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(54) Title: PLASMA OR CVD PRE-TREATMENT FOR LUBRICATED PHARMACEUTICAL PACKAGE, COATING PROCESS AND APPARATUS

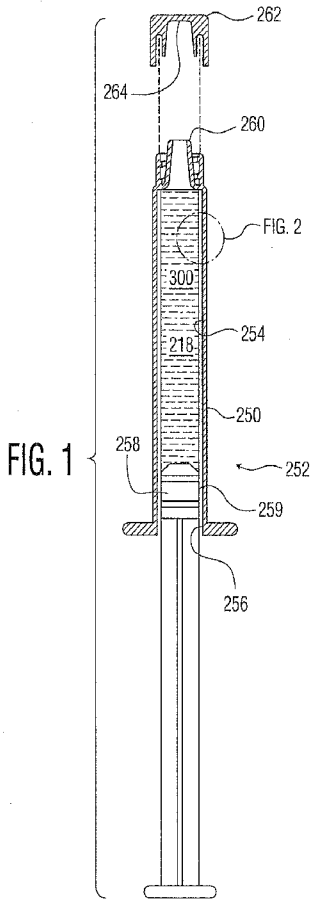

FIG. 1

(57) Abstract: A syringe comprising a wall having a generally cylindrical interior surface defining a lumen with a primer coating or layer between 1 and 1000 nm thick of SiOx Cy Hz, in which x is from about 0.5 to about 2.4, y is from about 0.6 to about 3, and z is from about 2 to about 9, on at least a portion of the interior surface, the primer coating or layer having an outside surface facing the interior surface of the barrel and an inside surface facing the lumen. A deposit of fluid lubricant on the inside surface of the primer coating or layer is further provided.

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PLASMA OR CVD PRE-TREATMENT FOR LUBRICATED PHARMACEUTICAL PACKAGE, COATING PROCESS AND APPARATUS

[0001] This application claims the priority of U.S. Provisional Appl. 61/771,644, filed March 1, 2013, all of which is incorporated by reference here to provide continuity of disclosure.

[0002] U.S. Provisional Serial Nos. 61/177,984 filed May 13, 2009; 61/222,727, filed July 2, 2009; 61/213,904, filed July 24, 2009; 61/234,505, filed Aug. 17, 2009; 61/261,321, filed November 14, 2009; 61/263,289, filed November 20, 2009; 61/285,813, filed December 11, 2009; 61/298,159, filed January 25, 2010; 61/299,888, filed January 29, 2010; 61/318,197, filed March 26, 2010; 61/333,625, filed May 11, 2010; 61/413,334, filed November 12, 2010; 61/636,377, filed April 20, 2012; 61/654,612, filed June 1, 2012; 12/779,007, filed May 12, 2010, now U.S. Pat. No. 7,985,188; International Application PCT/US11/36097, filed May 11, 2011; and U.S. Ser. No. 61/558,885, filed November 11, 2011; are all incorporated here by reference in their entirety.

[0003] Also incorporated by reference in their entirety are the following European patent applications: EP10162755.2 filed May 12, 2010; EP10162760.2 filed May 12, 2010; EP10162756.0 filed May 12, 2010; EP10162758.6 filed May 12, 2010; EP10162761.0 filed May 12, 2010; and EP10162757.8 filed May 12, 2010. These European patent applications describe apparatus, vessels, precursors, coatings or layers and methods (in particular coating methods and test methods for examining the coatings or layers) which can generally be used in performing the present invention, unless stated otherwise herein. They also describe SiO_x barrier coatings or layers to which reference is made herein.

FIELD OF THE INVENTION

[0004] The present invention relates to the technical field of lubricated and siliconized surfaces, for example interior surfaces of pharmaceutical packages or other vessels for storing or other contact with fluids. (A “deposit of lubricant” as defined in this specification also includes deposits of “lubricants” for non-lubricating uses, for example siliconization of a vessel wall to prevent adherence of a fluid stored in the vessel.)

[0005] The present invention also relates to a pharmaceutical package or other vessel and to a method for making a pharmaceutical package with a lubricated surface. The present invention also relates more generally to medical articles, including articles other than packages or vessels, for example catheters.

BACKGROUND OF THE INVENTION

[0006] In glass syringes and other pharmaceutical packages, silicone oil is typically used as a lubricant to allow the plunger tip to slide in the barrel, and/or to promote draining of the intended deliverable fluid from the syringe surfaces.

[0007] Glass pharmaceutical packages or other vessels are prone to breakage or degradation during manufacture, filling operations, shipping and use, which means that glass particulates may enter the drug. The presence of glass particles has led to many FDA Warning Letters and to product recalls.

[0008] Glass-forming processes do not yield the tight dimensional tolerances required for some of the newer auto-injectors and delivery systems. Glass is also more difficult and expensive to fabricate into syringes than injection molded plastics.

[0009] An important consideration regarding medical syringes is to ensure that the plunger can move at a constant speed and with a constant force when it is pressed into the barrel during use, with a low initiation or breakout force, F_i, and a low maintenance force, F_m. A similar consideration making lubrication desirable applies to vessels such as pharmaceutical vials which have to be closed by a closure, for example a plunger tip, septum or stopper, and to the septum or stopper itself, and more generally to any surface which desirably provides smooth operation of moving parts and/or is protectively coated.

[0010] One factor affecting the magnitude and aging of the breakout force is the surface composition and topology of the syringe. Specifically, the breakout force is lower for glass syringes than for plastic syringes due to the surface energy differences between glass and plastic (glass is a hydrophilic surface and plastic is a hydrophobic surface). PDMS is hydrophobic. It would be useful to provide a similar breakout force

profile on plastic and glass syringes, and for the effect of aging on the breakout force to be minimal.

SUMMARY OF THE INVENTION

[0011] A non-limiting aspect of the invention is a syringe comprising a wall, a primer coating, and a deposit of fluid lubricant.

[0012] The wall has a generally cylindrical interior surface defining a lumen and adapted to receive a plunger

[0013] The primer coating or layer is between 1 and 1000 nm thick. It comprises $SiO_xC_yH_z$, in which x is from about 0.5 to about 2.4 as measured by X-ray photoelectron spectroscopy (XPS), y is from about 0.6 to about 3 as measured by XPS, and z is from about 2 to about 9, on at least a portion of the interior surface. The primer coating or layer has an outside surface facing the interior surface of the barrel and an inside surface facing the lumen.

[0014] The deposit of fluid lubricant is deposited on the inside surface of the primer coating or layer.

[0015] The primer coating or layer improves the lubrication between the relatively sliding parts. More evenly distributed lubricant might be a factor in lowering the sliding friction and making the sliding friction more uniform. As another potential result, in a medical vessel coated on the interior wall with the primer coating or layer and a deposit of lubricant, the more evenly distributed lubricant can improve draining of the vessel. As a third potential result, the more evenly distributed lubricant can be used in a smaller quantity to obtain the same technical effect or advantage, thus potentially reducing the amount of lubricant available to mix with the contents of the vessel. Some potential examples of the lubricant mixing with the contents of the vessel are mechanical or chemical emulsification of the lubricant and a drug or other contents of the vessel.

[0016] Optionally, the primer coating or layer itself, without a deposit of lubricant, can improve draining of the vessel.

[0017] Optionally, a similar breakout force profile can be obtained on plastic and glass syringes if the plastic syringes are treated as described in this specification.

[0018] Another non-limiting aspect of the invention is a method of making a syringe as described above.

[0019] A syringe is provided having a surface to be lubricated.

[0020] A primer coating or layer of SiO_xC_y or SiN_xC_y, in which x is from about 0.5 to about 2.4 and y is from about 0.6 to about 3, is applied to the surface. The primer coating or layer can be applied by chemical vapor deposition of a polysiloxane or polysilazane precursor, typically in the presence of oxygen. The primer coating or layer is applied either directly to the syringe surface or with one or more intervening coatings or layers between the primer coating or layer and the syringe surface. The primer coating or layer has a first primer surface facing away from the syringe surface and a second primer surface facing the syringe surface.

[0021] A deposit of lubricant is applied to the first primer surface.

[0022] Another non-limiting aspect of the invention is a prefilled syringe comprising a syringe as described above containing a fluid to be dispensed and closed with a plunger. The fluid to be dispensed can be any of the inhalation anesthetics, injectable drugs, liquid drugs (non-injectable), drug classes, diagnostic test materials, or other materials recited in the specification or claims.

[0023] Many other embodiments of the present invention are expressly contemplated, as recited in the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] FIG. 1 is an exploded longitudinal view, partly in section, of a syringe, plunger, and cap assembly according to the present invention.

[0025] FIG. 2 is a detail view of FIG. 1 showing the coatings on the wall of the syringe barrel.

[0026] FIG. 3 is a plot of F_i, the force required to initiate movement of a plunger within the barrel of a syringe, for syringes having a treated plunger tip.

[0027] FIG. 4 is another plot of F_i, the force required to initiate movement of a plunger within the barrel of a syringe, for syringes having a treated plunger tip.

[0028] FIG. 5 is a plot showing the aging effect on initiation force for SiO_x bilayer syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0029] FIG. 6 is a plot showing the aging effect on initiation force for Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0030] FIG. 7 is a plot showing the aging effect on Maximum maintenance force for SiO_x bilayer syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, and Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, each under wet vs. dry storage.

[0031] FIG. 8 is a plot showing the aging effect on initiation force for SiO_x bilayer syringes having a 6.50 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0032] FIG. 9 is a plot comparing initiation force for SiO_x bilayer syringes 6.35 mm ID vs. 6.50 mm ID, lubricated with 1,000 cSt PDMS, dry storage.

[0033] FIG. 10 is a plot comparing initiation force for SiO_x bilayer syringes 6.50mm ID to Hypak® glass syringes having a 6.35 mm ID, both lubricated with 1,000 cSt PDMS, dry storage.

[0034] FIG.11 is a plot comparing initiation force for SiO_x bilayer syringes 6.50mm ID to Hypak® glass syringes having a 6.35 mm ID, both lubricated with 1,000 cSt PDMS, wet storage.

[0035] FIG. 12 is a plot showing the aging effect on maximum maintenance force for SiO_x bilayer syringes having a 6.50 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0036] FIG. 13 is a plot showing the aging effect on initiation force for SiO_x bilayer syringes having a 6.35 mm ID, lubricated with 12,500 cSt PDMS, wet vs. dry storage.

[0037] FIG. 14 is a plot showing the aging effect on initiation force for Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0038] FIG. 15 is a plot comparing initiation force for SiO_x bilayer syringes 6.35 mm ID lubricated with 1,000 cSt. vs.12,500 cSt. PDMS, dry storage.

[0039] FIG. 16 is a plot comparing initiation force for SiO_x bilayer syringes 6.35 mm ID lubricated with 1,000 cSt vs. 12,500 cSt, wet storage.

[0040] FIG. 17 is a plot showing the aging effect on Maximum maintenance force for SiO_x bilayer syringes having a 6.35 mm ID, lubricated with 12,500 cSt PDMS, and Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0041] FIG. 18 is a plot showing the aging effect on initiation force for trilayer syringes, 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0042] FIG. 19 is a plot showing the aging effect on initiation force for trilayer syringes, 6.50 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0043] FIG. 20 is a plot showing the aging effect on initiation force for trilayer syringes, 6.65 mm ID, lubricated with 1,000 cSt PDMS, wet vs. dry storage.

[0044] FIG. 21 is a plot comparing initiation force between SiO_x bilayer and trilayer syringes, 6.35 mm ID, lubricated with 1,000 cSt PDMS, dry storage.

[0045] FIG. 22 is a plot comparing initiation force between SiO_x bilayer and trilayer syringes, 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet storage.

[0046] FIG. 23 is a plot comparing initiation force between SiO_x bilayer and trilayer syringes 6.50 mm ID, lubricated with 1,000 cSt PDMS, dry storage.

[0047] FIG. 24 is a plot comparing initiation force Between SiO_x bilayer and trilayer syringes 6.50 mm ID, lubricated with 1,000 cSt PDMS, wet storage.

[0048] FIG. 25 is a plot comparing initiation force for trilayer syringes and Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, dry storage.

[0049] FIG. 26 is a plot comparing initiation force for trilayer syringes and Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet storage.

[0050] FIG. 27 is a plot comparing aging effect on Maximum maintenance force for trilayer syringes, ID 6.35, 6.5, or 6.65, vs. BD Hypak® glass syringes having a 6.35 mm ID, all lubricated with 1,000 cSt PDMS, wet storage.

[0051] FIG. 28 is a plot comparing silicon dissolution over time for

- bilayer syringes, ID 6.35 and 6.5 mm, lubricated with 1,000 cSt. PDMS, wet storage;
- bilayer syringes, ID 6.35 mm, lubricated with 12,000 cSt. PDMS, wet storage;
- trilayer syringes, ID 6.35, 6.5, or 6.65 mm, lubricated with 1,000 cSt PDMS, wet storage.

[0052] FIG. 29 is a plot comparing silicon dissolution over Time for BD Hypak® glass syringes having a 6.35 mm ID, lubricated with 1,000 cSt PDMS, wet storage.

[0053] The following reference characters are used in the drawing figures:

62	Data points, group 1A
64	Data points, group 1B
66	Data points, group 1C
68	Data points, group 1D
70	Data points, group 2A
72	Data points, group 2B
74	Data points, group 3A
76	Data points, group 3B
78	Data points, group 3C
80	Data points, group 3D
82	Data points, group 4A
84	Data points, group 4B
86	Data points, group 4C
88	Data points, group 4D
90	Data points, group 4E
92	Data points, group 4F
94	F_i, FIG. 30
96	F_m, FIG. 30
98	CCI failure rate, FIG. 30
214	Wall
216	Exterior surface (of 241)
218	Fluid
250	Syringe barrel
252	Syringe
254	Inner or interior surface (of 250)
256	Back end (of 250)
258	Plunger (of 252) (relatively sliding part)
259	Outer sliding surface
260	Front end (of 250)
262	Cap
264	Inner or interior surface (of 262)
266	Adhesion layer
286	Primer coating or layer
287	Fluid lubricant
288	Barrier coating or layer
300	Lumen (of 250)
650	Exemplary data point, COP syringe without plasma treatment (comparative example)
652	Exemplary data point, COP syringe with PECVD plasma treatment applying SiO_x barrier layer and SiO_xC_y pH protective layer (inventive example)
654	Exemplary data point, COP syringe with PECVD plasma treatment applying SiO_x barrier layer as the outer layer (inventive example)
656	Exemplary data point, glass syringe (comparative example)
658	Exemplary data point, glass syringe (comparative example)
660	Exemplary data point, plasma treatment without organosilicon precursor (inventive example)

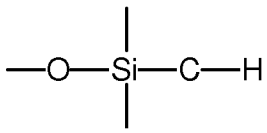
DEFINITION SECTION

[0054] In the context of the present invention, the following definitions and abbreviations are used:

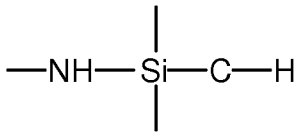
[0055] The term “at least” in the context of the present invention means “equal or more” than the integer following the term. The word “comprising” does not exclude other elements or steps, and the indefinite article “a” or “an” does not exclude a plurality unless indicated otherwise. Whenever a parameter range is indicated, it is intended to disclose the parameter values given as limits of the range and all values of the parameter falling within said range.

[0056] “First” and “second” or similar references to, for example, deposits of lubricant, processing stations or processing devices refer to the minimum number of deposits, processing stations or devices that are present, but do not necessarily represent the order or total number of deposits, processing stations and devices or require additional deposits, processing stations and devices beyond the stated number. These terms do not limit the number of processing stations or the particular processing carried out at the respective stations.

[0057] For purposes of the present invention, an “organosilicon precursor” is a compound having at least one of the linkages:



or



which is a tetravalent silicon atom connected to an oxygen or nitrogen atom and an organic carbon atom (an organic carbon atom being a carbon atom bonded to at least one hydrogen atom). A volatile organosilicon precursor, defined as such a precursor that can be supplied as a vapor in a PECVD apparatus, is an optional organosilicon

precursor. Optionally, the organosilicon precursor is selected from the group consisting of a linear siloxane, a monocyclic siloxane, a polycyclic siloxane, a polysilsesquioxane, an alkyl trimethoxysilane, linear silazane, a monocyclic silazane, a polycyclic silazane, or a combination of any two or more of these precursors, and preferably comprises octamethylenecyclotetrasiloxane (OMCTS), tetramethyldisiloxane (TMDSO), hexamethyldisiloxane (HMDSO), or a combination of two or more of these precursors.

[0058] The feed amounts of PECVD precursors, gaseous reactant or process gases, and carrier gas are sometimes expressed in "standard volumes" in the specification and claims. The standard volume of a charge or other fixed amount of gas is the volume the fixed amount of the gas would occupy at a standard temperature and pressure (without regard to the actual temperature and pressure of delivery). Standard volumes can be measured using different units of volume, and still be within the scope of the present disclosure and claims. For example, the same fixed amount of gas could be expressed as the number of standard cubic centimeters, the number of standard cubic meters, or the number of standard cubic feet. Standard volumes can also be defined using different standard temperatures and pressures, and still be within the scope of the present disclosure and claims. For example, the standard temperature might be 0°C and the standard pressure might be 760 Torr (as is conventional), or the standard temperature might be 20°C and the standard pressure might be 1 Torr. But whatever standard is used in a given case, when comparing relative amounts of two or more different gases without specifying particular parameters, the same units of volume, standard temperature, and standard pressure are to be used relative to each gas, unless otherwise indicated.

[0059] The corresponding feed rates of PECVD precursors, gaseous reactant or process gases, and carrier gas are expressed in standard volumes per unit of time in the specification. For example, in the working examples the flow rates are expressed as standard cubic centimeters per minute, abbreviated as sccm. As with the other parameters, other units of time can be used, such as seconds or hours, but consistent parameters are to be used when comparing the flow rates of two or more gases, unless otherwise indicated.

[0060] The present syringes optionally can be used as pharmaceutical packages or other vessels in which the lumen has a void volume of from 0.5 to 50 mL, optionally from 1 to 10 mL, optionally from 0.5 to 5 mL, optionally from 1 to 3 mL. The substrate surface can be part or all of the inner or interior surface of a vessel having at least one opening and an inner or interior surface.

[0061] A "hydrophobic layer" in the context of the present invention means that the coating or layer lowers the wetting tension of a surface coated with the coating or layer, compared to the corresponding uncoated surface. Hydrophobicity is thus a function of both the uncoated substrate and the coating or layer. The same applies with appropriate alterations for other contexts wherein the term "hydrophobic" is used. The term "hydrophilic" means the opposite, i.e. that the wetting tension is increased compared to reference sample. The present hydrophobic layers are primarily defined by their hydrophobicity and the process conditions providing hydrophobicity

[0062] The values of w, x, y, and z as applicable to the empirical composition $Si_wO_xC_yH_z$ throughout this specification should be understood as ratios or an empirical formula (for example for a coating or layer), rather than as a limit on the number or type of atoms in a molecule. For example, octamethylcyclotetrasiloxane, which has the molecular composition $Si_4O_4C_8H_{24}$, can be described by the following empirical formula, arrived at by dividing each of w, x, y, and z in the molecular formula by 4, the largest common factor: $Si_1O_1C_2H_6$. The values of w, x, y, and z are also not limited to integers. For example, (acyclic) octamethyltrisiloxane, molecular composition $Si_3O_2C_8H_{24}$, is reducible to $Si_1O_{0.67}C_{2.67}H_8$. Also, although $SiO_xC_yH_z$ is described as equivalent to SiO_xC_y, it is not necessary to show the presence of hydrogen in any proportion to show the presence of SiO_xC_y.

[0063] "Wetting tension" is a specific measure for the hydrophobicity or hydrophilicity of a surface. An optional wetting tension measurement method in the context of the present invention is ASTM D 2578 or a modification of the method described in ASTM D 2578. This method uses standard wetting tension solutions (called dyne solutions) to determine the solution that comes nearest to wetting a plastic film surface for exactly two seconds. This is the film's wetting tension. The procedure

utilized is varied herein from ASTM D 2578 in that the substrates are not flat plastic films, but are tubes made according to the Protocol for Forming PET Tube and (except for controls) coated according to the Protocol for coating Tube Interior with Hydrophobic Coating or Layer (see Example 9 of EP2251671 A2).

[0064] A "primer coating or layer" according to the present invention is a coating or layer which is more receptive than the uncoated surface to a deposit of lubricant, The deposit of lubricant reduces the frictional resistance of the coated surface in comparison to a reference surface that is uncoated. The primer coating or layer optionally can have a composition according to the empirical composition SiO_x, or according to the empirical composition $Si_wO_xC_yH_z$, (or its equivalent SiO_xC_y) as defined herein, which omits hydrogen because it is not measured by the XPS (X-ray photoelectron spectroscopy) method used in this specification to define the composition of a plasma treated surface or a CVD or chemical vapor deposition coating or layer. The primer coating or layer generally has an atomic ratio $Si_wO_xC_y$ (or its equivalent SiO_xC_y) wherein w is 1, x is from about 0.5 to about 2.4, y is from about 0.6 to about 3, as measured by XPS.

[0065] Where it is desired to determine the proportion of hydrogen, and thus the value of z in $Si_wO_xC_yH_z$, this can be done using well-known techniques such as Rutherford backscattering (RBS) or hydrogen forward scattering (HFS).

[0066] Typically, expressed as the formula $Si_wO_xC_y$, the atomic ratios of Si, O, and C in the "primer coating or layer" are, as several options:

Si 100 : O 50–150 : C 90-200 (i.e. w = 1, x = 0.5 to 1.5, y = 0.9 to 2);
Si 100 : O 70–130 : C 90-200 (i.e. w = 1, x = 0.7 to 1.3, y = 0.9 to 2)
Si 100 : O 80–120 : C 90-150 (i.e. w = 1, x = 0.8 to 1.2, y = 0.9 to 1.5)
Si 100 : O 90-120 : C 90-140 (i.e. w = 1, x = 0.9 to 1.2, y = 0.9 to 1.4), or
Si 100 : O 92-107 : C 116-133 (i.e. w = 1, x = 0.92 to 1.07, y = 1.16 to 1.33)

[0067] The atomic ratio can be determined by XPS. Taking into account the H atoms, which are not measured by XPS, the coating or layer may thus in one aspect have the formula $Si_wO_xC_yH_z$ (or its equivalent SiO_xC_y), for example where w is 1. X is from about 0.5 to about 2.4, optionally between 0.5 and 1.5, preferably between 0.7 and 1.3, more preferably between 0.8 and 1.2, still more preferably between 0.9 and 1.2. Y

is from about 0.6 to about 3, optionally between 0.9 and 2, preferably between 0.9 and 1.5, more preferably between 0.9 and 1.4. Z is from about 2 to about 9. Typically, such coating or layer would hence contain 36% to 41% carbon normalized to 100% carbon plus oxygen plus silicon.

[0068] "Frictional resistance" can be static frictional resistance and/or kinetic frictional resistance.

[0069] One of the optional embodiments of the present invention is a syringe part, for example a syringe or plunger tip, coated with a deposit of lubricant on a primer coating or layer. In this contemplated embodiment, the relevant static frictional resistance in the context of the present invention is the breakout force as defined herein, and the relevant kinetic frictional resistance in the context of the present invention is the plunger sliding force as defined herein. For example, the plunger sliding force as defined and determined herein is suitable to determine the presence or absence and the lubricity and/or protective characteristics of a deposit of lubricant on a primer coating or layer in the context of the present invention whenever the coating or layer is applied to any syringe or syringe part, for example to the inner wall of a syringe. The breakout force is of particular relevance for evaluation of the coating or layer effect on a prefilled syringe, i.e. a syringe which is filled after coating and can be stored for some time, for example several months or even years, before the plunger tip is moved again (has to be "broken out").

[0070] The "plunger sliding force" (synonym to "glide force," "maintenance force", or F_m, also used in this description) in the context of the present invention is the force required to maintain movement of a plunger tip in a syringe, for example during aspiration or dispense. It can advantageously be determined using the ISO 7886-1:1993 test described herein and known in the art. A synonym for "plunger sliding force" often used in the art is "plunger force" or "pushing force".

[0071] The "plunger breakout force" (synonym to "breakout force", "break loose force", "initiation force", F_i, also used in this description) in the context of the present invention is the initial force required to move the plunger tip in a syringe, for example in a prefilled syringe.

[0072] Both "plunger sliding force" and "plunger breakout force" and methods for their measurement are described in more detail in subsequent parts of this description. These two forces can be expressed in N, lbs or kg. These units correlate as follows: 1N = 0.102 kg = 0.2248 lbs (pounds).

[0073] Sliding force and breakout force are sometimes used herein to describe the forces required to advance a stopper or other closure into a pharmaceutical package or other vessel, such as a medical sample tube or a vial, to seat the stopper in a vessel to close the vessel. Its use is analogous to use in the context of a syringe and its plunger tip, and the measurement of these forces for a vessel and its closure are contemplated to be analogous to the measurement of these forces for a syringe, except that at least in most cases no liquid is ejected from a vessel when advancing the closure to a seated position.

[0074] "Slidably" means that the plunger tip, closure, or other removable part is permitted to slide in a syringe or other vessel.

DETAILED DESCRIPTION

[0075] The present invention will now be described more fully, with reference to the accompanying drawings, in which several embodiments are shown. This invention can, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth here. Rather, these embodiments are examples of the invention, which has the full scope indicated by the language of the claims. Like numbers refer to like or corresponding elements throughout. The following disclosure relates to all embodiments unless specifically limited to a certain embodiment.

[0076] Referring to FIGS. 1 and 2 showing an embodiment, a syringe 252 comprises a syringe barrel 250 having a PECVD treated generally cylindrical interior surface 254 defining an inner sliding surface; and a deposit of fluid lubricant 287 on the PECVD treated surface 254. The syringe barrel optionally is made of injection molded material, for example cyclic olefin polymer (COP).

[0077] The syringe as illustrated includes a plunger 258 having an outer sliding surface 259 configured to slide within the lumen 300 along the inner sliding surface 254. Optionally, the outer sliding surface 259 can be a PECVD treated surface as well.

[0078] The term "syringe," as used here, is broadly defined to include cartridges, injection "pens," and other types of barrels or reservoirs adapted to be assembled with one or more other components to provide a functional syringe. "Syringe" is also broadly defined to include related articles such as auto-injectors, which provide a mechanism for dispensing the contents.

[0079] Optionally, the syringe, in particular a surface of a syringe such as the interior surface 254 to be lubricated, comprises a first deposit of lubricant 287 applied to the primer surface.

[0080] Optionally for any of the embodiments, at least a portion of the wall 214 of the vessel 250 comprises or consists essentially of a polymer, for example a polyolefin (for example a cyclic olefin polymer, a cyclic olefin copolymer, or polypropylene), a polyester, for example polyethylene terephthalate, polyethylene naphthalate, a polycarbonate, or any combination or copolymer of any of these. Specific contemplated wall materials include COC (cyclic olefin copolymer), COP (cyclic olefin polymer), PET (polyethylene terephthalate), polypropylene (PP), or a combination of two or more of these. Optionally, at least a portion of the wall 214 of the vessel 250 comprises or consists essentially of glass, for example borosilicate glass.

[0081] The plunger can be made of a variety of materials. For example, at least a portion of the plunger can be made of chlorobutyl rubber, bromobutyl rubber, silicone rubber, or a combination of any two or none or these.

[0082] Optionally, the outer diameter of the plunger when unconstrained by the syringe barrel is from about 0.05 mm to about 0.3 mm greater, preferably from 0.1 to about 0.3 mm, greater, more preferably from 0.15 mm to 0.25 mm greater, still more preferably about 0.2 mm greater than the average inner diameter of the interior surface.

[0083] Optionally, the PECVD treated surface comprises a primer coating or layer 286 of SiO_xC_y, in which x is from about 0.5 to about 2.4 and y is from about 0.6 to about

3. Optionally, x is between 0.5 and 1.5 and y is between 0.9 and 2. Optionally, x is between 0.7 and 1.3 and y is between 0.9 and 2. Optionally, x is between 0.8 and 1.2 and y is between 0.9 and 1.5. Optionally, x is between 0.9 and 1.2 and y is between 0.9 and 1.4. Optionally, x is between 0.92 and 1.07 and y is between 1.16 and 1.33.

[0084] As another option, the PECVD treated surface comprises a primer coating or layer 286 of SiO_x, in which x is from 1.5 to 2.9.

[0085] Optionally, the primer coating or layer 286 is between 10 and 1000 nm thick. Optionally, the primer coating or layer is between 10 and 1000 nm thick. Optionally, the primer coating or layer is between 50 and 800 nm thick. Optionally, the primer coating or layer is between 100 and 700 nm thick. Optionally, the primer coating or layer is between 300 and 600 nm thick.

[0086] Optionally, the primer coating or layer 286 contacting the fluid is between 10 and 1000 nm thick two years after the article is assembled. Optionally, the primer coating or layer contacting the fluid is between 20 and 700 nm thick two years after the article is assembled. Optionally, the primer coating or layer contacting the fluid is between 50 and 500 nm thick two years after the article is assembled. Optionally, the primer coating or layer contacting the fluid is between 100 and 400 nm thick two years after the article is assembled. Optionally, the primer coating or layer contacting the fluid is between 150 and 300 nm thick two years after the article is assembled.

[0087] Optionally, the fluid removes the primer coating or layer at a rate of 1 nm or less of primer coating or layer thickness per 44 hours of contact with the fluid. Optionally, the fluid removes the primer coating or layer at a rate of 1 nm or less of primer coating or layer thickness per 88 hours of contact with the fluid. Optionally, the fluid removes the primer coating or layer at a rate of 1 nm or less of primer coating or layer thickness per 175 hours of contact with the fluid. Optionally, the fluid removes the primer coating or layer at a rate of 1 nm or less of primer coating or layer thickness per 250 hours of contact with the fluid. Optionally, the fluid removes the primer coating or layer at a rate of 1 nm or less of primer coating or layer thickness per 350 hours of contact with the fluid.

[0088] Optionally, the primer has a contact angle (with distilled water) of from 70° to 130°. Optionally, the interior surface of the primer has a contact angle (with distilled water) of from 90° to 110°. Optionally, the interior surface of the primer has a contact angle (with distilled water) of from 80° to 120°.

[0089] Optionally, the fluid lubricant 287 comprises polydimethylsiloxane. For several examples, it can comprise non-reactive silicone fluid, nonreactive silicone emulsion, curable silicone fluid, or a combination of two or more of these.

[0090] A deposit of fluid lubricant 287 can be formed on the CVD treated surface 254 in any convenient manner, such as by spraying a liquid lubricant or by applying it using an applicator. Optionally, the lubricant has a molecular weight of from about 1900 to about 37,000. Optionally, the lubricant has a viscosity of from about 20 CSt. to about 13,000 CSt., alternatively from 500 to 30,000 cSt, preferably from 1000 to 25,000 cSt, more preferably from 5,000 to 20,000 cSt, still more preferably from 10,000 to 15,000 cSt, optionally about 12,500 cSt.

[0091] Optionally, the breakout force, F_i, of the plunger is between 0.5 and 15 N, alternatively between 1 and 10 N, alternatively between 5 and 15 N, after a park time of 3 days, alternatively 10 days, alternatively 30 days, alternatively 3 months, alternatively 6 months, alternatively 9 months, alternatively 12 months, alternatively 15 months, alternatively 18 months, alternatively two years.

[0092] Optionally, the maintenance force, F_m, of the plunger is between 0.5 and 15 N, alternatively between 1 and 10 N, alternatively between 5 and 15 N, after a park time of 3 days, alternatively 10 days, alternatively 30 days, alternatively 3 months, alternatively 6 months, alternatively 9 months, alternatively 12 months, alternatively 15 months, alternatively 18 months, alternatively two years.

[0093] Optionally, the lubricant has a contact angle (with distilled water) of from 90° to 150°.203. Optionally, the lubricant has a contact angle (with distilled water) of from 90° to 110°. Optionally, the lubricant has a contact angle (with distilled water) of from 90° to 120°. Optionally, the lubricant has a contact angle (with distilled water) of from 0° to 35° greater than the contact angle (with distilled water) of the primer coating or layer.

[0094] Optionally, the deposit of lubricant on the primer coating or layer is effective to provide a lower frictional resistance than the uncoated syringe surface between the syringe surface and a relatively sliding part at least one year after the syringe is assembled with a plunger. the frictional resistance is reduced by at least 25% in comparison to the uncoated article surface. Optionally, the frictional resistance is reduced by at least 45% in comparison to the uncoated article surface. Optionally, the frictional resistance is reduced by at least 60% in comparison to the uncoated article surface. Optionally, the deposit of lubricant is effective to reduce the frictional resistance between a portion of the article surface contacted by the fluid and a relatively sliding part after the article is assembled. Optionally, the deposit of lubricant is effective to reduce the frictional resistance between the article surface and a relatively sliding part at least one year after the article is assembled. Optionally, the deposit of lubricant is effective to reduce the frictional resistance between the article surface and a relatively sliding part at least eighteen months after the article is assembled. Optionally, the deposit of lubricant is effective to reduce the frictional resistance between the article surface and a relatively sliding part at least two years after the article is assembled.

[0095] Further PECVD coatings or layers are contemplated, in addition to the primer coating or layer 286.

[0096] Optionally, a barrier coating or layer 288 can be provided between the primer coating or layer 286 and the syringe surface 254. The barrier coating or layer 288 can be made at least in part of SiO_x, wherein x is from 1.5 to 2.9, from 2 to 1000 nm thick. The barrier coating or layer of SiOx has an interior surface facing the lumen and an outer surface facing the wall inner or article surface 254. The barrier coating or layer 288 is effective to reduce the ingress of atmospheric gas into the lumen 212, compared to an uncoated container otherwise the same as the pharmaceutical package or other vessel 210.

[0097] As another option, an adhesion layer 266 can be provided between the barrier coating or layer 288 and the syringe surface 254.

[0098] A method of making a syringe as previously described is also contemplated. To carry out the method, a syringe is provided having a surface to be

lubricated. A primer coating or layer of SiO_xC_y or SiN_xC_y is applied to the surface; in these formulas x can be from about 0.5 to about 2.4 and y can be from about 0.6 to about 3. The primer coating or layer can be applied by chemical vapor deposition of a polysiloxane or polysilazane precursor, in the presence of oxygen. The primer coating or layer can be applied either directly to the syringe surface or with one or more intervening coatings or layers between the primer coating or layer and the syringe surface.

[0099] The primer coating or layer can have a first primer surface facing away from the syringe surface and a second primer surface facing the syringe surface. A first deposit of lubricant can be adhered to the first primer surface.

[00100] Optionally, a fluid can be placed in the lumen via the opening, optionally for extended storage, and the opening can be closed with a closure such as the plunger 258. The fluid can be an aqueous liquid, for example a drug. The drug can be a parenteral drug, as one example. Other examples of suitable fluids are a food, a nutritional supplement, an inhalation anesthetic, or a diagnostic test material.

