

**(12) STANDARD PATENT**  
**(19) AUSTRALIAN PATENT OFFICE**

(11) Application No. **AU 2007209856 B2**

(54) Title  
**Methods of applying a hydrophilic coating to a substrate, and substrates having a hydrophilic coating**

(51) International Patent Classification(s)  
**A61L 29/08** (2006.01) **A61L 29/14** (2006.01)

(21) Application No: **2007209856** (22) Date of Filing: **2007.01.30**

(87) WIPO No: **WO07/089784**

(30) Priority Data

(31) Number	(32) Date	(33) Country
<b>60/764,151</b>	<b>2006.02.01</b>	<b>US</b>

(43) Publication Date: **2007.08.09**

(44) Accepted Journal Date: **2013.06.13**

(71) Applicant(s)  
**Hollister Incorporated**

(72) Inventor(s)  
**Gilman, Thomas H.**

(74) Agent / Attorney  
**Shelston IP, L 21 60 Margaret St, Sydney, NSW, 2000**

(56) Related Art  
**D1. US 5670558 A (ONISHI et al) 23 September 1997**

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
9 August 2007 (09.08.2007)

PCT

(10) International Publication Number  
**WO 2007/089784 A2**

(51) International Patent Classification:  
A61L 29/08 (2006.01) A61L 29/14 (2006.01)

(21) International Application Number:  
PCT/US2007/002545

(22) International Filing Date: 30 January 2007 (30.01.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/764,151 1 February 2006 (01.02.2006) US

(71) Applicant (for all designated States except US): **HOLLISTER INCORPORATED** [US/US]; 2000 Hollister Drive, Libertyville, IL 60048 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **GILMAN, Thomas, H.** [US/US]; 7209 Ridge Court, Spring Grove, IL 60081 (US).

(74) Agent: **LAWRENCE, Andrew, M.**; MARSHALL GERSTEIN & BORUN LLP, 233 S. Wacker Drive, Suite 6300, Sears Tower, Chicago, IL 60606-6357 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF APPLYING A HYDROPHILIC COATING TO A SUBSTRATE, AND SUBSTRATES HAVING A HYDROPHILIC COATING

(57) Abstract: This invention relates to methods of applying to a substrate a hydrophilic coating that becomes lubricious when activated with water or wat vapor, and to substrates having such a hydrophilic coating.



**WO 2007/089784 A2**

**METHODS OF APPLYING A HYDROPHILIC COATING TO A  
SUBSTRATE, AND SUBSTRATES HAVING A HYDROPHILIC COATING**

**CROSS-REFERENCE TO RELATED APPLICATION**

The benefit under 35 U.S.C. §119(e) of U.S. provisional patent application  
5 serial no. 60/764,151 filed February 1, 2006, the entire disclosure of which is  
incorporated herein by reference, is hereby claimed.

**FIELD OF THE INVENTION**

This invention relates to methods of applying to a substrate a hydrophilic  
coating that becomes lubricious when activated with water or water vapor, and to  
10 substrates having such a hydrophilic coating.

**BACKGROUND**

In the medical field, and in other fields as well, there has developed a need for  
substrates with surfaces that become lubricious upon contact with water. A main use  
of lubricious materials involves catheters, catheter guide wires, and other medical  
15 devices that are meant to be inserted into the body. The lubricious nature of such  
materials allows the insertion (and subsequent removal) of a catheter or other medical  
device to be accomplished with minimum resistance, thereby reducing discomfort and  
possible injury.

In many cases, it is easy to prepare a functional lubricious coating for a  
20 substrate surface. However, it is more difficult to prepare a lubricious coating that is  
securely anchored to the substrate surface. Secure anchoring of a lubricious coating  
to a substrate surface is generally desirable, and particularly useful in the medical  
field, where secure anchorage of the coating is often an important requirement.

U.S. Patent 4,642,267 to Creasy *et al.* discloses a hydrophilic polymer blend  
25 comprising a thermoplastic polyurethane and a poly(N-vinyl lactam). When used as a  
coating material, the polymer blend components are co-dissolved in an organic  
solvent capable of solubilizing both polymers, a substrate is dip coated in the solution,  
and the solvent is then driven off by a drying process so as to form a hydrophilic

coating on the substrate surface. However, the coating attachment to the substrate is considered to lack the security desired. Another disadvantage of the '267 patent is that high boiling point and potentially toxic solvents are used to deliver the coating formulation, and thus significant costs must be incurred to drive off the solvent  
5 residuals from the coated product so as to obtain the desired biocompatibility.

