolymer, or an oxygen permeable polymer matrix with the oxygen absorber or scavenger. The protective sheath oxygen absorbers or scavengers inside the enclosure and adjacent to the drug device will locally absorb any oxygen gas that may enter the inner chamber of the container **10** during sterilization and storage and minimize oxygen gas in the vicinity of the drug device.

[**0041**] **FIG. 9** illustrates container **10** that is similar to the container shown in **FIGS. 5 and 6** or has oxygen absorbers or scavengers similar to that shown in **FIG. 7**. The container **10** is disposed within the interior of an outer enclosure **34**. Oxygen absorbers or scavengers are provided in the outer enclosure such as in a packet **60** as shown to reduce the oxygen level within the enclosure **34** to prevent penetration into the interior **18** of the container **10**. Moreover, such scavengers can reduce the oxygen level within the interior **18** through the permeable portion of the container since oxygen is freely transported through the permeable portion of the container and that the scavengers attract the oxygen gas. Optionally, desiccants may be placed inside the interior of the outer and/or containers to reduce, maintain and/or control the moisture content of the container.

[**0042**] The present invention relies upon gas sterilization where the articles to be sterilized are first placed and sealed within a container. At least a portion of the container is gas permeable so that one or more articles within the interior of the container may be sterilized by placing the container in an environment of the sterilizing gas, typically an environment of essentially all ethylene oxide. Once the one or more articles are placed in the interior of the container, the interior may be evacuated to remove ambient gases which may be present. Sterilizing gas is introduced into the container interior through the permeable portion of the container and maintained within the container interior at sufficient levels to sterilize the articles therein. After sterilization is complete, the interior is preferably evacuated to remove the sterilizing gas, and the container is modified, partitioned, replaced into a secondary enclosure, or otherwise placed in a condition so that further gas exchange between the exterior and interior of the container is inhibited or prevented. The method and system of the present invention provide for convenient and effective sterilization of articles using a conventional gas sterilant, and prevent the degradation of the sterilized articles or portions thereof by subsequent exposure to oxygen, water, or other ambient gases.

[**0043**] EtO sterilization and packaging according to the present invention usually employs five major steps, including: pre-sterilization conditioning, sterilization, evacuation, air wash, and aeration. The conditioning step includes placing the one or more articles to be sterilized into the interior of the container, sealing the container and evacuating the gas from the container interior. The sterilization step includes introducing the sterilant into the interior of the container by passing a sterilizing gas through the permeable portion of the container, establishing the appropriate operating parameters, such as temperature, pressure, and relative humidity, within the inner chamber and keeping these conditions in the chamber for a pre-determined period of time for effective sterilization of the articles. The container may be placed in a sterilization vessel with the atmosphere surrounding the container within the vessel being adjusted to control the procedure. The evacuation step after sterilization includes the removal of EtO from the container interior by one or more vacuum washes and/or one or more purges with air or nitrogen, or combinations thereof. In order to further remove residual EtO from the inner chamber, the container package then undergoes aeration which can be performed in either the sterilization vessel or in a separate aeration chamber.

[**0044**] The EtO sterilization process embodying features of the present invention is performed at process parameters which are particularly useful and effective in the sterilization of an article which is at least in part formed of a reactive or labile material, such as a therapeutic agent coated on the device, while minimizing adverse effects on the integrity of the reactive or labile material during and post sterilization process. The packaged device sterilized according to the present invention enables enhanced product shelf-life and greater confidence in the integrity and suitability of the sterilized aged device.

[**0045**] The sterilization step is preferably carried out at a temperature below 30° C. with a dwell time of about 6 to 18 hours or greater. While ethylene oxide is reactive in both liquid and gaseous phase, it is preferred to employ EtO in gaseous phase to increase penetration of the gas into the device/package and its reactivity. Either or both, higher temperature and lower pressure as well as relative humidity can increase gas penetration and/or reactivity.

[**0046**] The boiling point for ethylene oxide at atmospheric pressure is about 10° C. (51° F.) where EtO is in gaseous state. Therefore, this temperature of 1° C. is the preferred lowest temperature at which to perform the sterilization step at atmospheric pressure. Alternatively, the temperature of the container interior can further be reduced below 10° C. by further reducing the pressure to below atmospheric pressure. By way of example, the sterilization step can effectively be performed at a temperature of 0° C. by reducing the pressure within the container interior to about 4 psi (pounds per square inch).

