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1**UNITED STATES PATENT APPLICATION**

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 FOR: **BLOOD COLLECTION TUBE ASSEMBLY**

10 **BACKGROUND OF THE INVENTION**

 1. **Field of the Invention**

15 This invention relates to a multi-layer barrier coating for
 providing an effective barrier against gas and water permeability for
 containers, especially plastic blood collection tubes.

 2. **Description of the Related Art**

20 With the increased emphasis on the use of plastic medical
 products, a special need exists for improving the barrier properties of
 articles made of polymers.

25 Such medical products that would derive a considerable benefit
 from improving their barrier properties include, but are not limited to,
 collection tubes and particularly those used for blood collection.

 Blood collection tubes require certain performance standards to
30 be acceptable for use in medical applications. Such performance
 standards include the ability to maintain greater than about 90%
 original draw volume over a one year period, to be radiation
 sterilizable and to be non-interfering in tests and analysis.

35 Therefore, a need exists to improve the barrier properties of
 articles made of polymers and in particular plastic evacuated blood



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collection tubes wherein certain performance standards would be met and the article would be effective and usable in medical applications.

SUMMARY OF THE INVENTION

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The present invention is a plastic composite container with a multi-layer barrier coating comprising at least two barrier materials disposed over the outer or inner surface of the previously formed composite container. Desirably, the barrier materials comprise a first
10 layer of a polymeric material applied to the outer surface of the previously formed composite container, a second layer of an inorganic material applied over the first layer and optionally a third layer of organic material applied over the second layer.

15

The first layer, a primer coating, is preferably a heterocyclic compound such as ethylene oxides. This type of compound is frequently called an epoxide, although the formal IUPAC nomenclature is oxirane. The coating may be formed either on an interior surface portion, on an exterior surface portion, or both of the container.

20

The second layer of the barrier coating may preferably be a silicon oxide based composition, such as SiO_x wherein x is from 1.0 to about 2.5; or an aluminium oxide based composition. Most preferably, the second layer is a silicon oxide based composition applied over the
25 first layer.

The optional third layer of the barrier coating preferably an organic barrier composition, such as poly (vinylidene chloride) (PVDC), is most preferably applied over the second layer.

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Desirably, the primer coating is formed by an application of an uncured polyamine polyepoxide mixture, followed by exposure to a photolytic or thermal curing source.

Preferably, the primer coating is a highly cross-linked polyamine/polyepoxide mixture as described in International Patent WO 93/07068 and United States Patent No. 4,478,874, the disclosures of which are herein incorporated by reference.

5

Preferably, the thickness of the epoxide primer coating is about 100 microns to about 300 microns and most preferably from about 100 microns to about 175 microns.

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A desirable second layer which is disposed over the first layer preferably comprises a silicon oxide based composition, such as SiO_x . Such a film desirably is derived from volatile organosilicon compounds.

15

The silicon oxide based composition provides a dense, vapor-impervious coating over the primer organic coating. Preferably, the thickness of the silicon oxide based layer is about 100 to about 2,000 Angstroms ($\text{\AA}$) and most preferably from about 500 to about 1,000 $\text{\AA}$. A coating above 5,000 $\text{\AA}$ may crack and therefore be ineffective as a barrier.

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A desirable optional third layer which is disposed over the second layer preferably comprises vinylidene chloride - methyl methacrylate - methacrylate acrylic acid polymer (PVDC), thermosetting epoxy coatings, parylene polymers or polyesters.

25

Preferably, the thickness of the PVDC layer is about 2 to about 15 microns and most preferably from about 3 to about 5 microns.

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The process for applying the primer coating to a container is preferably carried out as described in International Publication No. 93/07068 and U.S. Patent No. 4,478,874 wherein said mixture is coated into a blood collection tube and cured by thermal methods. The

deposition and curing steps may be repeated until the desired number of layers has been achieved.

5 A method for depositing a silicon oxide based film is as follows: (a) pretreating the first layer on the container with a first plasma coating of oxygen; (b) controllably flowing a gas stream including an organosilicon compound into a plasma; and (c) depositing a silicon oxide onto the first layer while maintaining a pressure of less than about 500 mm. H_g during the depositing.

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Although the pretreatment step is optional, it is believed that the pretreatment step provides for improved adherence qualities between the second layer and the primer coating.

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The organosilicon compound is preferably combined with oxygen and optionally helium or another inert gas such as argon or nitrogen and at least a portion of the plasma is preferably magnetically confined adjacent to the surface of the first layer during the depositing, most preferably by an unbalanced magnetron.