U.S. Patent 5,702,754 to Zhong discloses coating a substrate surface with a polymer having reactive functional groups and an excess of cross-linking agent. The polymer is cured to form a coating. Then, a second coating comprising a hydrophilic polymer having the same type of reactive functional groups is applied thereover.  
10 When the hydrophilic polymer is then cured, the second coating becomes covalently bonded to the first coating because the first coating includes an excess of cross-linking agent thereby permitting covalent bonding between the first coating and the hydrophilic polymer. Disadvantages of this approach include the fact that multiple steps are required and multiple polymer solutions are involved. There are also  
15 significant limitations in the selection of lubricious polymers and cross-linking agents.

Any discussion of the prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of common general knowledge in the field.

It is an object of the present invention to overcome or ameliorate at least one  
20 of the disadvantages of the prior art, or to provide a useful alternative.

### **SUMMARY OF THE INVENTION**

According to a first aspect, the invention provides a method of applying a hydrophilic coating to a substrate surface comprising:

25 providing a substrate having a surface comprising at least in part a water-swella-  
ble material;

contacting the substrate surface with a solution to swell the water-swella-  
ble material, said solution comprising at least one of (i) a water-soluble polymer capable  
of being cross-linked to form a cross-linked, lubricious, hydrophilic coating and (ii) a

water-soluble monomer capable of being polymerized to form a cross-linked, lubricious, hydrophilic coating; and

forming the cross-linked, lubricious, hydrophilic coating, said coating being entangled with and securely anchored to the substrate surface.

5           The water-soluble polymer can be cross-linked in the presence of the swollen substrate surface to provide a cross-linked coating that is entangled with and securely anchored to the substrate surface. Similarly, the monomer can either form a crosslinked hydrogel network as it is polymerized, or can be polymerized and then subsequently cross-linked, in the presence of the swollen substrate surface, to provide  
10 a cross-linked coating that is entangled with and securely anchored to the substrate surface. The substrate includes a first or outer layer comprising a water-swella-  
ble material. The substrate may further include an optional second or support layer, which comprises non-water-swella-  
ble materials and/or water-swella-  
ble materials.

          According to a second aspect, the invention provides a substrate made  
15 according to the method of the first aspect.

          According to a third aspect, the invention provides a substrate having a cross-linked hydrophilic coating, disposed on a substrate comprising:

          a substrate having a surface comprising at least in part a water-swella-  
ble material; and,

20           an interpenetrating polymer network disposed on the surface, the interpenetrating polymer network comprising the network that comprises the water-swella-  
ble substrate surface physically entangled with the network that comprises the cross-linked hydrophilic coating, said coating being securely anchored to the substrate surface.

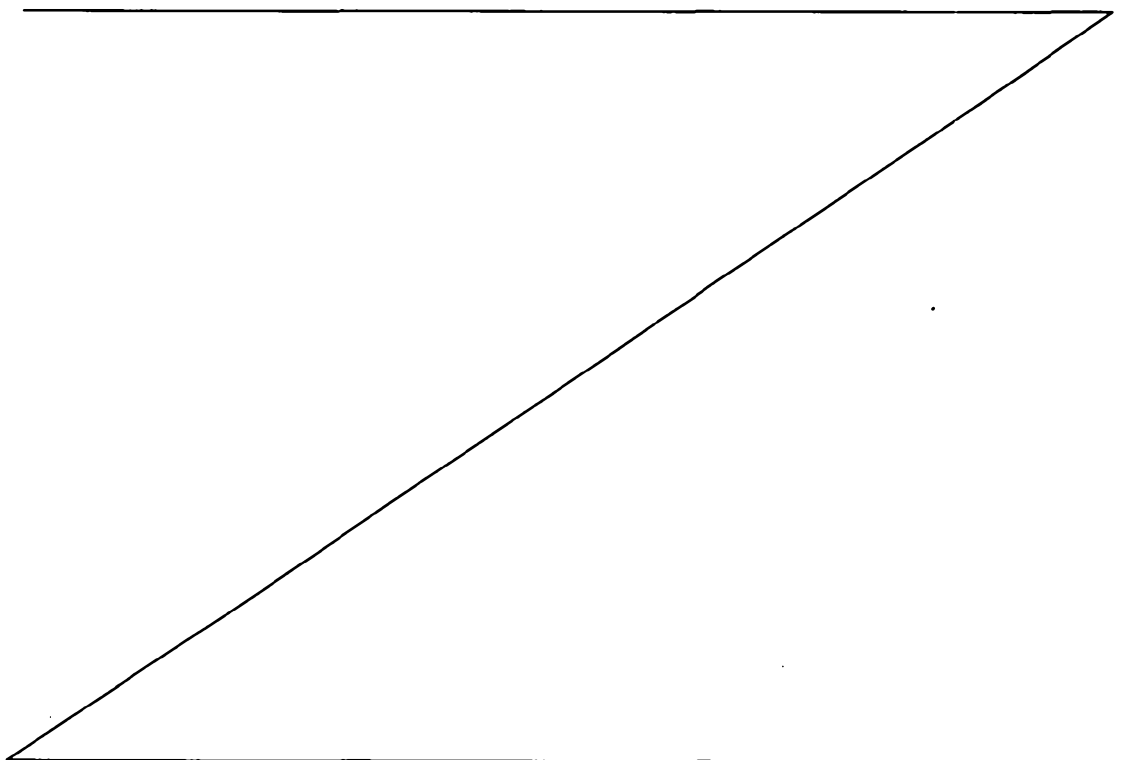
25           Unless the context clearly requires otherwise, throughout the description and the claims, the words "comprise", "comprising", and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of "including, but not limited to".