[0047] The following examples are offered by way of illustration, not by way of limitation.

EXAMPLE 1

[0048] A drug eluting stent mounted onto the balloon of a stent delivery catheter (a drug eluting stent system) is packaged in a foil pouch that has a permeable portion or patch formed of Tyvek®. The pouch is subjected to a vacuum within the inner chamber with a surrounding atmosphere of EtO gas at temperatures of 60° C. to sterilize the drug eluting stent and delivery catheter. After sterilization, the pouch is resealed with the stent and delivery system within the post seal area and the Tyvek patch outside the post-seal area. The foil pouch minimizes the light exposure as well the oxygen and moisture exposure to the sterilized contents of the container.

EXAMPLE 2

[0049] A drug eluting stent mounted onto the balloon of a stent delivery catheter is packaged in a Tyvek pouch along with ferrous oxide as an oxygen absorber and desiccant. The pouch is closed, subjected to ethylene oxide gas which permeates the pouch. After sterilization, the Tyvek pouch is evacuated and purged with nitrogen and air to remove essentially all EtO and then placed inside a gas impermeable foil pouch. The foil pouch is evacuated by vacuum to remove the remaining air and nitrogen gas, and then finally sealed. The foil pouch minimizes the exposure of the sterilized product within the Tyvek pouch to light and to oxygen and moisture, thus providing a long shelf life.

EXAMPLE 3

[0050] A drug eluting stent crimped onto a PTCA catheter or a drug eluting stent system is packaged on Tyvek pouch along with ferrous oxide oxygen absorbers and desiccant. The pouch is sterilized by ethylene oxide gas with sterilization temperatures of about 55° C. After sterilization, the sterilized Tyvek pouch with the stent system sealed inside is inserted inside a foil pouch. The foil pouch is sealed using a vacuum sealer that first purge the bag with nitrogen gas which replaces the air inside the foil pouch and that finally seal the foil pouch. This minimizes the light exposure as well as limit oxygen and moisture exposure.

EXAMPLE 4

[0051] A drug eluting stent mounted onto the balloon of a stent delivery catheter is packaged in an essentially gas impermeable foil container that has a Tyvek patch which allows for gas permeability through the gas permeable patch. The pouch is exposed to ethylene oxide gas using the following cycle:

	Set Point
Chamber Temperature	77° F. (25° C.)
Preconditioning Time	3 hrs
Initial Evacuation Pressure	1 psia
EtO Dwell Pressure	7 psia
EtO Exposure Time	14 hrs
Number of Air Wash after sterilization	12 times
Air Wash Time	10 hrs
Room Temperature (20° C.) Aeration	3 days

EXAMPLE 5

[0052] A drug eluting stent mounted onto the balloon of a stent delivery catheter is packaged on foil pouch that has a Tyvek patch (i.e., breathable). The pouch is exposed to ethylene oxide gas using the following cycle:

	Set Point
Chamber Temperature	84° F. (29° C.)
Preconditioning Time	3 hrs
Initial Evacuation Pressure	1 psia
EtO Dwell Pressure	7 psia
EtO Exposure Time	14 hrs
Number of Air Washes	12 times
Air Wash Time	10 hrs
Room Temperature (20° C.) Aeration	3 days

EXAMPLE 6

[0053] A drug eluting stent is crimped onto the balloon of a stent delivery catheter. A protective sheath made from ethylene-cyclohexenylmethyl acrylate copolymer (an oxygen absorber) is inserted over the drug eluting device. The drug eluting stent and delivery catheter is packaged in a Tyvek pouch, the pouch is sealed and then sterilized by ethylene oxide gas at normal sterilization parameters. The protective sheath formed of oxygen absorbing polymer material minimizes the oxidative degradation of the drug eluting stent by limiting exposure to oxygen gas.