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The PVDC layer may be applied over the second layer by dipping or spraying techniques.

25 Most preferably, the method for depositing a barrier coating on a substrate, such as a plastic collection tube comprises the following steps:

- 30 (a) applying an uncured polyamine polyepoxide mixture onto the outer surface of a container;
- (b) curing said mixture;
- (c) vaporizing an organosilicon component and admixing the volatilized organosilicon component with an oxidizer component and optionally an inert gas component to form a gas stream exterior to the chamber;

- (d) establishing a glow discharge plasma in the chamber from one or more of the gas stream components;
- (e) controllably flowing the gas stream into the plasma while confining at least a portion of the plasma therein; and
- 5 (f) depositing a second layer of a silicon oxide coating adjacent said first layer.

Optionally, a PVDC coating may be applied over the second layer by dipping or spraying techniques. An emulsion based PVDC
10 solution may be used for dipping the container surface, followed by thermal curing. Solvent based PVDC solutions, where the solvent is CHCl_3 , CCl_4 and the like, may be used for spray-coating, followed by thermal curing.

15 Optionally, the container and/or the first layer may be flame-treated or plasma oxygen treated or corona discharge treated prior to applying the multi-layer coatings.

Plastic tubes coated with the multi-layer barrier coating,
20 comprising the primer coating, and an oxide layer and an overcoating layer are able to maintain substantially far better vacuum retention, draw volume and thermomechanical integrity retention than previous tubes comprised of polymer compositions and blends thereof without a coating of barrier materials or of tubes comprising only an oxide
25 coating. In addition, the tube's resistance to impact is much better than that of glass. Most notably is the clarity of the multi-layer coating and its durability to substantially withstand resistance to impact and abrasion.

30 Most preferably, the container of the present invention is a blood collection device. The blood collection device can be either an evacuated blood collection tube or a non-evacuated blood collection tube. The blood collection tube is desirably made of polyethylene

terephthalate, polypropylene, polyethylene naphthalate or copolymers thereof.

Printing may be placed on the multi-layer barrier coating applied to the container of interest. For example, a product identification, bar code, brand name, company logo, lot number, expiration date and other data and information may all be included on the barrier coating. Moreover, a matte finish or a corona discharged surface may be developed on the barrier coating so as to make the surface appropriate for writing additional information on the label. Furthermore, a pressure sensitive adhesive label may be placed over the barrier coating so as to accommodate various hospital over-labels, for example.

Preferably, the multi-layer barrier coating of the present invention provides a transparent or colorless appearance and may have printed matter applied thereon.

A further advantage is that the method of the present invention provides a reduction in the gas permeability of three-dimensional objects that has not been achieved with conventional deposition method typically used with thin films.

It has been found in the present invention that the organic material, epoxide provides a good platform for the growth of the dense SiO_x barrier material.

It has been found that the epoxide layer improves the adhesion between a plastic surface and SiO_x and overall improves the thermomechanical stability of the coated system. In addition, acrylate primer coating has a role of a planarization (leveling) layer, covering the particles and imperfections on the surface of a polymer and reducing the defect density in the deposited inorganic coatings. The good bonding properties of the acrylate are also due to the fact that

acrylate is polar and the polarity provides means for good bond formation between the SiO_x and the acrylate. In addition, it has been found that a good bond formation is made between plastic tubes made of polypropylene and acrylate. Thus, the present invention provides the means of substantially improving the barrier properties of polypropylene tubes. The adhesion properties of both the acrylate coating and the oxide coating can be further substantially improved by surface pretreatment methods such as flame or oxygen plasma. Therefore, a significant reduction in permeability of the article is due to the substantially improved SiO_x surface coverage that is obtained by the use of a primer coating of acrylate on the plastic article surface.

The layer of PVDC improves the layer of SiO_x because it plugs the defects and/or irregularities in the SiO_x layer. Furthermore, the PVDC layer improves the abrasion resistance of the SiO_x layer.

A plastic blood collection tube coated with the multi-layer barrier coating of the present invention will not interfere with testing and analysis that is typically performed on blood in a tube. Such tests include but are not limited to, routine chemical analysis, biological inertness, hematology, blood chemistry, blood typing, toxicology analysis or therapeutic drug monitoring and other clinical tests involving body fluids. Furthermore, a plastic blood collection tube coated with the barrier coating is capable of being subjected to automated machinery such as centrifuges and may be exposed to certain levels of radiation in the sterilization process with substantially no change in optical or mechanical and functional properties.

DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of a typical blood collection tube with a stopper.

FIG. 2 is a longitudinal sectional view of the tube of FIG. 1 taken along line 2-2.

FIG. 3 is a longitudinal sectional view of a tube-shaped container similar to the tube of FIG. 1 without a stopper, comprising a multi-layer barrier coating.

FIG. 4 is a longitudinal sectional view of a tube-shaped container, similar to the tube of FIG. 1 with a stopper, comprising a multi-layer barrier coating.

FIG. 5 is a longitudinal sectional view of a further embodiment of the invention illustrating the tube with a stopper similar to FIG. 1 and with the multi-layer barrier coating encompassing both the tube and stopper thereof.

FIG. 6 illustrates a plasma deposition system.

FIG. 7 is a general schematic diagram illustrating the layers being deposited on a substrate.

DETAILED DESCRIPTION

The present invention may be embodied in other specific forms and is not limited to any specific embodiment described in detail which is merely exemplary. Various other modifications will be apparent to and readily made by those skilled in the art without departing from the scope and spirit of the invention. The scope of the invention will be measured by the appended claims and their equivalents.

Referring to the drawings in which like reference characters refer to like parts throughout the several views thereof, FIGS. 1 and 2 show a typical blood collection tube 10, having a sidewall 11 extending from an open end 16 to a closed end 18 and a stopper 14 which

includes a lower annular portion or skirt 15 which extends into and presses against the inner surface 12 of the sidewall for maintaining stopper 14 in place.

5 FIG. 2 schematically illustrates that there are three mechanisms for a change in vacuum in a blood collection tube: (A) gas permeation through the stopper material; (B) gas permeation through the tube and (C) leak at the stopper tube interface. Therefore, when there is substantially no gas permeation and no leak, there is good vacuum
10 retention and good draw volume retention.

FIG. 3 shows the preferred embodiment of the invention, a plastic tube coated with at least two layers of barrier materials. The preferred embodiment includes many components which are
15 substantially identical to the components of FIGS. 1 and 2. Accordingly, similar components performing similar functions will be numbered identically to those components of FIGS. 1 and 2, except that a suffix "a" will be used to identify those components in FIG. 3.

20 Referring now to FIG. 3, the preferred embodiment of the invention, collection tube assembly 20 comprises a plastic tube 10a, having a sidewall 11a extending from an opened end 16a to a closed end 18a. A barrier coating 25 extends over a substantial portion of the outer surface of the tube with the exception of open end 16a. Barrier
25 coating 25 comprises a first layer 26 of a polymer material such as an epoxide material and a second layer 27 an inorganic material such as a silicon oxide based composition and a third layer 28 of an organic overcoating layer such as PVDC.

30 FIG. 4 illustrates an alternate embodiment of the invention, wherein collection tube assembly 40 comprises stopper 48 in place for closing open end 41 of tube 42. As can be seen, sidewall 43 extends from open end 41 to closed end 44 and stopper 48 includes an annular upper portion 50 which extends over the top edge of tube 42. Stopper

48 includes a lower annular portion or skirt 49 which extends into and presses against the inside inner surface 46 of sidewall 43 for maintaining stopper 48 in place. Also, the stopper has a septum portion 52 for receiving a cannula therethrough.

5

Thus, the user, once receiving a container such as that shown in FIG. 4 with a sample contained therein, may insert a cannula through septum 52 for receiving part or all of the contents in tube 42 to perform various tests on a sample. Covering a substantial portion of the length
10 of the tube is a multi-layer barrier coating 45. Multi-layer barrier coating 45 covers substantially most of the tube with the exception of open end 41 thereof. Multi-layer barrier coating 45 comprises a first layer 54 of a polymer material such as an epoxide, a second layer 56 of an inorganic material such as a silicon oxide material and a third layer
15 57 of an organic barrier material such as PVDC. FIG. 4 differs from the embodiment in FIG. 3 in that the tube may be evacuated with the simultaneous placement of stopper 48 therein after the application of layers 54 and 56 over the tube. Alternatively, the multi-layer barrier coating may be applied to the tube after it has been evacuated.

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FIG. 5 shows an additional embodiment of the barrier coating and a tube. The alternate embodiment functions in a similar manner to the embodiment illustrated in FIG. 4. Accordingly, similar components performing similar functions will be numbered identically to those
25 components in the embodiment of FIG. 4, except that a suffix "a" will be used to identify those components in FIG. 5.