### **DETAILED DESCRIPTION**

One embodiment of the invention relates to methods of applying a lubricious, hydrophilic coating to a substrate. An additional embodiment of the invention relates to substrates having such a lubricious, hydrophilic coating.

- 5           As used herein, the term "lubricious coating" refers to a coating that provides a substrate surface having a coefficient of friction value less than about 0.3, less than about 0.1, and/or less than about 0.05, for example, 0.03, or even 0.01.

- The invention involves creating an interpenetrating polymer network *in situ* on a substrate surface. For example, a substrate surface comprising a water-swella-
- 10   material is contacted with a solution comprising a water-soluble hydrophilic polymer capable of being cross-linked to form a cross-linked, lubricious hydrophilic coating. Alternatively, a water-soluble monomer, either capable of being polymerized to form a cross-linked, lubricious, hydrophilic coating, or of being polymerized and then cross-linked to form a cross-linked, lubricious, hydrophilic coating, may be used in
- 15   place of, or in addition to, the water-soluble hydrophilic polymer. The coating is typically then cured, for example, by exposure to UV light, in order to cross-link the water-soluble polymer and/or polymer formed from the water-soluble monomer.



- 4 -

The use of one or more water-soluble polymers is typically preferred relative to the use of one or more water-soluble monomers, however, particularly for medical applications, because residual unpolymerized monomer can present biocompatibility issues for medical device applications.

5           Because the water-swellaable material of the substrate swells in the presence of water and/or alcohol, it is believed to become physically entangled with the water-soluble hydrophilic polymer before cross-linking, and those entanglements are locked in during cross-linking. Thus, a coating comprising the interpenetrating polymer network is formed by polymerizing the water-soluble polymer in the presence of the  
10   water-swellaable substrate surface when the water-swellaable substrate surface is in a swollen state, and results in the lubricious coating being securely anchored to the substrate (after cross-linking thereof). Essentially, the method allows two hydrogels to be linked together mechanically on a molecular scale.

Advantageously, the hydrophilic coating can be secured to the surface without  
15   the need for covalent interactions between the hydrophilic coating and the first layer. Another advantage is that the coating formulation can be carried using solvents such as water and lower alcohols, which are inexpensive, biocompatible, and relatively easy to drive off from the coated product. Still another advantage is the versatility of the invention; the invention will provide secure anchorage for any hydrophilic coating  
20   formed from a water-soluble polymer and/or water-soluble monomer, which can be coated from an aqueous or alcohol based solution, without the need for a primer layer or other polymer solution based anchorage means. This versatility allows a wide number of polymer / cross-linking agent systems and/or monomer / initiator / cross-linking systems to be utilized, and thus for an optimal system to be implemented for  
25   any given application.