[00101] The fluid can be a member selected from the group consisting of:

INHALATION ANESTHETICS

Aliflurane
Chloroform
Cyclopropane
Desflurane (Suprane)
Diethyl Ether
Enflurane (Ethrane)
Ethyl Chloride
Ethylene
Halothane (Fluothane)
Isoflurane (Forane, Isoflo)
Isopropenyl vinyl ether
Methoxyflurane

methoxyflurane,

Methoxypropane

Nitrous Oxide

Roflurane

Sevoflurane (Sevorane, Ultane, Sevoflo)

Teflurane

Trichloroethylene

Vinyl Ether

Xenon

INJECTABLE DRUGS

Ablavar (Gadofosveset Trisodium Injection)

Abarelix Depot

Abobotulinumtoxin A Injection (Dysport)

ABT-263

ABT-869

ABX-EFG

Accretropin (Somatropin Injection)

Acetadote (Acetylcysteine Injection)

Acetazolamide Injection (Acetazolamide Injection)

Acetylcysteine Injection (Acetadote)

Actemra (Tocilizumab Injection)

Acthrel (Corticorelin Ovine Triflutate for Injection)

Actummune

Activase

Acyclovir for Injection (Zovirax Injection)

Adacel

Adalimumab

Adenoscan (Adenosine Injection)

Adenosine Injection (Adenoscan)

Adrenaclick

AdreView (Iobenguane I 123 Injection for Intravenous Use)

Afluria
Ak-Fluor (Fluorescein Injection)
Aldurazyme (Laronidase)
Alglucerase Injection (Ceredase)
Alkeran Injection (Melphalan Hcl Injection)
Allopurinol Sodium for Injection (Aloprim)
Aloprim (Allopurinol Sodium for Injection)
Alprostadil
Alsuma (Sumatriptan Injection)
ALTU-238
Amino Acid Injections
Aminosyn
Apidra
Apremilast
Alprostadil Dual Chamber System for Injection (Caverject Impulse)
AMG 009
AMG 076
AMG 102
AMG 108
AMG 114
AMG 162
AMG 220
AMG 221
AMG 222
AMG 223
AMG 317
AMG 379
AMG 386
AMG 403
AMG 477
AMG 479

AMG 517

AMG 531

AMG 557

AMG 623

AMG 655

AMG 706

AMG 714

AMG 745

AMG 785

AMG 811

AMG 827

AMG 837

AMG 853

AMG 951

Amiodarone HCl Injection (Amiodarone HCl Injection)

Amobarbital Sodium Injection (Amytal Sodium)

Amytal Sodium (Amobarbital Sodium Injection)

Anakinra

Anti-Abeta

Anti-Beta7

Anti-Beta20

Anti-CD4

Anti-CD20

Anti-CD40

Anti-IFNalpha

Anti-IL13

Anti-OX40L

Anti-oxLDS

Anti-NGF

Anti-NRP1

Arixtra

Amphadase (Hyaluronidase Inj)

Ammonul (Sodium Phenylacetate and Sodium Benzoate Injection)

Anaprox

Anzemet Injection (Dolasetron Mesylate Injection)

Apidra (Insulin Glulisine [rDNA origin] Inj)

Apomab

Aranesp (darbepoetin alfa)

Argatroban (Argatroban Injection)

Arginine Hydrochloride Injection (R-Gene 10)

Aristocort

Aristospan

Arsenic Trioxide Injection (Trisenox)

Articane HCl and Epinephrine Injection (Septocaine)

Arzerra (Ofatumumab Injection)

Asclera (Polidocanol Injection)

Ataluren

Ataluren-DMD

Atenolol Inj (Tenormin I.V. Injection)

Atracurium Besylate Injection (Atracurium Besylate Injection)

Avastin

Azactam Injection (Aztreonam Injection)

Azithromycin (Zithromax Injection)

Aztreonam Injection (Azactam Injection)

Baclofen Injection (Lioresal Intrathecal)

Bacteriostatic Water (Bacteriostatic Water for Injection)

Baclofen Injection (Lioresal Intrathecal)

Bal in Oil Ampules (Dimercarprol Injection)

BayHepB

BayTet

Benadryl

Bendamustine Hydrochloride Injection (Treanda)

Benztropine Mesylate Injection (Cogentin)

Betamethasone Injectable Suspension (Celestone Soluspan)

Bexxar

Bicillin C-R 900/300 (Penicillin G Benzathine and Penicillin G Procaine Injection)

Blenoxane (Bleomycin Sulfate Injection)

Bleomycin Sulfate Injection (Blenoxane)

Boniva Injection (Ibandronate Sodium Injection)

Botox Cosmetic (OnabotulinumtoxinA for Injection)

BR3-FC

Bravelle (Urofollitropin Injection)

Bretylium (Bretylium Tosylate Injection)

Brevital Sodium (Methohexital Sodium for Injection)

Brethine

Briobacept

BTT-1023

Bupivacaine HCl

Byetta

Ca-DTPA (Pentetate Calcium Trisodium Inj)

Cabazitaxel Injection (Jevtana)

Caffeine Alkaloid (Caffeine and Sodium Benzoate Injection)

Calcijex Injection (Calcitrol)

Calcitrol (Calcijex Injection)

Calcium Chloride (Calcium Chloride Injection 10%)

Calcium Disodium Versenate (Edetate Calcium Disodium Injection)

Campath (Altemtuzumab)

Camptosar Injection (Irinotecan Hydrochloride)

Canakinumab Injection (Ilaris)

Capastat Sulfate (Capreomycin for Injection)

Capreomycin for Injection (Capastat Sulfate)

Cardiolite (Prep kit for Technetium Tc99 Sestamibi for Injection)

Carticel

Cathflo

Cefazolin and Dextrose for Injection (Cefazolin Injection)

Cefepime Hydrochloride

Cefotaxime

Ceftriaxone

Cerezyme

Carnitor Injection

Caverject

Celestone Soluspan

Celsior

Cerebyx (Fosphenytoin Sodium Injection)

Ceredase (Alglucerase Injection)

Ceretec (Technetium Tc99m Exametazime Injection)

Certolizumab

CF-101

Chloramphenicol Sodium Succinate (Chloramphenicol Sodium Succinate Injection)

Chloramphenicol Sodium Succinate Injection (Chloramphenicol Sodium Succinate)

Cholestagel (Colesevelam HCL)

Choriogonadotropin Alfa Injection (Ovidrel)

Cimzia

Cisplatin (Cisplatin Injection)

Clolar (Clofarabine Injection)

Clomiphine Citrate

Clonidine Injection (Duraclon)

Cogentin (Benztropine Mesylate Injection)

Colistimethate Injection (Coly-Mycin M)

Coly-Mycin M (Colistimethate Injection)

Compath

Conivaptan Hcl Injection (Vaprisol)

Conjugated Estrogens for Injection (Premarin Injection)

Copaxone

Corticorelin Ovine Triflutate for Injection (Acthrel)

Corvert (Ibutilide Fumarate Injection)

Cubicin (Daptomycin Injection)

CF-101

Cyanokit (Hydroxocobalamin for Injection)

Cytarabine Liposome Injection (DepoCyt)

Cyanocobalamin

Cytovene (ganciclovir)

D.H.E. 45

Dacetuzumab

Dacogen (Decitabine Injection)

Dalteparin

Dantrium IV (Dantrolene Sodium for Injection)

Dantrolene Sodium for Injection (Dantrium IV)

Daptomycin Injection (Cubicin)

Darbepoietin Alfa

DDAVP Injection (Desmopressin Acetate Injection)

Decavax

Decitabine Injection (Dacogen)

Dehydrated Alcohol (Dehydrated Alcohol Injection)

Denosumab Injection (Prolia)

Delatestryl

Delestrogen

Delteparin Sodium

Depacon (Valproate Sodium Injection)

Depo Medrol (Methylprednisolone Acetate Injectable Suspension)

DepoCyt (Cytarabine Liposome Injection)

DepoDur (Morphine Sulfate XR Liposome Injection)

Desmopressin Acetate Injection (DDAVP Injection)

Depo-Estradiol

Depo-Provera 104mg/ml

Depo-Provera 150mg/ml

Depo-Testosterone

Dexrazoxane for Injection, Intravenous Infusion Only (Totect)

Dextrose / Electrolytes

Dextrose and Sodium Chloride Inj (Dextrose 5% in 0.9% Sodium Chloride)

Dextrose

Diazepam Injection (Diazepam Injection)

Digoxin Injection (Lanoxin Injection)

Dilaudid-HP (Hydromorphone Hydrochloride Injection)

Dimercarprol Injection (Bal in Oil Ampules)

Diphenhydramine Injection (Benadryl Injection)

Dipyridamole Injection (Dipyridamole Injection)

DMOAD

Docetaxel for Injection (Taxotere)

Dolasetron Mesylate Injection (Anzemet Injection)

Doribax (Doripenem for Injection)

Doripenem for Injection (Doribax)

Doxercalciferol Injection (Hectorol Injection)

Doxil (Doxorubicin Hcl Liposome Injection)

Doxorubicin Hcl Liposome Injection (Doxil)

Duraclon (Clonidine Injection)

Duramorph (Morphine Injection)

Dysport (Abobotulinumtoxin A Injection)

Ecallantide Injection (Kalbitor)

EC-Naprosyn (naproxen)

Edetate Calcium Disodium Injection (Calcium Disodium Versenate)

Edex (Alprostadil for Injection)

Engerix

Edrophonium Injection (Enlon)

Eliglustat Tartate

Eloxatin (Oxaliplatin Injection)

Emend Injection (Fosaprepitant Dimeglumine Injection)

Enalaprilat Injection (Enalaprilat Injection)

Enlon (Edrophonium Injection)

Enoxaparin Sodium Injection (Lovenox)

Eovist (Gadoxetate Disodium Injection)

Enbrel (etanercept)

Enoxaparin

Epicel

Epinepherine

Epipen

Epipen Jr.

Epratuzumab

Erbitux

Ertapenem Injection (Invanz)

Erythropoieten

Essential Amino Acid Injection (Nephramine)

Estradiol Cypionate

Estradiol Valerate

Etanercept

Exenatide Injection (Byetta)

Evlotra

Fabrazyme (Adalsidase beta)

Famotidine Injection

FDG (Fludeoxyglucose F 18 Injection)

Feraheme (Ferumoxytol Injection)

Feridex I.V. (Ferumoxides Injectable Solution)

Fertinex

Ferumoxides Injectable Solution (Feridex I.V.)

Ferumoxytol Injection (Feraheme)

Flagyl Injection (Metronidazole Injection)

Fluarix

Fludara (Fludarabine Phosphate)

Fludeoxyglucose F 18 Injection (FDG)

Fluorescein Injection (Ak-Fluor)

Follistim AQ Cartridge (Follitropin Beta Injection)

Follitropin Alfa Injection (Gonal-f RFF)

Follitropin Beta Injection (Follistim AQ Cartridge)

Folotyn (Pralatrexate Solution for Intravenous Injection)

Fondaparinux

Forteo (Teriparatide (rDNA origin) Injection)

Fostamatinib

Fosaprepitant Dimeglumine Injection (Emend Injection)

Foscarnet Sodium Injection (Foscavir)

Foscavir (Foscarnet Sodium Injection)

Fosphenytoin Sodium Injection (Cerebyx)

Fospropofol Disodium Injection (Lusedra)

Fragmin

Fuzeon (enfuvirtide)

GA101

Gadobenate Dimeglumine Injection (Multihance)

Gadofosveset Trisodium Injection (Ablavar)

Gadoteridol Injection Solution (ProHance)

Gadoversetamide Injection (OptiMARK)

Gadoxetate Disodium Injection (Eovist)

Ganirelix (Ganirelix Acetate Injection)

Gardasil

GC1008

GDFD

Gemtuzumab Ozogamicin for Injection (Mylotarg)

Genotropin

Gentamicin Injection

GENZ-112638

Golimumab Injection (Simponi Injection)
Gonal-f RFF (Follitropin Alfa Injection)
Granisetron Hydrochloride (Kytril Injection)
Gentamicin Sulfate
Glatiramer Acetate
Glucagen
Glucagon
HAE1
Haldol (Haloperidol Injection)
Havrix
Hectorol Injection (Doxercalciferol Injection)
Hedgehog Pathway Inhibitor
Heparin
Herceptin
hG-CSF
Humalog
Human Growth Hormone
Humatrope
HuMax
Humegon
Humira
Humulin
Ibandronate Sodium Injection (Boniva Injection)
Ibuprofen Lysine Injection (NeoProfen)
Ibutilide Fumarate Injection (Corvert)
Idamycin PFS (Idarubicin Hydrochloride Injection)
Idarubicin Hydrochloride Injection (Idamycin PFS)
Ilaris (Canakinumab Injection)
Imipenem and Cilastatin for Injection (Primaxin I.V.)
Imitrex
Incobotulinumtoxin A for Injection (Xeomin)

Increlex (Mecasermin [rDNA origin] Injection)

Indocin IV (Indomethacin Inj)

Indomethacin Inj (Indocin IV)

Infanrix

Innohep

Insulin

Insulin Aspart [rDNA origin] Inj (NovoLog)

Insulin Glargine [rDNA origin] Injection (Lantus)

Insulin Glulisine [rDNA origin] Inj (Apidra)

Interferon alfa-2b, Recombinant for Injection (Intron A)

Intron A (Interferon alfa-2b, Recombinant for Injection)

Invanz (Ertapenem Injection)

Invega Sustenna (Paliperidone Palmitate Extended-Release Injectable Suspension)

Invirase (saquinavir mesylate)

Iobenguane I 123 Injection for Intravenous Use (AdreView)

Iopromide Injection (Ultravist)

Ioversol Injection (Optiray Injection)

Iplex (Mecasermin Rinfabate [rDNA origin] Injection)

Iprivask

Irinotecan Hydrochloride (Camptosar Injection)

Iron Sucrose Injection (Venofer)

Istodax (Romidepsin for Injection)

Itraconazole Injection (Sporanox Injection)

Jevtana (Cabazitaxel Injection)

Jonexa

Kalbitor (Ecallantide Injection)

KCL in D5NS (Potassium Chloride in 5% Dextrose and Sodium Chloride Injection)

KCL in D5W

KCL in NS

Kenalog 10 Injection (Triamcinolone Acetonide Injectable Suspension)

Kepivance (Palifermin)

Keppra Injection (Levetiracetam)

Keratinocyte

KFG

Kinase Inhibitor

Kineret (Anakinra)

Kinlytic (Urokinase Injection)

Kinrix

Klonopin (clonazepam)

Kytril Injection (Granisetron Hydrochloride)

lacosamide Tablet and Injection (Vimpat)

Lactated Ringer's

Lanoxin Injection (Digoxin Injection)

Lansoprazole for Injection (Prevacid I.V.)

Lantus

Leucovorin Calcium (Leucovorin Calcium Injection)

Lente (L)

Leptin

Levemir

Leukine Sargramostim

Leuprolide Acetate

Levothyroxine

Levetiracetam (Keppra Injection)

Lovenox

Levocarnitine Injection (Carnitor Injection)

Lexiscan (Regadenoson Injection)

Lioresal Intrathecal (Baclofen Injection)

Liraglutide [rDNA] Injection (Victoza)

Lovenox (Enoxaparin Sodium Injection)

Lucentis (Ranibizumab Injection)

Lumizyme

Lupron (Leuprolide Acetate Injection)

Lusedra (Fospropofol Disodium Injection)

Maci

Magnesium Sulfate (Magnesium Sulfate Injection)

Mannitol Injection (Mannitol IV)

Marcaine (Bupivacaine Hydrochloride and Epinephrine Injection)

Maxipime (Cefepime Hydrochloride for Injection)

MDP Multidose Kit of Technetium Injection (Technetium Tc99m Medronate Injection)

Mecasermin [rDNA origin] Injection (Increlex)

Mecasermin Rinfabate [rDNA origin] Injection (Iplex)

Melphalan Hcl Injection (Alkeran Injection)

Methotrexate

Menactra

Menopur (Menotropins Injection)

Menotropins for Injection (Repronex)

Methohexital Sodium for Injection (Brevital Sodium)

Methyldopate Hydrochloride Injection, Solution (Methyldopate Hcl)

Methylene Blue (Methylene Blue Injection)

Methylprednisolone Acetate Injectable Suspension (Depo Medrol)

MetMab

Metoclopramide Injection (Reglan Injection)

Metrodin (Urofollitropin for Injection)

Metronidazole Injection (Flagyl Injection)

Miacalcin

Midazolam (Midazolam Injection)

Mimpara (Cinacalet)

Minocin Injection (Minocycline Inj)

Minocycline Inj (Minocin Injection)

Mipomersen

Mitoxantrone for Injection Concentrate (Novantrone)

Morphine Injection (Duramorph)

Morphine Sulfate XR Liposome Injection (DepoDur)

Morrhuate Sodium (Morrhuate Sodium Injection)

Motesanib

Mozobil (Plerixafor Injection)

Multihance (Gadobenate Dimeglumine Injection)

Multiple Electrolytes and Dextrose Injection

Multiple Electrolytes Injection

Mylotarg (Gemtuzumab Ozogamicin for Injection)

Myozyme (Alglucosidase alfa)

Nafcillin Injection (Nafcillin Sodium)

Nafcillin Sodium (Nafcillin Injection)

Naltrexone XR Inj (Vivitrol)

Naprosyn (naproxen)

NeoProfen (Ibuprofen Lysine Injection)

Nandrol Decanoate

Neostigmine Methylsulfate (Neostigmine Methylsulfate Injection)

NEO-GAA

NeoTect (Technetium Tc 99m Depreotide Injection)

Nephramine (Essential Amino Acid Injection)

Neulasta (pegfilgrastim)

Neupogen (Filgrastim)

Novolin

Novolog

NeoRecormon

Neutrexin (Trimetrexate Glucuronate Inj)

NPH (N)

Nexterone (Amiodarone HCl Injection)

Norditropin (Somatropin Injection)

Normal Saline (Sodium Chloride Injection)

Novantrone (Mitoxantrone for Injection Concentrate)

Novolin 70/30 Innolet (70% NPH, Human Insulin Isophane Suspension and 30% Regular, Human Insulin Injection)

NovoLog (Insulin Aspart [rDNA origin] Inj)

Nplate (romiplostim)

Nutropin (Somatropin (rDNA origin) for Inj)

Nutropin AQ

Nutropin Depot (Somatropin (rDNA origin) for Inj)

Octreotide Acetate Injection (Sandostatin LAR)

Ocrelizumab

Ofatumumab Injection (Arzerra)

Olanzapine Extended Release Injectable Suspension (Zyprexa Relprevv)

Omnitarg

Omnitrope (Somatropin [rDNA origin] Injection)

Ondansetron Hydrochloride Injection (Zofran Injection)

OptiMARK (Gadoversetamide Injection)

Optiray Injection (Ioversol Injection)

Orencia

Osmitrol Injection in Aviva (Mannitol Injection in Aviva Plastic Vessel)

Osmitrol Injection in Viaflex (Mannitol Injection in Viaflex Plastic Vessel)

Osteoprotegrin

Ovidrel (Choriogonadotropin Alfa Injection)

Oxacillin (Oxacillin for Injection)

Oxaliplatin Injection (Eloxatin)

Oxytocin Injection (Pitocin)

Paliperidone Palmitate Extended-Release Injectable Suspension (Invega Sustenna)

Pamidronate Disodium Injection (Pamidronate Disodium Injection)

Panitumumab Injection for Intravenous Use (Vectibix)

Papaverine Hydrochloride Injection (Papaverine Injection)

Papaverine Injection (Papaverine Hydrochloride Injection)

Parathyroid Hormone

Paricalcitol Injection Fliptop Vial (Zemplar Injection)

PARP Inhibitor

Pediarix

PEGIntron

Peginterferon

Pegfilgrastim

Penicillin G Benzathine and Penicillin G Procaine

Pentetate Calcium Trisodium Inj (Ca-DTPA)

Pentetate Zinc Trisodium Injection (Zn-DTPA)

Pepcid Injection (Famotidine Injection)

Pergonal

Pertuzumab

Phentolamine Mesylate (Phentolamine Mesylate for Injection)

Physostigmine Salicylate (Physostigmine Salicylate (injection))

Physostigmine Salicylate (injection) (Physostigmine Salicylate)

Piperacillin and Tazobactam Injection (Zosyn)

Pitocin (Oxytocin Injection)

Plasma-Lyte 148 (Multiple Electrolytes Inj)

Plasma-Lyte 56 and Dextrose (Multiple Electrolytes and Dextrose Injection in Viaflex Plastic Vessel)

PlasmaLyte

Plerixafor Injection (Mozobil)

Polidocanol Injection (Asclera)

Potassium Chloride

Pralatrexate Solution for Intravenous Injection (Folotyn)

Pramlintide Acetate Injection (Symlin)

Premarin Injection (Conjugated Estrogens for Injection)

Prep kit for Technetium Tc99 Sestamibi for Injection (Cardiolite)

Prevacid I.V. (Lansoprazole for Injection)

Primaxin I.V. (Imipenem and Cilastatin for Injection)

Prochymal

Procrit

Progesterone

ProHance (Gadoteridol Injection Solution)

Prolia (Denosumab Injection)

Promethazine HCl Injection (Promethazine Hydrochloride Injection)

Propranolol Hydrochloride Injection (Propranolol Hydrochloride Injection)

Quinidine Gluconate Injection (Quinidine Injection)

Quinidine Injection (Quinidine Gluconate Injection)

R-Gene 10 (Arginine Hydrochloride Injection)

Ranibizumab Injection (Lucentis)

Ranitidine Hydrochloride Injection (Zantac Injection)

Raptiva

Reclast (Zoledronic Acid Injection)

Recombivarix HB

Regadenoson Injection (Lexiscan)

Reglan Injection (Metoclopramide Injection)

Remicade

Renagel

Renvela (Sevelamer Carbonate)

Repronex (Menotropins for Injection)

Retrovir IV (Zidovudine Injection)

rhApo2L/TRAIL

Ringer's and 5% Dextrose Injection (Ringers in Dextrose)

Ringer's Injection (Ringers Injection)

Rituxan

Rituximab

Rocephin (ceftriaxone)

Rocuronium Bromide Injection (Zemuron)

Roferon-A (interferon alfa-2a)

Romazicon (flumazenil)

Romidepsin for Injection (Istodax)

Saizen (Somatropin Injection)

Sandostatin LAR (Octreotide Acetate Injection)

Sclerostin Ab

Sensipar (cinacalcet)
Sensorcaine (Bupivacaine HCl Injections)
Septocaine (Articane HCl and Epinephrine Injection)
Serostim LQ (Somatropin (rDNA origin) Injection)
Simponi Injection (Golimumab Injection)
Sodium Acetate (Sodium Acetate Injection)
Sodium Bicarbonate (Sodium Bicarbonate 5% Injection)
Sodium Lactate (Sodium Lactate Injection in AVIVA)
Sodium Phenylacetate and Sodium Benzoate Injection (Ammonul)
Somatropin (rDNA origin) for Inj (Nutropin)
Sporanox Injection (Itraconazole Injection)
Stelara Injection (Ustekinumab)
Stemgen
Sufenta (Sufentanil Citrate Injection)
Sufentanil Citrate Injection (Sufenta)
Sumavel
Sumatriptan Injection (Alsuma)
Symlin
Symlin Pen
Systemic Hedgehog Antagonist
Synvisc-One (Hylan G-F 20 Single Intra-articular Injection)
Tarceva
Taxotere (Docetaxel for Injection)
Technetium Tc 99m
Telavancin for Injection (Vibativ)
Temsirolimus Injection (Torisel)
Tenormin I.V. Injection (Atenolol Inj)
Teriparatide (rDNA origin) Injection (Forteo)
Testosterone Cypionate
Testosterone Enanthate
Testosterone Propionate

Tev-Tropin (Somatropin, rDNA Origin, for Injection)

tgAAC94

Thallous Chloride

Theophylline

Thiotepa (Thiotepa Injection)

Thymoglobulin (Anti-Thymocyte Globulin (Rabbit)

Thyrogen (Thyrotropin Alfa for Injection)

Ticarcillin Disodium and Clavulanate Potassium Galaxy (Timentin Injection)

Tigan Injection (Trimethobenzamide Hydrochloride Injectable)

Timentin Injection (Ticarcillin Disodium and Clavulanate Potassium Galaxy)

TNKase

Tobramycin Injection (Tobramycin Injection)

Tocilizumab Injection (Actemra)

Torisel (Temsirolimus Injection)

Totect (Dexrazoxane for Injection, Intravenous Infusion Only)

Trastuzumab-DM1

Travasol (Amino Acids (Injection))

Treanda (Bendamustine Hydrochloride Injection)

Trelstar (Triptorelin Pamoate for Injectable Suspension)

Triamcinolone Acetonide

Triamcinolone Diacetate

Triamcinolone Hexacetonide Injectable Suspension (Aristospan Injection 20 mg)

Triesence (Triamcinolone Acetonide Injectable Suspension)

Trimethobenzamide Hydrochloride Injectable (Tigan Injection)

Trimetrexate Glucuronate Inj (Neutrexin)

Triptorelin Pamoate for Injectable Suspension (Trelstar)

Twinject

Trivaris (Triamcinolone Acetonide Injectable Suspension)

Trisenox (Arsenic Trioxide Injection)

Twinrix

Typhoid Vi

Ultravist (Iopromide Injection)

Urofollitropin for Injection (Metrodin)

Urokinase Injection (Kinlytic)

Ustekinumab (Stelara Injection)

Ultralente (U)

Valium (diazepam)

Valproate Sodium Injection (Depacon)

Valtropin (Somatropin Injection)

Vancomycin Hydrochloride (Vancomycin Hydrochloride Injection)

Vancomycin Hydrochloride Injection (Vancomycin Hydrochloride)

Vaprisol (Conivaptan Hcl Injection)

VAQTA

Vasovist (Gadofosveset Trisodium Injection for Intravenous Use)

Vectibix (Panitumumab Injection for Intravenous Use)

Venofer (Iron Sucrose Injection)

Verteporfin Inj (Visudyne)

Vibativ (Telavancin for Injection)

Victoza (Liraglutide [rDNA] Injection)

Vimpat (lacosamide Tablet and Injection)

Vinblastine Sulfate (Vinblastine Sulfate Injection)

Vincasar PFS (Vincristine Sulfate Injection)

Victoza

Vincristine Sulfate (Vincristine Sulfate Injection)

Visudyne (Verteporfin Inj)

Vitamin B-12

Vivitrol (Naltrexone XR Inj)

Voluven (Hydroxyethyl Starch in Sodium Chloride Injection)

Xeloda

Xenical (orlistat)

Xeomin (Incobotulinumtoxin A for Injection)

Xolair

Zantac Injection (Ranitidine Hydrochloride Injection)

Zemplar Injection (Paricalcitol Injection Fliptop Vial)

Zemuron (Rocuronium Bromide Injection)

Zenapax (daclizumab)

Zevalin

Zidovudine Injection (Retrovir IV)

Zithromax Injection (Azithromycin)

Zn-DTPA (Pentetate Zinc Trisodium Injection)

Zofran Injection (Ondansetron Hydrochloride Injection)

Zingo

Zoledronic Acid for Inj (Zometa)

Zoledronic Acid Injection (Reclast)

Zometa (Zoledronic Acid for Inj)

Zosyn (Piperacillin and Tazobactam Injection)

Zyprexa Relprevv (Olanzapine Extended Release Injectable Suspension)

LIQUID DRUGS (NON-INJECTABLE)

Abilify

AccuNeb (Albuterol Sulfate Inhalation Solution)

Actidose Aqua (Activated Charcoal Suspension)

Activated Charcoal Suspension (Actidose Aqua)

Advair

Agenerase Oral Solution (Amprenavir Oral Solution)

Akten (Lidocaine Hydrochloride Ophthalmic Gel)

Alamast (Pemirolast Potassium Ophthalmic Solution)

Albumin (Human) 5% Solution (Buminate 5%)

Albuterol Sulfate Inhalation Solution

Alinia

Alocril

Alphagan

Alrex

Alvesco

Amprenavir Oral Solution

Analpram-HC

Arformoterol Tartrate Inhalation Solution (Brovana)

Aristospan Injection 20 mg (Triamcinolone Hexacetonide Injectable Suspension)

Asacol

Asmanex

Astepro

Astepro (Azelastine Hydrochloride Nasal Spray)

Atrovent Nasal Spray (Ipratropium Bromide Nasal Spray)

Atrovent Nasal Spray .06

Augmentin ES-600

Azasite (Azithromycin Ophthalmic Solution)

Azelaic Acid (Finacea Gel)

Azelastine Hydrochloride Nasal Spray (Astepro)

Azelex (Azelaic Acid Cream)

Azopt (Brinzolamide Ophthalmic Suspension)

Bacteriostatic Saline

Balanced Salt

Bepotastine

Bactroban Nasal

Bactroban

Beclovent

Benzac W

Betimol

Betoptic S

Bepreve

Bimatoprost Ophthalmic Solution

Bleph 10 (Sulfacetamide Sodium Ophthalmic Solution 10%)

Brinzolamide Ophthalmic Suspension (Azopt)

Bromfenac Ophthalmic Solution (Xibrom)

Bromhist

Brovana (Arformoterol Tartrate Inhalation Solution)

Budesonide Inhalation Suspension (Pulmicort Respules)

Cambia (Diclofenac Potassium for Oral Solution)

Capex

Carac

Carboxine-PSE

Carnitor

Cayston (Aztreonam for Inhalation Solution)

Cellcept

Centany

Cerumenex

Ciloxan Ophthalmic Solution (Ciprofloxacin HCL Ophthalmic Solution)

Ciprodex

Ciprofloxacin HCL Ophthalmic Solution (Ciloxan Ophthalmic Solution)

Clemastine Fumarate Syrup (Clemastine Fumarate Syrup)

CoLyte (PEG Electrolytes Solution)

Combiven

Comtan

Condylox

Cordran

Cortisporin Ophthalmic Suspension

Cortisporin Otic Suspension

Cromolyn Sodium Inhalation Solution (Intal Nebulizer Solution)

Cromolyn Sodium Ophthalmic Solution (Opticrom)

Crystalline Amino Acid Solution with Electrolytes (Aminosyn Electrolytes)

Cutivate

Cuvposa (Glycopyrrolate Oral Solution)

Cyanocobalamin (CaloMist Nasal Spray)

Cyclosporine Oral Solution (Gengraf Oral Solution)

Cyclogyl

Cysview (Hexaminolevulinate Hydrochloride Intravesical Solution)

DermOtic Oil (Fluocinolone Acetonide Oil Ear Drops)

Desmopressin Acetate Nasal Spray

DDAVP

Derma-Smoothe/FS

Dexamethasone Intensol

Dianeal Low Calcium

Dianeal PD

Diclofenac Potassium for Oral Solution (Cambia)

Didanosine Pediatric Powder for Oral Solution (Videx)

Differin

Dilantin 125 (Phenytoin Oral Suspension)

Ditropan

Dorzolamide Hydrochloride Ophthalmic Solution (Trusopt)

Dorzolamide Hydrochloride-Timolol Maleate Ophthalmic Solution (Cosopt)

Dovonex Scalp (Calcipotriene Solution)

Doxycycline Calcium Oral Suspension (Vibramycin Oral)

Efudex

Elaprase (Idursulfase Solution)

Elestat (Epinastine HCl Ophthalmic Solution)

Elocon

Epinastine HCl Ophthalmic Solution (Elestat)

Epivir HBV

Epogen (Epoetin alfa)

Erythromycin Topical Solution 1.5% (Staticin)

Ethiodol (Ethiodized Oil)

Ethosuximide Oral Solution (Zarontin Oral Solution)

Eurax

Extraneal (Icodextrin Peritoneal Dialysis Solution)

Felbatol

Feridex I.V. (Ferumoxides Injectable Solution)

Flovent

Floxin Otic (Ofloxacin Otic Solution)

Flo-Pred (Prednisolone Acetate Oral Suspension)

Fluoroplex

Flunisolide Nasal Solution (Flunisolide Nasal Spray .025%)

Fluorometholone Ophthalmic Suspension (FML)

Flurbiprofen Sodium Ophthalmic Solution (Ocufen)

FML

Foradil

Formoterol Fumarate Inhalation Solution (Perforomist)

Fosamax

Furadantin (Nitrofurantoin Oral Suspension)

Furoxone

Gammagard Liquid (Immune Globulin Intravenous (Human) 10%)

Gantrisin (Acetyl Sulfisoxazole Pediatric Suspension)

Gatifloxacin Ophthalmic Solution (Zymar)

Gengraf Oral Solution (Cyclosporine Oral Solution)

Glycopyrrolate Oral Solution (Cuvposa)

Halcinonide Topical Solution (Halog Solution)

Halog Solution (Halcinonide Topical Solution)

HEP-LOCK U/P (Preservative-Free Heparin Lock Flush Solution)

Heparin Lock Flush Solution (Hepflush 10)

Hexaminolevulinate Hydrochloride Intravesical Solution (Cysview)

Hydrocodone Bitartrate and Acetaminophen Oral Solution (Lortab Elixir)

Hydroquinone 3% Topical Solution (Melquin-3 Topical Solution)

IAP Antagonist

Isopto

Ipratropium Bromide Nasal Spray (Atrovent Nasal Spray)

Itraconazole Oral Solution (Sporanox Oral Solution)

Ketorolac Tromethamine Ophthalmic Solution (Acular LS)

Kaletra

Lanoxin

Lexiva

Leuprolide Acetate for Depot Suspension (Lupron Depot 11.25 mg)

Levobetaxolol Hydrochloride Ophthalmic Suspension (Betaxon)

Levocarnitine Tablets, Oral Solution, Sugar-Free (Carnitor)

Levofloxacin Ophthalmic Solution 0.5% (Quixin)

Lidocaine HCl Sterile Solution (Xylocaine MPF Sterile Solution)

Lok Pak (Heparin Lock Flush Solution)

Lorazepam Intensol

Lortab Elixir (Hydrocodone Bitartrate and Acetaminophen Oral Solution)

Lotemax (Loteprednol Etabonate Ophthalmic Suspension)

Loteprednol Etabonate Ophthalmic Suspension (Alrex)

Low Calcium Peritoneal Dialysis Solutions (Dianeal Low Calcium)

Lumigan (Bimatoprost Ophthalmic Solution 0.03% for Glaucoma)

Lupron Depot 11.25 mg (Leuprolide Acetate for Depot Suspension)

Megestrol Acetate Oral Suspension (Megestrol Acetate Oral Suspension)

MEK Inhibitor

Mepron

Mesnex

Mestinon

Mesalamine Rectal Suspension Enema (Rowasa)

Melquin-3 Topical Solution (Hydroquinone 3% Topical Solution)

MetMab

Methyldopate Hcl (Methyldopate Hydrochloride Injection, Solution)

Methylin Oral Solution (Methylphenidate HCl Oral Solution 5 mg/5 mL and 10 mg/5 mL)

Methylprednisolone Acetate Injectable Suspension (Depo Medrol)

Methylphenidate HCl Oral Solution 5 mg/5 mL and 10 mg/5 mL (Methylin Oral Solution)

Methylprednisolone sodium succinate (Solu Medrol)

Metipranolol Ophthalmic Solution (Optipranolol)

Migranal

Miochol-E (Acetylcholine Chloride Intraocular Solution)

Micro-K for Liquid Suspension (Potassium Chloride Extended Release Formulation for Liquid Suspension)

Minocin (Minocycline Hydrochloride Oral Suspension)

Nasacort

Neomycin and Polymyxin B Sulfates and Hydrocortisone

Nepafenac Ophthalmic Suspension (Nevanac)

Nevanac (Nepafenac Ophthalmic Suspension)

Nitrofurantoin Oral Suspension (Furadantin)

Noxafil (Posaconazole Oral Suspension)

Nystatin (oral) (Nystatin Oral Suspension)

Nystatin Oral Suspension (Nystatin (oral))

Ocufen (Flurbiprofen Sodium Ophthalmic Solution)

Ofloxacin Ophthalmic Solution (Ofloxacin Ophthalmic Solution)

Ofloxacin Otic Solution (Floxin Otic)

Olopatadine Hydrochloride Ophthalmic Solution (Pataday)

Opticrom (Cromolyn Sodium Ophthalmic Solution)

Optipranolol (Metipranolol Ophthalmic Solution)

Patanol

Pediapred

PerioGard

Phenytoin Oral Suspension (Dilantin 125)

Phisohex

Posaconazole Oral Suspension (Noxafil)

Potassium Chloride Extended Release Formulation for Liquid Suspension (Micro-K for Liquid Suspension)

Pataday (Olopatadine Hydrochloride Ophthalmic Solution)

Patanase Nasal Spray (Olopatadine Hydrochloride Nasal Spray)

PEG Electrolytes Solution (CoLyte)

Pemirolast Potassium Ophthalmic Solution (Alamast)

Penlac (Ciclopirox Topical Solution)

PENNSAID (Diclofenac Sodium Topical Solution)