Referring now to FIG. 5, a further embodiment 60 of the invention wherein multi-layer barrier coating 45a incorporates both
30 upper portion 50a of stopper 48a, as well as the entire outer surface of tube 42a. Multi-layer barrier coating 45a includes serrations 62 at the tube, stopper interface. The serrations are registered so that it can be determined if the sealed container has been tampered with. Such an embodiment may be utilized, for example, for sealing the container

with the stopper in place. Once a sample has been placed in the tube, the sample cannot be tampered with by removal of the stopper. Additionally, the serrations may be registered so that it can be determined if the sealed container has been tampered with. Such an
5 arrangement may be appropriate, for example, in drug abuse testing, specimen identification and quality control.

In an alternate embodiment of the invention, multi-layer barrier coating 45 is repeatedly or sequentially applied to the inner and/or
10 outer surface of the tube. Preferably, the coating is applied at least twice.

It will be understood by practitioners-in-the-art, that such tubes may contain reagents in the form of additives or coatings on the inner
15 wall of the tube.

The multi-layer barrier coating forms a substantially clear or translucent barrier. Therefore, the contents of a plastic tube with a multi-layer barrier coating comprising at least two layers of barrier
20 materials are substantially visible to the observer at the same time identifying information may be displayed over the multi-layer barrier coating after it is applied to the plastic tube.

The first layer of the multi-layer barrier coating may be formed
25 on the tube by dip-coating, roll-coating or spray-coating ethylene oxide or oxirane monomers on the surface to be coated, followed by UV or thermal curing.

The second layer of the multi-layer barrier coating, an inorganic
30 material, may be formed over the first layer by radio frequency discharge, direct or dual ion beam deposition, sputtering or plasma chemical vapor deposition, as described in U.S. Patent Nos. 4,698,256, 4,809,876, 4,992,298 and 5,055,318, the disclosures of which are herein incorporated by reference.

For example, a method of depositing an oxide coating is provided by establishing a glow discharge plasma in a previously evacuated chamber. The plasma is derived from one or more of the gas stream components, and preferably is derived from the gas stream itself. The article is positioned in the plasma, preferably adjacent the confined plasma, and the gas stream is controllably flowed into the plasma. A silicon oxide based film is deposited on the substrate to a desired thickness. The thickness of the oxide coating is about 100 Angstroms ($\text{\AA}$) to about 10,000 $\text{\AA}$. A thickness of less than about 5,000 $\text{\AA}$ may not provide sufficient barrier and a thickness of greater than about 5,000 $\text{\AA}$ may crack, thus decreasing the effective barrier. Most preferably, the thickness of the oxide coating is about 1,000 $\text{\AA}$ to about 3,000 $\text{\AA}$.

Another method of depositing an oxide coating is by confining a plasma with magnets. Preferably, the magnetically enhanced method for depositing a silicon oxide based film on a substrate is preferably conducted in a previously evacuated chamber of glow discharge from a gas stream. The gas stream preferably comprises at least two components: a volatilized organosilicon component, an oxidizer component such as oxygen, nitrous oxide, carbon dioxide or air and an optionally inert gas component.

Examples of suitable organosilicon compounds useful for the gas stream in the plasma deposition methods are liquid or gas at about ambient temperature and when volatilized have a boiling point about 0°C to about 150°C and include dimethylsilane, trimethylsilane, diethylsilane, propylsilane, phenylsilane, hexamethyldisilane, 1,1,2,2-tetramethyldisilane, bis (trimethylsilane)methane, bis (dimethylsilyl)methane, hexamethyldisiloxane, vinyl trimethoxy silane, vinyl triethoxysilane, ethylmethoxysilane, ethyltrimethoxysilane, divinyltetramethyldisiloxane, hexamethyldsilazane divinyl-

hexamethyltrisiloxane, trivinylpentamethyltrisiloxazane,
tetraethoxysilane and tetramethoxysilane.

5 Among the preferred organosilicons are 1,1,3,3-
tetramethyldisiloxane, trimethylsilane, hexamethyldisiloxane,
vinyltrimethylsilane, methyltrimethoxysilane, vinyltrimethoxysilane
and hexamethyldisilazane. These preferred organosilicon compounds
have boiling points of 71°C, 55.5°C, 102°C, 123°C and 127°C
respectively.

10

The optional inert gas of the gas stream preferably is helium,
argon or nitrogen.

15 The volatilized organosilicon component is preferably
admixed with the oxygen component and the inert gas component
before being flowed into the chamber. The quantities of these gases
being so admixed are controlled by flow controllers so as to
adjustably control the flow rate ratio of the gas stream components.