In one embodiment, the terms "well-anchored" or "securely anchored" refers to a coating that, after an abrasion protocol is conducted on the substrate carrying the coating, results in a substrate having a final coefficient of friction value, when the coating is activated, for example, by water immersion, that is not more than ten times,  
30   not more than five times, and/or not more than two times the original coefficient of friction value prior to abrasion. A suitable abrasion protocol includes passing a

- 5 -

coated tube through a hole which is about 10% smaller diameter than the outside diameter of the tubing 100 times, while keeping the coating wet during the abrasion cycles. After this abrasion protocol, the tube is immersed in deionized water for about 30 seconds so as to activate the coating, and the coefficient of friction can be  
5 determined using standard means.

A substrate, such as a catheter tube, to be coated by the methods of this invention, is formed in a way that provides it with a surface or surface layer comprised at least in part of a water-swellaable material. That may be accomplished in a variety of ways including but not limited to coextruding a substrate having a first or  
10 outer layer comprising any suitable water-swellaable material, and a second or inner support layer comprised of non-water-swellaable materials and/or water-swellaable materials.

Generally, any water swellaable materials or mixtures thereof could be used for the first or outer layer. Suitable water-swellaable materials include but are not limited  
15 to water-swellaable polyamide-based copolymers, water-swellaable polyester-based copolymers, water-swellaable urethane-based copolymers, and mixtures thereof. Any of a variety of thermoplastic polymers, thermoplastic elastomers, and/or thermoplastic alloys, which are capable of swelling in the presence of water (e.g., an aqueous solution) may be used. In general, such water swellaable polymers will also swell in  
20 lower alcohols such as methanol, ethanol, propanol, isopropanol, butanol, and the like. Higher alcohols such as hexanol and octanol may also be used, but lower alcohols are typically preferred because of their increased volatility relative to water.

Preferably, the first layer is comprised of a water-swellaable thermoplastic elastomer comprising a block copolymer having rigid and flexible blocks. Suitable  
25 rigid blocks include polyamide blocks, polyester blocks, and polyurethane blocks, but other rigid polymer blocks may be used. The rigid block is preferably either glassy or crystalline at room temperature. Suitable flexible blocks include flexible polyether blocks such as flexible polyethylene oxide blocks, flexible poly-N-vinyl lactam blocks such as flexible polyvinylpyrrolidone blocks, flexible polyalcohol blocks, and  
30 flexible polyacid blocks. Of course, other flexible blocks could also be used.



- 6 -

Suitable water-swellaable thermoplastic elastomers include but are not limited to polyether/polyamide block elastomers such as those sold under the PEBAX<sup>®</sup> trade name (Arkema, PA), for example, such as PEBAX<sup>®</sup> 1647, PEBAX<sup>®</sup> 1074, and PEBAX<sup>®</sup> MX1652, and polyester elastomers such as those sold under the HYTREL<sup>®</sup> trade name (Du Pont de Nemours, DE), for example, such as HYTREL<sup>®</sup> 8171 and HYTREL<sup>®</sup> 8206. Other suitable water-swellaable thermoplastic elastomers include but are not limited to thermoplastic polyurethanes such as polyether thermoplastic polyurethanes sold under the ESTANE<sup>®</sup> and the TECOPHILIC<sup>®</sup> trade names (Noveon Inc., OH) and polyester thermoplastic polyurethanes such as those sold under the ESTANE<sup>®</sup> and CARBOTHANE<sup>®</sup> trade names (Noveon Inc., OH).

The substrate can be made entirely from a water-swellaable material. Polymer blends including at least one water-swellaable material can alternatively be used. Surprisingly, even polymer blends where a water-swellaable material comprises only a minority of the polymer blend will provide securely anchored hydrophilic coatings. This allows flexibility in designing substrates, for example, as a homoextrusion that will have the mechanical properties needed for a given application. For example, tubing made of 40 weight percent (wt.%) PEBAX<sup>®</sup> 1074 (a water-swellaable thermoplastic elastomer) and 60 wt.% PEBAX<sup>®</sup> 3533 (a non-water-swellaable thermoplastic elastomer) has desirable properties for a urinary catheter application, and provides many or all of the advantages of this invention.

Alternatively, the substrate can have an outer layer made from a water-swellaable material, or an outer layer made from a blend comprised of water-swellaable and non-water-swellaable materials. The substrate can then have an inner or support layer comprised of one or more non-water-swellaable materials. Of course, the inner or support layer may be made from or further include one or more water-swellaable materials.