Perforomist (Formoterol Fumarate Inhalation Solution)

Peritoneal Dialysis Solution

Phenylephrine Hydrochloride Ophthalmic Solution (Neo-Synephrine)

Phospholine Iodide (Echothiophate Iodide for Ophthalmic Solution)

Podofilox (Podofilox Topical Solution)

Pred Forte (Prednisolone Acetate Ophthalmic Suspension)

Pralatrexate Solution for Intravenous Injection (Folotyn)

Pred Mild

Prednisone Intensol

Prednisolone Acetate Ophthalmic Suspension (Pred Forte)

Prevacid

PrismaSol Solution (Sterile Hemofiltration Hemodiafiltration Solution)

ProAir

Proglycem

ProHance (Gadoteridol Injection Solution)

Proparacaine Hydrochloride Ophthalmic Solution (Alcaine)

Propine

Pulmicort

Pulmozyme

Quixin (Levofloxacin Ophthalmic Solution 0.5%)

QVAR

Rapamune

Rebetol

Relacon-HC

Rotarix (Rotavirus Vaccine, Live, Oral Suspension)

Rotavirus Vaccine, Live, Oral Suspension (Rotarix)

Rowasa (Mesalamine Rectal Suspension Enema)

Sabril (Vigabatrin Oral Solution)

Sacrosidase Oral Solution (Sucraid)

Sandimmune

Sepra

Serevent Diskus

Solu Cortef (Hydrocortisone Sodium Succinate)

Solu Medrol (Methylprednisolone sodium succinate)

Spiriva

Sporanox Oral Solution (Itraconazole Oral Solution)

Staticin (Erythromycin Topical Solution 1.5%)

Stalevo

Starlix

Sterile Hemofiltration Hemodiafiltration Solution (PrismaSol Solution)

Stimate

Sucralfate (Carafate Suspension)

Sulfacetamide Sodium Ophthalmic Solution 10% (Bleph 10)

Synarel Nasal Solution (Nafarelin Acetate Nasal Solution for Endometriosis)

Taclonex Scalp (Calcipotriene and Betamethasone Dipropionate Topical Suspension)

Tamiflu

Tobi

TobraDex

Tobradex ST (Tobramycin / Dexamethasone Ophthalmic Suspension 0.3%/0.05%)

Tobramycin / Dexamethasone Ophthalmic Suspension 0.3%/0.05% (Tobradex ST)

Timolol

Timoptic

Travatan Z

Treprostinil Inhalation Solution (Tyvaso)

Trusopt (Dorzolamide Hydrochloride Ophthalmic Solution)

Tyvaso (Treprostinil Inhalation Solution)

Ventolin

Vfend

Vibramycin Oral (Doxycycline Calcium Oral Suspension)

Videx (Didanosine Pediatric Powder for Oral Solution)

Vigabatrin Oral Solution (Sabril)

Viokase

Viracept
Viramune
Vitamin K1 (Fluid Colloidal Solution of Vitamin K1)
Voltaren Ophthalmic (Diclofenac Sodium Ophthalmic Solution)
Zarontin Oral Solution (Ethosuximide Oral Solution)
Ziagen
Zyvox
Zymar (Gatifloxacin Ophthalmic Solution)
Zymaxid (Gatifloxacin Ophthalmic Solution)

DRUG CLASSES

5-alpha-reductase inhibitors
5-aminosalicylates
5HT3 receptor antagonists
adamantane antivirals
adrenal cortical steroids
adrenal corticosteroid inhibitors
adrenergic bronchodilators
agents for hypertensive emergencies
agents for pulmonary hypertension
aldosterone receptor antagonists
alkylating agents
alpha-adrenoreceptor antagonists
alpha-glucosidase inhibitors
alternative medicines
amebicides
aminoglycosides
aminopenicillins
aminosalicylates
amylin analogs
Analgesic Combinations
Analgesics

androgens and anabolic steroids
angiotensin converting enzyme inhibitors
angiotensin II inhibitors
anorectal preparations
anorexiants
antacids
anthelmintics
anti-angiogenic ophthalmic agents
anti-CTLA-4 monoclonal antibodies
anti-infectives
antiadrenergic agents, centrally acting
antiadrenergic agents, peripherally acting
antiandrogens
antianginal agents
antiarrhythmic agents
antiasthmatic combinations
antibiotics/antineoplastics
anticholinergic antiemetics
anticholinergic antiparkinson agents
anticholinergic bronchodilators
anticholinergic chronotropic agents
anticholinergics/antispasmodics
anticoagulants
anticonvulsants
antidepressants
antidiabetic agents
antidiabetic combinations
antidiarrheals
antidiuretic hormones
antidotes
antiemetic/antivertigo agents

antifungals
antigonadotropic agents
antigout agents
antihistamines
antihyperlipidemic agents
antihyperlipidemic combinations
antihypertensive combinations
antihyperuricemic agents
antimalarial agents
antimalarial combinations
antimalarial quinolines
antimetabolites
antimigraine agents
antineoplastic detoxifying agents
antineoplastic interferons
antineoplastic monoclonal antibodies
antineoplastics
antiparkinson agents
antiplatelet agents
antipseudomonal penicillins
antipsoriatics
antipsychotics
antirheumatics
antiseptic and germicides
antithyroid agents
antitoxins and antivenins
antituberculosis agents
antituberculosis combinations
antitussives
antiviral agents
antiviral combinations

antiviral interferons
anxiolytics, sedatives, and hypnotics
aromatase inhibitors
atypical antipsychotics
azole antifungals
bacterial vaccines
barbiturate anticonvulsants
barbiturates
BCR-ABL tyrosine kinase inhibitors
benzodiazepine anticonvulsants
benzodiazepines
beta-adrenergic blocking agents
beta-lactamase inhibitors
bile acid sequestrants
biologicals
bisphosphonates
bone resorption inhibitors
bronchodilator combinations
bronchodilators
calcitonin
calcium channel blocking agents
carbamate anticonvulsants
carbapenems
carbonic anhydrase inhibitor anticonvulsants
carbonic anhydrase inhibitors
cardiac stressing agents
cardioselective beta blockers
cardiovascular agents
catecholamines
CD20 monoclonal antibodies
CD33 monoclonal antibodies

CD52 monoclonal antibodies
central nervous system agents
cephalosporins
cerumenolytics
chelating agents
chemokine receptor antagonist
chloride channel activators
cholesterol absorption inhibitors
cholinergic agonists
cholinergic muscle stimulants
cholinesterase inhibitors
CNS stimulants
coagulation modifiers
colony stimulating factors
contraceptives
corticotropin
coumarins and indandiones
cox-2 inhibitors
decongestants
dermatological agents
diagnostic radiopharmaceuticals
dibenzazepine anticonvulsants
digestive enzymes
dipeptidyl peptidase 4 inhibitors
diuretics
dopaminergic antiparkinsonism agents
drugs used in alcohol dependence
echinocandins
EGFR inhibitors
estrogen receptor antagonists
estrogens

expectorants
factor Xa inhibitors
fatty acid derivative anticonvulsants
fibric acid derivatives
first generation cephalosporins
fourth generation cephalosporins
functional bowel disorder agents
gallstone solubilizing agents
gamma-aminobutyric acid analogs
gamma-aminobutyric acid reuptake inhibitors
gamma-aminobutyric acid transaminase inhibitors
gastrointestinal agents
general anesthetics
genitourinary tract agents
GI stimulants
glucocorticoids
glucose elevating agents
glycopeptide antibiotics
glycoprotein platelet inhibitors
glycylcyclines
gonadotropin releasing hormones
gonadotropin-releasing hormone antagonists
gonadotropins
group I antiarrhythmics
group II antiarrhythmics
group III antiarrhythmics
group IV antiarrhythmics
group V antiarrhythmics
growth hormone receptor blockers
growth hormones
H. pylori eradication agents

H2 antagonists
hematopoietic stem cell mobilizer
heparin antagonists
heparins
HER2 inhibitors
herbal products
histone deacetylase inhibitors
hormone replacement therapy
hormones
hormones/antineoplastics
hydantoin anticonvulsants
illicit (street) drugs
immune globulins
immunologic agents
immunosuppressive agents
impotence agents
in vivo diagnostic biologicals
incretin mimetics
inhaled anti-infectives
inhaled corticosteroids
inotropic agents
insulin
insulin-like growth factor
integrase strand transfer inhibitor
interferons
intravenous nutritional products
iodinated contrast media
ionic iodinated contrast media
iron products
ketolides
laxatives

leprostatics
leukotriene modifiers
lincomycin derivatives
lipoglycopeptides
local injectable anesthetics
loop diuretics
lung surfactants
lymphatic staining agents
lysosomal enzymes
macrolide derivatives
macrolides
magnetic resonance imaging contrast media
mast cell stabilizers
medical gas
meglitinides
metabolic agents
methylxanthines
mineralocorticoids
minerals and electrolytes
miscellaneous agents
miscellaneous analgesics
miscellaneous antibiotics
miscellaneous anticonvulsants
miscellaneous antidepressants
miscellaneous antidiabetic agents
miscellaneous antiemetics
miscellaneous antifungals
miscellaneous antihyperlipidemic agents
miscellaneous antimalarials
miscellaneous antineoplastics
miscellaneous antiparkinson agents

miscellaneous antipsychotic agents
miscellaneous antituberculosis agents
miscellaneous antivirals
miscellaneous anxiolytics, sedatives and hypnotics
miscellaneous biologicals
miscellaneous bone resorption inhibitors
miscellaneous cardiovascular agents
miscellaneous central nervous system agents
miscellaneous coagulation modifiers
miscellaneous diuretics
miscellaneous genitourinary tract agents
miscellaneous GI agents
miscellaneous hormones
miscellaneous metabolic agents
miscellaneous ophthalmic agents
miscellaneous otic agents
miscellaneous respiratory agents
miscellaneous sex hormones
miscellaneous topical agents
miscellaneous uncategorized agents
miscellaneous vaginal agents
mitotic inhibitors
monoamine oxidase inhibitors
monoclonal antibodies
mouth and throat products
mTOR inhibitors
mTOR kinase inhibitors
mucolytics
multikinase inhibitors
muscle relaxants
mydriatics

narcotic analgesic combinations
narcotic analgesics
nasal anti-infectives
nasal antihistamines and decongestants
nasal lubricants and irrigations
nasal preparations
nasal steroids
natural penicillins
neuraminidase inhibitors
neuromuscular blocking agents
next generation cephalosporins
nicotinic acid derivatives
nitrates
NNRTIs
non-cardioselective beta blockers
non-iodinated contrast media
non-ionic iodinated contrast media
non-sulfonylureas
nonsteroidal anti-inflammatory agents
norepinephrine reuptake inhibitors
norepinephrine-dopamine reuptake inhibitors
nucleoside reverse transcriptase inhibitors (NRTIs)
nutraceutical products
nutritional products
ophthalmic anesthetics
ophthalmic anti-infectives
ophthalmic anti-inflammatory agents
ophthalmic antihistamines and decongestants
ophthalmic diagnostic agents
ophthalmic glaucoma agents
ophthalmic lubricants and irrigations

ophthalmic preparations
ophthalmic steroids
ophthalmic steroids with anti-infectives
ophthalmic surgical agents
oral nutritional supplements
otic anesthetics
otic anti-infectives
otic preparations
otic steroids
otic steroids with anti-infectives
oxazolidinedione anticonvulsants
parathyroid hormone and analogs
penicillinase resistant penicillins
penicillins
peripheral opioid receptor antagonists
peripheral vasodilators
peripherally acting antiobesity agents
phenothiazine antiemetics
phenothiazine antipsychotics
phenylpiperazine antidepressants
plasma expanders
platelet aggregation inhibitors
platelet-stimulating agents
polyenes
potassium-sparing diuretics
probiotics
progesterone receptor modulators
progestins
prolactin inhibitors
prostaglandin D2 antagonists
protease inhibitors

proton pump inhibitors
psoralens
psychotherapeutic agents
psychotherapeutic combinations
purine nucleosides
pyrrolidine anticonvulsants
quinolones
radiocontrast agents
radiologic adjuncts
radiologic agents
radiologic conjugating agents
radiopharmaceuticals
RANK ligand inhibitors
recombinant human erythropoietins
renin inhibitors
respiratory agents
respiratory inhalant products
rifamycin derivatives
salicylates
sclerosing agents
second generation cephalosporins
selective estrogen receptor modulators
selective serotonin reuptake inhibitors
serotonin-norepinephrine reuptake inhibitors
serotoninergic neuroenteric modulators
sex hormone combinations
sex hormones
skeletal muscle relaxant combinations
skeletal muscle relaxants
smoking cessation agents
somatostatin and somatostatin analogs

spermicides
statins
sterile irrigating solutions
streptomyces derivatives
succinimide anticonvulsants
sulfonamides
sulfonylureas
synthetic ovulation stimulants
tetracyclic antidepressants
tetracyclines
therapeutic radiopharmaceuticals
thiazide diuretics
thiazolidinediones
thioxanthenes
third generation cephalosporins
thrombin inhibitors
thrombolytics
thyroid drugs
tocolytic agents
topical acne agents
topical agents
topical anesthetics
topical anti-infectives
topical antibiotics
topical antifungals
topical antihistamines
topical antipsoriatics
topical antivirals
topical astringents
topical debriding agents
topical depigmenting agents

topical emollients
topical keratolytics
topical steroids
topical steroids with anti-infectives
toxoids
triazine anticonvulsants
tricyclic antidepressants
trifunctional monoclonal antibodies
tumor necrosis factor (TNF) inhibitors
tyrosine kinase inhibitors
ultrasound contrast media
upper respiratory combinations
urea anticonvulsants
urinary anti-infectives
urinary antispasmodics
urinary pH modifiers
uterotonic agents
vaccine
vaccine combinations
vaginal anti-infectives
vaginal preparations
vasodilators
vasopressin antagonists
vasopressors
VEGF/VEGFR inhibitors
viral vaccines
viscosupplementation agents
vitamin and mineral combinations
vitamins
DIAGNOSTIC TESTS
17-Hydroxyprogesterone

ACE (Angiotensin I converting enzyme)
Acetaminophen
Acid phosphatase
ACTH
Activated clotting time
Activated protein C resistance
Adrenocorticotropic hormone (ACTH)
Alanine aminotransferase (ALT)
Albumin
Aldolase
Aldosterone
Alkaline phosphatase
Alkaline phosphatase (ALP)
Alpha1-antitrypsin
Alpha-fetoprotein
Alpha-fetoprotien
Ammonia levels
Amylase
ANA (antinuclear antbodies)
ANA (antinuclear antibodies)
Angiotensin-converting enzyme (ACE)
Anion gap
Anticardiolipin antibody
Anticardiolipin antivbodies (ACA)
Anti-centromere antibody
Antidiuretic hormone
Anti-DNA
Anti-Dnase-B
Anti-Gliadin antibody
Anti-glomerular basement membrane antibody
Anti-HBc (Hepatitis B core antibodies

Anti-HBs (Hepatitis B surface antibody
Antiphospholipid antibody
Anti-RNA polymerase
Anti-Smith (Sm) antibodies
Anti-Smooth Muscle antibody
Antistreptolysin O (ASO)
Antithrombin III
Anti-Xa activity
Anti-Xa assay
Apolipoproteins
Arsenic
Aspartate aminotransferase (AST)
B12
Basophil
Beta-2-Microglobulin
Beta-hydroxybutyrate
B-HCG
Bilirubin
Bilirubin, direct
Bilirubin, indirect
Bilirubin, total
Bleeding time
Blood gases (arterial)
Blood urea nitrogen (BUN)
BUN
BUN (blood urea nitrogen)
CA 125
CA 15-3
CA 19-9
Calcitonin
Calcium

Calcium (ionized)

Carbon monoxide (CO)

Carcinoembryonic antigen (CEA)

CBC

CEA

CEA (carcinoembryonic antigen)

Ceruloplasmin

CH50Chloride

Cholesterol

Cholesterol, HDL

Clot lysis time

Clot retraction time

CMP

CO2

Cold agglutinins

Complement C3

Copper

Corticotrophin releasing hormone (CRH) stimulation test

Cortisol

Cortrosyn stimulation test

C-peptide

CPK (Total)

CPK-MB

C-reactive protein

Creatinine

Creatinine kinase (CK)

Cryoglobulins

DAT (Direct antiglobulin test)

D-Dimer

Dexamethasone suppression test

DHEA-S

Dilute Russell viper venom

Elliptocytes

Eosinophil

Erythrocyte sedimentation rate (ESR)

Estradiol

Estriol

Ethanol

Ethylene glycol

Euglobulin lysis

Factor V Leiden

Factor VIII inhibitor

Factor VIII level

Ferritin

Fibrin split products

Fibrinogen

Folate

Folate (serum

Fractional excretion of sodium (FENA)

FSH (follicle stimulating factor)

FTA-ABS

Gamma glutamyl transferase (GGT)

Gastrin

GGTP (Gamma glutamyl transferase)

Glucose

Growth hormone

Haptoglobin

HBeAg (Hepatitis Be antigen)

HBs-Ag (Hepatitis B surface antigen)

Helicobacter pylori

Hematocrit

Hematocrit (HCT)

Hemoglobin
Hemoglobin A1C
Hemoglobin electrophoresis
Hepatitis A antibodies
Hepatitis C antibodies
IAT (Indirect antiglobulin test)
Immunofixation (IFE)
Iron
Lactate dehydrogenase (LDH)
Lactic acid (lactate)
LDH
LH (Leutinizing hormone
Lipase
Lupus anticoagulant
Lymphocyte
Magnesium
MCH (mean corpuscular hemoglobin
MCHC (mean corpuscular hemoglobin concentration)
MCV (mean corpuscular volume)
Methylmalonate
Monocyte
MPV (mean platelet volume)
Myoglobin
Neutrophil
Parathyroid hormone (PTH)
Phosphorus
Platelets (plt)
Potassium
Prealbumin
Prolactin
Prostate specific antigen (PSA)

Protein C

Protein S

PSA (prostate specific antigen)

PT (Prothrombin time)

PTT (Partial thromboplastin time)

RDW (red cell distribution width)

Renin

Rennin

Reticulocyte count

reticulocytes

Rheumatoid factor (RF)

Sed Rate

Serum glutamic-pyruvic transaminase (SGPT

Serum protein electrophoresis (SPEP)

Sodium

T3-resin uptake (T3RU)

T4, Free

Thrombin time

Thyroid stimulating hormone (TSH)

Thyroxine (T4)

Total iron binding capacity (TIBC)

Total protein

Transferrin

Transferrin saturation

Triglyceride (TG)

Troponin

Uric acid

Vitamin B12

White blood cells (WBC)

Widal test

EXAMPLES

Protocol for Coating Syringe Barrel Interior with SiO_x

[00102] The apparatus and protocol generally as found in U.S. Patent No. 7,985,188 were used for coating syringe barrel interiors with an SiO_x barrier coating or layer, in some cases with minor variations. A similar apparatus and protocol were used for coating vials with an SiO_x barrier coating or layer, in some cases with minor variations.

Protocol for Coating Syringe Barrel Interior with Primer Coating or Layer

[00103] Syringe barrels already interior coated with a barrier coating or layer of SiO_x, as previously identified, are further interior coated with a primer coating or layer of SiO_xC_y as previously identified, generally following the protocols of U.S. Patent No. 7,985,188 for applying the lubricity coating or layer, except with modified conditions in certain instances.

Protocol for F_i (breakout or initiation force) Measurement

[00104] Convenient methods for measuring the breakout or initiation force required to initiate travel of a previously parked plunger in a syringe are described in Examples 11, 12, or 21 of U.S. Patent No. 7,985,188, which are incorporated here by reference.

Protocol for Total Silicon Measurement

[00105] This protocol is used to determine the total amount of silicon coatings present on the entire vessel wall. A supply of 0.1 N potassium hydroxide (KOH) aqueous solution is prepared, taking care to avoid contact between the solution or ingredients and glass. The water used is purified water, 18 MΩ quality. A Perkin Elmer Optima Model 7300DV ICP-OES instrument is used for the measurement except as otherwise indicated.

[00106] Each device (vial, syringe, tube, or the like) to be tested and its cap and crimp (in the case of a vial) or other closure are weighed empty to 0.001 g, then filled completely with the KOH solution (with no headspace), capped, crimped, and reweighed to 0.001g. In a digestion step, each vial is placed in an autoclave oven (liquid cycle) at 121°C for 1 hour. The digestion step is carried out to quantitatively remove the silicon coatings from the vessel wall into the KOH solution. After this digestion step, the vials are removed from the autoclave oven and allowed to cool to room temperature. The contents of the vials are transferred into ICP tubes. The total Si concentration is run on each solution by ICP/OES following the operating procedure for the ICP/OES.

[00107] The total Si concentration is reported as parts per billion of Si in the KOH solution. This concentration represents the total amount of silicon coatings that were on the vessel wall before the digestion step was used to remove it.

[00108] The total Si concentration can also be determined for fewer than all the silicon layers on the vessel, as when an SiO_x barrier layer is applied, an SiO_xC_y second layer (for example, a lubricity layer or a primer coating or layer) is then applied, and it is desired to know the total silicon concentration of just the SiO_xC_y layer. This determination is made by preparing two sets of vessels, one set to which only the SiO_x layer is applied and the other set to which the same SiO_x layer is applied, followed by the SiO_xC_y layer or other layers of interest. The total Si concentration for each set of vessels is determined in the same manner as described above. The difference between the two Si concentrations is the total Si concentration of the SiO_xC_y second layer.

Protocol for Measuring Dissolved Silicon in a Vessel

[00109] In some of the working examples, the amount of silicon dissolved from the wall of the vessel by a test solution is determined, in parts per billion (ppb), for example to evaluate the dissolution rate of the test solution. This determination of dissolved silicon is made by storing the test solution in a vessel provided with an SiO_x and/or SiO_xC_y coating or layer under test conditions, then removing a sample of the solution from the vessel and testing the Si concentration of the sample. The test is done in the same manner as the Protocol for Total Silicon Measurement, except that the digestion

step of that protocol is replaced by storage of the test solution in the vessel as described in this protocol. The total Si concentration is reported as parts per billion of Si in the test solution

Protocol for Determining Average Dissolution Rate

[00110] The average dissolution rates reported in the working examples are determined as follows. A series of test vessels having a known total total silicon measurement are filled with the desired test solution analogous to the manner of filling the vials with the KOH solution in the Protocol for Total Silicon Measurement. (The test solution can be a physiologically inactive test solution as employed in the present working examples or a physiologically active pharmaceutical preparation intended to be stored in the vessels to form a pharmaceutical package). The test solution is stored in respective vessels for several different amounts of time, then analyzed for the Si concentration in parts per billion in the test solution for each storage time. The respective storage times and Si concentrations are then plotted. The plots are studied to find a series of substantially linear points having the steepest slope.

The plot of dissolution amount (ppb Si) versus days decreases in slope with time, even though it does not appear thatthe Si layer has been fully digested by the test solution.

[00111] For the PC194 test data in Table 3, linear plots of dissolution versus time data are prepared by using a least squares linear regression program to find a linear plot corresponding to the first five data points of each of the experimental plots. The slope of each linear plot is then determined and reported as representing the average dissolution rate applicable to the test, measured in parts per billion of Si dissolved in the test solution per unit of time.

Protocol for Determining Calculated Shelf Life

[00112] The calculated shelf life values reported in the working examples below are determined by extrapolation of the total silicon measurements and average dissolution rates, respectively determined as described in the Protocol for Total Silicon

Measurement and the Protocol for Determining Average Dissolution Rate. The assumption is made that under the indicated storage conditions the SiO_xC_y primer coating or layer will be removed at the average dissolution rate until the coating is entirely removed. Thus, the total silicon measurement for the vessel, divided by the dissolution rate, gives the period of time required for the test solution to totally dissolve the SiO_xC_y coating. This period of time is reported as the calculated shelf life. Unlike commercial shelf life calculations, no safety factor is calculated. Instead, the calculated shelf life is the calculated time to failure.

[00113] It should be understood that because the plot of ppb Si versus hours decreases in slope with time, an extrapolation from relatively short measurement times to relatively long calculated shelf lives is believed to be a "worst case" test that tends to underestimate the calculated shelf life actually obtainable.

Examples 1-3

[00114] Syringe samples 1-3, employing three different primer coatings or layers, were produced under the following PECVD conditions:

- OMCTS –2.5 sccm
- Argon gas –7.6 sccm (when used)
- Oxygen 0.38 sccm (when used)
- Power – 3 watts
- Power on time – 10 seconds

[00115] Syringe 1 had a three-component primer coating or layer employing OMCTS, oxygen, and carrier gas. Syringe 2 had a two component primer coating or layer employing OMCTS and oxygen, but no carrier gas. Syringe 3 had a one-component primer coating or layer (OMCTS only). The primer coatings or layers produced according to these working examples are contemplated to function as protective coatings or layers to increase the shelf life of the vessels, compared to similar vessels provided with a barrier coating or layer but no primer coating or layer.

Examples 4-6

[00116] [03] HMDSO was used as the precursor in Examples 4-6. The results are shown in Table 1. The coatings produced according to these working examples are contemplated to function as primer coatings or layers, and also as protective coatings or layers to increase the shelf life of the vessels, compared to similar vessels provided with a barrier coating or layer but no primer coating or layer.

Example 7: Primer Coating or Layer Extractables

[00117] Silicon extractables from syringes were measured using ICP-MS analysis as described in the Protocol for Measuring Dissolved Silicon in a Vessel. The syringes were evaluated in both static and dynamic situations. The Protocol for Measuring Dissolved Silicon in a Vessel, modified as follows, describes the test procedure:

- Syringe filled with 2 ml of 0.9% saline solution
- Syringe placed in a stand – stored at 50°C for 72 hours.
- After 72 hours saline solution test for dissolved silicon
- Dissolved silicon measured before and after saline solution expelled through syringe.

[00118] The extractable Silicon Levels from a silicone oil coated glass syringe and a protective coated and SiO_x coated COC syringe are shown in Table 2. Precision of the ICP-MS total silicon measurement is +/- 3%.

Comparative Example 8: Dissolution of SiO_x Coating Versus pH

[00119] The Protocol for Measuring Dissolved Silicon in a Vessel is followed, except as modified here. Test solutions – 50 mM buffer solutions at pH 3, 6, 7, 8, 9, and 12 are prepared. Buffers are selected having appropriate pKa values to provide the pH values being studied. A potassium phosphate buffer is selected for pH 3, 7, 8 and 12, a sodium citrate buffer is utilized for pH 6 and tris buffer is selected for pH 9. 3 ml of each test solution is placed in borosilicate glass 5 ml pharmaceutical vials and SiO_x

coated 5 ml thermoplastic pharmaceutical vials. The vials are all closed with standard coated stoppers and crimped. The vials are placed in storage at 20 - 25°C and pulled at various time points for inductively coupled plasma spectrometer (ICP) analysis of Si content in the solutions contained in the vials, in parts per billion (ppb) by weight, for different storage times.

[00120] The Protocol for Determining Average Dissolution Rate Si content is used to monitor the rate of glass dissolution, except as modified here. The data is plotted to determine an average rate of dissolution of borosilicate glass or SiO_x coating at each pH condition.

[00121] The rate of Si dissolution in ppb is converted to a predicted thickness (nm) rate of Si dissolution by determining the total weight of Si removed, then using a surface area calculation of the amount of vial surface (11.65 cm^2) exposed to the solution and a density of SiO_x of 2.2 g/cm^3. The predicted initial thickness of the SiO_x coating required, based on the conditions and assumptions of this example (assuming a residual SiO_x coating of at least 30 nm at the end of the desired shelf life of two years, and assuming storage at 20 to 25°C) is about 36 nm at pH 5, about 80 nm at pH 6, about 230 nm at pH 7, about 400 nm at pH 7.5, about 750 nm at pH 8, and about 2600 nm at pH 9.

[00122] The coating thicknesses represent atypically harsh case scenarios for pharma and biotech products. Most biotech products and many pharma products are stored at refrigerated conditions and none are typically recommended for storage above room temperature. As a general rule of thumb, storage at a lower temperature reduces the thickness required, all other conditions being equivalent.

[00123] The following conclusions are reached, based on this test. First, the amount of dissolved Si in the SiO_x coating or glass increases exponentially with increasing pH. Second, the SiO_x coating dissolves more slowly than borosilicate glass at a pH lower than 8. The SiO_x coating shows a linear, monophasic dissolution over time, whereas borosilicate glass tends to show a more rapid dissolution in the early hours of exposure to solutions, followed by a slower linear dissolution. This may be due to surface accumulation of some salts and elements on borosilicate during the forming process relative to the uniform composition of the SiO_x coating. This result incidentally

suggests the utility of an SiO_x coating on the wall of a borosilicate glass vial to reduce dissolution of the glass at a pH lower than 8. Third, PECVD applied barrier coatings for vials in which pharmaceutical preparations are stored will need to be adapted to the specific pharmaceutical preparation and proposed storage conditions (or vice versa), at least in some instances in which the pharmaceutical preparation interacts with the barrier coating significantly.

Example 9

[00124] An experiment is conducted with vessels coated with SiO_x coating + OMCTS primer coating or layer, to test the primer coating or layer for its functionality as a protective coating or layer. The vessels are 5 mL vials (the vials are normally filled with product to 5 mL; their capacity without headspace, when capped, is about 7.5 mL) composed of cyclic olefin co-polymer (COC, Topas® 6013M-07).

[00125] Sixty vessels are coated on their interior surfaces with an SiO_x coating produced in a plasma enhanced chemical vapor deposition (PECVD) process using a HMDSO precursor gas according to the Protocol for Coating Tube Interior with SiO_x set forth above, except that equipment suitable for coating a vial is used. The following conditions are used.

- HMDSO flow rate: 0.47 sccm
- Oxygen flow rate: 7.5 sccm
- RF power: 70 Watts
- Coating time: 12 seconds (includes a 2-sec RF power ramp-up time)

[00126] Next the SiO_x coated vials are coated over the SiO_x with an SiO_xC_y coating produced in a PECVD process using an OMCTS precursor gas according to the Protocol for Coating COC Syringe Barrel Interior with OMCTS Lubricity Coating set forth above, except that the same coating equipment is used as for the SiO_x coating. Thus, the special adaptations in the protocol for coating a syringe are not used. The following conditions are used.

- OMCTS flow rate: 2.5 sccm
- Argon flow rate: 10 sccm
- Oxygen flow rate: 0.7 sccm
- RF power: 3.4 Watts
- Coating time: 5 seconds

[00127] Eight vials are selected and the total deposited quantity of PECVD coating (SiO_x + SiO_xC_y) is determined with a Perkin Elmer Optima Model 7300DV ICP-OES instrument, using the Protocol for Total Silicon Measurement set forth above. This measurement determines the total amount of silicon in both coatings, and does not distinguish between the respective SiO_x and SiO_xC_y coatings. The results are shown below.

Vial	Total Silicon ug/L
1	13844
2	14878
3	14387
4	13731
5	15260
6	15017
7	15118
8	12736
Mean	**14371**
StdDev	**877**

Quantity of SiO_x + Lubricity layer on Vials

[00128] In the following work, except as indicated otherwise in this example, the Protocol for Determining Average Dissolution Rate is followed. Two buffered pH test solutions are used in the remainder of the experiment, respectively at pH 4 and pH 8 to test the effect of pH on dissolution rate. Both test solutions are 50 mM buffers using potassium phosphate as the buffer, diluted in water for injection (WFI) (0.1 um sterilized, filtered). The pH is adjusted to pH 4 or 8, respectively, with concentrated nitric acid.

[00129] 25 vials are filled with 7.5 ml per vial of pH 4 buffered test solution and 25 other vials are filled with 7.5 ml per vial of pH 4 buffered test solution (note the fill level is to the top of the vial – no head space). The vials are closed using prewashed butyl

stoppers and aluminum crimps. The vials at each pH are split into two groups. One group at each pH containing 12 vials is stored at 4°C and the second group of 13 vials is stored at 23°C

[00130] The vials are sampled at Days 1, 3, 6, and 8. The Protocol for Measuring Dissolved Silicon in a Vessel is used, except as otherwise indicated in this example. The analytical result is reported on the basis of parts per billion of silicon in the buffered test solutions of each vial. A dissolution rate is calculated in terms of parts per billion per day as described above in the Protocol for Determining Average Dissolution Rate. The results at the respective storage temperatures follow:

	Shelf Life Conditions 23º C	
	Vial SiO_x + Lubricity Coating at pH4	Vial SiO_x + Lubricity Coating at pH8
Si Dissolution Rate (PPB/day)	31	7

	Shelf Life Conditions 4º C	
	Vial SiO_x + Lubricity Coating at pH4	Vial SiO_x + Lubricity Coating at pH8
Si Dissolution Rate (PPB/day)	7	11

[00131] The observations of Si dissolution versus time for the OMCTS-based coating at pH8 and pH 4 indicate the pH 4 rates are higher at ambient conditions. Thus, the pH 4 rates are used to determine how much material would need to be initially applied to leave a coating of adequate thickness at the end of the shelf life, taking account of the amount of the initial coating that would be dissolved. The results of this calculation are:

	Vial SiO_x + Lubricity Coating at pH4
Si Dissolution Rate (PPB/day)	31
Mass of Coating Tested (Total Si)	14,371
Shelf Life (days) at 23º C	464
Shelf Life (years) at 23º C	1.3

	Vial SiO_x + Lubricity Coating at pH4
Required Mass of Coating (Total Si) – 2 years	22,630
Required Mass of Coating (Total Si) – 3 years	33,945

Shelf Life Calculation

[00132] Based on this calculation, the OMCTS protective layer needs to be about 2.5 times thicker – resulting in dissolution of 33945 ppb versus the 14,371 ppb representing the entire mass of coating tested – to achieve a 3-year calculated shelf life.

Example 10

[00133] The results of Comparative Example 8 and Example 9 above can be compared as follows, where the "primer coating or layer" is the coating of SiO_xC_y referred to in Example 9.

	Shelf Life Conditions - - pH8 and 23º C	
	Vial SiO_x	Vial SiO_x + Lubricity Coating
Si Dissolution Rate (PPB/day)	1,250	7

[00134] This data shows that the silicon dissolution rate of SiO_x alone is reduced by more than 2 orders of magnitude at pH 8 in vials also coated with SiO_xC_y coatings.

[00135] Another comparison is shown by the data in Table 5 from several different experiments carried out under similar accelerated dissolution conditions.

[00136] Ta le 5, Row A (SiO_x with OMCTS coating) versus C (SiO_x without OMCTS coating) show that the OMCTS primer coating or layer is also an effective protective coating or layer to the SiO_x coating at pH 8. The OMCTS coating reduced the one-day dissolution rate from 2504 ug/L ("u" or µ or the Greek letter "mu" as used herein are identical, and are abbreviations for "micro") to 165 ug/L. This data also shows that an HMDSO-based $Si_wO_xC_y$ (or its equivalent SiO_xC_y) overcoat (Row D) provided a far higher dissolution rate than an OMCTS-based $Si_wO_xC_y$ (or its equivalent SiO_xC_y) overcoat (Row A).

Example 11

[00137] An experiment similar to Example 9 was carried out, modified as indicated in this example and in Table 3 (where the results are tabulated). 100 5 mL COP vials were made and coated with an SiO_x barrier layer and an OMCTS-based primer coating or layer as described previously, except that for Sample PC194 only the primer coating or layer was applied. The coating quantity was again measured in parts per billion extracted from the surfaces of the vials to remove the entire primer coating or layer, as reported in Table 3.

[00138] In this example, several different coating dissolution conditions were employed. The test solutions used for dissolution contained either 0.02 or 0.2 wt.% polysorbate-80 surfactant, as well as a buffer to maintain a pH of 8. Dissolution tests were carried out at either 23°C or 40°C.