[0054] While the invention has been described herein primarily in terms of packaging medical devices, and in particular to drug eluting stents, it is also suitable for sterilization and packaging of other articles, including foods, pharmaceuticals, diagnostic and assay systems, sensitive electrical components, chemical system components, and the like, where the ability to sterilize articles after initial packaging has been completed is desirable. The methods and systems of the present invention are simple to perform, require minimum changes from existing packaging practices, and provide a package to the end user which is as convenient and easy to use as prior packaging systems.

[0055] Many other alterations and modifications may be made by those of ordinary skill in this art, without departing from the spirit and scope of this invention. For example, the method and packaging may be utilized for packaging articles treated by gases other than sterilizing gases The illustrated embodiments have been shown only for purposes of clarity and the examples should not be taken as limiting the invention as defined in the following claims. The claims are intended to include all equivalents, whether now or later devised.

[0056] Moreover, individual features of embodiments of the invention may be shown in some drawings and not in

others, but those skilled in the art will recognize that individual features of one embodiment of the invention can be combined with one or more features of another embodiment. Accordingly, it is not intended that the invention be limited to the specific embodiments illustrated or described. It is therefore intended that this invention to be defined by the scope of the appended claims as broadly as the prior art will permit.

[0057] Terms such a "element,""member,""component,""device,""section,""portion,""means,""steps" and words of similar import when used herein shall not be construed as invoking the provisions of 35 U.S.C. §112(6) unless the following claims expressly use the term "means" followed by a particular function without specific structure or expressly use the term "step" followed by a particular function without specific action. All patents and patent applications referred to above are hereby incorporated by reference in their entirety.

What is claimed is:

1. A method for packaging a sterile article, comprising:

a. providing a container which has a wall defining at least in part an interior and which has at least one portion permeable to sterilizing gas;

b. placing an article into the interior of the container;

c. exposing at least one permeable portion of the container to an exterior environment which includes a sterilizing gas under conditions such that the sterilizing gas permeates through at least one permeable portion of the container into the interior of the container; and

d. removing sterilizing gas from the interior of the container after the articles therein are sterilized.

2. The method of claim 1 wherein the at least one permeable region of the container is sealed after the sterilizing gas is removed from the interior to prevent gas permeation while the article remains in the interior.

3. A method as in claim 1, wherein the sterilizing gas is at least in part ethylene oxide.

4. A method as in claim 1, wherein the sterilizing gas is removed from the interior of the container by applying a vacuum to the interior.

5. A method as in claim 1, wherein the sterilized gas is removed from the interior of the container by purging the interior of the container with a non-active gas.

6. A method as in claim 1, wherein sealing comprises partitioning the container to isolate the article within an impermeable portion of the container interior.

7. A method as in claim 6, further comprising removing the gas permeable portion of the container.

8. A method as in claim 1, wherein sealing comprises deploying the container into an impermeable enclosure.

9. A method as in claim 1, wherein the container is sealed by applying a gas impermeable barrier over the gas permeable portion of the container.

10. A method as in claim 1, wherein the article within the interior of the container is a medical device.

11. A method as in claim 10, wherein the medical device is formed at least in part of a labile material which is degradable in an atmosphere containing oxygen and/or water vapor.

12. A method as in claim 10, wherein the medical device is a stent coated with a therapeutic or diagnostic agent.

13. A method as in claim 12 wherein the interior of the container has less than about 150 ppm sterilizing gas or residuals.

14. A method as in claim 12 wherein the container interior has about 10 ppm to about 50 ppm sterilizing gas or residuals.

15. A method as in claim 1 wherein the sterilizing gas is selected from the group consisting of ethylene oxide, ethylene oxide and nitrogen, ethylene oxide and carbon dioxide, ethylene oxide with one or more chlorofluorocarbon diluents, Oxyfume 2000 series of sterilant, ozone, hydrogen peroxide gas plasma, chlorine dioxide and mixtures thereof.

16. A sterile packaging system for one or more sterile articles, comprising:

a. a container which has a wall, an interior defined at least in part by the container wall and configured to receive at least one article and at least one portion that is permeable to sterilizing gas and is in fluid communication with the interior, and

b. a patch of impermeable material on the permeable portions to prevent permeation of gas into the interior through the permeable portions.

17. The sterile packaging system as in claim 16 wherein the container interior is essentially free of sterilizing gas.

18. The sterile packaging system as in claim 16 wherein the container interior has less than about 150 ppm sterilizing gas or residuals.