As used herein, the term "water-swellaable" generally refers to a material that swells in the presence of water or alcohol. In various embodiments, the term refers to a material that increases in at least one dimension by at least 0.5%, at least 1%, at least 2%, at least 5%, at least 10%, at least 25%, or even greater when immersed in water for a period of approximately 90 minutes. In accordance with the foregoing

- 7 -

embodiments, a 1 inch by 1 inch by 1 mil square of material can be immersed in water for a period of 90 minutes, and the increase in the height or length can be determined relative to the original height or length so as to ascertain whether a certain material swells sufficiently to be considered a water-swellable material in accordance with the invention. If so, the material can generally be considered suitable for use as a water-swellable material in the invention.

Generally, any material can be used in forming the optional second or support layer, but materials capable of being extruded or otherwise melt-processed are generally preferred. Suitable materials for use in the optional second or support layer include but are not limited to thermoplastic resins, such as, for example, olefin polymers, particularly, polyethylenes, polypropylenes, polyvinylchlorides, polytetrafluoroethylenes, polyvinylacetates, polystyrenes, polyesters, polyurethanes, polyamides, other suitable polymers, and mixtures thereof. Metals, ceramics, and other materials may also be used as the support layer, but then the outer layer needs to be affixed or coupled to the second layer by a mechanism different than co-extrusion, for example, by spin-casting, dip-coating, wire extrusion coating, or otherwise affixing, coupling, or adhering the water-swellable surface layer (or substrate comprising same) to the second layer.

The substrate can be a medical device. Exemplary medical devices that may be coated with the lubricious coatings in accordance with the invention include but are not limited to contact lenses, medical implants including but not limited to pacemakers and wire leads for same, intravascular implants including but not limited to arterial stents, and catheters including but not limited to urinary catheters, fecal catheters, catheters for administration of intravenous fluids, medications, and nutrition, and coronary catheters such as angioplasty catheters. Further still, in certain medical device applications it may be desirable to incorporate a drug into the coating solution, or to add a drug after formation of the coating on the medical device. For example, stents having a coating in accordance with the invention can comprise a drug, for example, taxol to prevent late stenosis, or heparin to prevent the formation of a thrombus.

- 8 -

Additionally, non-medical device applications of the invention can also be envisioned where surfaces having a low coefficient of friction in a wet environment are desired because the invention can provide a highly lubricious coating to any product that is used in a wet environment. Possible non-limiting examples include  
5 marine uses, for example, such as wet suits or boat hulls where the coating could be applied to reduce drag.

The untreated substrate is typically dipped or otherwise coated with a polymer solution in which the coating polymer is dissolved in water, alcohol, or a solution containing both water and alcohol. If a catheter is being coated, a mandrel can be  
10 inserted into the catheter structure in order to prevent any coating solution from contacting and/or coating the inside of the catheter when the coating solution is applied.

Any suitable hydrophilic polymer capable of being cross-linked and of swelling and becoming lubricious when exposed to water or water vapor may be used  
15 to provide the hydrophilic coating. Upon being cross-linked, the network of the coating polymer forms an interpolymer with the swollen water-swellaable material, for example, with the flexible (or soft) blocks of the substrate surface block polymer, resulting in a coating that is securely anchored to the substrate. Suitable water-soluble hydrophilic polymers include but are not limited to polyacrylic acids, acrylic acid  
20 copolymers such as acrylamide/acrylic acid copolymers, polyvinylpyrrolidones, polyvinylalcohols, water-soluble polymers containing carboxylic acid functional groups, and mixtures thereof. Other water-soluble polymers that can be cross-linked to form a hydrophilic coating may also be used.

Similarly, any suitable hydrophilic monomer capable of being polymerized to  
25 form a cross-linked network and becoming lubricious when exposed to water or water vapor may be used to provide the hydrophilic coating. Suitable water-soluble hydrophilic monomers that can be used include but are not limited to vinyl monomers, for example, vinyl alcohols, vinylpyrrolidones, acrylamides, methacrylates, acrylic acids, and mixtures thereof. Some of these can be copolymerized with  
30 multifunctional monomer to form a network *in situ*, others can be polymerized and subsequently cross-linked using methods well known in the art. Various initiators, for

- 9 -

example, photoinitiators including but not limited to benzophenone can be used to polymerize the monomers.