[00139] Multiple syringes were filled with each test solution, stored at the indicated temperature, and analyzed at several intervals to determine the extraction profile and the amount of silicon extracted. An average dissolution rate for protracted storage times was then calculated by extrapolating the data obtained according to the Protocol for Determining Average Dissolution Rate. The results were calculated as described previously and are shown in Table 3. Of particular note, as shown on Table 3, were the very long calculated shelf lives of the filled packages provided with a PC 194 primer coating or layer:

- 21045 days (over 57 years) based on storage at a pH of 8, 0.02 wt.% polysorbate-80 surfactant, at 23°C;
- 38768 days (over 100 years) based on storage at a pH of 8, 0.2 wt.% polysorbate-80 surfactant, at 23°C;
- 8184 days (over 22 years) based on storage at a pH of 8, 0.02 wt.% polysorbate-80 surfactant, at 40°C; and
- 14732 days (over 40 years) based on storage at a pH of 8, 0.2 wt.% polysorbate-80 surfactant, at 40°C.

[00140] Referring to Table 3, the longest calculated shelf lives corresponded with the use of an RF power level of 150 Watts and a corresponding high W/FM value. It is believed that the use of a higher power level causes higher cross-link density of the primer coating or layer.

Example 12 –Deposit of Lubricant

[00141] A preliminary study was conducted to compare the relative amounts of free (i.e. readily removable) Dow Corning 360 Medical Fluid (PMDS non-reactive silicone fluid) on:

- borosilicate glass vials,
- SiO_x barrier-coated COP vials, and
- SiO_x barrier-coated COP vials further coated with an OMCTS primer coating or layer.

[00142] The SiO_x barrier coatings were applied according to the Protocol for Coating Syringe Barrel Interior with SiO_x. The OMCTS primer coating or layer was applied according to the Protocol for Coating Syringe Barrel Interior with OMCTS Primer Coating or Layer.

[00143] This study was carried out by applying a deposit of Dow Corning 360 Medical Fluid (having a viscosity of 350 CST) to the test vials

[00144] To carry out the preliminary study, the vials were filled with a 50 mM potassium phosphate solution of pH 8 with 0.2% Tween®-80. The filled vials were closed with a prewashed stopper and aluminum crimp and stored for up to 600 hours at a temperature of 40°C, then the solutions from the vials were tested for PMDS non-reactive silicone fluid content according to the Protocol for Determining Average Dissolution Rate.

[00145] This preliminary study showed that the OMCTS primer coating or layer prevented significant amounts of PMDS non-reactive silicone fluid from dissolving into a Tween solution, while significant amounts of PMDS non-reactive silicone fluid dissolved in solution from the borosilicate glass vials and SiO_x barrier-coated COP vials. The

OMCTS primer coating or layer appeared to have a great affinity for PMDS non-reactive silicone fluid, compared to the other substrates tested.

Example 13 – Hypothetical Example of Deposit of Lubricant

[00146] A more rigorous study similar to Example 12 is conducted, using as the substrates:

- borosilicate glass vials,
- uncoated COP vials,
- SiO_x barrier-coated COP vials, and
- SiO_x barrier-coated COP vials further coated with an OMCTS primer coating or layer.

[00147] One set of each type of vial is provided with a deposit of PMDS non-reactive silicone fluid, except that, as indicated above, some of the test vials receiving the deposit of lubricanthave not previously been coated with a primer coating or layer. A second set of each type of vial does not receive a deposit of lubricant and serves as controls.

[00148] The vials are filled with one of the following test solutions:

- 50 mM aqueous phosphate solutions with pHs of 4.0, 6.5, 8.0, 8.0, each also containing 0.2% Tween®-80
- water for injection (wfi) and
- 300 mM aqueous sodium chloride (NaCl).

[00149] All vials with solution are incubated at 40°C and samples pulled at the intervals shown in the table below for testing. The following tests are performed:

- Dissolved Si in solution, a measure of silicone oil and dissolved SiO2
- Total Organic Carbon (TOC) on solution not containing tween, to determine amount of silicone oil in solution

- Particulates focusing on low micron channels to measure micelles of silicone oil
- pH of wfi solutions
- Oxygen transmission rate (OTR) as deemed appropriate to verify integrity of barrier coatings

[00150] The study is expected to demonstrate that the application of a primer coating or layer as described in this specification improves the retention of the PMDS non-reactive silicone fluid on the vials.

Example 14 – Measurement of Contact Angle

[00151] The test purpose was to determine the contact angle or surface energy on the inside surface of two kinds of plastic vials and one kind of glass vial

[00152] The specimens that underwent testing and analysis reported here are three kinds of vials. The specimens are (A) an uncoated COP vial, (B) an SiO_x + primer layer coated COP vial prepared according to the above Protocol for Coating Syringe Barrel Interior with SiO_x, followed by the Protocol for Coating Syringe Barrel Interior with OMCTS Primer Coating or Layer, and (C) a glass vial. Small pieces were obtained by cutting the plastic vials or crushing the glass vial in order to test the inside surface.

[00153] The analysis instrument for the contact angle tests is the Contact Angle Meter model DM-701, made by Kyowa Interface Science Co., Ltd. (Tokyo, Japan). To obtain the contact angle, five water droplets were deposited on the inside surface of small pieces obtained from each specimen. The testing conditions and parameters are summarized below. Both plastic vials were cut and trimmed, while the glass vial needed to be crushed. The best representative pieces for each specimen were selected for testing. A dropsize of 1 µL (one microliter) was used for all samples. Due to the curvature of the specimens, a curvature correction routine was used to accurately measure the contact angle. The second table below contains the values for the radius of curvature used for each specimen.

Contact Angle Testing Conditions and Parameters

Test instrument - DM-701 Contact Angle Meter

Liquid Dispenser - 22 gauge stainless steel needle

Drop Size - 1 µL

Test liquid Distilled water

Environment Ambient air, room temperature

Radius of Curvature for each Vial Specimen

Specimen	Radius of Curvature (µm, micrometers)
COP	9240
COP plus primer	9235
Glass	9900

[00154] The contact angle results for each specimen are provided in an accompanying table.

[00155] The COP plus primer coated specimen had the highest average contact angle of all tested specimens. The average contact angle for the COP plus primer coating or layer specimen was 99.1°. The average contact angle for the uncoated COP specimen was 90.5°. The glass specimen had a significantly lower average contact angle at 10.6°. This data shows the utility of the primer coating to raise the contact angle of the uncoated COP vessel. It is expected that an SiO_x coated vessel without the primer coating or layer would exhibit a result similar to glass, which shows a hydrophilic coating relative to the primer coating or layer.

Contact Angle Result for Each Tested Specimen (degrees)							
Specimen	Test 1	Test 2	Test 3	Test 4	Test 5	Ave	Std. Dev.
COP	88.9	91.9	89.1	91.4	91.1	90.5	1.4
COP/Primer	98.9	96.8	102.2	98.3	99.5	99.1	2.0
Glass	11.6	10.6	10.1	10.4	10.4	10.6	0.6

Example 15

[00156] The purpose of this example was to evaluate the recoverability or drainage of a slightly viscous aqueous solution from glass, COP and coated vials,

[00157] This study evaluated the recovery of a 30 cps (centipoise) carbohydrate solution in water-for-injection from (A) an uncoated COP vial, (B) an SiO_x + primer layer coated COP vial prepared according to the above Protocol for Coating Syringe Barrel Interior with SiO_x, followed by the Protocol for Coating Syringe Barrel Interior with OMCTS Primer Coating or Layer, and (C) a glass vial.

[00158] 2.0 ml of the carbohydrate solution was pipetted into 30 vials each of glass, COP and primer coated vials. The solution was aspirated from the vials with a 10 ml syringe, through a 23 gauge, 1.5" needle. The vials were tipped to one side as the solution was aspirated to maximize the amount recovered. The same technique and similar withdrawal time was used for all vials. The vials were weighed empty, after placing 2.0 ml of the solution to the vial and at the conclusion of aspirating the solution from the vial. The amount delivered to the vial (A) was determined by subtracting the weight of the empty vial from the weight of the vial with the 2.0 ml of solution. The weight of solution not recovered (B) was determined by subtracting the weight of the empty vial from the weight of the vials after aspirating the solution from the vial. The percent unrecovered was determined by dividing B by A and multiplying by 100.

[00159] It was observed during the aspiration of drug product that the glass vials remained wetted with the solution. The COP vial repelled the liquid and as the solution was aspirated from the vials. This helped with recovery but droplets were observed to bead on the sidewalls of the vials during the aspiration. The primer coated vials also repelled the liquid during aspiration but no beading of solution on the sidewalls was observed.

[00160] The conclusion was that primer coated vials do not wet with aqueous solutions as do glass vials, leading to superior recovery of drug product relative to glass. Primer coated vials were not observed to cause beading of solution on sidewall during aspiration of aqueous products therefore coated vials performed better than uncoated COP vials in product recovery experiments.

Example 16—PECVD Treatments and Lubricity Testing

[00161] Multiple syringe samples of each type defined below are plasma processed (except the comparative examples), lubricated with polydimethylsiloxane (PDMS), assembled and filled, and then tested for breakout force. The plasma treating processes and PECVD primer coating formulations used on the syringes tested in this example are among those defined by the parameters set out in Table 4 (employing HMDSO to deposit a PECVD coating, or no HMDSO to effect a plasma treatment without coating, or no HMDSO to effect a plasma treatment of the SiO_xC_y or SiN_xC_y coated surface), and the data obtained is presented in FIG. 3.

[00162] The treatment conditions and data identified as "421-48 COP" relate to plastic syringe samples composed of cyclic olefin polymer (COP) that has not been plasma treated (Comparative example).

[00163] The treatment conditions and data identified as "EO-4 bilayer" relate to plastic syringe samples composed of cyclic olefin polymer. A bi-layer coating (an SiO_x barrier coating or layer, followed by an SiO_xC_y pH protective coating or layer) is applied to the interior surface of the syringe using a PECVD process. The top (pH protective) layer is hydrophobic. After PDMS is applied onto the top layer the syringe is treated with ethylene oxide (sterilization).

[00164] The treatment conditions and data identified as "EO-1 SiO_x" relate to plastic syringe samples composed of cyclic olefin polymer. A SiO_x coating is applied to the interior surface of the syringe using a PECVD process. The SiO_x layer is hydrophilic. PDMS is applied on to the SiO_x layer. The syringe has been treated with ethylene oxide (sterilization).

[00165] The treatment conditions and data identified as "BD" relate to a glass syringe commercially available from Becton, Dickinson and Company or a related company, which is coated by the supplier with 1000 cst PDMS (Comparative example).

[00166] The treatment conditions and data identified as "Schott" relate to a glass syringe commercially available from Schott AG or a related company, which is coated by the supplier with 1000 cst PDMS (Comparative example).

[00167] The barrel interior of each of the above-listed samples except the glass syringes is coated with approximately 1 mg of PDMS (Dow 360 Medical Fluid, 1,000 cst) using an IVEK Multispense 2000 coater under the following conditions:

- Volume – 0.8 – 1.0 mL
- Dispense Rate – 10 L / sec
- Atomizing Pressure – 5 – 8 psi (x N/cm^2)
- Back Pressure – 25 – 30 psi (x N/cm^2)

[00168] The syringe barrels are then assembled with Grey Stelmi plunger tips, which are parked in the syringe for the amount of time indicated in FIG. 3, then tested for F_i (breakout force). Breakout force testing is then conducted similarly to the testing in Example 21 of U.S. Patent 7,985,188.

[00169] The results of this testing are shown in FIG. 3. F_i in Newtons (N) is shown in the vertical scale.and hours are shown in the horizontal scale.

[00170] The following guide is provided to assist interpretation of the test results represented in FIG. 3. A high breakout force is undesirable because it indicates that a user administering medication to a patient using the syringe needs to apply a large force to start the plunger moving. Typically, the force to keep the plunger moving is lower than the breakout force, so the syringe typically is prone to jerking after breakout when administration of a medicament is started, causing discomfort to the recipient. A rapidly increasing breakout force versus park time is undesirable because it indicates that the syringe will soon age as the park time increases, to the point where the breakout force is high with the disadvantage noted above. Thus, a rapidly increasing breakout force with park time indicates a syringe with a short useful shelf life.

[00171] As FIG. 3 illustrates, the data points such as 650 represent the breakout force data for the lubricated, non-plasma treated COP syringe. This syringe type has the highest breakout force after any tested park time, and the breakout force increases substantially with park time – for example at 0.25 hours (15 minutes) park time the breakout force is about 6 N but at 24 hours the breakout force is about 18 N – three times as great.

[00172] The bilayer syringe samples represented by the data points 652 of FIG. 3 have a much lower breakout force and a much lower rate of increase of breakout force with park time than the non-plasma-treated samples represented by the data points 650. Thus, at 0.25 hours (15 minutes) park time the breakout force is about 3.5 N, while at 24 hours park time the breakout force is about 7.6 N.

[00173] The SiO_x barrier coated syringe samples represented by the data points 654 of FIG. 3 have a much lower breakout force and rate of increase with park time than the samples described above represented by the data points 650 and 652. Thus, at 0.25 hours, 15 minutes, the SiO_x barrier coated syringe samples have a breakout force of less than 2 N, comparable to that of the glass-coated syringes represented by the overlapping data points 656 and 658, and at 24 hours the overlap is similar and the breakout force is about 3.5 N. Under the test conditions, therefore, the COP syringes that are barrier coated and lubricated with PDMS perform about as well as the glass syringes. This is a surprising result, showing that the barrier coating on a plastic syringe makes its breakout performance substantially that of a much more expensive and breakable glass syringe.

Example 17 – PECVD and Plasma Treatments and Lubricity Testing.

[00174] Example 17 is carried out comparably to Example 16, except that in addition to the above types of samples, all represented by data points having the same reference numbers in FIG. 4 as in FIG. 3, another type of samples, represented by data points such as 660, represented among the surface modifications in Table 4 employing no monomer ("NA"), was also prepared and tested. These represent plasma treatment without PECVD coating, or plasma treatment after applying a pH protective layer by PECVD. FIG. 4 shows similar results again, and for the plasma treatment only samples represented by the points 660, the results are surprisingly similar to those obtained using glass or SiO_x barrier coated syringe barrels.

[00175] The working examples thus show several different types of plasma treatments, with and without deposition of a PECVD coating, improving the breakout

force and the rate of increase of breakout force with park time in a molded plastic syringe.

Examples 18-25

[00176] These working examples compare the effects of aging lubricated 1 mL syringe barrels on their lubricity properties: breakout or initial force, F_i, and maintenance force, F_m, with dry storage at room temperature (RT) and wet storage at 40°C. Wet storage is defined as filling the syringe with 0.8 mL of water balanced to pH 8 and containing 0.2% Tween® 80 surfactant. Dry storage is of the unfilled syringe barrel.

[00177] Referring to FIGS. 1 and 2, the bilayer syringe model used in these examples was an injection molded cyclic olefin polymer (COP) syringe barrel 250 that underwent two PECVD processes to apply two different silicon based coatings on the inside of the syringe barrel. The first layer, called the adhesion layer 266 or alternatively a tie layer, is a layer typically from about 1 to several nanometers thick (although it can be thicker or thinner), composed of $SiO_xC_yH_z$, provided to create a rugged connection between the COP syringe barrel 250 and a second thicker SiO_x barrier layer 288. The purpose of the SiO_x barrier layer 288 is to provide a barrier to oxygen permeation through the syringe and into its contents. Because of the chemical properties of the SiO_x barrier layer 288, aqueous solutions having a pH of 4 or higher are able to react and dissolve away this layer over time. Generally speaking, the higher the pH of a solution, the faster it dissolves away the SiO_x barrier layer 288. The SiOx layer also served in the present context as a primer coating or layer. The $SiO_xC_yH_z$ coating 286 was not present in the bilayer syringe model.

[00178] Still referring to FIGS. 1 and 2, the trilayer syringe model used in other trials had the syringe barrel 250, adhesion layer 266, and barrier layer 288 of the bilayer syringe model described in the previous paragraph, and in addition underwent a third PECVD process to apply a separate primer coating or layer 286 -- another $SiO_xC_yH_z$ layer. This primer coating or layer 286, also referred to as a pH protective coating or layer, protects the barrier layer from the contents of the syringe. It has the ability to hold up against solutions having a pH greater than 4, including base solutions, without

dissolving, or with reduced dissolution, over time. This primer coating or layer 286 was formed using TMDSO as a precursor.

[00179] The bilayer and trilayer syringe barrels were evaluated with barrel inner diameters (ID) of 6.35 and 6.50 mm. The barrel inner diameters were measured at the midpoint between the front walls of the syringe barrels bearing the needle and the rear flange and opening of the syringe barrel, as is conventional.

[00180] For low-viscosity trials, the bilayer syringe barrels and trilayer syringe barrels were coated with 1 mg per syringe barrel of 1,000 centistoke (cSt) polydimethylsiloxane (PDMS). For high-viscosity trials, the bilayer and trilayer syringe barrels were coated with 1 mg of 12,500 cSt PDMS. The PDMS coatings are shown as 287 in FIG. 2.

[00181] To apply the polydimethylsiloxane (PDMS) or silicone oil to the syringe barrels, the PDMS was sent through an IVEK 40 Point Linear Actuator that can dispense the PDMS at a specific rate and volume. For this experiment, the actuator was set to dispense a volume of 1.75 µL at a rate of 1.00 µL/min. Pressurized air is then mixed with the PDMS to aerosolize and spray it into the inside of the syringe. The syringe barrels were set aside for 8 days to allow the PDMS time to evenly disperse throughout the syringe and cure. The 1,000 cSt and 12,500 cSt PDMS materials used for this experiment were each 360 Dow Corning Medical Fluid. Due to the high viscosity of 12,500 cSt PDMS, the pressurized air was heated to 205°F, and the PDMS was heated to 250°F before they were combined.

[00182] Commercial PDMS-coated BD Hypak® glass syringe barrels with 6.35 mm ID served as a benchmark under both storage conditions. These BD syringe barrels were coated with about 0.4 mg of 1000 cSt PDMS.

[00183] Except as otherwise indicated, 6.7 mm nominal diameter Stelmi plunger tips were inserted in the syringe barrels. The plunger depth was set to 15mm from the bottom of the flange to the tip of the plunger, using a molded puck for consistent manual loading with a plunger rod. Each group contained 30 syringe barrels for five time data points after plunger insertion (3 hours, 1 day, 3 days, 7 days, 21 days), with 6 syringe barrels per time point. Syringe barrels were tested at each time point, except as noted.

[00184] Many of the sets of data points were extrapolated to a storage time of two years (740 days). Various combinations of data sets were plotted, and are presented as FIGS. 5-29. The two-year (740-day) data points are all extrapolated from the data for shorter storage periods.

[00185] For convenient reference, Table 6 shows all the types of syringe barrels tested and identifies the test conditions and corresponding data points in FIGS. 5-29.

[00186] Plunger Initiation Force, F_i, and Plunger Maintenance Force, F_m, were analyzed by the linear regression of log (F_i) vs. log (time), and a two year estimate was generated by extrapolation of this regression. The upper and lower prediction limits (UPL and LPL) of this two year estimate were calculated by a 100(1-α) % Prediction Interval using the t-distribution, with a 95% confidence interval. All error bars in FIGS. 5-29 are two times the sample standard deviation, with the exception of the two year estimates which are the UPL and LPL.

Example 18 – 6.35 mm ID Bilayer Syringes

[00187] FIG. 6 reports the test results for Becton-Dickinson (BD) Hypak® commercial glass syringe barrels, all 6.35 mm inner diameter (ID), which maintained a low F_i of under 10 Newtons (N) for 3 months, in both dry (data points 66) and wet (data points 68) storage, with two year estimates of 15 N and 27 N for dry and wet storage, respectively. FIG. 5 reports the test results for the SiO_x bilayer syringe barrels with 6.35 mm ID, dry (data points 62) and wet (data points 64) storage. For the bilayer syringe barrels, F_i rose above 20 N after 3 months for both wet and dry storage conditions, and 2 year estimates of 68 N and 63 N for dry and wet storage were calculated, respectively. The BD Hypak® commercial glass syringe barrels performed consistently between samples, while the SiO_x bilayer syringe barrels had larger variations between samples.

[00188] FIG. 7 is a plot of maintenance force, F_m, versus time for the data points represented by reference characters 62, 64, 66, and 68 in Table 6. In terms of Maximum Maintenance Force, which is the maximum force required to maintain

movement of the plunger at any point along the barrel, $F_{m,max}$ values 62 for SiO_x bilayer syringe barrels under dry storage were comparable to BD syringe barrel values 68 and 66 under wet and dry storage. Under wet storage, there was a slight rise in $F_{m,max}$ from the 7 to 21 days stretch for BD syringe barrels, but this was regarded as insignificant compared to the rise and variation of the SiO_x bilayer syringe barrels.

Example 19 – 6.5 mm ID Bilayer Syringes

[00189] Next, SiO_x bilayer syringe barrels with 1 mg PDMS (1,000 cSt) and a larger (6.50 mm) barrel ID were tested, as shown in FIG. 8. F_i and F_m performance for dry storage (data points 70) and wet storage (data points 72), compare with BD Groups 1C and 1D.

[00190] FIG. 9 compares the dry storage results for SiO_x bilayer 6.35mm ID (data points 62) and 6.50mm ID (data points 70) syringe barrels. There was significant improvement in performance, in terms of F_i, by simply increasing the barrel ID to 6.50 mm. Two year dry storage estimates dropped from above 60 N for 6.35 mm ID to 13 N for 6.5mm ID.

[00191] FIG. 10 shows that the SiO_x bilayer syringe with a 6.50mm ID (data points 70) can deliver lubricity performance equal to BD syringe barrels with a 6.35 mm ID (data points 66) for dry storage. For wet storage, FIG. 11, the performance of the bilayer syringe (data points 72) is comparable to BD (data points 64).

[00192] A larger barrel ID decreases compression on the plunger tip, which reduces the friction forces between the plunger and the barrel wall.

[00193] FIG. 12 shows the aging effect on maximum maintenance force for SiO_x bilayer, 6.50 mm ID syringe barrels under wet conditions (data points 72) and dry conditions (data points 70). $F_{m,max}$ values are reduced and are much more consistent between samples for SiO_x bilayer syringe barrels with 6.50 mm IDs than those with 6.35 mm IDs (FIG. 7). The dry storage syringe barrels (data points 70) were comparable to BD, and the wet storage syringe barrels (data points 72) were approaching BD.

[00194] Based on this data, the use of 1000 cSt PDMS on 6.50 mm ID COP trilayer syringe barrels with a thin SiO2 layer deposited on the standard tri-layer coating is contemplated to be useful to deliver lubrication performance equal to the benchmark BD glass syringe. The SiO_x bilayer 6.50 mm syringe barrels show F_i performance equivalent to the BD 6.35 mm syringe in both wet and dry conditions. The SiO_x bilayer 6.50 mm syringe shows $F_{m,max}$ approaching that of the BD 6.35 mm syringe in dry and wet conditions.

Example 20 – 12,500 cSt. PDMS, Bilayer Syringes

[00195] FIGS. 13-17 are tests showing the influence of increasing the viscosity of the PDMS lubricant from 1,000 cSt. to 12,500 cSt. on F_i and F_m performance. SiO_x bilayer syringe barrels with 1 mg PDMS (12,500 cSt) with 6.35 mm barrel ID are represented by data points 74 (dry storage) and 76 (wet storage) in FIG. 13. F_i and F_m performance data of the BD glass syringe for dry (data points 78) and wet (data points 80) storage is presented in FIG. 14.

[00196] FIG. 15 compares Initiation Force for SiO_x bilayer 6.35 mm syringes lubricated with 1,000 cSt (data points 62) vs. 12,500 cSt (data points 74) PDMS, both after dry storage.

[00197] FIG. 16 compares Initiation Force for SiO_x bilayer 6.35 mm syringes lubricated with 1,000 cSt (data points 64) vs. 12,500 cSt (data points 76), Wet Storage.

[00198] FIG. 17 determines the Aging Effect on Maximum Maintenance Force for SiO_x bilayer, 6.35 mm ID, 12,500 cSt PDMS, with wet storage (data points 76) and dry storage (data points 74), and BD Control with wet storage (data points 80) and dry storage (data points 78).

[00199] The F_i at the time of plunger insertion observed for 12,500 cSt PDMS coated on the SiO_x bilayer 6.35 mm syringe barrels is greater than that observed with 1,000 PDMS coated on equivalent syringe barrels, for both dry and wet storage. However, the increase in F_i over time, under both storage conditions, with 12,500 cSt

PDMS is slower than that of 1,000 cSt PDMS. The extrapolations suggest the 12,500 cSt PDMS lubricant will have lower F_i at long storage times.

[00200] In FIG. 17, $F_{m,max}$ appears to have greater variation between samples with the 12,500 cSt PDMS than with the 1,000 cSt PDMS. This is believed to be an artifact of the lubrication process, and not an inherent difference. Wet storage still appears to be the worst performance scenario, but it does level off at 5 N, which is a low level of friction, and performs better than wet storage with 1,000 cSt PDMS (FIG. 7).

[00201] 12,500 cSt PDMS also has other advantages as a lubricant for syringes. It is less mobile when applied to the syringe barrel, and is believed to provide fewer sub-visible PDMS emulsion particles than 1,000 Cstk PDMS.

Example 21 – 6.35 mm ID, 6.5 mm ID, and 6.65 mm ID Trilayer Syringes

[00202] FIGS. 18-20 show the initiation force F_i, after both dry and wet storage, for trilayer, 1,000 cSt PDMS lubricated syringe barrels in three sizes -- . 6.35 mm ID, 6.5 mm ID, and 6.65 mm ID. FIGS. 18-20 show that F_i improves for both wet and dry storage as the barrel inner diameter increases, with small differences between wet and dry storage over the 21 days of storage.

Example 22 – Bilayer vs. Trilayer Syringes

[00203] FIGS. 21 and 22 compare the initiation force for bilayer and trilayer syringe barrels at 6.35 mm ID, respectively under dry and wet storage conditions. FIGS. 23 and 24 compare the initiation force for bilayer and trilayer syringe barrels at 6.5 mm ID, respectively under dry and wet storage conditions. Every measured F_i value, under dry storage, is greater for the trilayer syringes than that observed with the bilayer syringes at the same time after plunger insertion. However, the slope of the $\log(F_i)$ vs. $\log(t)$ plot is less than that of SiO_x bilayer for dry and wet storage (See FIGS. 21 through 24), indicating that F_i is changing more slowly with the trilayer syringes than SiO_x bilayer in these experiments.

Example 23 – Trilayer Syringes vs. BD Hypak® Syringes

[00204] FIGS. 25 and 26 compare the initation force of 6.35 mm ID, 6.5 mm ID, and 6.65 mm ID trilayer syringe barrels and the 6.35 mm ID BD Hypak® syringe barrels, respectively under wet and dry conditions. These data show a clear trend of lower initiation force with increasing syringe barrel diameter of the trilayer syringe barrels.

[00205] FIGS. 25 and 26 further illustrate that every measured F_i value under dry storage is above that of BD. However the slope of the log plots show that F_i is changing more slowly with trilayer syringes. It should also be noted that the wet performance is better on trilayer syringes, which approaches BD performance. The two-year extrapolated initiation force data for these examples is presented in Table 7, and shows the same trend. The extrapolated initiation force of the trilayer 6.65 mm ID syringe barrel after wet storage is less than that of the BD glass syringe.

[00206] FIG. 27 shows the maintenance force (F_m) data for the respective trilayer syringe diameters under wet storage conditions, with both force and time shown on a linear scale. The 6.35 mm ID trilayer syringe barrels require a greater maintenance force than the larger-diameter trilayer syringe barrels or the BD glass syringe barrel, which all require about the same, quite low maintenance force. By increasing the ID to just 6.50 mm, there is significant improvement that is comparable to BD.

Example 24 – Silicon Dissolution Data

[00207] FIGS. 28 and 29, both having linear scales, show the silicon dissolution rate for PDMS coated bilayer, trilayer, and glass (BD Hypak®) syringe barrels, measured as indicated previously in this specification. Data points 64 represent 6.35 mm ID bilayer syringe barrels lubricated with 1,000 cSt. PDMS, data points 72 represent 6.5 mm ID bilayer syringe barrels lubricated with 1,000 cSt. PDMS, and data points 76 represent 6.35 mm ID bilayer syringe barrels lubricated with 12,500 cSt. PDMS. The SiO_x surface of the bilayer syringe barrels dissolved in less than a week, after which the amount of silicon in solution reached a steady state at about 25 micrograms (µg) of silicon. In comparison, the tri-layer system, represented by data points 88 and 92, is more stable under the same storage conditions, with less than 1.5 µg of Si dissolved

after 20 days. The surface of the trilayer syringe barrels exposed to the fluid under wet storage conditions is an SiO_xC_y pH protective coating or layer that guards the underlying SiO_x coating or layer against dissolution.

[00208] FIG. 29 shows the silicon dissolution data for the BD Hypak® glass syringe barrels. Data points 68 and 80 are two groups of nominally identical syringe barrels, showing dissolution of over 5 µg of Si in less than 3 weeks under wet storage conditions. This data shows that more silicon is dissolved from the glass syringe barrels over the period of this experiment than from the trilayer syringe barrels discussed in the preceding paragraph.

Example 25 – Container Closure Integrity (CCI) vs. Barrel ID

[00209] Referring to FIG. 30, the relation between F_i, F_m, and container closure integrity failure data is shown for trilayer syringes having 6.48 mm ID to 6.67 mm ID. In this work, Datwyler Omniflex Plungers were used, having a nominal diameter (expressed as the average maximum rib outside diameter) of 6.77 mm, thus exceeding the respective syringe barrel IDs identified in FIG. 30 by the amounts shown in Table 8.

[00210] This data shows that increasing the syringe ID to reduce initiation and sliding forces when dispensing from the syringe increases the failure rate resulting from loss of container closure integrity. This data shows that a plunger 0.2 mm larger than the Barrel ID provided a 3% failure rate in container closure integrity of the COP trilayer syringe barrel, while a plunger 0.1 mm larger than the Barrel ID provided a 100% failure rate with the same barrel.

[00211] Finally, the solution of increasing the barrel ID, used in this data to improve the initiation and maintenance forces of COP syringe barrels, is not as practical for improving a glass syringe barrel because the barrel ID tolerance of a glass syringe barrel is much greater than the barrel ID tolerance of an injection molded COP barrel, due to the different manufacturing methods used for glass vs. injection molded resin. For example, each member of a lot of 25 COP syringe barrels, nominally 0.2544 inch (6.462 mm) ID, was found to have a standard deviation of 0.0002 inch (0.005 mm),

while a lot of BD Hypak® glass syringe barrels, nominally 0.2506 inch (6.365 mm) ID, had a standard deviation of 0.0012 inch (0.03 mm) – six times as great as for the COP syringe barrels. This larger statistical deviation of the glass syringe barrels means that glass outliers having the greatest ID are much more likely to cross the threshold of breakdown of CCI than COP outliers in a lot having the same nominal diameter.

[00212] To summarize this experimentation:

[00213] COP trilayer syringes with PDMS performed better during chemical aging than a BD glass syringe with PDMS (see FIGS. 28-29).

[00214] COP trilayer syringes with PDMS aged in a wet environment showed a slower increase in F_i over time than a BD syringe PDMS on glass.

[00215] Increasing the COP syringe barrel ID from 6.35 mm to 6.50 reduced the F_i/F_m with PDMS, for both bilayer and trilayer syringe barrels. A plastic, injection molded syringe has better dimensional tolerances than a glass syringe. Better dimensional tolerances mean that the nominal syringe ID can be increased from 6.35 mm (used in glass syringes) to 6.50 mm (for COP syringes) without degrading the seal integrity between the plunger and the syringe barrel.
COP bilayer 6.50 mm ID syringe barrels with PDMS had similar F_i/F_m characteristics to BD Hypak® glass syringe barrels using PDMS on glass.

[00216] Employing 12,500 Cstk PDMS, having a higher viscosity and molecular weight compared with 1,000 Cstk. PDMS, has several advantages. The comparative studies with 12,500 and 1,000 Cstk PDMS with COP and SiO2 coated COP syringes show that the rate of increase in force over time (aging) is slower with 12,500 Cstk PDMS. Thus, the magnitude of forces F_i/F_m is higher with 12,500 than 1,000 Cstk PDMS at early times, but the relative magnitude reverses at long storage times after plunger insertion

TABLES

TABLE 1: primer coating or layer

Example	OMCTS (sccm)	O_2 (sccm)	Ar (sccm)
I	2.5	0.38	7.6
J	2.5	0.38	-
K	2.5	-	-

TABLE 2

Silicon Extractables Comparison of Lubricity Coatings		
Package Type	Static (ug/L)	Dynamic (ug/L)
Cyclic Olefin Syringe with CV Holdings SiOCH Lubricity Coating	70	81
Borocilicate Glass Syringe with silicone oil	825	835

TABLE 3

Sample	OMCTS Flow Rate (sccm)	Argon Flow Rate (sccm)	O_2 Flow Rate (sccm)	Power (W)	Plasma Duration (sec)	W/FM (kJ/kg)	Total Si (ppb) (OMCTS) layer)	Calculated Shelf-life (days)	Average Rate of Dissolution (ppb/day)
	Process Parameters						Si Dissolution @ pH8/23ºC/0.02% Tween®-80		
PC194	0.5	20	0.5	150	20	1223335	73660	21045	3.5
018	1.0	20	0.5	18	15	77157	42982	1330	32.3
	Process Parameters						Si Dissolution @ pH8/23ºC/0.2% Tween®-80		
PC194	0.5	20	0.5	150	20	1223335	73660	38768	1.9
018	1.0	20	0.5	18	15	77157	42982	665	64.6
048	4	80	2	35	20	37507	56520	1074	52.62
	Process Parameters						Si Dissolution @ pH8/40ºC/0.02% Tween®-80		
PC194	0.5	20	0.5	150	20	1223335	73660	8184	9
018	1.0	20	0.5	18	15	77157	42982	511	84
	Process Parameters						Si Dissolution @ pH8/40ºC/0.2% Tween®-80		
PC194	0.5	20	0.5	150	20	1223335	73660	14732	5
018	1.0	20	0.5	18	15	77157	42982	255	168

TABLE 4

Surface Mod	Monomer	Monomer (sccm)	Argon (sccm)	Oxygen (sccm)	Power (W)	Time (sec)
1	HMDSO	about 3	0	25	35	2.5
2	HMDSO		0	25	35	5
3	HMDSO		0	25	35	10
4	HMDSO		0	25	40	5
5	HMDSO		0	50	40	5
6	HMDSO		0	75	40	5
7	None	NA	50	0	40	5
8	None	NA	25	25	40	5
9	None	NA	0	50	40	5

TABLE 5	Silicon Dissolution with pH 8 at 40°C						
	(ug/L)						
Vial Coating Description	**1 day**	**2 days**	**3 days**	4 days	7 days	**10 days**	**15 days**
A. SiO_x made with HMDSO Plasma + $Si_wO_xC_y$ or its equivalent SiO_xC_y made with OMCTS Plasma	165	211	226	252	435	850	1,364
B. $Si_wO_xC_y$ or its equivalent SiO_xC_y made with OMCTS Plasma	109	107	76	69	74	158	198
C. SiO_x made with HMDSO Plasma	2,504	4,228	5,226	5,650	9,292	10,177	9,551
D. SiO_x made with HMDSO Plasma + $Si_wO_xC_y$ or its equivalent SiO_xC_y made with HMDSO Plasma	1,607	1,341	3,927	10,182	18,148	20,446	21,889
E. $Si_wO_xC_y$ or its equivalent SiO_xC_y made	1,515	1,731	1,813	1,743	2,890	3,241	3,812

TABLE 5	Silicon Dissolution with pH 8 at 40°C						
	(ug/L)						
Vial Coating Description	**1 day**	**2 days**	**3 days**	4 days	7 days	**10 days**	**15 days**
with HMDSO Plasma							

TABLE 6

Ref. Char.	Group	Substrate	Viscosity (cSt)	Barrel ID (mm)	Solution	Storage (ºC)
62	1A	Bilayer	1,000	6.35	Dry	RT
64	1B	Bilayer	1,000	6.35	Wet	40
70	2A	Bilayer	1,000	6.50	Dry	RT
72	2B	Bilayer	1,000	6.50	Wet	40
74	3A	Bilayer	12,500	6.35	Dry	RT
76	3B	Bilayer	12,500	6.35	Wet	40
82	4A	Trilayer	1,000	6.35	Dry	RT
84	4B	Trilayer	1,000	6.35	Wet	40
86	4C	Trilayer	1,000	6.50	Dry	RT
88	4D	Trilayer	1,000	6.50	Wet	40
90	4E	Trilayer	1,000	6.65	Dry	RT
92	4F	Trilayer	1,000	6.65	Wet	40
66	1C	BD Hypak	1,000	6.35	Dry	RT
68	1D	BD Hypak	1,000	6.35	Wet	40
78	3C	BD Hypak	1,000	6.35	Dry	RT
80	3D	BD Hypak	1,000	6.35	Wet	40

TABLE 7

Extrapolated 2 Year Estimates on F_i for Trilayer and BD.