19. The sterile packaging system as in claim 16 wherein the sterilizing gas is selected from the group consisting of ethylene oxide, ethylene oxide and nitrogen, ethylene oxide and carbon dioxide, ethylene oxide with one or more chlorofluorocarbon diluents, Oxyfume 2000 series of sterilant, ozone, hydrogen peroxide gas plasma, chlorine dioxide and mixtures thereof.

20. A system as in claim 16, wherein the at least one gas permeable portion is formed of material which is impermeable to liquid.

21. A system as in claim 16, wherein the at least one gas permeable portion is at least in part formed of a spun olefin.

22. A system as in claim 16, wherein the patch sealing the permeable portion is formed of a material which is moisture and gas impermeable and is non-transmissive for light and UV radiation.

23. A system as in claim 16, wherein the sealing patch is part of a gas impermeable enclosure which receives the container.

24. The system of claim 23 wherein the impermeable enclosure is sealed about the container to isolate the container from an atmosphere containing oxygen and moisture.

25. A system as in claim 23, wherein the enclosure is formed of a polymer film which is impermeable to oxygen and moisture.

26. A system as in claim 16, wherein the container has a first portion which is impermeable to gas and a second portion which is permeable to gas, and wherein the first portion impermeable to gas contains the one or more articles and the second portion permeable to gas is sealed from the first portion by a partition line which can be selectively adhered to isolate the portion of the interior of the container within the gas impermeable portion from the inner portion of the gas permeable portion.

27. A system as in claim 16, wherein the enclosure receiving the container is a pouch having a sealable open end

and a receptacle portion formed from a non-gas permeable material and wherein the gas permeable portion lies between the receptacle portion and the open end and a partition line lies between the gas permeable portion and the receptacle portion.

28. The system of claim 16 wherein the container has oxygen absorbers or scavengers.

29. The system of claim 28 wherein oxygen absorbers or scavengers are provided in fluid communication with the interior of the container.

30. The system of claim 28 wherein the oxygen absorbers or scavengers are inside the permeable portion of the container.

31. The system of claim 28 wherein an oxygen absorber is incorporated into or coated on the permeable portion of the container.

32. The system of claim 28 wherein an oxygen absorber is incorporated into or coated on the impermeable portion of the container.

33. The system of claim 28 wherein the oxygen absorber is coated onto an interior surface of the container.

34. The system of claim 28 wherein the oxygen absorber is coated onto an exterior surface of the container.

35. The system of claim 28 wherein the oxygen absorber is selected from the group consisting of ethylene-cyclohexenylmethyl acrylate copolymer and ethylene-methylacrylate-cyclohexeneylmethyl acrylate terpolymer.

36. The system of claim 28 wherein the oxygen scavenger is selected from the group of materials consisting of ethylenically unsaturated polymers, ferrous oxide, titanium oxide, activated carbon with sodium ascorbate, diethylhydroxylamine, carbohydrazide, combinations of these materials.

37. The system of claim 28 wherein the oxygen absorbers or scavengers are packaged in a packet made from oxygen permeable material that has an oxygen permeability coefficient greater than 30 $cm^3/100\ in^2$/day-atm.

38. The system of claim 28 wherein the oxygen absorbers or scavengers are packaged in a packet made from oxygen permeable material that has an oxygen Permeability Coefficient greater than 100 $cm^3/100\ in^2$/day-atm.

39. The system of claim 28 wherein the oxygen absorbers or scavengers are packaged in a packet made from oxygen permeable material that has an oxygen permeability coefficient greater than about 300 $cm^3/100\ in^2$/day-atm.

40. The system of claim 28 wherein the oxygen absorbers or scavengers are incorporated into a protective sheath that is disposed proximate to the sterilized medical device.

41. A sterilized package, comprising:

a. a sealed container which has an interior defined at least in part by a wall, which has at least a portion permeable to sterilizing gas and which has at least one sterilized article within the interior; and

b. an atmosphere within the interior of the container which is substantially free of sterilizing gas.

42. The sterilized package of claim 41 wherein the container portion permeable to sterilizing gas is sealed to prevent penetration of non-sterilizing gas exterior to the container into the interior of the container.