An important advantage of this method is that it is relatively easy to prepare a substrate with a securely anchored hydrophilic coating. Since the outer layer of the substrate generally includes a thermoplastic polymer, known manufacturing methods that are uncomplicated, direct, and economical, such as extrusion, co-extrusion, or injection molding, may be used to produce a substrate having a water-swella-  
5 surface. The coating method is applicable to any system of hydrophilic coating polymer and cross-linking method that can be achieved using a water- or alcohol-based solvent system. Similarly, the coating method is applicable to any system of hydrophilic monomer, initiator, and cross-linking method that can be achieved using a water- or alcohol-based solvent system.

Suitable cross-linking agents are well known in the art and include but are not limited to UV activatable cross-linking agents, carbodiimides, aziridines, melamine  
15 formaldehydes, and multifunctional carboxylic acid cross-linking agents. Exemplary UV activatable cross-linking agents include polymeric hydroxyl ketones sold under the ESACURE™ trade name (Sartomer Company, PA), for example, ESACURE™ KIP 150 and ESACURE™ ONE. Exemplary carbodiimide cross-linking agents are sold under the CARBODILITE™ trade name (Nisshinbo Industries, Inc., JP), for  
20 example, CARBODILITE™ V-02-L2 and CARBODILITE™ E-02. Exemplary aziridine cross-linking agents are sold under the cross-linker CX-100 trade name (DSM NeoResins, DSM, NL). Heat and/or light can also be used to cross-link some water-soluble polymers.

The methods of applying a hydrophilic coating to a substrate and substrates  
25 having such a hydrophilic coating in accordance with the invention can be better understood in light of the following examples. However, the foregoing description and the following examples are merely illustrative, and therefore no unnecessary limitations should be understood therefrom as numerous modifications and variations are expected to occur to those skilled in the art.

30

- 10 -

### EXAMPLE 1

A coating polymer solution was prepared in an approximately 70:30 weight/weight isopropyl alcohol/water solvent system, where the polymer was polyvinylpyrrolidone K-90 at about 9 wt./vol. Included in the solution was about 0.03 wt.% UV activatable cross-linking agent (ESACURE™ KIP 150, Sartomer).

A thermoplastic substrate was employed in the form of a coextruded tube having an outside diameter of about 0.180 inches and an inside diameter of about 0.123 inches. The tube had an outer layer of about 0.003 inches thick that was a blend of a polyether/polyamide block elastomer (PEBAX® 1074, a water-swella-  
10 thermoplastic elastomer available from Arkema, PA) with an ethylene acid copolymer resin (NUCREL® 2806, a non-water-swella- thermoplastic elastomer available from Du Pont de Nemours, DE) at a weight ratio of about 40:60. The inner layer of the tube was a blend of thermoplastic, non-water-swella- resins designed to give the  
15 the coating solution and held therein for about 10 minutes prior to withdrawal. After withdrawal, the tube was air dried for about 30 minutes. Thereafter, the coated tube was exposed to UV light for about 5 minutes.

The tube with its cured coating was immersed in deionized water for 30 seconds. At that point, the surface of the tube was found to be highly lubricious, and  
20 the lubricious coating was securely adhered to the tube.

### EXAMPLE 2

Another approach is to use a separate, second solution that contains a cross-linking agent for the coating polymer. The second solution can be applied to the substrate having a water-swella- outer surface either before, or after, the coating  
25 polymer solution is applied. After both solutions have been applied, the coating is then cross-linked.

A coextruded tube was prepared having an outer layer of a polyether/polyamide block elastomer (PEBAX® 1074, Arkema, PA), and an inner layer of a polyether/polyamide block elastomer (PEBAX® 2533, a non-water-  
30 swella- thermoplastic elastomer available from Arkema, PA). The tube was first

- 11 -

dipped in an approximately 70:30 weight/weight isopropyl alcohol/water solution containing about 12 wt.% of a carbodiimide cross-linking agent (CARBODILITE™ V-02-L2, Nisshinbo, Japan) , and held therein for ten minutes prior to withdrawal. The tube was then air dried for ten minutes, subsequently dipped in an approximately  
5 70:30 weight/weight isopropyl alcohol/water solution containing about 7.5 wt.% of a water-soluble polymer containing carboxylic acid functional groups (GANTREZ™ S-97BF, ISP Technologies, Inc.), and then withdrawn immediately. After withdrawal, the tube was air dried for ten minutes.