Syringe	Dry Storage	Wet Storage
Trilayer 6.35 mm	33 N	49 N
Trilayer 6.50 mm	36 N	34 N
Trilayer 6.65 mm	29 N	18 N
BD Hypak®	15 N	28 N

TABLE 8

Barrel ID	Difference, Plunger OD vs. Barrel ID	Compression of Plunger in Barrel	CCI Failure Rate, FIG. 30
6.48 mm	0.29 mm	4.28%	0%
6.52 mm	0.25 mm	--	6%
6.55 mm	0.22 mm	3.25%	0%
6.57 mm	0.20 mm	--	3%
6.67 mm	0.10 mm	1.48%	100%

CLAIMS

1. A syringe comprising:
   - a wall having a generally cylindrical interior surface defining a lumen and adapted to receive a plunger;
   - a primer coating or layer between 1 and 1000 nm thick of $SiO_xC_yH_z$, in which x is from about 0.5 to about 2.4 as measured by X-ray photoelectron spectroscopy (XPS), y is from about 0.6 to about 3 as measured by XPS, and z is from about 2 to about 9, on at least a portion of the interior surface, the primer coating or layer having an outside surface facing the interior surface of the barrel and an inside surface facing the lumen; and
   - a deposit of fluid lubricant on the inside surface of the primer coating or layer.

2. The syringe of claim 1, further comprising a plunger seated in the barrel against the interior surface.

3. The syringe of claim 2, in which the plunger has an outer sliding surface configured to slide along the interior surface.

4. The syringe of a preceding claim 2 or 3, in which the outer diameter of the plunger when unconstrained by the barrel is from about 0.05 mm to about 0.3 mm greater, preferably from 0.1 to about 0.3 mm, greater, more preferably from 0.15 mm to 0.25 mm greater, still more preferably about 0.2 mm greater than the average inner diameter of the interior surface.

5. The syringe of a preceding claim 3 or 4, in which the plunger outer sliding surface has a primer coating or layer.

6. The syringe of a preceding claim 2-5, in which the breakout force, Fi, of the plunger is between 0.5 and 15 N, alternatively between 1 and 10 N, alternatively between 5 and 15 N, after a park time of 3 days, alternatively 10 days, alternatively 30

days, alternatively 3 months, alternatively 6 months, alternatively 9 months, alternatively 12 months, alternatively 15 months, alternatively 18 months, alternatively two years.

7. The syringe of a preceding claim 2-6, in which the maintenance force, Fm, of the plunger is between 0.5 and 15 N, alternatively between 1 and 10 N, alternatively between 5 and 15 N, after a park time of 3 days, alternatively 10 days, alternatively 30 days, alternatively 3 months, alternatively 6 months, alternatively 9 months, alternatively 12 months, alternatively 15 months, alternatively 18 months, alternatively two years.

8. The syringe of a preceding claim 1-7, in which the barrel comprises injection molded material.

9. The syringe of a preceding claim 1-8, in which the syringe barrel adjacent to the interior surface comprises a polyolefin, a polyester, or a combination of a polyolefin and a polyester, and preferably comprises COC (cyclic olefin copolymer), COP (cyclic olefin polymer), PET (polyethylene terephthalate), polypropylene (PP), or a combination of two or more of these.

10. The syringe of a preceding claim 1-9, in which z is measured by Rutherford back scattering (RBS).

11. The syringe of a preceding claim 1-10, in which z is measured by Hydrogen forward scattering (HFS).

12. The syringe of a preceding claim 1-11 in which, in $SiO_xC_yH_z$,

- x is between 0.5 and 1.5, preferably between 0.7 and 1.3, more preferably between 0.8 and 1.2, still more preferably between 0.9 and 1.2; and
- y is between 0.9 and 2, preferably between 0.9 and 1.5, more preferably between 0.9 and 1.4 .

13. The syringe of a preceding claim 1-12, in which the primer coating or layer is between between 10 and 1000 nm thick, preferably between 50 and 800 nm thick, more preferably between 100 and 700 nm thick, still more preferably between 300 and 600 nm thick.

14. The syringe of a preceding claim 1-13, in which the primer coating or layer is deposited under conditions effective to form a coating from a precursor selected from a linear siloxane, a monocyclic siloxane, a polycyclic siloxane, a polysilsesquioxane, a linear silazane, a monocyclic silazane, a polycyclic silazane, or a combination of any two or more of these precursors, and preferably comprises octamethylenecyclotetrasiloxane (OMCTS), tetramethyldisiloxane (TMDSO), hexamethyldisiloxane (HMDSO), or a combination of two or more of these.

15. The syringe of a preceding claim 1-14, in which the interior surface of the primer coating or layer has a contact angle (with distilled water) of from 90° to 110°, optionally from 80° to 120°, optionally from 70° to 130°.

16. The syringe of a preceding claim 1-15, in which the fluid lubricant comprises polydimethylsiloxane, and preferably comprises non-reactive silicone fluid, nonreactive silicone emulsion, curable silicone fluid, or a combination of two or more of these.

17. The syringe of a preceding claim 1-16, in which the viscosity of the fluid lubricant is from 500 to 30,000 cSt, preferably from 1000 to 25,000 cSt, more preferably from 5,000 to 20,000 cSt, still more preferably from 10,000 to 15,000 cSt, optionally about 12,500 cSt.

18. The syringe of a preceding claim 1-17, in which the deposit of fluid lubricant is formed on the primer coating or layer by spraying the fluid lubricant.

19. The syringe of a preceding claim 1-18, further comprising a barrier coating or layer of SiO_x, in which x is from 1.5 to 2.9 as measured by XPS, located between the primer coating or layer and the interior surface.

20. The syringe of a preceding claim 1-19, further comprising an adhesion coating or layer of the $SiO_xC_yH_z$, located between the barrier coating or layer and the interior surface.

21. The syringe of a preceding claim 1-20, in which the deposit of lubricant and primer coating or layer is effective to provide a lower frictional resistance than the uncoated barrel interior surface.

22. The syringe of claim 21, in which the frictional resistance is reduced by at least 25% in comparison to the uncoated barrel interior surface.

23. The syringe of claim 21, in which the frictional resistance is reduced by at least 45% in comparison to the uncoated barrel interior surface.

24. The syringe of claim 21, in which the frictional resistance is reduced by at least 60% in comparison to the uncoated barrel interior surface.

25. The syringe of a preceding claim 1-24, in which the deposit of lubricant is effective to reduce the frictional resistance between a portion of the barrel interior surface contacted by the deposit of fluid lubricant and a relatively sliding part after the syringe is assembled.

26. The syringe of a preceding claim 1-25, in which the deposit of fluid lubricant is effective to reduce the frictional resistance between the barrel interior surface and a relatively sliding part at least one year after the syringe is assembled.

27. The syringe of a preceding claim 1-26, in which the deposit of fluid lubricant is effective to reduce the frictional resistance between the barrel interior surface and a relatively sliding part at least eighteen months after the syringe is assembled.

28. The syringe of a preceding claim 1-27, in which the deposit of fluid lubricant is effective to reduce the frictional resistance between the barrel interior surface and a relatively sliding part at least two years after the syringe is assembled.

29. The syringe of a preceding claim 1-28, further comprising a fluid stored in the lumen in contact with the deposit of fluid lubricant.

30. The syringe of claim 29, in which the fluid comprises a food.

31. The syringe of claim 29, in which the fluid comprises a nutritional supplement.

32. The syringe of a claim 29, in which the fluid is a water solution or dispersion.

33. The syringe of claim 29, in which the fluid comprises a drug.

34. The syringe of claim 29, in which the fluid consists essentially of a drug.

35. The syringe of claim 33 or 34, in which the drug is a parenteral drug.

36. The syringe of claim 29, in which the fluid comprises an inhalation anesthetic.

37. The syringe of claim 29, in which the fluid comprises a diagnostic test material.

38. The syringe of claim 29, in which the fluid comprises a member selected from the group consisting of:

INHALATION ANESTHETICS

Aliflurane
Chloroform
Cyclopropane
Desflurane (Suprane)
Diethyl Ether
Enflurane (Ethrane)
Ethyl Chloride
Ethylene

Halothane (Fluothane)
Isoflurane (Forane, Isoflo)
Isopropenyl vinyl ether
Methoxyflurane
methoxyflurane,
Methoxypropane
Nitrous Oxide
Roflurane
Sevoflurane (Sevorane, Ultane, Sevoflo)
Teflurane
Trichloroethylene
Vinyl Ether
Xenon

INJECTABLE DRUGS

Ablavar (Gadofosveset Trisodium Injection)
Abarelix Depot
Abobotulinumtoxin A Injection (Dysport)
ABT-263
ABT-869
ABX-EFG
Accretropin (Somatropin Injection)
Acetadote (Acetylcysteine Injection)
Acetazolamide Injection (Acetazolamide Injection)
Acetylcysteine Injection (Acetadote)
Actemra (Tocilizumab Injection)
Acthrel (Corticorelin Ovine Triflutate for Injection)
Actummune
Activase
Acyclovir for Injection (Zovirax Injection)
Adacel

Adalimumab

Adenoscan (Adenosine Injection)

Adenosine Injection (Adenoscan)

Adrenaclick

AdreView (Iobenguane I 123 Injection for Intravenous Use)

Afluria

Ak-Fluor (Fluorescein Injection)

Aldurazyme (Laronidase)

Alglucerase Injection (Ceredase)

Alkeran Injection (Melphalan Hcl Injection)

Allopurinol Sodium for Injection (Aloprim)

Aloprim (Allopurinol Sodium for Injection)

Alprostadil

Alsuma (Sumatriptan Injection)

ALTU-238

Amino Acid Injections

Aminosyn

Apidra

Apremilast

Alprostadil Dual Chamber System for Injection (Caverject Impulse)

AMG 009

AMG 076

AMG 102

AMG 108

AMG 114

AMG 162

AMG 220

AMG 221

AMG 222

AMG 223

AMG 317

AMG 379
AMG 386
AMG 403
AMG 477
AMG 479
AMG 517
AMG 531
AMG 557
AMG 623
AMG 655
AMG 706
AMG 714
AMG 745
AMG 785
AMG 811
AMG 827
AMG 837
AMG 853
AMG 951
Amiodarone HCl Injection (Amiodarone HCl Injection)
Amobarbital Sodium Injection (Amytal Sodium)
Amytal Sodium (Amobarbital Sodium Injection)
Anakinra
Anti-Abeta
Anti-Beta7
Anti-Beta20
Anti-CD4
Anti-CD20
Anti-CD40
Anti-IFNalpha
Anti-IL13

Anti-OX40L

Anti-oxLDS

Anti-NGF

Anti-NRP1

Arixtra

Amphadase (Hyaluronidase Inj)

Ammonul (Sodium Phenylacetate and Sodium Benzoate Injection)

Anaprox

Anzemet Injection (Dolasetron Mesylate Injection)

Apidra (Insulin Glulisine [rDNA origin] Inj)

Apomab

Aranesp (darbepoetin alfa)

Argatroban (Argatroban Injection)

Arginine Hydrochloride Injection (R-Gene 10)

Aristocort

Aristospan

Arsenic Trioxide Injection (Trisenox)

Articane HCl and Epinephrine Injection (Septocaine)

Arzerra (Ofatumumab Injection)

Asclera (Polidocanol Injection)

Ataluren

Ataluren-DMD

Atenolol Inj (Tenormin I.V. Injection)

Atracurium Besylate Injection (Atracurium Besylate Injection)

Avastin

Azactam Injection (Aztreonam Injection)

Azithromycin (Zithromax Injection)

Aztreonam Injection (Azactam Injection)

Baclofen Injection (Lioresal Intrathecal)

Bacteriostatic Water (Bacteriostatic Water for Injection)

Baclofen Injection (Lioresal Intrathecal)

Bal in Oil Ampules (Dimercarprol Injection)

BayHepB

BayTet

Benadryl

Bendamustine Hydrochloride Injection (Treanda)

Benztropine Mesylate Injection (Cogentin)

Betamethasone Injectable Suspension (Celestone Soluspan)

Bexxar

Bicillin C-R 900/300 (Penicillin G Benzathine and Penicillin G Procaine Injection)

Blenoxane (Bleomycin Sulfate Injection)

Bleomycin Sulfate Injection (Blenoxane)

Boniva Injection (Ibandronate Sodium Injection)

Botox Cosmetic (OnabotulinumtoxinA for Injection)

BR3-FC

Bravelle (Urofollitropin Injection)

Bretylium (Bretylium Tosylate Injection)

Brevital Sodium (Methohexital Sodium for Injection)

Brethine

Briobacept

BTT-1023

Bupivacaine HCl

Byetta

Ca-DTPA (Pentetate Calcium Trisodium Inj)

Cabazitaxel Injection (Jevtana)

Caffeine Alkaloid (Caffeine and Sodium Benzoate Injection)

Calcijex Injection (Calcitrol)

Calcitrol (Calcijex Injection)

Calcium Chloride (Calcium Chloride Injection 10%)

Calcium Disodium Versenate (Edetate Calcium Disodium Injection)

Campath (Altemtuzumab)

Camptosar Injection (Irinotecan Hydrochloride)

Canakinumab Injection (Ilaris)

Capastat Sulfate (Capreomycin for Injection)

Capreomycin for Injection (Capastat Sulfate)

Cardiolite (Prep kit for Technetium Tc99 Sestamibi for Injection)

Carticel

Cathflo

Cefazolin and Dextrose for Injection (Cefazolin Injection)

Cefepime Hydrochloride

Cefotaxime

Ceftriaxone

Cerezyme

Carnitor Injection

Caverject

Celestone Soluspan

Celsior

Cerebyx (Fosphenytoin Sodium Injection)

Ceredase (Alglucerase Injection)

Ceretec (Technetium Tc99m Exametazime Injection)

Certolizumab

CF-101

Chloramphenicol Sodium Succinate (Chloramphenicol Sodium Succinate Injection)

Chloramphenicol Sodium Succinate Injection (Chloramphenicol Sodium Succinate)

Cholestagel (Colesevelam HCL)

Choriogonadotropin Alfa Injection (Ovidrel)

Cimzia

Cisplatin (Cisplatin Injection)

Clolar (Clofarabine Injection)

Clomiphine Citrate

Clonidine Injection (Duraclon)

Cogentin (Benztropine Mesylate Injection)

Colistimethate Injection (Coly-Mycin M)

Coly-Mycin M (Colistimethate Injection)

Compath

Conivaptan Hcl Injection (Vaprisol)

Conjugated Estrogens for Injection (Premarin Injection)

Copaxone

Corticorelin Ovine Triflutate for Injection (Acthrel)

Corvert (Ibutilide Fumarate Injection)

Cubicin (Daptomycin Injection)

CF-101

Cyanokit (Hydroxocobalamin for Injection)

Cytarabine Liposome Injection (DepoCyt)

Cyanocobalamin

Cytovene (ganciclovir)

D.H.E. 45

Dacetuzumab

Dacogen (Decitabine Injection)

Dalteparin

Dantrium IV (Dantrolene Sodium for Injection)

Dantrolene Sodium for Injection (Dantrium IV)

Daptomycin Injection (Cubicin)

Darbepoietin Alfa

DDAVP Injection (Desmopressin Acetate Injection)

Decavax

Decitabine Injection (Dacogen)

Dehydrated Alcohol (Dehydrated Alcohol Injection)

Denosumab Injection (Prolia)

Delatestryl

Delestrogen

Delteparin Sodium

Depacon (Valproate Sodium Injection)

Depo Medrol (Methylprednisolone Acetate Injectable Suspension)

DepoCyt (Cytarabine Liposome Injection)

DepoDur (Morphine Sulfate XR Liposome Injection)

Desmopressin Acetate Injection (DDAVP Injection)

Depo-Estradiol

Depo-Provera 104mg/ml

Depo-Provera 150mg/ml

Depo-Testosterone

Dexrazoxane for Injection, Intravenous Infusion Only (Totect)

Dextrose / Electrolytes

Dextrose and Sodium Chloride Inj (Dextrose 5% in 0.9% Sodium Chloride)

Dextrose

Diazepam Injection (Diazepam Injection)

Digoxin Injection (Lanoxin Injection)

Dilaudid-HP (Hydromorphone Hydrochloride Injection)

Dimercarprol Injection (Bal in Oil Ampules)

Diphenhydramine Injection (Benadryl Injection)

Dipyridamole Injection (Dipyridamole Injection)

DMOAD

Docetaxel for Injection (Taxotere)

Dolasetron Mesylate Injection (Anzemet Injection)

Doribax (Doripenem for Injection)

Doripenem for Injection (Doribax)

Doxercalciferol Injection (Hectorol Injection)

Doxil (Doxorubicin Hcl Liposome Injection)

Doxorubicin Hcl Liposome Injection (Doxil)

Duraclon (Clonidine Injection)

Duramorph (Morphine Injection)

Dysport (Abobotulinumtoxin A Injection)

Ecallantide Injection (Kalbitor)

EC-Naprosyn (naproxen)

Edetate Calcium Disodium Injection (Calcium Disodium Versenate)

Edex (Alprostadil for Injection)

Engerix

Edrophonium Injection (Enlon)

Eliglustat Tartate

Eloxatin (Oxaliplatin Injection)

Emend Injection (Fosaprepitant Dimeglumine Injection)

Enalaprilat Injection (Enalaprilat Injection)

Enlon (Edrophonium Injection)

Enoxaparin Sodium Injection (Lovenox)

Eovist (Gadoxetate Disodium Injection)

Enbrel (etanercept)

Enoxaparin

Epicel

Epinepherine

Epipen

Epipen Jr.

Epratuzumab

Erbitux

Ertapenem Injection (Invanz)

Erythropoieten

Essential Amino Acid Injection (Nephramine)

Estradiol Cypionate

Estradiol Valerate

Etanercept

Exenatide Injection (Byetta)

Evlotra

Fabrazyme (Adalsidase beta)

Famotidine Injection

FDG (Fludeoxyglucose F 18 Injection)

Feraheme (Ferumoxytol Injection)

Feridex I.V. (Ferumoxides Injectable Solution)

Fertinex

Ferumoxides Injectable Solution (Feridex I.V.)

Ferumoxytol Injection (Feraheme)

Flagyl Injection (Metronidazole Injection)

Fluarix

Fludara (Fludarabine Phosphate)

Fludeoxyglucose F 18 Injection (FDG)

Fluorescein Injection (Ak-Fluor)

Follistim AQ Cartridge (Follitropin Beta Injection)

Follitropin Alfa Injection (Gonal-f RFF)

Follitropin Beta Injection (Follistim AQ Cartridge)

Folotyn (Pralatrexate Solution for Intravenous Injection)

Fondaparinux

Forteo (Teriparatide (rDNA origin) Injection)

Fostamatinib

Fosaprepitant Dimeglumine Injection (Emend Injection)

Foscarnet Sodium Injection (Foscavir)

Foscavir (Foscarnet Sodium Injection)

Fosphenytoin Sodium Injection (Cerebyx)

Fospropofol Disodium Injection (Lusedra)

Fragmin

Fuzeon (enfuvirtide)

GA101

Gadobenate Dimeglumine Injection (Multihance)

Gadofosveset Trisodium Injection (Ablavar)

Gadoteridol Injection Solution (ProHance)

Gadoversetamide Injection (OptiMARK)

Gadoxetate Disodium Injection (Eovist)

Ganirelix (Ganirelix Acetate Injection)

Gardasil

GC1008

GDFD

Gemtuzumab Ozogamicin for Injection (Mylotarg)

Genotropin

Gentamicin Injection

GENZ-112638

Golimumab Injection (Simponi Injection)

Gonal-f RFF (Follitropin Alfa Injection)

Granisetron Hydrochloride (Kytril Injection)

Gentamicin Sulfate

Glatiramer Acetate

Glucagen

Glucagon

HAE1

Haldol (Haloperidol Injection)

Havrix

Hectorol Injection (Doxercalciferol Injection)

Hedgehog Pathway Inhibitor

Heparin

Herceptin

hG-CSF

Humalog

Human Growth Hormone

Humatrope

HuMax

Humegon

Humira

Humulin

Ibandronate Sodium Injection (Boniva Injection)

Ibuprofen Lysine Injection (NeoProfen)

Ibutilide Fumarate Injection (Corvert)

Idamycin PFS (Idarubicin Hydrochloride Injection)

Idarubicin Hydrochloride Injection (Idamycin PFS)

Ilaris (Canakinumab Injection)

Imipenem and Cilastatin for Injection (Primaxin I.V.)

Imitrex

Incobotulinumtoxin A for Injection (Xeomin)

Increlex (Mecasermin [rDNA origin] Injection)

Indocin IV (Indomethacin Inj)

Indomethacin Inj (Indocin IV)

Infanrix

Innohep

Insulin

Insulin Aspart [rDNA origin] Inj (NovoLog)

Insulin Glargine [rDNA origin] Injection (Lantus)

Insulin Glulisine [rDNA origin] Inj (Apidra)

Interferon alfa-2b, Recombinant for Injection (Intron A)

Intron A (Interferon alfa-2b, Recombinant for Injection)

Invanz (Ertapenem Injection)

Invega Sustenna (Paliperidone Palmitate Extended-Release Injectable Suspension)

Invirase (saquinavir mesylate)

Iobenguane I 123 Injection for Intravenous Use (AdreView)

Iopromide Injection (Ultravist)

Ioversol Injection (Optiray Injection)

Iplex (Mecasermin Rinfabate [rDNA origin] Injection)

Iprivask

Irinotecan Hydrochloride (Camptosar Injection)

Iron Sucrose Injection (Venofer)

Istodax (Romidepsin for Injection)

Itraconazole Injection (Sporanox Injection)

Jevtana (Cabazitaxel Injection)

Jonexa

Kalbitor (Ecallantide Injection)

KCL in D5NS (Potassium Chloride in 5% Dextrose and Sodium Chloride Injection)
KCL in D5W
KCL in NS
Kenalog 10 Injection (Triamcinolone Acetonide Injectable Suspension)
Kepivance (Palifermin)
Keppra Injection (Levetiracetam)
Keratinocyte
KFG
Kinase Inhibitor
Kineret (Anakinra)
Kinlytic (Urokinase Injection)
Kinrix
Klonopin (clonazepam)
Kytril Injection (Granisetron Hydrochloride)
lacosamide Tablet and Injection (Vimpat)
Lactated Ringer's
Lanoxin Injection (Digoxin Injection)
Lansoprazole for Injection (Prevacid I.V.)
Lantus
Leucovorin Calcium (Leucovorin Calcium Injection)
Lente (L)
Leptin
Levemir
Leukine Sargramostim
Leuprolide Acetate
Levothyroxine
Levetiracetam (Keppra Injection)
Lovenox
Levocarnitine Injection (Carnitor Injection)
Lexiscan (Regadenoson Injection)
Lioresal Intrathecal (Baclofen Injection)

Liraglutide [rDNA] Injection (Victoza)

Lovenox (Enoxaparin Sodium Injection)

Lucentis (Ranibizumab Injection)

Lumizyme

Lupron (Leuprolide Acetate Injection)

Lusedra (Fospropofol Disodium Injection)

Maci

Magnesium Sulfate (Magnesium Sulfate Injection)

Mannitol Injection (Mannitol IV)

Marcaine (Bupivacaine Hydrochloride and Epinephrine Injection)

Maxipime (Cefepime Hydrochloride for Injection)

MDP Multidose Kit of Technetium Injection (Technetium Tc99m Medronate Injection)

Mecasermin [rDNA origin] Injection (Increlex)

Mecasermin Rinfabate [rDNA origin] Injection (Iplex)

Melphalan Hcl Injection (Alkeran Injection)

Methotrexate

Menactra

Menopur (Menotropins Injection)

Menotropins for Injection (Repronex)

Methohexital Sodium for Injection (Brevital Sodium)

Methyldopate Hydrochloride Injection, Solution (Methyldopate Hcl)

Methylene Blue (Methylene Blue Injection)

Methylprednisolone Acetate Injectable Suspension (Depo Medrol)

MetMab

Metoclopramide Injection (Reglan Injection)

Metrodin (Urofollitropin for Injection)

Metronidazole Injection (Flagyl Injection)

Miacalcin

Midazolam (Midazolam Injection)

Mimpara (Cinacalet)

Minocin Injection (Minocycline Inj)

Minocycline Inj (Minocin Injection)

Mipomersen

Mitoxantrone for Injection Concentrate (Novantrone)

Morphine Injection (Duramorph)

Morphine Sulfate XR Liposome Injection (DepoDur)

Morrhuate Sodium (Morrhuate Sodium Injection)

Motesanib

Mozobil (Plerixafor Injection)

Multihance (Gadobenate Dimeglumine Injection)

Multiple Electrolytes and Dextrose Injection

Multiple Electrolytes Injection

Mylotarg (Gemtuzumab Ozogamicin for Injection)

Myozyme (Alglucosidase alfa)

Nafcillin Injection (Nafcillin Sodium)

Nafcillin Sodium (Nafcillin Injection)

Naltrexone XR Inj (Vivitrol)

Naprosyn (naproxen)

NeoProfen (Ibuprofen Lysine Injection)

Nandrol Decanoate

Neostigmine Methylsulfate (Neostigmine Methylsulfate Injection)

NEO-GAA

NeoTect (Technetium Tc 99m Depreotide Injection)

Nephramine (Essential Amino Acid Injection)

Neulasta (pegfilgrastim)

Neupogen (Filgrastim)

Novolin

Novolog

NeoRecormon

Neutrexin (Trimetrexate Glucuronate Inj)

NPH (N)

Nexterone (Amiodarone HCl Injection)

Norditropin (Somatropin Injection)

Normal Saline (Sodium Chloride Injection)

Novantrone (Mitoxantrone for Injection Concentrate)

Novolin 70/30 Innolet (70% NPH, Human Insulin Isophane Suspension and 30%

Regular, Human Insulin Injection)

NovoLog (Insulin Aspart [rDNA origin] Inj)

Nplate (romiplostim)

Nutropin (Somatropin (rDNA origin) for Inj)

Nutropin AQ

Nutropin Depot (Somatropin (rDNA origin) for Inj)

Octreotide Acetate Injection (Sandostatin LAR)

Ocrelizumab

Ofatumumab Injection (Arzerra)

Olanzapine Extended Release Injectable Suspension (Zyprexa Relprevv)

Omnitarg

Omnitrope (Somatropin [rDNA origin] Injection)

Ondansetron Hydrochloride Injection (Zofran Injection)

OptiMARK (Gadoversetamide Injection)

Optiray Injection (Ioversol Injection)

Orencia

Osmitrol Injection in Aviva (Mannitol Injection in Aviva Plastic Vessel)

Osmitrol Injection in Viaflex (Mannitol Injection in Viaflex Plastic Vessel)

Osteoprotegrin

Ovidrel (Choriogonadotropin Alfa Injection)

Oxacillin (Oxacillin for Injection)

Oxaliplatin Injection (Eloxatin)

Oxytocin Injection (Pitocin)

Paliperidone Palmitate Extended-Release Injectable Suspension (Invega Sustenna)

Pamidronate Disodium Injection (Pamidronate Disodium Injection)

Panitumumab Injection for Intravenous Use (Vectibix)

Papaverine Hydrochloride Injection (Papaverine Injection)

Papaverine Injection (Papaverine Hydrochloride Injection)

Parathyroid Hormone

Paricalcitol Injection Fliptop Vial (Zemplar Injection)

PARP Inhibitor

Pediarix

PEGIntron

Peginterferon

Pegfilgrastim

Penicillin G Benzathine and Penicillin G Procaine

Pentetate Calcium Trisodium Inj (Ca-DTPA)

Pentetate Zinc Trisodium Injection (Zn-DTPA)

Pepcid Injection (Famotidine Injection)

Pergonal

Pertuzumab

Phentolamine Mesylate (Phentolamine Mesylate for Injection)

Physostigmine Salicylate (Physostigmine Salicylate (injection))

Physostigmine Salicylate (injection) (Physostigmine Salicylate)

Piperacillin and Tazobactam Injection (Zosyn)

Pitocin (Oxytocin Injection)

Plasma-Lyte 148 (Multiple Electrolytes Inj)

Plasma-Lyte 56 and Dextrose (Multiple Electrolytes and Dextrose Injection in Viaflex Plastic Vessel)

PlasmaLyte

Plerixafor Injection (Mozobil)

Polidocanol Injection (Asclera)

Potassium Chloride

Pralatrexate Solution for Intravenous Injection (Folotyn)

Pramlintide Acetate Injection (Symlin)

Premarin Injection (Conjugated Estrogens for Injection)

Prep kit for Technetium Tc99 Sestamibi for Injection (Cardiolite)

Prevacid I.V. (Lansoprazole for Injection)

Primaxin I.V. (Imipenem and Cilastatin for Injection)

Prochymal

Procrit

Progesterone

ProHance (Gadoteridol Injection Solution)

Prolia (Denosumab Injection)

Promethazine HCl Injection (Promethazine Hydrochloride Injection)

Propranolol Hydrochloride Injection (Propranolol Hydrochloride Injection)

Quinidine Gluconate Injection (Quinidine Injection)

Quinidine Injection (Quinidine Gluconate Injection)

R-Gene 10 (Arginine Hydrochloride Injection)

Ranibizumab Injection (Lucentis)

Ranitidine Hydrochloride Injection (Zantac Injection)

Raptiva

Reclast (Zoledronic Acid Injection)

Recombivarix HB

Regadenoson Injection (Lexiscan)

Reglan Injection (Metoclopramide Injection)

Remicade

Renagel

Renvela (Sevelamer Carbonate)

Repronex (Menotropins for Injection)

Retrovir IV (Zidovudine Injection)

rhApo2L/TRAIL

Ringer's and 5% Dextrose Injection (Ringers in Dextrose)

Ringer's Injection (Ringers Injection)

Rituxan

Rituximab

Rocephin (ceftriaxone)

Rocuronium Bromide Injection (Zemuron)

Roferon-A (interferon alfa-2a)

Romazicon (flumazenil)

Romidepsin for Injection (Istodax)

Saizen (Somatropin Injection)

Sandostatin LAR (Octreotide Acetate Injection)

Sclerostin Ab

Sensipar (cinacalcet)

Sensorcaine (Bupivacaine HCl Injections)

Septocaine (Articane HCl and Epinephrine Injection)

Serostim LQ (Somatropin (rDNA origin) Injection)

Simponi Injection (Golimumab Injection)

Sodium Acetate (Sodium Acetate Injection)

Sodium Bicarbonate (Sodium Bicarbonate 5% Injection)

Sodium Lactate (Sodium Lactate Injection in AVIVA)

Sodium Phenylacetate and Sodium Benzoate Injection (Ammonul)

Somatropin (rDNA origin) for Inj (Nutropin)

Sporanox Injection (Itraconazole Injection)

Stelara Injection (Ustekinumab)

Stemgen

Sufenta (Sufentanil Citrate Injection)

Sufentanil Citrate Injection (Sufenta)

Sumavel

Sumatriptan Injection (Alsuma)

Symlin

Symlin Pen

Systemic Hedgehog Antagonist

Synvisc-One (Hylan G-F 20 Single Intra-articular Injection)

Tarceva

Taxotere (Docetaxel for Injection)

Technetium Tc 99m

Telavancin for Injection (Vibativ)

Temsirolimus Injection (Torisel)

Tenormin I.V. Injection (Atenolol Inj)

Teriparatide (rDNA origin) Injection (Forteo)

Testosterone Cypionate

Testosterone Enanthate

Testosterone Propionate

Tev-Tropin (Somatropin, rDNA Origin, for Injection)

tgAAC94

Thallous Chloride

Theophylline

Thiotepa (Thiotepa Injection)

Thymoglobulin (Anti-Thymocyte Globulin (Rabbit)

Thyrogen (Thyrotropin Alfa for Injection)

Ticarcillin Disodium and Clavulanate Potassium Galaxy (Timentin Injection)

Tigan Injection (Trimethobenzamide Hydrochloride Injectable)

Timentin Injection (Ticarcillin Disodium and Clavulanate Potassium Galaxy)

TNKase

Tobramycin Injection (Tobramycin Injection)

Tocilizumab Injection (Actemra)

Torisel (Temsirolimus Injection)

Totect (Dexrazoxane for Injection, Intravenous Infusion Only)

Trastuzumab-DM1

Travasol (Amino Acids (Injection))

Treanda (Bendamustine Hydrochloride Injection)

Trelstar (Triptorelin Pamoate for Injectable Suspension)

Triamcinolone Acetonide

Triamcinolone Diacetate

Triamcinolone Hexacetonide Injectable Suspension (Aristospan Injection 20 mg)

Triesence (Triamcinolone Acetonide Injectable Suspension)

Trimethobenzamide Hydrochloride Injectable (Tigan Injection)

Trimetrexate Glucuronate Inj (Neutrexin)

Triptorelin Pamoate for Injectable Suspension (Trelstar)

Twinject

Trivaris (Triamcinolone Acetonide Injectable Suspension)

Trisenox (Arsenic Trioxide Injection)

Twinrix

Typhoid Vi

Ultravist (Iopromide Injection)

Urofollitropin for Injection (Metrodin)

Urokinase Injection (Kinlytic)

Ustekinumab (Stelara Injection)

Ultralente (U)

Valium (diazepam)

Valproate Sodium Injection (Depacon)

Valtropin (Somatropin Injection)

Vancomycin Hydrochloride (Vancomycin Hydrochloride Injection)

Vancomycin Hydrochloride Injection (Vancomycin Hydrochloride)

Vaprisol (Conivaptan Hcl Injection)

VAQTA

Vasovist (Gadofosveset Trisodium Injection for Intravenous Use)

Vectibix (Panitumumab Injection for Intravenous Use)

Venofer (Iron Sucrose Injection)

Verteporfin Inj (Visudyne)

Vibativ (Telavancin for Injection)

Victoza (Liraglutide [rDNA] Injection)

Vimpat (lacosamide Tablet and Injection)

Vinblastine Sulfate (Vinblastine Sulfate Injection)

Vincasar PFS (Vincristine Sulfate Injection)

Victoza

Vincristine Sulfate (Vincristine Sulfate Injection)

Visudyne (Verteporfin Inj)

Vitamin B-12

Vivitrol (Naltrexone XR Inj)

Voluven (Hydroxyethyl Starch in Sodium Chloride Injection)

Xeloda

Xenical (orlistat)

Xeomin (Incobotulinumtoxin A for Injection)

Xolair

Zantac Injection (Ranitidine Hydrochloride Injection)

Zemplar Injection (Paricalcitol Injection Fliptop Vial)

Zemuron (Rocuronium Bromide Injection)

Zenapax (daclizumab)

Zevalin

Zidovudine Injection (Retrovir IV)

Zithromax Injection (Azithromycin)

Zn-DTPA (Pentetate Zinc Trisodium Injection)

Zofran Injection (Ondansetron Hydrochloride Injection)

Zingo

Zoledronic Acid for Inj (Zometa)

Zoledronic Acid Injection (Reclast)

Zometa (Zoledronic Acid for Inj)

Zosyn (Piperacillin and Tazobactam Injection)