20

Various optical methods known in the art may be used to
determine the thickness of the deposited film while in the deposition
chamber, or the film thickness can be determined after the article is
removed from the deposition chamber.

25

The deposition method of the present invention is preferably
practiced at relatively high power and quite low pressure. A pressure
less than about 500 millitorr (mTorr) should be maintained during the
deposition, and preferably the chamber is at a pressure between about
43 to about 490 millitorr during the deposition of film. Low system
30 pressure results in lower deposition rates whereas higher system
pressure provides faster deposition rates. When the plastic article to
be coated is heat sensitive, a higher system pressure may be used to
minimize the amount of heat the substrate is exposed to during
deposition because high substrate temperatures are to be avoided for

low Tg polymers such as polypropylene and PET (Tg is -10°C and 60°C respectively).

5 The substrate is electrically isolated from the deposition system (except for electrical contact with the plasma) and is at a temperature of less than about 80°C during the depositing. That is, the substrate is not deliberately heated.

10 Referring to FIG. 6, the system for depositing a silicon oxide based film comprises an enclosed reaction chamber 170 in which a plasma is formed and in which a substrate or tube 171, is placed for depositing a thin film of material on a sample holder 172. The substrate can be any vacuum compatible material, such as plastic. One or more gases are supplied to the reaction chamber by a gas
15 supply system 173. An electric field is created by a power supply 174.

The reaction chamber can be of an appropriate type to perform any of the plasma-enhanced chemical vapor deposition
20 (PECVD) or plasma polymerization process. Furthermore, the reaction chamber may be modified so that one or more articles may be coated with an oxide layer simultaneously within the chamber.

The pressure of the chamber is controlled by a mechanical
25 pump 188 connected to chamber 170 by a valve 190.

The tube to be coated is first loaded into chamber 170 in sample holder 172. The pressure of the chamber is reduced to about 5m Torr by mechanical pump 188. The operating pressure of the
30 chamber is about 90 to about 140 mTorr for a PECVD or plasma polymerization process and is achieved by flowing the process gases, oxygen and trimethyl silane, into the chamber through monomer inlet 176.

The thin film is deposited on the outer surface of the tube and has a desired uniform thickness or the deposition process may be interrupted periodically to minimize heating of the substrate and/or electrodes and/or physically remove particulate matter from the articles.

Magnets 196 and 198 are positioned behind electrode 200 to create an appropriate combination of magnetic and electrical fields in the plasma region around the tube.

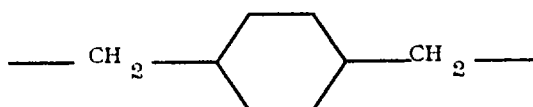
The system is suitable for low frequency operation. An example frequency is 40kHz. However, there can be some advantages from operating at a much high frequency, such as in the radio frequency range of several megahertz.

The silicon oxide based film or blends thereof used in accordance with this disclosure, may contain conventional additives and ingredients which do not adversely affect the properties of articles made therefrom.

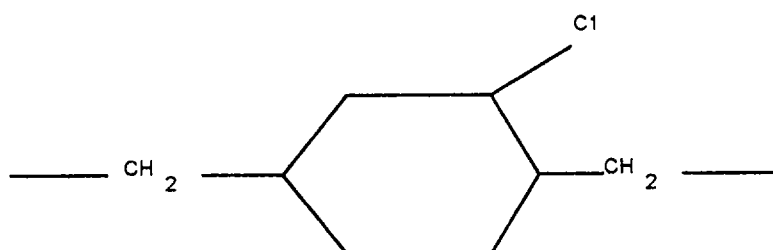
The third layer of the multi-layer barrier coating may be formed on the second layer by dip-coating, roll-coating or spraying an aqueous emulsion of the PVDC homopolymer, followed by thermal curing.

The third layer may preferably be vinylidene chloride-acrylonitrile-methyl methacrylate-methyl acrylate-acrylic acid copolymers, thermosetting epoxy coatings, parylene polymers, or polyesters.