The water-soluble polymer of this example is a methyl vinyl ether copolymer  
10 with maleic anhydride where the anhydride has been hydrolyzed into a diacid. The acid groups can be cross-linked by the carbodiimide cross-linking agent.

Curing was accomplished by heating the tubing to approximately 70° C for about 20 minutes in a conventional oven. The coating was neutralized by dipping it in a buffer solution. The resulting tube with its cured coating was then dipped in  
15 deionized water for 30 seconds. The surface of the wetted tube was slippery and the coating was securely adhered to the tube.

### EXAMPLE 3

A thermoplastic substrate was employed in the form of a coextruded tube having an outside diameter of about 0.181 inches and an inside diameter of about  
20 0.122 inches. The tube had an outer layer of about 0.003 inches thick, with the inner layer accounting for the balance of the tube. The inner tube layer comprised a blend of an ethylene octene copolymer (EXACT™ 5371, ExxonMobil Chemical Company, ExxonMobil, TX) with an ethylene acid copolymer resin (NUCREL® 2806, Du Pont de Nemours, DE) at a weight ratio of approximately 20:80, and the outer tube layer  
25 comprised a blend of a polyether/polyamide block elastomer (PEBAX® 1074, Arkema, PA) with an ethylene acid copolymer resin (NUCREL® 2806, Du Pont de Nemours, DE) at a weight ratio of approximately 40:60.

The tubing was coated by dipping in an approximately 70:30 weight/weight isopropyl alcohol/water solution containing about 5.5 wt.% polyvinylpyrrolidone K-  
30 90 (ICI Chemicals, England) and about 0.11 wt.% ESACURE™ One (Sartomer, PA).

- 12 -

The tubing was held in the coating solution for about 5 minutes in this solution and then withdrawn. After withdrawal, the coated tubing was air dried for about 50 minutes (at room temperature). Thereafter, the coated tube was exposed to UVC light for approximately 2.5 minutes.

5           The resulting tube with its cured coating was then immersed in deionized water for about 30 seconds. At that point, the surface of the tube was found to be highly lubricious, having an average coefficient of friction ( $n = 12$  samples tested) of about 0.02.

10           To test coating anchorage to the substrate tubing, an abrasion testing protocol was performed on the resulting coated tubing. The sample was passed through a hole in a 1/32" thick silicone rubber sheet, with the hole being about 10% smaller diameter than the outside diameter of the tubing. This was done 100 times, keeping the coating wet during the abrasion testing. After this abrasion protocol, the tube was again immersed in deionized water for about 30 seconds and tested for coefficient of  
15           friction. Again, the average coefficient of friction for the samples was about 0.02.

          Another group of samples was immersed for about 30 seconds in water to activate the coating, and then allowed to stand out in open air for about 10 minutes. Following this drying protocol, the average coefficient of friction ( $n = 12$  samples tested) was about 0.02.

20           Still another group of samples ( $n =$  three samples) were subjected to a thermoforming process to create a bullet shaped closed tip on one end in order to make a tipped tube suitable for use as a urinary catheter. This tipped tubing was subjected to a coating process as described in this example above, except the cure was by accomplished by exposure to UVC light for a period of about 3 minutes. After  
25           immersion in deionized water for about 20 minutes, the surface of the coated tubing was very slippery and the slippery coating was well adhered to both the formed tip portion of the tubing and the straight wall portion of the tubing.

          The foregoing examples demonstrate several advantages of the invention. For example, highly lubricious, highly adherent coatings have been achieved with two  
30           different water soluble polymer/cross-linker systems, and with three different

- 13 -

substrate constructions. Example 3 further demonstrates that it is possible to thermoform a multi-layered tube while maintaining the water-swellable properties of the outer layer surface, which allows a securely anchored coating to be achieved, even in the formed portion of the substrate. Example 3 also demonstrates that coatings  
5 made per this invention are able to maintain their slippery nature even after an extended period of air exposure. It is theorized that the water-swellable nature of the substrate surface helps in this regard, as the substrate surface will hold water and thus perhaps contribute to the ability of the coating to maintain hydration and therefore lubricity. This attribute of the invention is particularly advantageous for intermittent  
10 urinary catheters.

While embodiments of this invention have been disclosed in considerable detail herein for purposes of illustration, it will be understood by those skilled in the art that many of those details may be varied without departing from the spirit and scope of the invention. Accordingly, only such limitations as appear in the appended  
15 claims should be placed on the invention.