Zyprexa Relprevv (Olanzapine Extended Release Injectable Suspension)

LIQUID DRUGS (NON-INJECTABLE)

Abilify

AccuNeb (Albuterol Sulfate Inhalation Solution)

Actidose Aqua (Activated Charcoal Suspension)

Activated Charcoal Suspension (Actidose Aqua)

Advair

Agenerase Oral Solution (Amprenavir Oral Solution)

Akten (Lidocaine Hydrochloride Ophthalmic Gel)

Alamast (Pemirolast Potassium Ophthalmic Solution)

Albumin (Human) 5% Solution (Buminate 5%)

Albuterol Sulfate Inhalation Solution

Alinia

Alocril

Alphagan

Alrex

Alvesco

Amprenavir Oral Solution

Analpram-HC

Arformoterol Tartrate Inhalation Solution (Brovana)

Aristospan Injection 20 mg (Triamcinolone Hexacetonide Injectable Suspension)

Asacol

Asmanex

Astepro

Astepro (Azelastine Hydrochloride Nasal Spray)

Atrovent Nasal Spray (Ipratropium Bromide Nasal Spray)

Atrovent Nasal Spray .06

Augmentin ES-600

Azasite (Azithromycin Ophthalmic Solution)

Azelaic Acid (Finacea Gel)

Azelastine Hydrochloride Nasal Spray (Astepro)

Azelex (Azelaic Acid Cream)

Azopt (Brinzolamide Ophthalmic Suspension)

Bacteriostatic Saline

Balanced Salt

Bepotastine

Bactroban Nasal

Bactroban

Beclovent

Benzac W

Betimol

Betoptic S

Bepreve
Bimatoprost Ophthalmic Solution
Bleph 10 (Sulfacetamide Sodium Ophthalmic Solution 10%)
Brinzolamide Ophthalmic Suspension (Azopt)
Bromfenac Ophthalmic Solution (Xibrom)
Bromhist
Brovana (Arformoterol Tartrate Inhalation Solution)
Budesonide Inhalation Suspension (Pulmicort Respules)
Cambia (Diclofenac Potassium for Oral Solution)
Capex
Carac
Carboxine-PSE
Carnitor
Cayston (Aztreonam for Inhalation Solution)
Cellcept
Centany
Cerumenex
Ciloxan Ophthalmic Solution (Ciprofloxacin HCL Ophthalmic Solution)
Ciprodex
Ciprofloxacin HCL Ophthalmic Solution (Ciloxan Ophthalmic Solution)
Clemastine Fumarate Syrup (Clemastine Fumarate Syrup)
CoLyte (PEG Electrolytes Solution)
Combiven
Comtan
Condylox
Cordran
Cortisporin Ophthalmic Suspension
Cortisporin Otic Suspension
Cromolyn Sodium Inhalation Solution (Intal Nebulizer Solution)
Cromolyn Sodium Ophthalmic Solution (Opticrom)
Crystalline Amino Acid Solution with Electrolytes (Aminosyn Electrolytes)

Cutivate

Cuvposa (Glycopyrrolate Oral Solution)

Cyanocobalamin (CaloMist Nasal Spray)

Cyclosporine Oral Solution (Gengraf Oral Solution)

Cyclogyl

Cysview (Hexaminolevulinate Hydrochloride Intravesical Solution)

DermOtic Oil (Fluocinolone Acetonide Oil Ear Drops)

Desmopressin Acetate Nasal Spray

DDAVP

Derma-Smoothe/FS

Dexamethasone Intensol

Dianeal Low Calcium

Dianeal PD

Diclofenac Potassium for Oral Solution (Cambia)

Didanosine Pediatric Powder for Oral Solution (Videx)

Differin

Dilantin 125 (Phenytoin Oral Suspension)

Ditropan

Dorzolamide Hydrochloride Ophthalmic Solution (Trusopt)

Dorzolamide Hydrochloride-Timolol Maleate Ophthalmic Solution (Cosopt)

Dovonex Scalp (Calcipotriene Solution)

Doxycycline Calcium Oral Suspension (Vibramycin Oral)

Efudex

Elaprase (Idursulfase Solution)

Elestat (Epinastine HCl Ophthalmic Solution)

Elocon

Epinastine HCl Ophthalmic Solution (Elestat)

Epivir HBV

Epogen (Epoetin alfa)

Erythromycin Topical Solution 1.5% (Staticin)

Ethiodol (Ethiodized Oil)

Ethosuximide Oral Solution (Zarontin Oral Solution)

Eurax

Extraneal (Icodextrin Peritoneal Dialysis Solution)

Felbatol

Feridex I.V. (Ferumoxides Injectable Solution)

Flovent

Floxin Otic (Ofloxacin Otic Solution)

Flo-Pred (Prednisolone Acetate Oral Suspension)

Fluoroplex

Flunisolide Nasal Solution (Flunisolide Nasal Spray .025%)

Fluorometholone Ophthalmic Suspension (FML)

Flurbiprofen Sodium Ophthalmic Solution (Ocufen)

FML

Foradil

Formoterol Fumarate Inhalation Solution (Perforomist)

Fosamax

Furadantin (Nitrofurantoin Oral Suspension)

Furoxone

Gammagard Liquid (Immune Globulin Intravenous (Human) 10%)

Gantrisin (Acetyl Sulfisoxazole Pediatric Suspension)

Gatifloxacin Ophthalmic Solution (Zymar)

Gengraf Oral Solution (Cyclosporine Oral Solution)

Glycopyrrolate Oral Solution (Cuvposa)

Halcinonide Topical Solution (Halog Solution)

Halog Solution (Halcinonide Topical Solution)

HEP-LOCK U/P (Preservative-Free Heparin Lock Flush Solution)

Heparin Lock Flush Solution (Hepflush 10)

Hexaminolevulinate Hydrochloride Intravesical Solution (Cysview)

Hydrocodone Bitartrate and Acetaminophen Oral Solution (Lortab Elixir)

Hydroquinone 3% Topical Solution (Melquin-3 Topical Solution)

IAP Antagonist

Isopto

Ipratropium Bromide Nasal Spray (Atrovent Nasal Spray)

Itraconazole Oral Solution (Sporanox Oral Solution)

Ketorolac Tromethamine Ophthalmic Solution (Acular LS)

Kaletra

Lanoxin

Lexiva

Leuprolide Acetate for Depot Suspension (Lupron Depot 11.25 mg)

Levobetaxolol Hydrochloride Ophthalmic Suspension (Betaxon)

Levocarnitine Tablets, Oral Solution, Sugar-Free (Carnitor)

Levofloxacin Ophthalmic Solution 0.5% (Quixin)

Lidocaine HCl Sterile Solution (Xylocaine MPF Sterile Solution)

Lok Pak (Heparin Lock Flush Solution)

Lorazepam Intensol

Lortab Elixir (Hydrocodone Bitartrate and Acetaminophen Oral Solution)

Lotemax (Loteprednol Etabonate Ophthalmic Suspension)

Loteprednol Etabonate Ophthalmic Suspension (Alrex)

Low Calcium Peritoneal Dialysis Solutions (Dianeal Low Calcium)

Lumigan (Bimatoprost Ophthalmic Solution 0.03% for Glaucoma)

Lupron Depot 11.25 mg (Leuprolide Acetate for Depot Suspension)

Megestrol Acetate Oral Suspension (Megestrol Acetate Oral Suspension)

MEK Inhibitor

Mepron

Mesnex

Mestinon

Mesalamine Rectal Suspension Enema (Rowasa)

Melquin-3 Topical Solution (Hydroquinone 3% Topical Solution)

MetMab

Methyldopate Hcl (Methyldopate Hydrochloride Injection, Solution)

Methylin Oral Solution (Methylphenidate HCl Oral Solution 5 mg/5 mL and 10 mg/5 mL)

Methylprednisolone Acetate Injectable Suspension (Depo Medrol)

Methylphenidate HCl Oral Solution 5 mg/5 mL and 10 mg/5 mL (Methylin Oral Solution)
Methylprednisolone sodium succinate (Solu Medrol)
Metipranolol Ophthalmic Solution (Optipranolol)
Migranal
Miochol-E (Acetylcholine Chloride Intraocular Solution)
Micro-K for Liquid Suspension (Potassium Chloride Extended Release Formulation for Liquid Suspension)
Minocin (Minocycline Hydrochloride Oral Suspension)
Nasacort
Neomycin and Polymyxin B Sulfates and Hydrocortisone
Nepafenac Ophthalmic Suspension (Nevanac)
Nevanac (Nepafenac Ophthalmic Suspension)
Nitrofurantoin Oral Suspension (Furadantin)
Noxafil (Posaconazole Oral Suspension)
Nystatin (oral) (Nystatin Oral Suspension)
Nystatin Oral Suspension (Nystatin (oral))
Ocufen (Flurbiprofen Sodium Ophthalmic Solution)
Ofloxacin Ophthalmic Solution (Ofloxacin Ophthalmic Solution)
Ofloxacin Otic Solution (Floxin Otic)
Olopatadine Hydrochloride Ophthalmic Solution (Pataday)
Opticrom (Cromolyn Sodium Ophthalmic Solution)
Optipranolol (Metipranolol Ophthalmic Solution)
Patanol
Pediapred
PerioGard
Phenytoin Oral Suspension (Dilantin 125)
Phisohex
Posaconazole Oral Suspension (Noxafil)
Potassium Chloride Extended Release Formulation for Liquid Suspension (Micro-K for Liquid Suspension)
Pataday (Olopatadine Hydrochloride Ophthalmic Solution)

Patanase Nasal Spray (Olopatadine Hydrochloride Nasal Spray)

PEG Electrolytes Solution (CoLyte)

Pemirolast Potassium Ophthalmic Solution (Alamast)

Penlac (Ciclopirox Topical Solution)

PENNSAID (Diclofenac Sodium Topical Solution)

Perforomist (Formoterol Fumarate Inhalation Solution)

Peritoneal Dialysis Solution

Phenylephrine Hydrochloride Ophthalmic Solution (Neo-Synephrine)

Phospholine Iodide (Echothiophate Iodide for Ophthalmic Solution)

Podofilox (Podofilox Topical Solution)

Pred Forte (Prednisolone Acetate Ophthalmic Suspension)

Pralatrexate Solution for Intravenous Injection (Folotyn)

Pred Mild

Prednisone Intensol

Prednisolone Acetate Ophthalmic Suspension (Pred Forte)

Prevacid

PrismaSol Solution (Sterile Hemofiltration Hemodiafiltration Solution)

ProAir

Proglycem

ProHance (Gadoteridol Injection Solution)

Proparacaine Hydrochloride Ophthalmic Solution (Alcaine)

Propine

Pulmicort

Pulmozyme

Quixin (Levofloxacin Ophthalmic Solution 0.5%)

QVAR

Rapamune

Rebetol

Relacon-HC

Rotarix (Rotavirus Vaccine, Live, Oral Suspension)

Rotavirus Vaccine, Live, Oral Suspension (Rotarix)

Rowasa (Mesalamine Rectal Suspension Enema)
Sabril (Vigabatrin Oral Solution)
Sacrosidase Oral Solution (Sucraid)
Sandimmune
Sepra
Serevent Diskus
Solu Cortef (Hydrocortisone Sodium Succinate)
Solu Medrol (Methylprednisolone sodium succinate)
Spiriva
Sporanox Oral Solution (Itraconazole Oral Solution)
Staticin (Erythromycin Topical Solution 1.5%)
Stalevo
Starlix
Sterile Hemofiltration Hemodiafiltration Solution (PrismaSol Solution)
Stimate
Sucralfate (Carafate Suspension)
Sulfacetamide Sodium Ophthalmic Solution 10% (Bleph 10)
Synarel Nasal Solution (Nafarelin Acetate Nasal Solution for Endometriosis)
Taclonex Scalp (Calcipotriene and Betamethasone Dipropionate Topical Suspension)
Tamiflu
Tobi
TobraDex
Tobradex ST (Tobramycin / Dexamethasone Ophthalmic Suspension 0.3%/0.05%)
Tobramycin / Dexamethasone Ophthalmic Suspension 0.3%/0.05% (Tobradex ST)
Timolol
Timoptic
Travatan Z
Treprostinil Inhalation Solution (Tyvaso)
Trusopt (Dorzolamide Hydrochloride Ophthalmic Solution)
Tyvaso (Treprostinil Inhalation Solution)
Ventolin

Vfend
Vibramycin Oral (Doxycycline Calcium Oral Suspension)
Videx (Didanosine Pediatric Powder for Oral Solution)
Vigabatrin Oral Solution (Sabril)
Viokase
Viracept
Viramune
Vitamin K1 (Fluid Colloidal Solution of Vitamin K1)
Voltaren Ophthalmic (Diclofenac Sodium Ophthalmic Solution)
Zarontin Oral Solution (Ethosuximide Oral Solution)
Ziagen
Zyvox
Zymar (Gatifloxacin Ophthalmic Solution)
Zymaxid (Gatifloxacin Ophthalmic Solution)

DRUG CLASSES

5-alpha-reductase inhibitors
5-aminosalicylates
5HT3 receptor antagonists
adamantane antivirals
adrenal cortical steroids
adrenal corticosteroid inhibitors
adrenergic bronchodilators
agents for hypertensive emergencies
agents for pulmonary hypertension
aldosterone receptor antagonists
alkylating agents
alpha-adrenoreceptor antagonists
alpha-glucosidase inhibitors
alternative medicines
amebicides

aminoglycosides
aminopenicillins
aminosalicylates
amylin analogs
Analgesic Combinations
Analgesics
androgens and anabolic steroids
angiotensin converting enzyme inhibitors
angiotensin II inhibitors
anorectal preparations
anorexiants
antacids
anthelmintics
anti-angiogenic ophthalmic agents
anti-CTLA-4 monoclonal antibodies
anti-infectives
antiadrenergic agents, centrally acting
antiadrenergic agents, peripherally acting
antiandrogens
antianginal agents
antiarrhythmic agents
antiasthmatic combinations
antibiotics/antineoplastics
anticholinergic antiemetics
anticholinergic antiparkinson agents
anticholinergic bronchodilators
anticholinergic chronotropic agents
anticholinergics/antispasmodics
anticoagulants
anticonvulsants
antidepressants

antidiabetic agents
antidiabetic combinations
antidiarrheals
antidiuretic hormones
antidotes
antiemetic/antivertigo agents
antifungals
antigonadotropic agents
antigout agents
antihistamines
antihyperlipidemic agents
antihyperlipidemic combinations
antihypertensive combinations
antihyperuricemic agents
antimalarial agents
antimalarial combinations
antimalarial quinolines
antimetabolites
antimigraine agents
antineoplastic detoxifying agents
antineoplastic interferons
antineoplastic monoclonal antibodies
antineoplastics
antiparkinson agents
antiplatelet agents
antipseudomonal penicillins
antipsoriatics
antipsychotics
antirheumatics
antiseptic and germicides
antithyroid agents

antitoxins and antivenins
antituberculosis agents
antituberculosis combinations
antitussives
antiviral agents
antiviral combinations
antiviral interferons
anxiolytics, sedatives, and hypnotics
aromatase inhibitors
atypical antipsychotics
azole antifungals
bacterial vaccines
barbiturate anticonvulsants
barbiturates
BCR-ABL tyrosine kinase inhibitors
benzodiazepine anticonvulsants
benzodiazepines
beta-adrenergic blocking agents
beta-lactamase inhibitors
bile acid sequestrants
biologicals
bisphosphonates
bone resorption inhibitors
bronchodilator combinations
bronchodilators
calcitonin
calcium channel blocking agents
carbamate anticonvulsants
carbapenems
carbonic anhydrase inhibitor anticonvulsants
carbonic anhydrase inhibitors

cardiac stressing agents
cardioselective beta blockers
cardiovascular agents
catecholamines
CD20 monoclonal antibodies
CD33 monoclonal antibodies
CD52 monoclonal antibodies
central nervous system agents
cephalosporins
cerumenolytics
chelating agents
chemokine receptor antagonist
chloride channel activators
cholesterol absorption inhibitors
cholinergic agonists
cholinergic muscle stimulants
cholinesterase inhibitors
CNS stimulants
coagulation modifiers
colony stimulating factors
contraceptives
corticotropin
coumarins and indandiones
cox-2 inhibitors
decongestants
dermatological agents
diagnostic radiopharmaceuticals
dibenzazepine anticonvulsants
digestive enzymes
dipeptidyl peptidase 4 inhibitors
diuretics

dopaminergic antiparkinsonism agents
drugs used in alcohol dependence
echinocandins
EGFR inhibitors
estrogen receptor antagonists
estrogens
expectorants
factor Xa inhibitors
fatty acid derivative anticonvulsants
fibric acid derivatives
first generation cephalosporins
fourth generation cephalosporins
functional bowel disorder agents
gallstone solubilizing agents
gamma-aminobutyric acid analogs
gamma-aminobutyric acid reuptake inhibitors
gamma-aminobutyric acid transaminase inhibitors
gastrointestinal agents
general anesthetics
genitourinary tract agents
GI stimulants
glucocorticoids
glucose elevating agents
glycopeptide antibiotics
glycoprotein platelet inhibitors
glycylcyclines
gonadotropin releasing hormones
gonadotropin-releasing hormone antagonists
gonadotropins
group I antiarrhythmics
group II antiarrhythmics

group III antiarrhythmics
group IV antiarrhythmics
group V antiarrhythmics
growth hormone receptor blockers
growth hormones
H. pylori eradication agents
H2 antagonists
hematopoietic stem cell mobilizer
heparin antagonists
heparins
HER2 inhibitors
herbal products
histone deacetylase inhibitors
hormone replacement therapy
hormones
hormones/antineoplastics
hydantoin anticonvulsants
illicit (street) drugs
immune globulins
immunologic agents
immunosuppressive agents
impotence agents
in vivo diagnostic biologicals
incretin mimetics
inhaled anti-infectives
inhaled corticosteroids
inotropic agents
insulin
insulin-like growth factor
integrase strand transfer inhibitor
interferons

intravenous nutritional products
iodinated contrast media
ionic iodinated contrast media
iron products
ketolides
laxatives
leprostatics
leukotriene modifiers
lincomycin derivatives
lipoglycopeptides
local injectable anesthetics
loop diuretics
lung surfactants
lymphatic staining agents
lysosomal enzymes
macrolide derivatives
macrolides
magnetic resonance imaging contrast media
mast cell stabilizers
medical gas
meglitinides
metabolic agents
methylxanthines
mineralocorticoids
minerals and electrolytes
miscellaneous agents
miscellaneous analgesics
miscellaneous antibiotics
miscellaneous anticonvulsants
miscellaneous antidepressants
miscellaneous antidiabetic agents

miscellaneous antiemetics
miscellaneous antifungals
miscellaneous antihyperlipidemic agents
miscellaneous antimalarials
miscellaneous antineoplastics
miscellaneous antiparkinson agents
miscellaneous antipsychotic agents
miscellaneous antituberculosis agents
miscellaneous antivirals
miscellaneous anxiolytics, sedatives and hypnotics
miscellaneous biologicals
miscellaneous bone resorption inhibitors
miscellaneous cardiovascular agents
miscellaneous central nervous system agents
miscellaneous coagulation modifiers
miscellaneous diuretics
miscellaneous genitourinary tract agents
miscellaneous GI agents
miscellaneous hormones
miscellaneous metabolic agents
miscellaneous ophthalmic agents
miscellaneous otic agents
miscellaneous respiratory agents
miscellaneous sex hormones
miscellaneous topical agents
miscellaneous uncategorized agents
miscellaneous vaginal agents
mitotic inhibitors
monoamine oxidase inhibitors
monoclonal antibodies
mouth and throat products

mTOR inhibitors
mTOR kinase inhibitors
mucolytics
multikinase inhibitors
muscle relaxants
mydriatics
narcotic analgesic combinations
narcotic analgesics
nasal anti-infectives
nasal antihistamines and decongestants
nasal lubricants and irrigations
nasal preparations
nasal steroids
natural penicillins
neuraminidase inhibitors
neuromuscular blocking agents
next generation cephalosporins
nicotinic acid derivatives
nitrates
NNRTIs
non-cardioselective beta blockers
non-iodinated contrast media
non-ionic iodinated contrast media
non-sulfonylureas
nonsteroidal anti-inflammatory agents
norepinephrine reuptake inhibitors
norepinephrine-dopamine reuptake inhibitors
nucleoside reverse transcriptase inhibitors (NRTIs)
nutraceutical products
nutritional products
ophthalmic anesthetics

ophthalmic anti-infectives
ophthalmic anti-inflammatory agents
ophthalmic antihistamines and decongestants
ophthalmic diagnostic agents
ophthalmic glaucoma agents
ophthalmic lubricants and irrigations
ophthalmic preparations
ophthalmic steroids
ophthalmic steroids with anti-infectives
ophthalmic surgical agents
oral nutritional supplements
otic anesthetics
otic anti-infectives
otic preparations
otic steroids
otic steroids with anti-infectives
oxazolidinedione anticonvulsants
parathyroid hormone and analogs
penicillinase resistant penicillins
penicillins
peripheral opioid receptor antagonists
peripheral vasodilators
peripherally acting antiobesity agents
phenothiazine antiemetics
phenothiazine antipsychotics
phenylpiperazine antidepressants
plasma expanders
platelet aggregation inhibitors
platelet-stimulating agents
polyenes
potassium-sparing diuretics

probiotics
progesterone receptor modulators
progestins
prolactin inhibitors
prostaglandin D2 antagonists
protease inhibitors
proton pump inhibitors
psoralens
psychotherapeutic agents
psychotherapeutic combinations
purine nucleosides
pyrrolidine anticonvulsants
quinolones
radiocontrast agents
radiologic adjuncts
radiologic agents
radiologic conjugating agents
radiopharmaceuticals
RANK ligand inhibitors
recombinant human erythropoietins
renin inhibitors
respiratory agents
respiratory inhalant products
rifamycin derivatives
salicylates
sclerosing agents
second generation cephalosporins
selective estrogen receptor modulators
selective serotonin reuptake inhibitors
serotonin-norepinephrine reuptake inhibitors
serotoninergic neuroenteric modulators

sex hormone combinations
sex hormones
skeletal muscle relaxant combinations
skeletal muscle relaxants
smoking cessation agents
somatostatin and somatostatin analogs
spermicides
statins
sterile irrigating solutions
streptomyces derivatives
succinimide anticonvulsants
sulfonamides
sulfonylureas
synthetic ovulation stimulants
tetracyclic antidepressants
tetracyclines
therapeutic radiopharmaceuticals
thiazide diuretics
thiazolidinediones
thioxanthenes
third generation cephalosporins
thrombin inhibitors
thrombolytics
thyroid drugs
tocolytic agents
topical acne agents
topical agents
topical anesthetics
topical anti-infectives
topical antibiotics
topical antifungals

topical antihistamines
topical antipsoriatics
topical antivirals
topical astringents
topical debriding agents
topical depigmenting agents
topical emollients
topical keratolytics
topical steroids
topical steroids with anti-infectives
toxoids
triazine anticonvulsants
tricyclic antidepressants
trifunctional monoclonal antibodies
tumor necrosis factor (TNF) inhibitors
tyrosine kinase inhibitors
ultrasound contrast media
upper respiratory combinations
urea anticonvulsants
urinary anti-infectives
urinary antispasmodics
urinary pH modifiers
uterotonic agents
vaccine
vaccine combinations
vaginal anti-infectives
vaginal preparations
vasodilators
vasopressin antagonists
vasopressors
VEGF/VEGFR inhibitors

viral vaccines
viscosupplementation agents
vitamin and mineral combinations
vitamins

DIAGNOSTIC TESTS

17-Hydroxyprogesterone
ACE (Angiotensin I converting enzyme)
Acetaminophen
Acid phosphatase
ACTH
Activated clotting time
Activated protein C resistance
Adrenocorticotropic hormone (ACTH)
Alanine aminotransferase (ALT)
Albumin
Aldolase
Aldosterone
Alkaline phosphatase
Alkaline phosphatase (ALP)
Alpha1-antitrypsin
Alpha-fetoprotein
Alpha-fetoprotien
Ammonia levels
Amylase
ANA (antinuclear antbodies)
ANA (antinuclear antibodies)
Angiotensin-converting enzyme (ACE)
Anion gap
Anticardiolipin antibody
Anticardiolipin antivbodies (ACA)

Anti-centromere antibody
Antidiuretic hormone
Anti-DNA
Anti-Dnase-B
Anti-Gliadin antibody
Anti-glomerular basement membrane antibody
Anti-HBc (Hepatitis B core antibodies
Anti-HBs (Hepatitis B surface antibody
Antiphospholipid antibody
Anti-RNA polymerase
Anti-Smith (Sm) antibodies
Anti-Smooth Muscle antibody
Antistreptolysin O (ASO)
Antithrombin III
Anti-Xa activity
Anti-Xa assay
Apolipoproteins
Arsenic
Aspartate aminotransferase (AST)
B12
Basophil
Beta-2-Microglobulin
Beta-hydroxybutyrate
B-HCG
Bilirubin
Bilirubin, direct
Bilirubin, indirect
Bilirubin, total
Bleeding time
Blood gases (arterial)
Blood urea nitrogen (BUN)

BUN

BUN (blood urea nitrogen)

CA 125

CA 15-3

CA 19-9

Calcitonin

Calcium

Calcium (ionized)

Carbon monoxide (CO)

Carcinoembryonic antigen (CEA)

CBC

CEA

CEA (carcinoembryonic antigen)

Ceruloplasmin

CH50Chloride

Cholesterol

Cholesterol, HDL

Clot lysis time

Clot retraction time

CMP

CO2

Cold agglutinins

Complement C3

Copper

Corticotrophin releasing hormone (CRH) stimulation test

Cortisol

Cortrosyn stimulation test

C-peptide

CPK (Total)

CPK-MB

C-reactive protein

Creatinine
Creatinine kinase (CK)
Cryoglobulins
DAT (Direct antiglobulin test)
D-Dimer
Dexamethasone suppression test
DHEA-S
Dilute Russell viper venom
Elliptocytes
Eosinophil
Erythrocyte sedimentation rate (ESR)
Estradiol
Estriol
Ethanol
Ethylene glycol
Euglobulin lysis
Factor V Leiden
Factor VIII inhibitor
Factor VIII level
Ferritin
Fibrin split products
Fibrinogen
Folate
Folate (serum
Fractional excretion of sodium (FENA)
FSH (follicle stimulating factor)
FTA-ABS
Gamma glutamyl transferase (GGT)
Gastrin
GGTP (Gamma glutamyl transferase)
Glucose

Growth hormone
Haptoglobin
HBeAg (Hepatitis Be antigen)
HBs-Ag (Hepatitis B surface antigen)
Helicobacter pylori
Hematocrit
Hematocrit (HCT)
Hemoglobin
Hemoglobin A1C
Hemoglobin electrophoresis
Hepatitis A antibodies
Hepatitis C antibodies
IAT (Indirect antiglobulin test)
Immunofixation (IFE)
Iron
Lactate dehydrogenase (LDH)
Lactic acid (lactate)
LDH
LH (Leutinizing hormone
Lipase
Lupus anticoagulant
Lymphocyte
Magnesium
MCH (mean corpuscular hemoglobin
MCHC (mean corpuscular hemoglobin concentration)
MCV (mean corpuscular volume)
Methylmalonate
Monocyte
MPV (mean platelet volume)
Myoglobin
Neutrophil

Parathyroid hormone (PTH)

Phosphorus

Platelets (plt)

Potassium

Prealbumin

Prolactin

Prostate specific antigen (PSA)

Protein C

Protein S

PSA (prostate specific antigen)

PT (Prothrombin time)

PTT (Partial thromboplastin time)

RDW (red cell distribution width)

Renin

Rennin

Reticulocyte count

reticulocytes

Rheumatoid factor (RF)

Sed Rate

Serum glutamic-pyruvic transaminase (SGPT

Serum protein electrophoresis (SPEP)

Sodium

T3-resin uptake (T3RU)

T4, Free

Thrombin time

Thyroid stimulating hormone (TSH)

Thyroxine (T4)

Total iron binding capacity (TIBC)

Total protein

Transferrin

Transferrin saturation

Triglyceride (TG)

Troponin

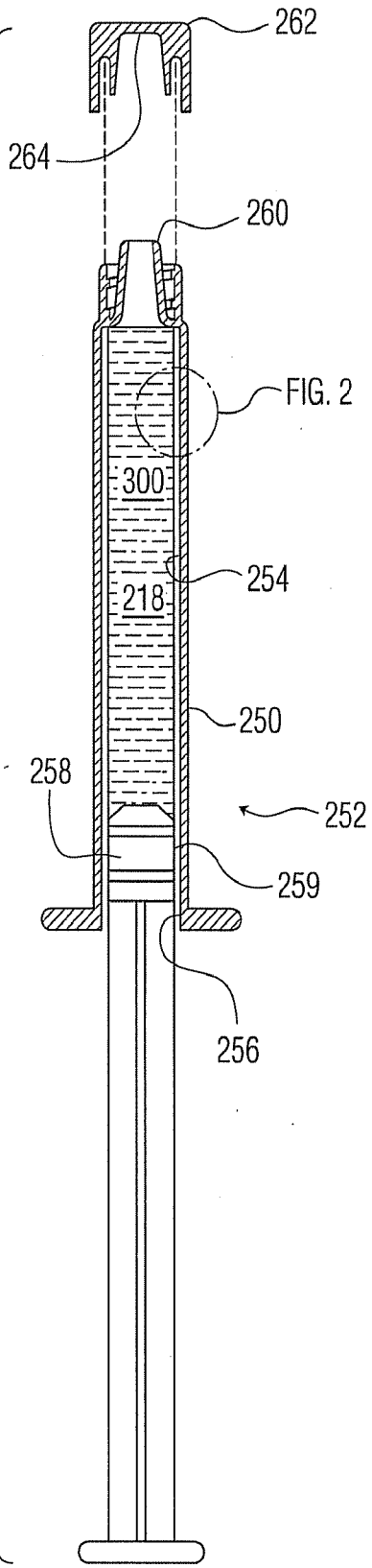
Uric acid

Vitamin B12

White blood cells (WBC)

Widal test

FIG. 1



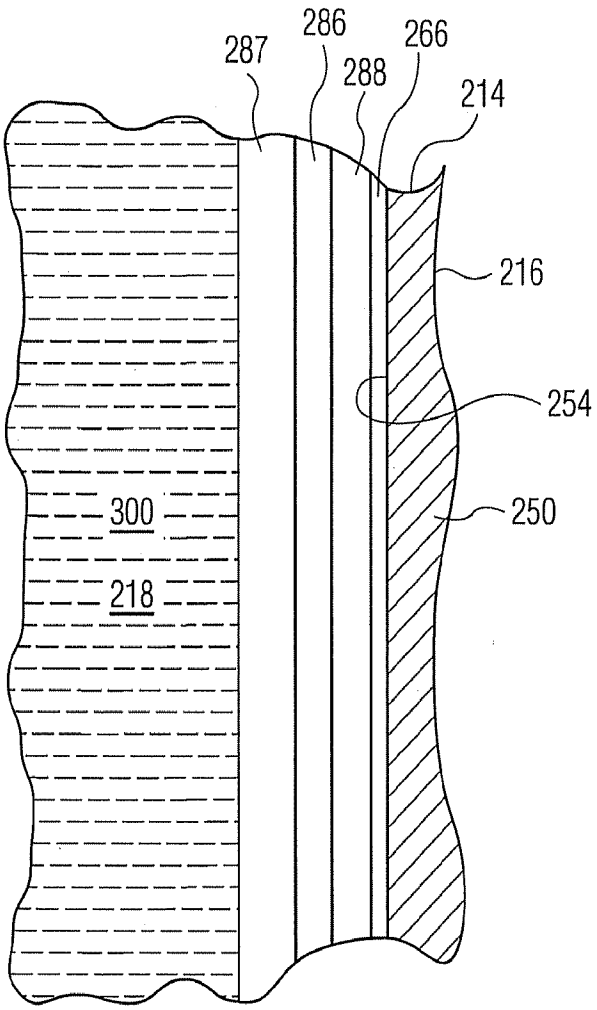


FIG. 2

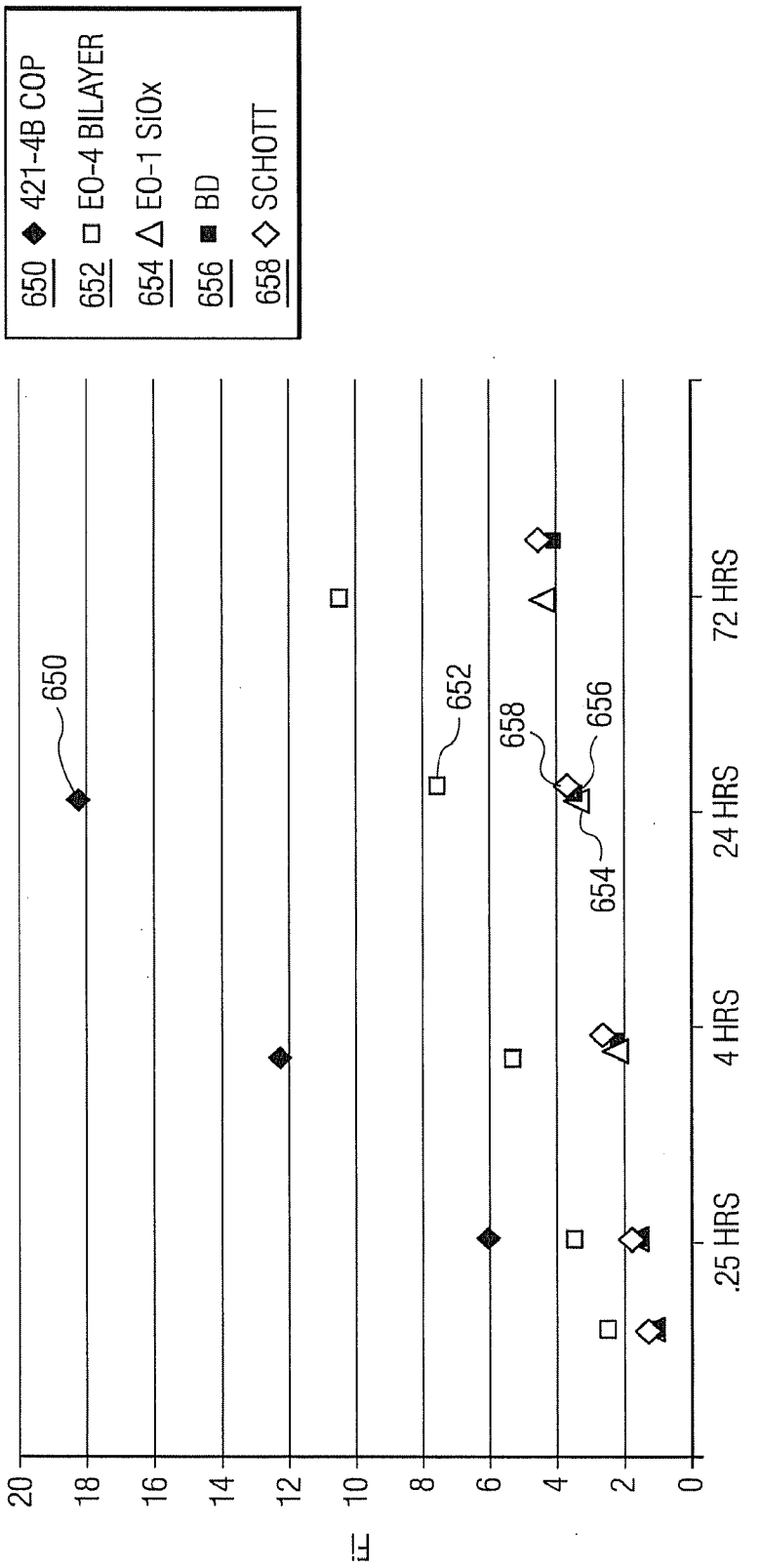

650 ◆ 421-4B COP
652 □ EO-4 BILAYER
654 △ EO-1 SiOx
656 ■ BD
658 ◇ SCHOTT
FI
20
18
16
14
12
10
8
6
4
2
0
.25 HRS
4 HRS
24 HRS
72 HRS
650
652
658
656
654