Preferably, the third layer is a parylene polymer. Parylene is the generic name for members of the polymer series developed by Union Carbide Corporation. The base member of the series, called parylene N, is poly-p-exlylene, a linear, crystalline material:

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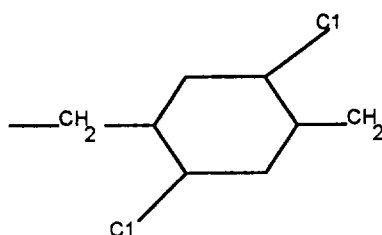
5 Parylene C, a second member of the parylene series is produced from the same monomer as parylene N and modified by the substitution of a chlorine atom for one other aromatic hydrogens:



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Parylene D, the third member of the parylene series is produced from the same monomer as parylene N and modified by the substitution of the chlorine atom for two of the aromatic hydrogens:

15



20 Most preferably, the polymer layer is a vinylidene chloride-methyl methacrylate-methacrylate acrylic acid polymer (PVDC). This polymer is available as DARAN® 8600-C (trademark of W.R.

Grace and Co.) sold by GRACE, Organic Chemicals Division, Lexington, Mass.

5 The third layer of the barrier coating, a polymer material, may be a parylene polymer applied to the second layer by a process similar to vacuum metallizing, as described in U.S. Patent Nos. 3,342,754 and 3,300,332, the disclosures of which are herein incorporated by reference. Alternatively, the third layer may be vinylidene chloride-acrylonitrile-methyl methacrylate-methyl acrylate-
10 acid acrylic polymer, applied to the second layer by dip-coating, roll-coating or spraying an aqueous emulsion of the polymer, followed by air drying of the coating, as described in U.S. Patent Nos. 5,093,194 and 4,497,859, the disclosure of which are herein incorporated by reference.

15

As shown in FIG. 7, the expoxide coating **A** and the silicon oxide based coating **B** may have defects or irregularities **C**. It is believed that complete coverage of the substrate **D** cannot be achieved with only the expoxide and silicon oxide based coatings.
20 Therefore, a third coating of PVDC, **E** is applied over the silicon oxide based coating to produce a substantially complete barrier coating over the substrate surface.

25 A variety of substrates can be coated with a barrier coating by the process of the present invention. Such substrates include, but are not limited to packaging, containers, bottles, jars, tubes and medical devices.

30 A plastic blood collection tube coated with the multi-layer barrier coating will not interfere with testing and analysis that is typically performed on blood in a tube. Such tests include but are not limited to, routine chemical analysis, biological inertness, hematology, blood chemistry, blood typing, toxicology analysis or therapeutic drug monitoring and other clinical tests involving body fluids. Furthermore,

a plastic blood collection tube coated with the barrier coating is capable of being subjected to automated machinery such as centrifuges and may be exposed to certain levels of radiation in the sterilization process with substantially no change in optical or mechanical and functional properties.

A plastic blood collection tube coated with the multi-layer barrier coating is able to maintain 90% original draw volume over a period of one year. Draw volume retention depends on the existence of a particle vacuum, or reduced pressure, inside the tube. The draw volume changes in direct proportion to the change in vacuum (reduced pressure). Therefore, draw volume retention is dependent on good vacuum retention. A plastic tube coated with a barrier coating substantially prevents gas permeation through the tube material so as to maintain and enhance the vacuum retention and draw volume retention of the tube. Plastic tubes without the multi-layer coating of the present invention may maintain about 90% draw volume for about 3 to 4 months.

If the multi-layer barrier coating is also coated or applied on the inner surface of the plastic blood collection tube, the barrier coating may be hemorepellent and/or have characteristics of a clot activator.

It will be understood that it makes no difference whether the plastic composite container is evacuated or not evacuated in accordance with this invention. The presence of a barrier coating on the outer surface of the container has the effect of maintaining the general integrity of the container holding a sample so that it may be properly disposed of without any contamination to the user. Notable is the clarity of the barrier coating as coated or applied on the container and its abrasion and scratch resistance.

The barrier coating used in accordance with this disclosure, may contain conventional additives and ingredients which do not adversely affect the properties of articles made therefrom.

- 5 The following examples are not limited to any specific embodiment of the invention, but are only exemplary.

EXAMPLE 1

10 **METHOD FOR COATING PLASTIC SUBSTRATES TUBES WITH MULTI-LAYER BARRIER COATING**

 A polyamine - polyepoxide coating was made by reacting 7 moles of tetra-ethylene pentamine with 6 moles of EPON 828 polyepoxide in 1-methoxy-2-propanol (Dowanol PM). To this mixture
15 was added 21g of diethanolamine, 36.1g of N, N, N¹, N¹ tetrakis, (oxiranylmethyl - 1, 3 - benzene dimethanamine, TETRAD X, Mitsubishi Gas Chemical Co.), 108.75 grams of additional Dowanol PM, 111.18g of 2-butoxyethanol and 6.7g of deionized water. This
20 mixture was applied to the substrate by dipping, spraying, or rolling the above described polyanine/polyepoxide mixture onto the substrate and baked for 15 - 20 minutes at 68°C.