43. The sterilized package of claim 41 wherein an oxygen scavenger is maintained in fluid communication with the interior of the container.

44. The sterilized package of claim 43 wherein the oxygen scavenger is in particulate form.

45. The sterilized package of claim 43 wherein the oxygen scavenger is incorporated within at least part of a wall defining the interior of the container.

46. The sterilized package of claim 41 wherein the container is sealed by disposing the container in a gas impermeable enclosure.

47. The sterilized package of claim 46 wherein the gas impermeable enclosure is formed at least in part of a polymer which is impermeable to vapor and moisture.

48. The sterilized package of claim 41 wherein the at least one article is a drug eluting stent.

49. The sterilized package of claim 48 wherein the stent is coated with a drug that is degraded by oxygen and/or water vapor.

50. The sterilized package of claim 48 wherein the stent is mounted on a balloon of a delivery catheter.

51. The sterilized package of claim 41 wherein the atmosphere within the container interior has less than about 150 ppm sterilizing gas or residuals.

52. A method of packaging and treating an article, comprising:

a. providing a container which has an interior defined at least in part by a wall, which has a portion permeable to treating gas and which has a article to be treated disposed within the interior of the container;

b. surrounding the permeable portion of the container with a treating gas under conditions which facilitate permeation of the treating gas through the permeable portion of the container into the container interior to treat the article disposed therein; and

c. removing treating gas from the inner chamber after the article has been treated.

53. The method of claim 52 wherein treating gas is removed from the interior of the container by purging the interior with innocuous gas.

54. The method of claim 53 wherein the container interior is purged with innocuous gas until substantially free of treating gas.

55. The method of claim 53 wherein the container interior has less than about 150 ppm treating gas or residuals.

56. The method of claim 54 wherein the permeable portion is sealed after the container interior is purged with innocuous gas.

57. The method of claim 52 wherein the article is a medical device.

58. The method of claim 57 wherein the medical device is a delivery catheter with an inflatable balloon and a drug eluting stent mounted on the balloon.

59. The method of packaging and sterilizing a medical device as in claim 52 wherein the sterilizing gas is removed from the container interior until essentially free of sterilizing gas.

60. The method of packaging and sterilizing a medical device as in claim 52 wherein the sterilizing gas is removed from the container interior until the interior has less than about 150 ppm sterilizing gas or residuals.

61. A method of packaging and sterilizing a medical device as in claim 52 wherein the sterilizing gas is selected from the group consisting of ethylene oxide, ethylene oxide and nitrogen, ethylene oxide and carbon dioxide, ethylene oxide with one or more chlorofluorocarbon diluents, Oxy-

fume 2000 series of sterilant, ozone, hydrogen peroxide gas plasma, chlorine dioxide and mixtures thereof.

62. A treated package, comprising:

a. a sealed container which has an interior defined at least in part by a wall, which has at least a portion permeable to treating gas and which has at least one treated article within the interior; and

b. an atmosphere within the interior of the container which is substantially free of treating gas.

63. A method for packaging one or more treated articles, comprising:

a. providing a container which has a wall defining at least in part an interior and which has at least one portion permeable to treating gas;

b. placing one or more articles into the interior of the container;

c. exposing at least one permeable portion of the container to an exterior environment which includes a treating gas under conditions such that the treating gas permeates through at least one permeable portion of the container into the interior of the container; and

d. removing treating gas from the interior of the container after the articles therein are treated.

64. A packaging system for one or more treated articles, comprising a container which has a wall, an interior defined at least in part by the container wall and configured to receive at least one article and a treating gas permeable means in fluid communication with the interior.

65. The packaging system of claim 64 wherein a patch of impermeable material covers at least part of the permeable means to prevent permeation of gas into the interior.

66. A method for packaging one or more treated articles, comprising:

a. a step of providing a container which has a wall defining at least in part an interior and which has at least one portion permeable to treating gas;

b. a step of placing one or more articles into the interior of the container; and

c. a step of exposing at least one permeable portion of the container to an exterior environment which includes a treating gas under conditions such that the treating gas permeates through at least one permeable portion of the container into the interior of the container.

67. The method of claim 66 including the step of removing treating gas from the interior of the container after the articles therein are treated.

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