FIG. 3

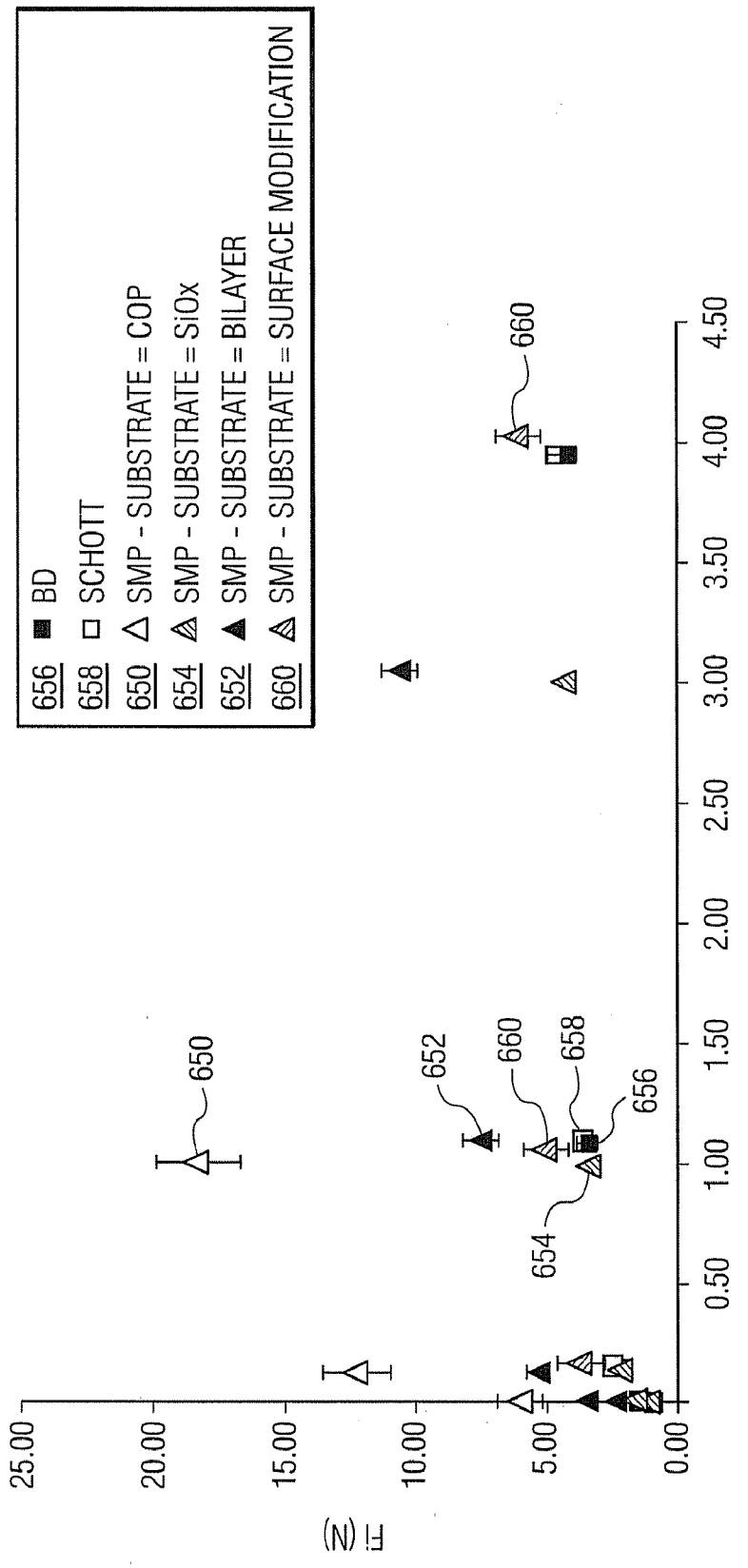

656 BD
658 SCHOTT
650 SMP - SUBSTRATE = COP
654 SMP - SUBSTRATE = SiOx
652 SMP - SUBSTRATE = BILAYER
660 SMP - SUBSTRATE = SURFACE MODIFICATION
Fi (N)
25.00
20.00
15.00
10.00
5.00
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
TIME (DAYS)
650
652
660
658
656
654
660

FIG. 4

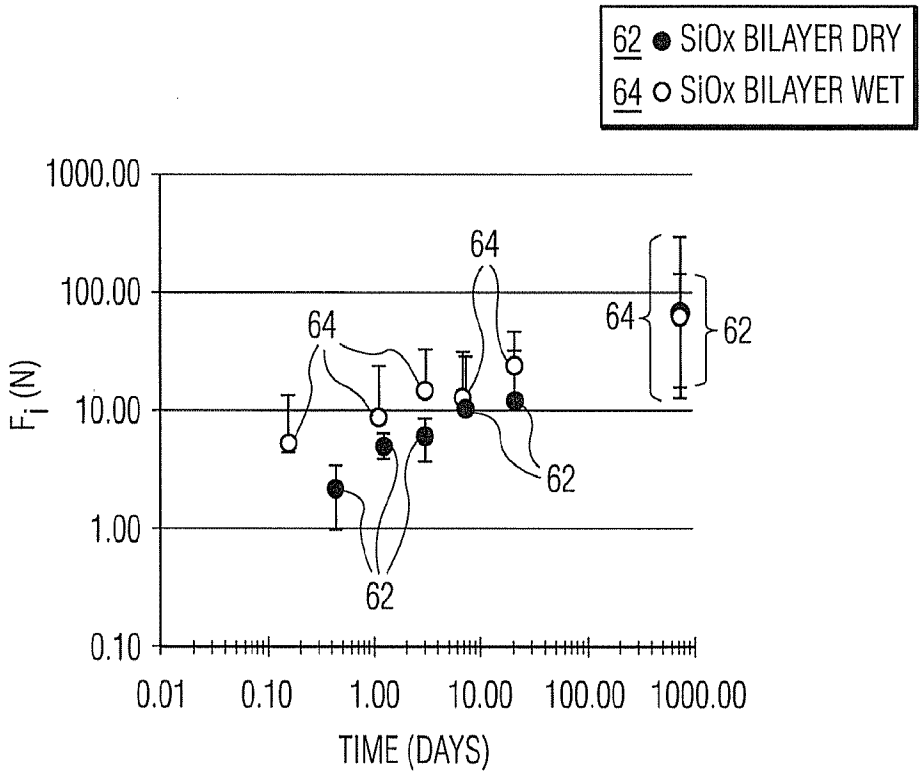

62 SiOx BILAYER DRY
64 SiOx BILAYER WET
1000.00
100.00
10.00
1.00
0.10
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
64
62

FIG. 5

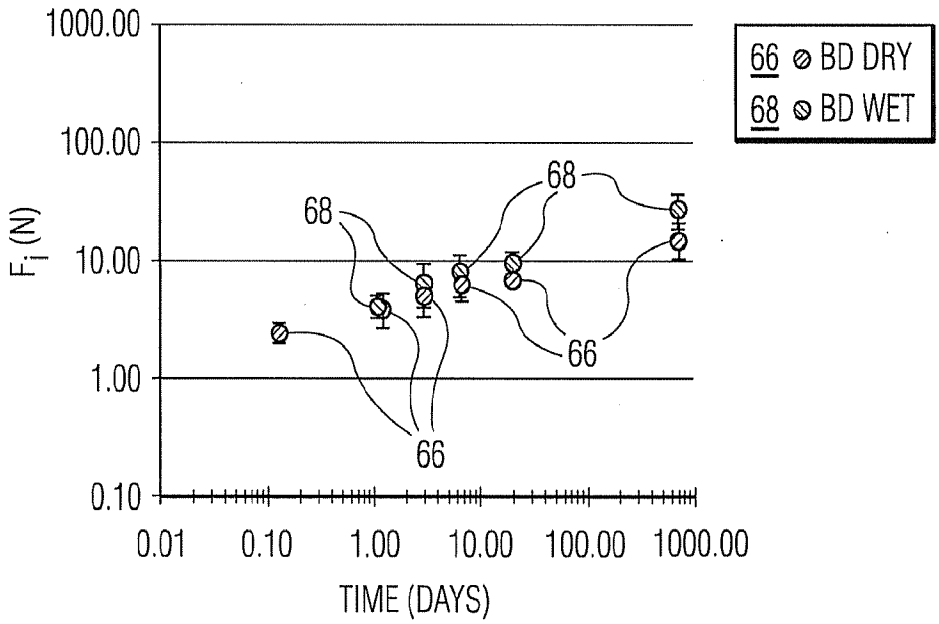

66 BD DRY
68 BD WET
1000.00
100.00
10.00
1.00
0.10
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
68
66

FIG. 6

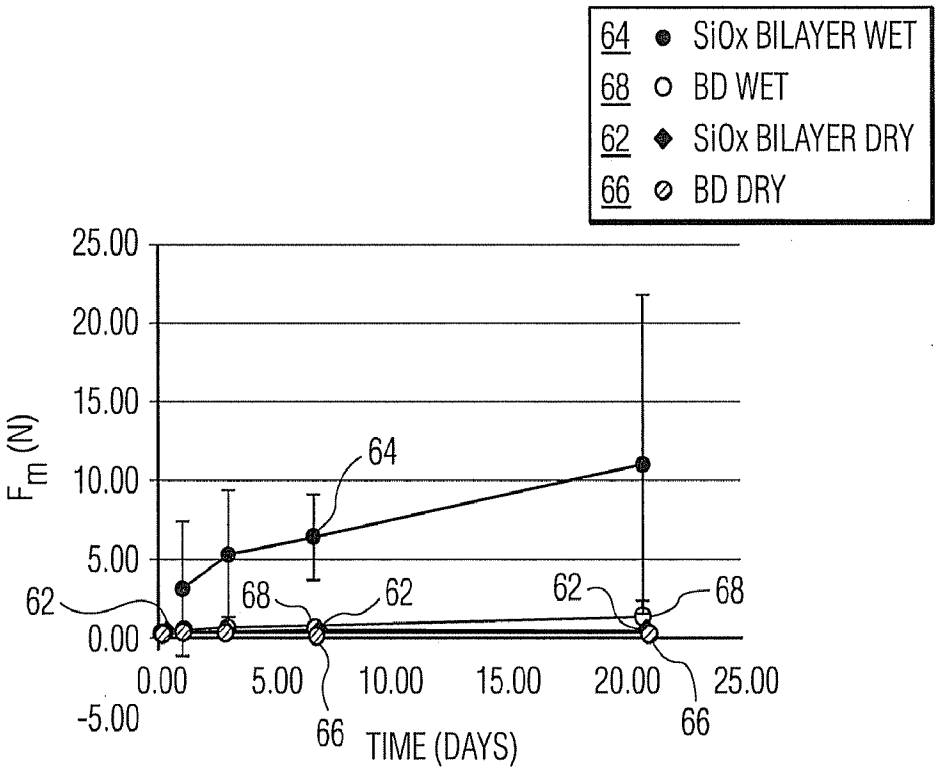

64 SiOx BILAYER WET
68 BD WET
62 SiOx BILAYER DRY
66 BD DRY
25.00
20.00
15.00
10.00
5.00
0.00
-5.00
F_m (N)
0.00
5.00
10.00
15.00
20.00
25.00
TIME (DAYS)
64
62
68
62
62
68
66
66

FIG. 7

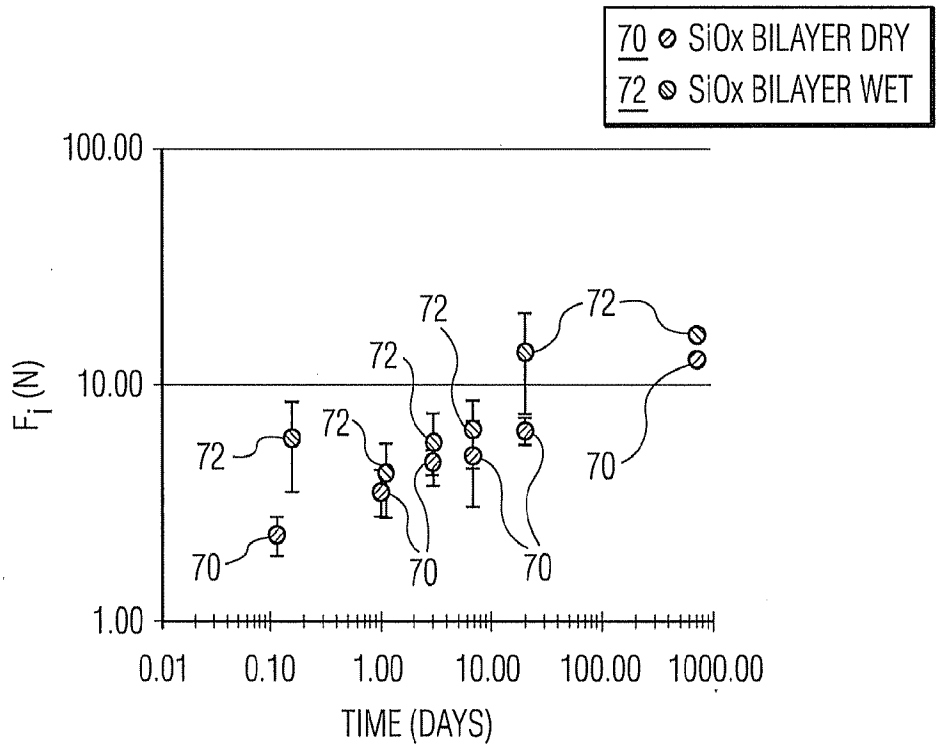

70 SiOx BILAYER DRY
72 SiOx BILAYER WET
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
72
72
72
72
72
70
70
70
70

FIG. 8

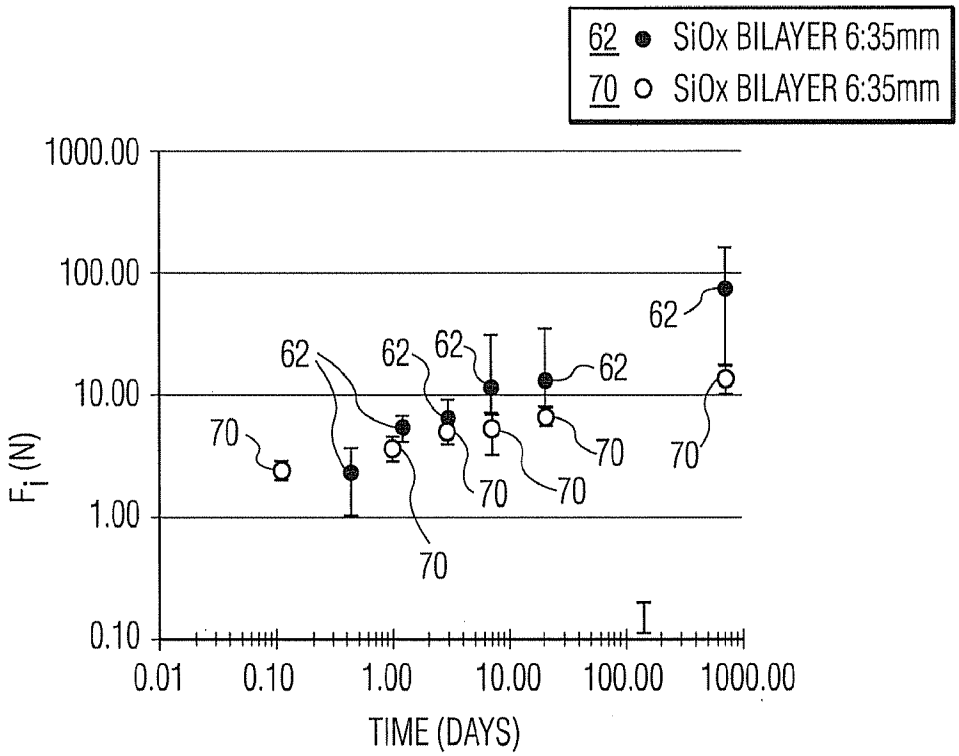

62 SiOx BILAYER 6:35mm
70 SiOx BILAYER 6:35mm
1000.00
100.00
10.00
1.00
0.10
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 9

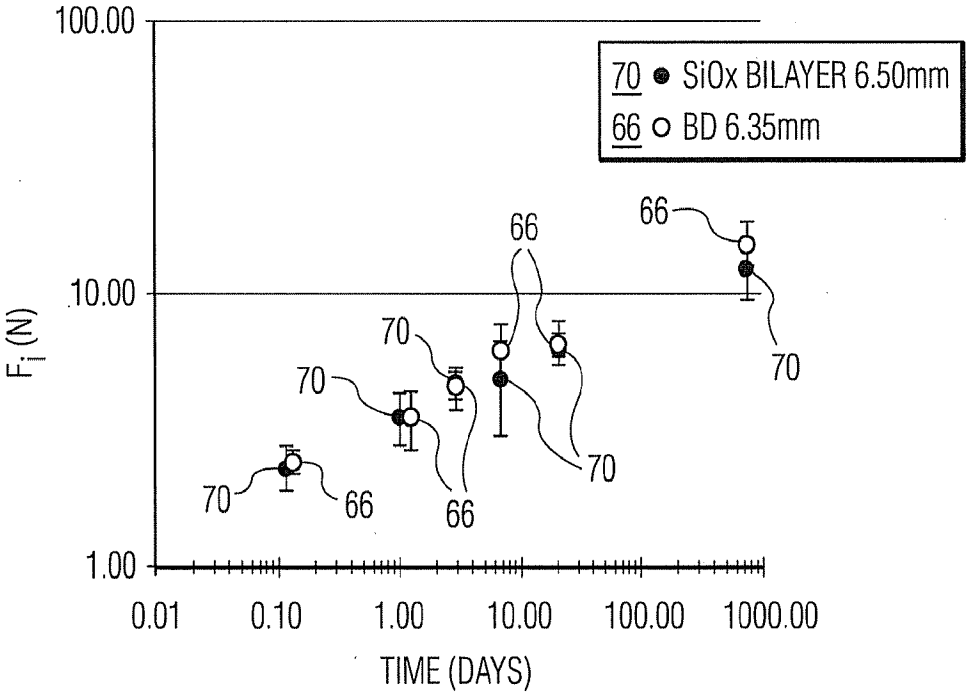

70 SiOx BILAYER 6.50mm
66 BD 6.35mm
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 10

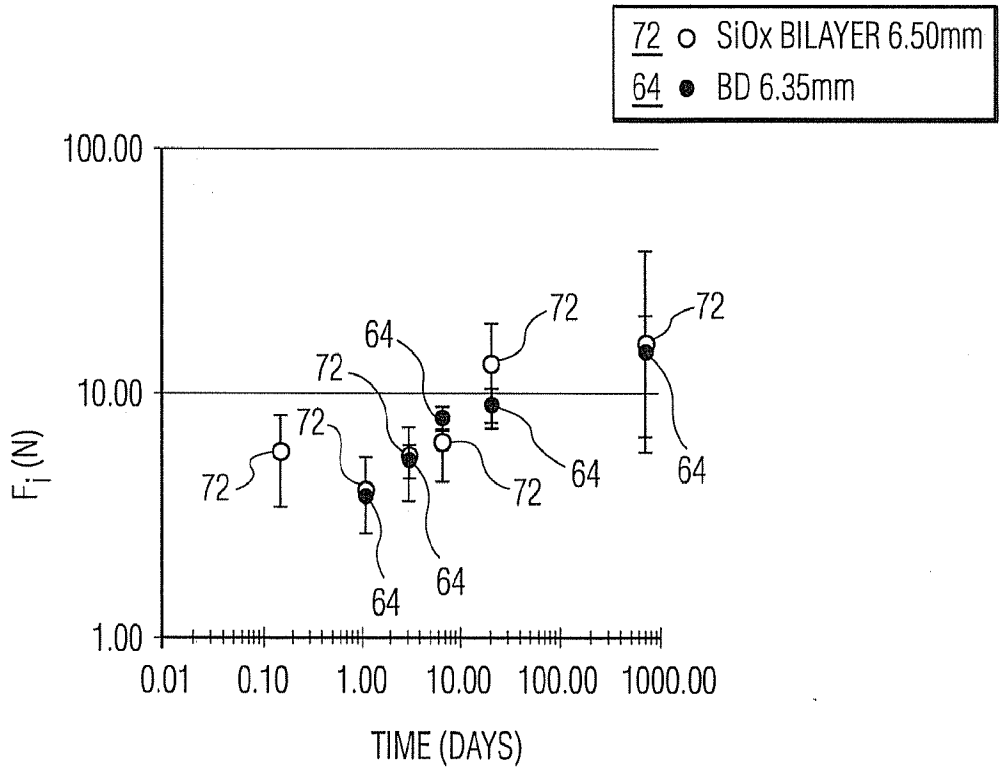

72 SiOx BILAYER 6.50mm
64 BD 6.35mm
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 11

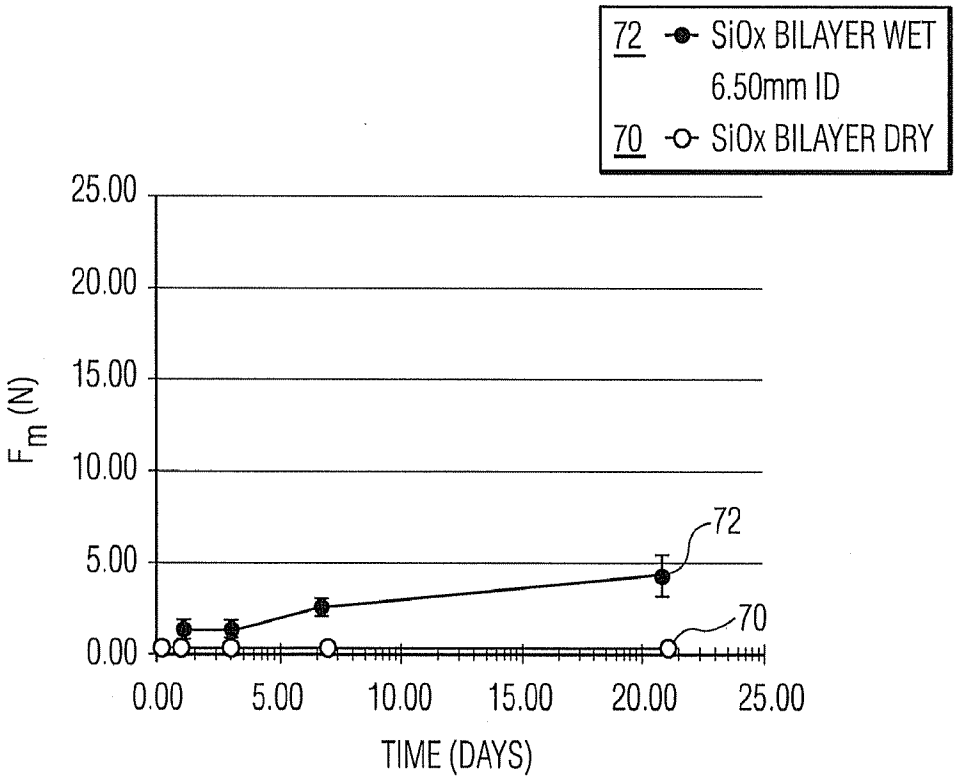

72 SiOx BILAYER WET
6.50mm ID
70 SiOx BILAYER DRY
25.00
20.00
15.00
10.00
5.00
0.00
F_m (N)
0.00
5.00
10.00
15.00
20.00
25.00
TIME (DAYS)

FIG. 12

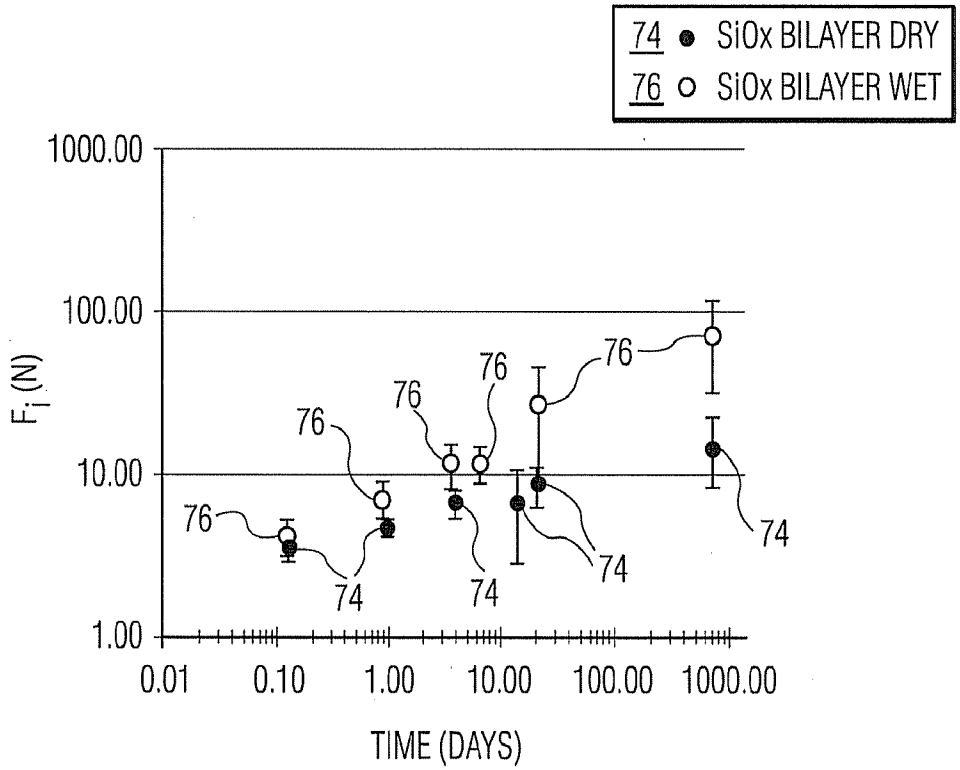

74 SiOx BILAYER DRY
76 SiOx BILAYER WET
1000.00
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 13

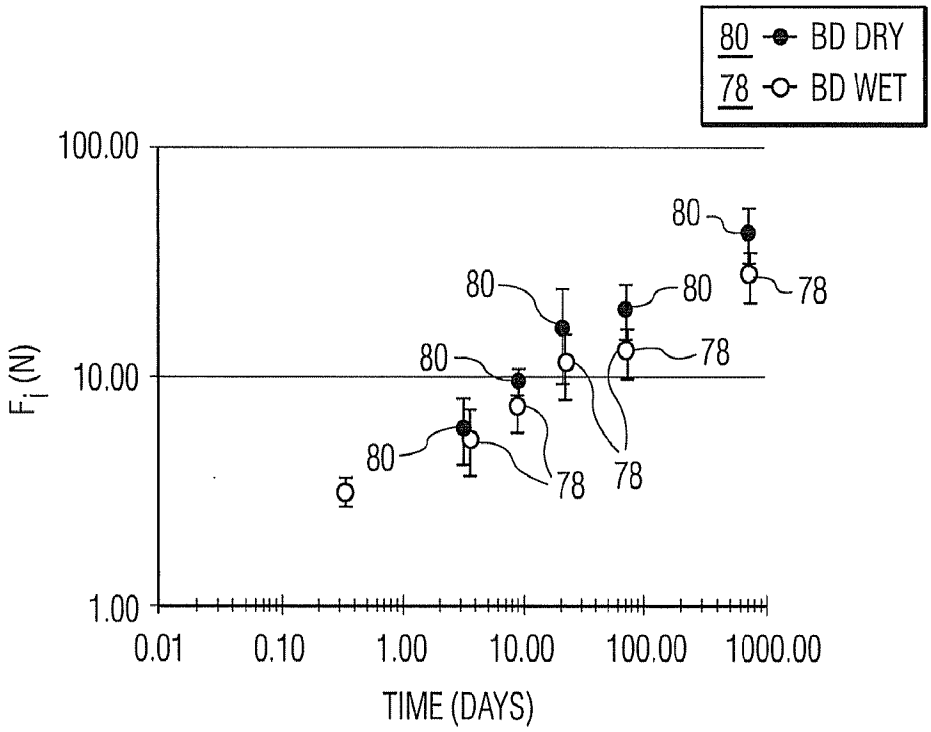

80 BD DRY
78 BD WET
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 14

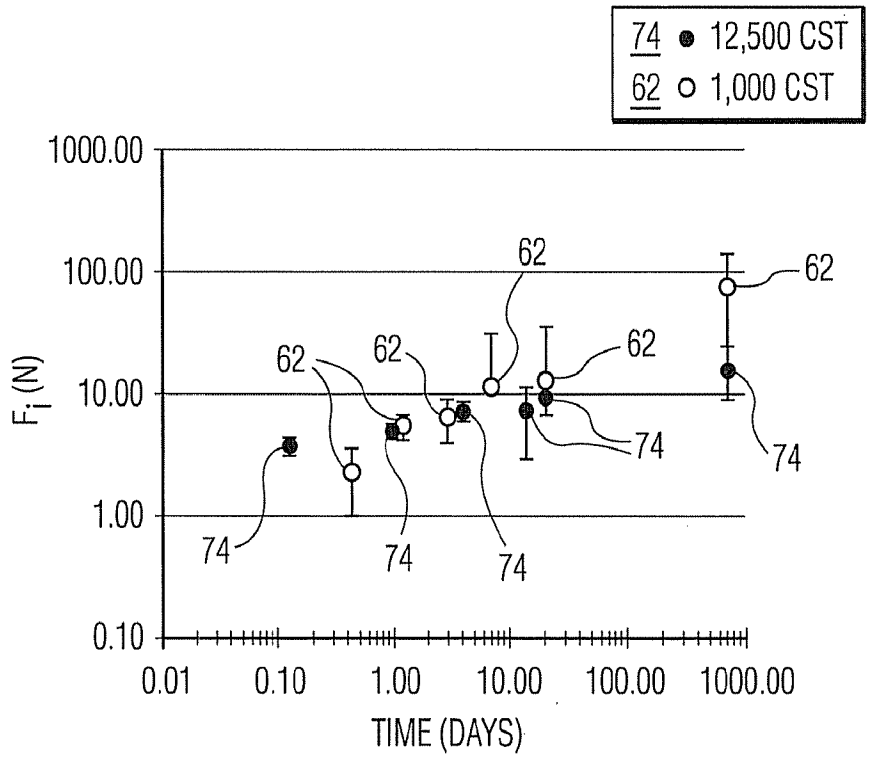

74 12,500 CST
62 1,000 CST
1000.00
100.00
10.00
1.00
0.10
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
62
74

FIG. 15

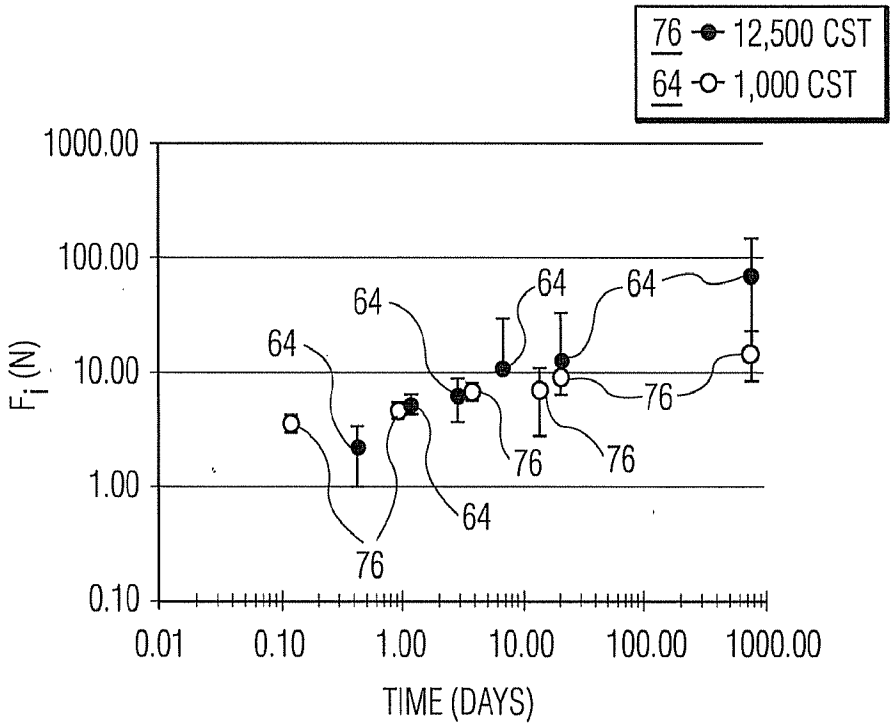

76 12,500 CST
64 1,000 CST
1000.00
100.00
10.00
1.00
0.10
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
64
76

FIG. 16

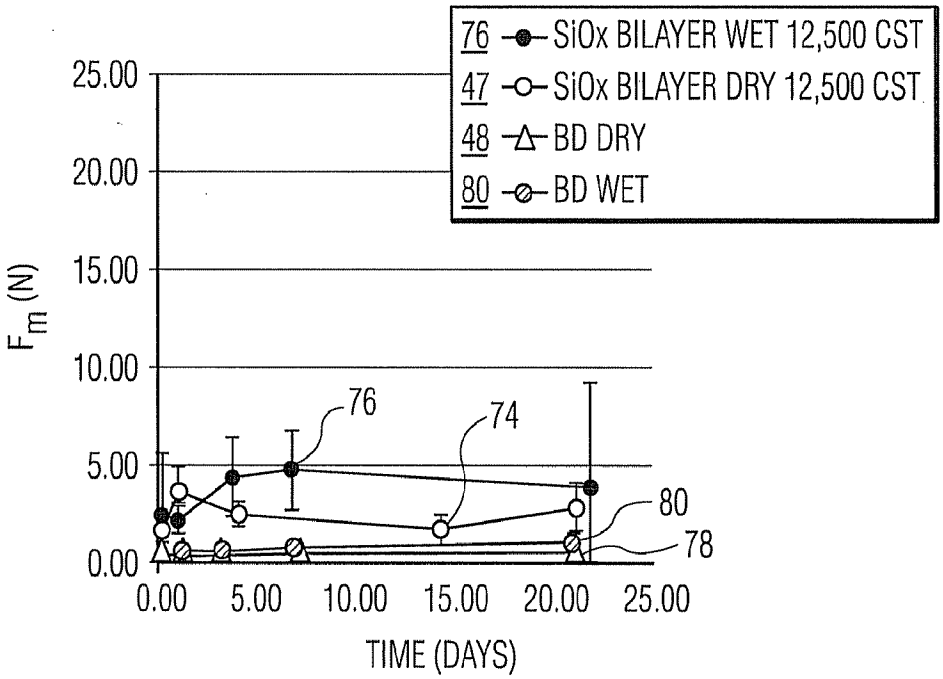

76 SiOx BILAYER WET 12,500 CST
47 SiOx BILAYER DRY 12,500 CST
48 BD DRY
80 BD WET
25.00
20.00
15.00
10.00
5.00
0.00
F_m (N)
76
74
80
78
0.00
5.00
10.00
15.00
20.00
25.00
TIME (DAYS)