 After aging for several days at ambient temperature, the
25 substrate coated with the polyanine/polyepoxide mixture was then cleaned with a mixture comprising equal parts of a micro detergent and de-ionized (DI) water solution. The substrate was rinsed thoroughly in DI water and allowed to air dry. The cleaned substrate was then stored in a vacuum oven at room temperature until it was to be coated.

30 The cleaned substrate was then attached to a holder which fits midway between the electrodes in the glass vacuum chamber. The chamber was closed and a mechanical pump was used to achieve a base pressure of 5 mTorr.

The electrode configuration is internally capacitively coupled with permanent magnets on the backside of the titanium electrodes. This special configuration provides the ability to confine the glow
 5 between the electrodes because of the increase in collision probability between electrons and reacting gas molecules. The net result of applying a magnetic field is similar to increasing the power applied to the electrodes, but without the disadvantages of higher bombardment energies and increased substrate heating. The use of magnetron
 10 discharge allows operation in the low pressure region and a substantial increase in polymer deposition rate.

The monomer which consists of a mixture of trimethylsilane (TMS) and oxygen was introduced through stainless steel tubing near
 15 the electrodes. The gases were mixed in the monomer inlet line before introduction into the chamber. Flow rates were manually controlled by stainless steel metering valves. A power supply operating at an audio frequency of 40 kHz was used to supply power to the electrodes. The system parameters used for thin film deposition of plasma polymerized
 20 TMS/O₂ on the polymer substrate were as follows:

25	Surface Pretreatment:	TMS Flow	=	0 sccm
		Base Pressure	=	5 mTorr
		Oxygen Flow	=	10 sccm
		System Pressure	=	140 mTorr
		Power	=	50 watts
		Time	=	2 minutes
30	Oxide Deposition:	TMS Flow	=	0.75 - 1.0 sccm
		Oxygen Flow	=	2.5 - 3.0 sccm
		System Pressure	=	90 - 100 mTorr
		Power	=	30 watts
		Deposition Time	=	5 minutes

After the thin film was deposited, the reactor was allowed to cool. The reactor was then opened, and the substrate was removed.

5 A protective topcoating of a water-based emulsion of PVDC copolymer was applied by dip coating and cured at 65° C for about 10 minutes to produce a final coating thickness averaging about 6 microns.

EXAMPLE 2

10 **COMPARISON OF SUBSTRATES WITH AND WITHOUT MULTI-LAYER BARRIER COATINGS**

All of the substrates prepared in accordance with Examples 1 and 2 above were evaluated for oxygen permeance (OTR) in the oxide
15 coatings as follows.

(i) Oxygen permeance (OTR):

Film or plaque samples were tested for oxygen permeance (OTR) using a MO CON Ox-TRAN 2/20 (sold by Modern Controls, Inc., 7500 Boone Avenue N., Minneapolis, MN 55428). A single
20 side of the film sample was exposed to 1 atm of 100% oxygen atmosphere. Oxygen permeating through the sample film was entrained in a nitrogen carrier gas stream on the opposite side of the film, and detected by a coulmetric sensor. An electrical signal was produced in proportion to the amount of oxygen permeating through
25 the sample. Samples were tested at 30°C and 0% relative humidity (R.H.). Samples were conditioned for 1 to 20 hours prior to determining oxygen permeance. The results are reported in Table 1 in units of cc/m²-atm-day.

30

Tube samples were tested for oxygen permeance (OTR) using a MOCON O_X-TRAN 1,000 (sold by Modern Controls, Inc., 7500 Boone Avenue N., Minneapolis, MN 55428). A package adapter was used for mounting the tubes in a manner that allowed the outside of the

5 tube to be immersed in a 100% O₂ atmosphere while the inside of tube is flushed with a nitrogen carrier gas. The tubes were then tested at 20°C and 50% R.H. The tubes were allowed to equilibrate for 2-14 days before a steady state permeability is determined. The results are reported in Table 1 in units of cc/m²-atm-day.