FIG. 17

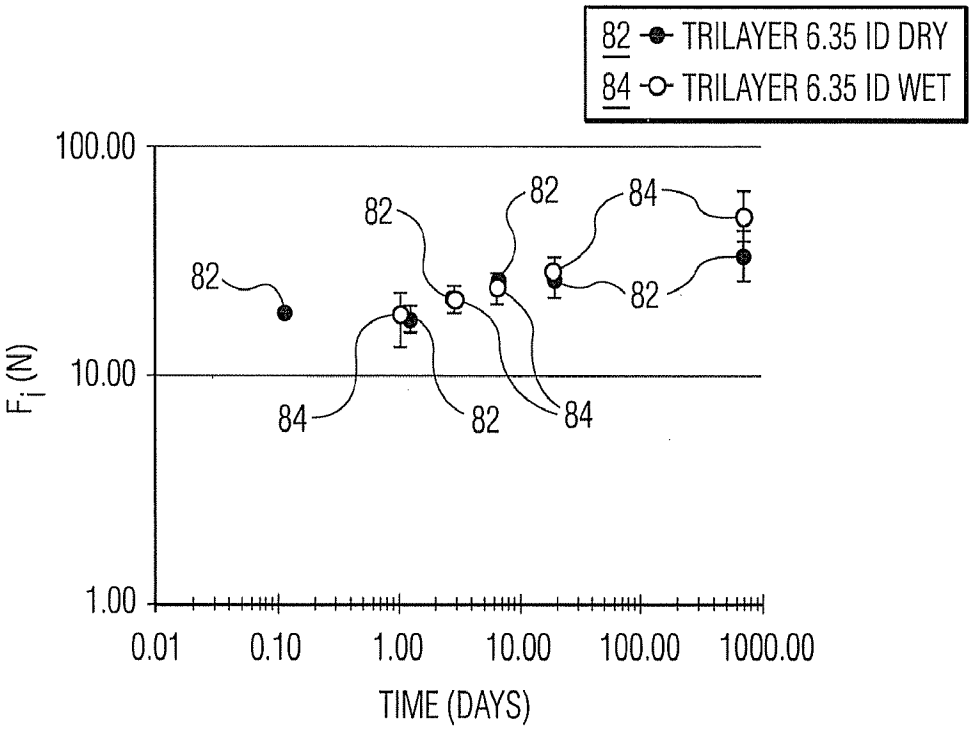

82 TRILAYER 6.35 ID DRY
84 TRILAYER 6.35 ID WET
100.00
10.00
1.00
F_i (N)
82
84
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 18

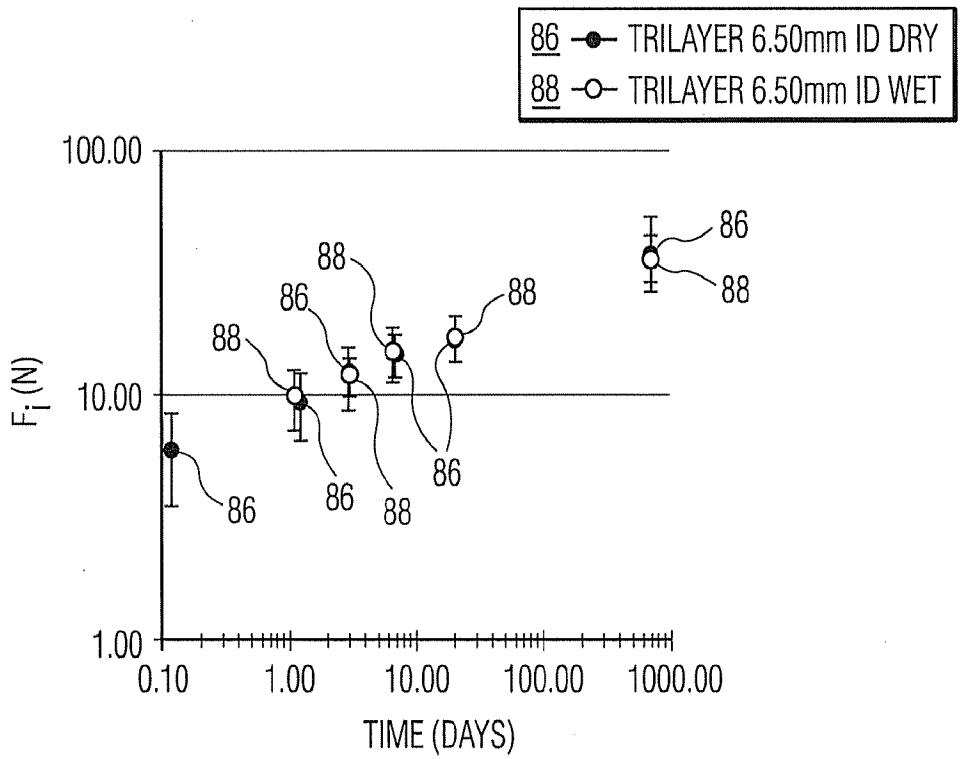

86 TRILAYER 6.50mm ID DRY
88 TRILAYER 6.50mm ID WET
100.00
10.00
1.00
F_i (N)
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 19

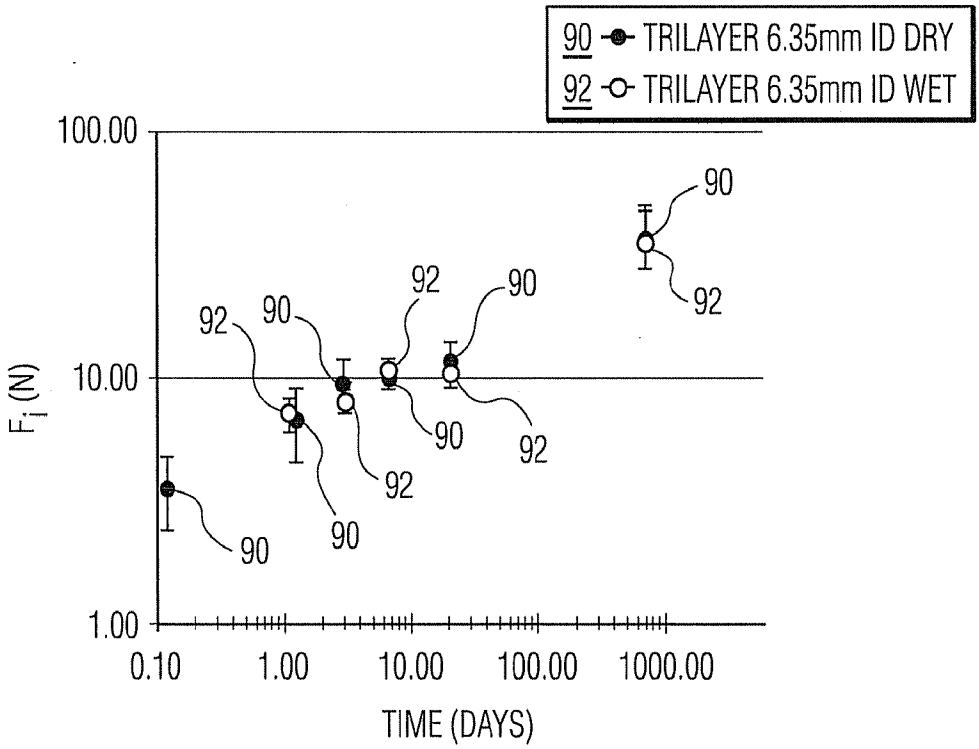

90 TRILAYER 6.35mm ID DRY
92 TRILAYER 6.35mm ID WET
100.00
10.00
1.00
F_i (N)
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 20

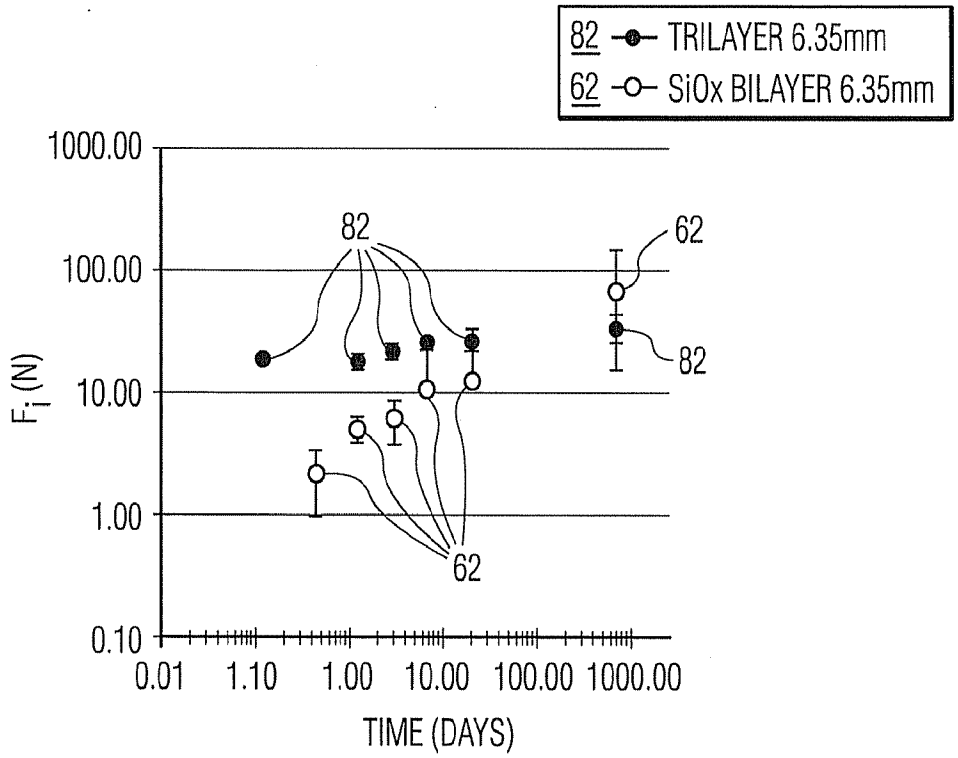

82 TRILAYER 6.35mm
62 SiOx BILAYER 6.35mm
1000.00
100.00
10.00
1.00
0.10
F_i (N)
0.01
1.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
82
62
82
62

FIG. 21

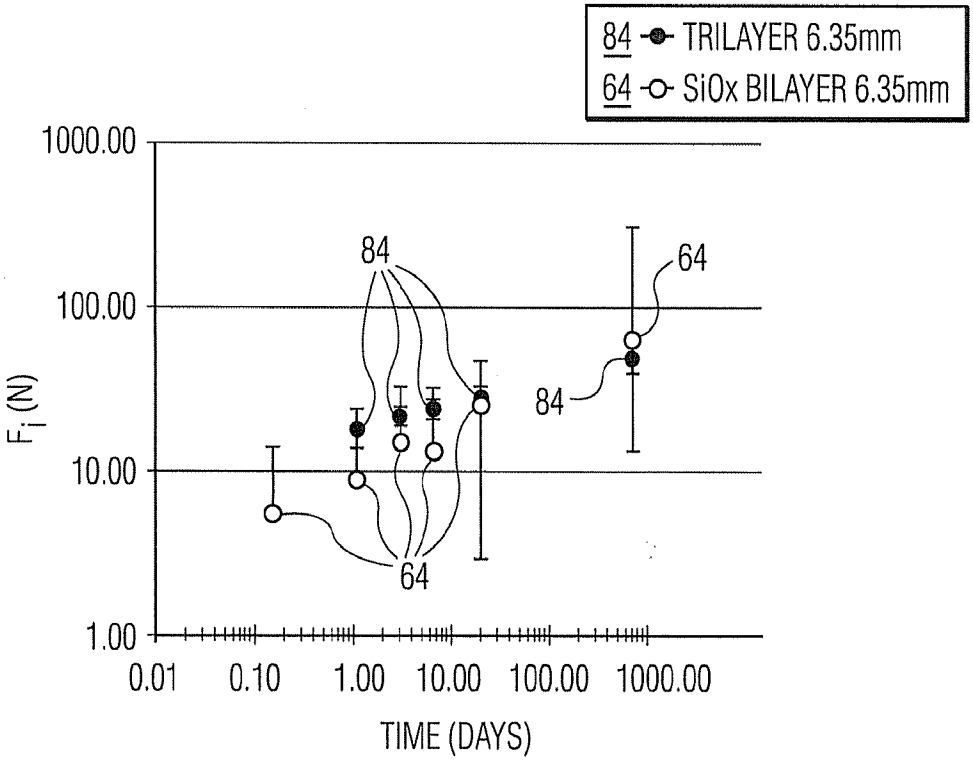

84 TRILAYER 6.35mm
64 SiOx BILAYER 6.35mm
1000.00
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)
84
64
84
64

FIG. 22

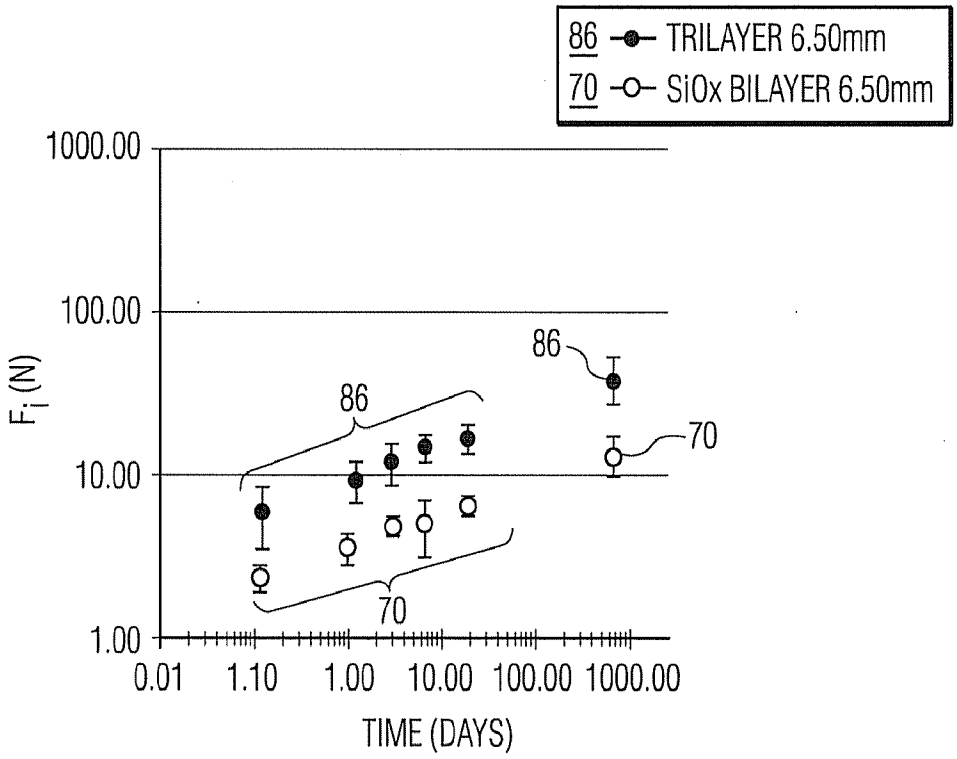

86 TRILAYER 6.50mm
70 SiOx BILAYER 6.50mm
1000.00
100.00
10.00
1.00
F_i (N)
86
70
0.01
1.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 23

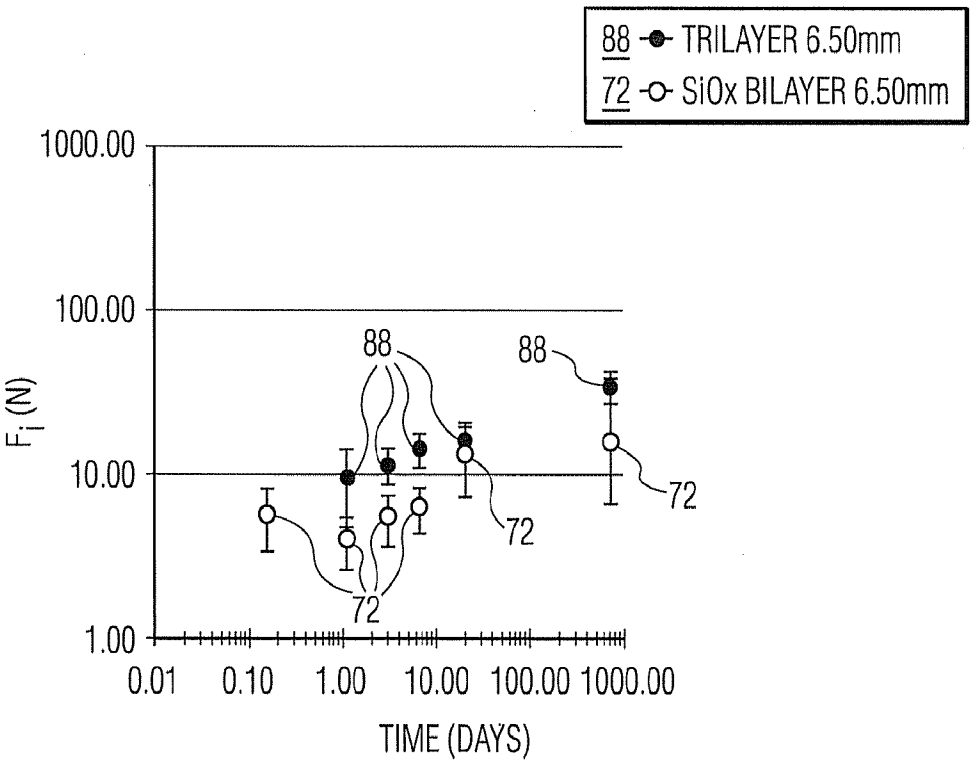

88 TRILAYER 6.50mm
72 SiOx BILAYER 6.50mm
1000.00
100.00
10.00
1.00
F_i (N)
88
72
0.01
0.10
1.00
10.00
100.00
1000.00
TIME (DAYS)

FIG. 24

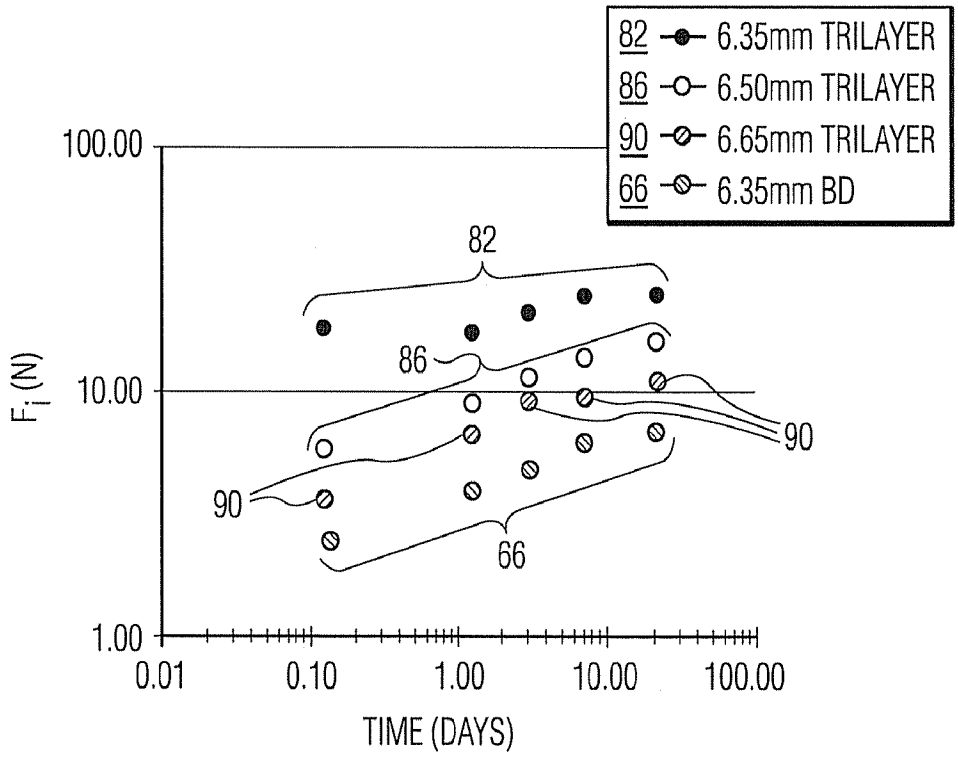

82 6.35mm TRILAYER
86 6.50mm TRILAYER
90 6.65mm TRILAYER
66 6.35mm BD
100.00
10.00
1.00
F_i (N)
0.01
0.10
1.00
10.00
100.00
TIME (DAYS)
82
86
90
90
66

FIG. 25

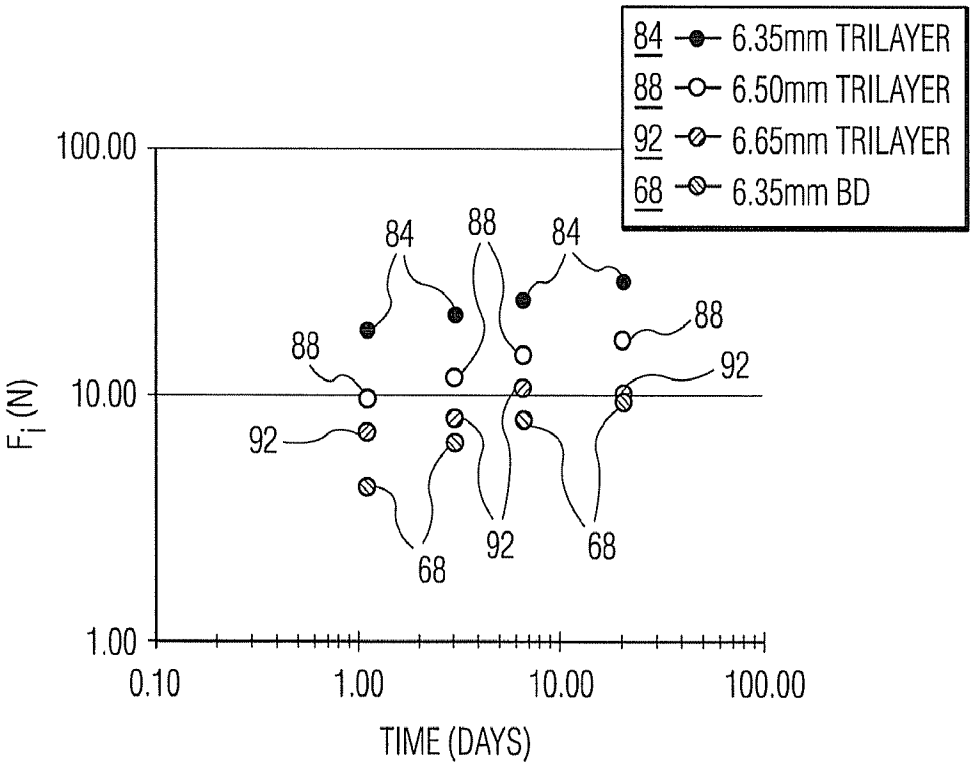

84 6.35mm TRILAYER
88 6.50mm TRILAYER
92 6.65mm TRILAYER
68 6.35mm BD
100.00
10.00
1.00
F_i (N)
0.10
1.00
10.00
100.00
TIME (DAYS)
84
88
84
88
88
92
92
68
92
68

FIG. 26

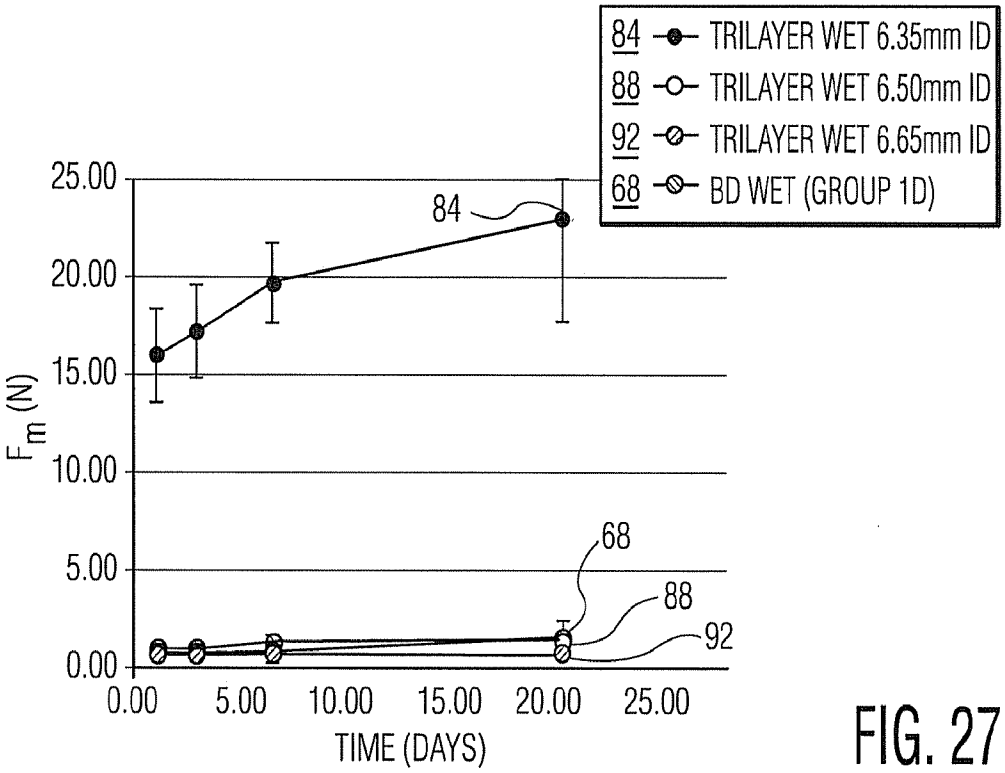

84 TRILAYER WET 6.35mm ID
88 TRILAYER WET 6.50mm ID
92 TRILAYER WET 6.65mm ID
68 BD WET (GROUP 1D)
25.00
20.00
15.00
10.00
5.00
0.00
F_m (N)
0.00 5.00 10.00 15.00 20.00 25.00
TIME (DAYS)
84
68
88
92

FIG. 27

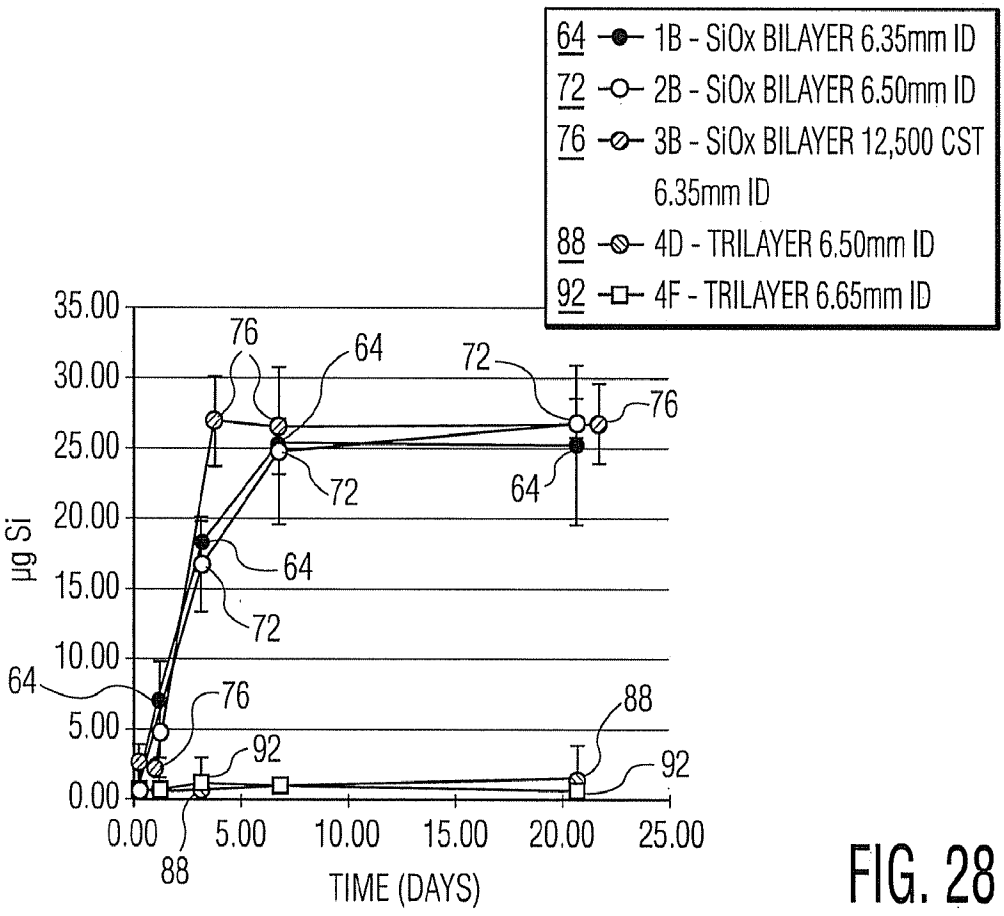

64 1B - SiOx BILAYER 6.35mm ID
72 2B - SiOx BILAYER 6.50mm ID
76 3B - SiOx BILAYER 12,500 CST 6.35mm ID
88 4D - TRILAYER 6.50mm ID
92 4F - TRILAYER 6.65mm ID
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
µg Si
0.00 5.00 10.00 15.00 20.00 25.00
TIME (DAYS)

FIG. 28

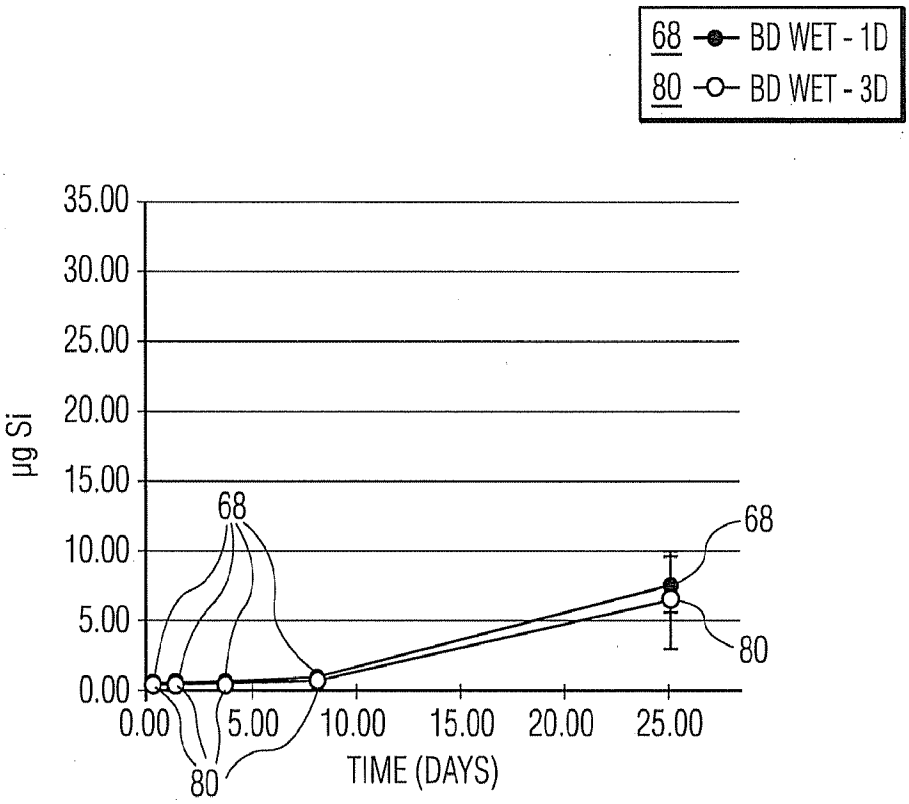

68 BD WET - 1D
80 BD WET - 3D
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
µg Si
0.00
5.00
10.00
15.00
20.00
25.00
TIME (DAYS)
68
68
80
80

FIG. 29

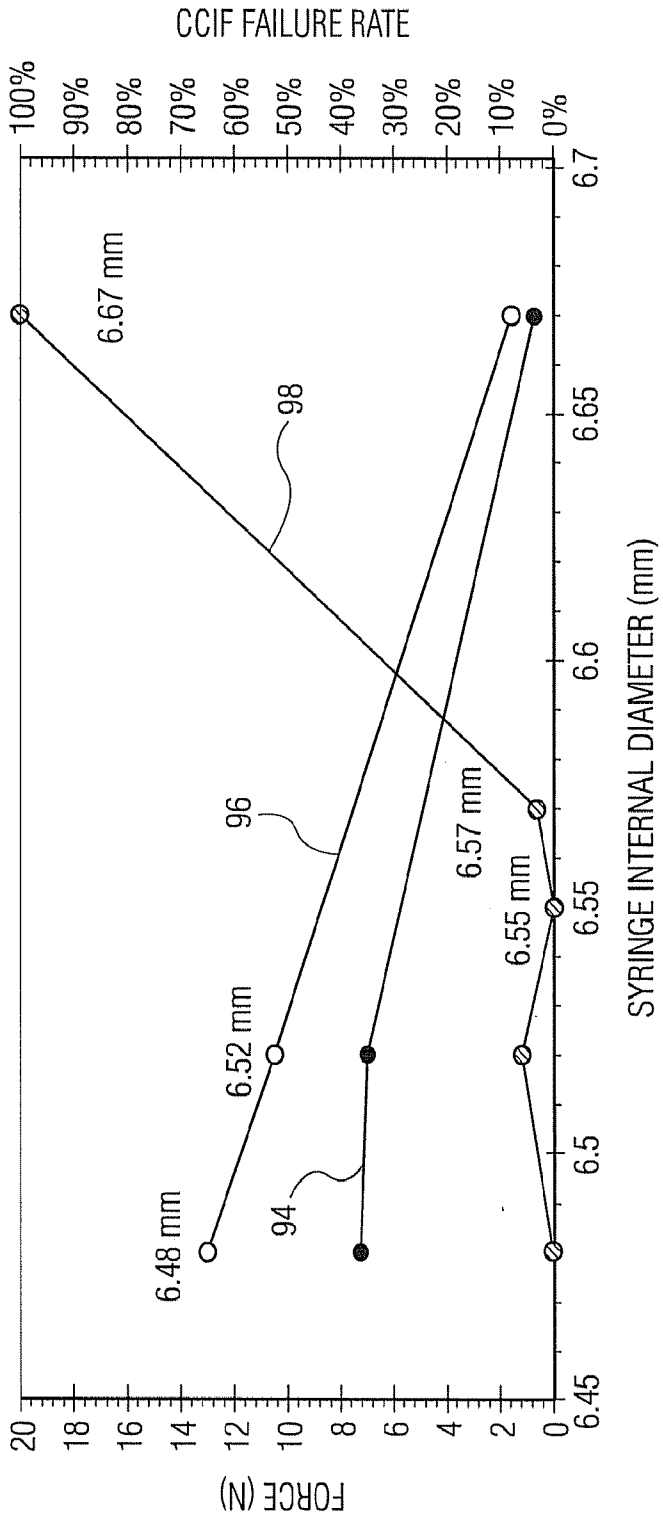

CCIF FAILURE RATE
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
6.67 mm
98
96
6.52 mm
6.48 mm
94
6.57 mm
6.55 mm
FORCE (N)
20
18
16
14
12
10
8
6
4
2
0
6.45
6.5
6.55
6.6
6.65
6.7
SYRINGE INTERNAL DIAMETER (mm)

FIG. 30

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/019684

A. CLASSIFICATION OF SUBJECT MATTER
INV. C23C16/40 A61M5/31
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C23C A61M

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 331 174 B1 (REINHARD MICHAEL [DE] ET AL) 18 December 2001 (2001-12-18) column 5, line 62 - column 8, line 13	1-38
Y	WO 2011/143509 A1 (CV HOLDINGS LLC [US]; FELTS JOHN T [US]; FISK THOMAS E [US]; ABRAMS RO) 17 November 2011 (2011-11-17) paragraph [0106]	1-38

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 May 2014	23/05/2014

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/019684

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 30-38(partially)
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Continuation of Box II.2

Claims Nos.: 30-38(partially)

Present claims 30-38 relates to an extremely large number of possible compositions in a prefilled medical syringe.
Many of the substances
listed over 52 pages are mentioned with their trade names rather than the exact compositions. This as such is objectionable under the clarity requirement of Article 6 PCT, since compositions sold under one name may not be the same at all times.
Moreover, some of the compositions listed
are vaguely described by their functions during particular uses and not their composition, effectively attempting to extend the scope of the claims to products not yet invented (and also not disclosed in the description) contrary to Articles 5 and 6 PCT.
The non-compliance with
the substantive provisions is to such an extent, that the search of these claims was limited to a prefilled syringe. See also PCT Guidelines 9.19 and 9.23.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2014/019684

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6331174 B1	18-12-2001	DE 4438360 A1	09-05-1996
		EP 0709105 A1	01-05-1996
		JP 3249035 B2	21-01-2002
		JP H08206201 A	13-08-1996
		US 6331174 B1	18-12-2001
WO 2011143509 A1	17-11-2011	NONE	