TABLE 1

Sample	Epoxide Coating	SiO _x Coating Method	PVDC Coating	Oxygen Transmission Rate (cc/m ² -atm-day) 30°C, 0% RH
PP tube, control	no	no	no	60-70
PP tube	no	yes	no	20-50
PP tube	yes	no	no	2.79
PP tube	yes	yes	no	0.58
PP tube	yes	yes	yes	0.15
PP tube	no	no	yes	15-30

Oxide Coatings = 1000 - 3000 Angstroms (as measured by Scanning Electron Microscope)

PP = polypropylene

tubes = nominal wall thickness of 40 mil

WHAT IS CLAIMED IS:

1. A sample assembly comprising:
a plastic container having an open end, a closed end, an inner surface and an outer surface; and
a multi-layer barrier coating associated over the outer surface of said container and extending over a major portion of said outer surface of said container, said coating having a first layer comprising an epoxide primer coating material, and a second layer on said first layer comprising a metal oxide.
2. The sample assembly of Claim 1 further comprising a third layer on said second layer comprising an organic material.
3. The assembly of Claim 1, further comprising a closure in said open end of said container whereby a container and closure interface is formed.
4. The assembly of Claim 3, wherein said plastic container is a tube and said closure is an elastomeric stopper.
5. The assembly of Claim 1, wherein said barrier coating extends substantially from said open end of said container to and over said closed end of said container.
6. The assembly of Claim 4, wherein said barrier coating extends from a portion of said elastomer stopper to a point adjacent said closed end of said container.
7. The assembly of Claim 3, wherein said tube is evacuated.
8. The assembly of Claim 6, wherein said multi-layer barrier coating includes registered tamper serrations adjacent to said container and said closure interface.

9 The assembly of Claim 1, wherein said second layer is aluminum oxide or silicon oxide based composition.

10 The assembly of Claim 9, wherein said second layer comprises silicon oxide.

11. The assembly of Claim 9, wherein said second layer is deposited by radio-frequency discharge, direct ion beam deposition, dual ion beam deposition, sputtering, plasma chemical vapor deposition or magnetically enhanced plasma systems.

12. The assembly of Claim 2, wherein said third layer is thermosetting epoxy, parylene polymer, vinylidene chloride-acrylonitrile-methyl methacrylate-methyl acrylate-acrylic acid polymer, or polyesters.

13. The assembly of Claim 2, wherein said second layer comprises silicon oxide and said third layer comprises polyvinylidene chloride.

14. The assembly of Claim 1, further comprising a multi-layer barrier coating over the inner surface of said container, having a first layer including an epoxide primer coating material, a second layer on said first layer of a metal oxide and a third layer of an organic material.

15. A multi-layer barrier coating comprising:

- a first layer comprising an epoxide material;
- a second layer on said first layer is silicon oxide;
- and a third layer on said second layer is polyvinylidene chloride.

16. The assembly of Claim 1, wherein said first layer is deposited on said outer surface of said container in a previously evacuated chamber comprising the following steps:

- (a) applying an uncured polyamine polyepoxide mixture onto the outer surface of said container; and
- (b) curing said mixture.

17. The assembly of Claim 16, wherein said second layer is deposited in said previously evacuated chamber onto said first layer by the following steps:

- (a) vaporizing an organosilicon component and admixing the volatilized organosilicon component with an oxidizer component and optionally an inert gas component to form a gas stream exterior to the chamber;
- (b) establishing a glow discharge plasma in the chamber from one or more of the gas stream components;
- (c) controllably flowing the gas stream into the plasma while confining at least a portion of the plasma therein; and
- (d) depositing a layer of silicon oxide adjacent said first layer.

18. The assembly of Claim 17, wherein said oxidizer component is oxygen nitrous oxide, carbon dioxide, air, or an inert compound.

19. The assembly of Claim 17, wherein the plastic substrate is electrically isolated from the chamber except for contact with the confined plasma.

20. The assembly of Claim 14, wherein said third layer is a parylene polymer.

21. The assembly of Claim 14, wherein said parylene polymer is parylene N, parylene C or parylene D.

22. A method of depositing a multilayer barrier coating on a plastic substrate in a previously evacuated chamber comprising:

- (a) applying an uncured polyamine polyepoxide mixture onto said plastic substrate;
- (b) curing said mixture;
- (c) vaporizing an organosilicon component and admixing the volatilized organosilicon component with an oxidizer component and optionally an inert gas component to form a gas stream exterior to the chamber;
- (d) establishing a glow discharge plasma in the chamber from one or more of the gas stream components;
- (e) controllably flowing the gas stream into the plasma while confining at least a portion of the plasma therein; and
- (f) depositing a second layer of silicon oxide adjacent said first layer.

23. The method of Claim 22 further comprising:

- (g) dip coating a third layer of PVDC onto said second layer.

24. The method of Claim 22 wherein said first layer is pretreated by oxygen plasma.