## CLAIMS

1. A method of applying a hydrophilic coating to a substrate surface, comprising:  
providing a substrate having a surface comprising at least in part a water-swella-  
ble material;  
5 contacting the substrate surface with a solution to swell the water-swella-  
ble material, said solution comprising at least one of (i) a water-soluble polymer capable  
of being cross-linked to form a cross-linked, lubricious, hydrophilic coating and (ii) a  
water-soluble monomer capable of being polymerized to form a cross-linked,  
lubricious, hydrophilic coating; and  
10 forming the cross-linked, lubricious, hydrophilic coating, said coating being  
entangled with and securely anchored to the substrate surface.
2. The method of claim 1, wherein the solution comprises at least one solvent  
selected from the group consisting of water, alcohols, and mixtures thereof.
3. The method of claim 2 wherein the solvent comprises water and isopropyl  
15 alcohol.
4. The method of any one of claims 1 to 3, wherein the substrate comprises a  
plurality of layers.
5. The method of claim 4, wherein at least one of the plurality of layers is made  
entirely of non-water swella-ble material.
- 20 6. The method of any one of the preceding claims, wherein the substrate  
comprises a medical device.
7. The method of claim 6, wherein the medical device is selected from the group  
consisting of medical implants, intravascular implants, catheters, and contact lenses.

8. The method of any one of the preceding claims, wherein the water-swella-  
ble material comprises a block copolymer.
9. The method of claim 8, wherein the block copolymer is selected from the  
group consisting of water-swella-  
ble polyester-based copolymers, water-swella-  
ble urethane-based copolymers, and  
mixtures thereof.
10. The method of any one of the preceding claims, wherein the water-soluble  
polymer is selected from the group consisting of polyacrylic acids, acrylic acid  
copolymers, poly-N-vinyl lactams, polyvinylalcohols, polyvinylalcohol copolymers,  
and mixtures thereof.
11. The method of claim 10, wherein the poly-N-vinyl lactam comprises  
polyvinylpyrrolidone.
12. The method of any one of the preceding claims, wherein the water-soluble  
monomer is selected from the group consisting of vinyl alcohols, vinylpyrrolidones,  
acrylamides, methacrylates, acrylic acids, and mixtures thereof.
13. The method of any one of the preceding claims, wherein the solution further  
comprises a cross-linking agent.
14. The method of any one of the preceding claims, wherein the hydrophilic  
coating is secured to the surface without covalent interactions between the hydrophilic  
coating and the surface.
15. The method of claim 13 or claim 14, wherein the cross-linking agent is  
selected from the group consisting of UV activatable cross-linking agents,  
carbodiimides, aziridines, melamine formaldehydes, and multifunctional carboxylic  
acid cross-linking agents.

16. The method of any one of the preceding claims, further comprising contacting the substrate with a solution comprising a cross-linking agent.
17. A substrate made according to the method of any one of the preceding claims.
18. A substrate having a cross-linked hydrophilic coating, disposed on a substrate  
5 comprising:  
a substrate having a surface comprising at least in part a water-swella-  
ble material; and,  
an interpenetrating polymer network disposed on the surface, the  
interpenetrating polymer network comprising the network that comprises the water-  
10 swella-  
ble substrate surface physically entangled with the network that comprises the  
cross-linked hydrophilic coating, said coating being securely anchored to the substrate  
surface.
19. The substrate of claim 18, wherein the substrate comprises a first layer, and a  
second layer, wherein the first layer comprises the water-swella-  
ble material.
- 15 20. The substrate of claim 19, wherein the second layer comprises a non-water-  
swella-  
ble material.
21. The substrate of any one of claims 18 to 20, wherein the substrate comprises a  
medical device.
22. The substrate of claim 21, wherein the medical device is selected from the  
20 group consisting of medical implants, intravascular implants, catheters, and contact  
lenses.
23. The substrate of any one of claims 18 to 22, wherein the water-swella-  
ble material comprises a block copolymer selected from the group consisting of water-  
swella-  
25 ble polyamide-based copolymers, water-swella-  
ble polyester-based copolymers,  
water-swella-  
ble urethane-based copolymers, and mixtures thereof.

24. The substrate of any one of claims 18 to 23, wherein the interpenetrating polymer network includes a water-soluble polymer that is selected from the group consisting of polyacrylic acids, acrylic acid copolymers, poly-N-vinyl lactams, polyvinylalcohols, polyvinylalcohol copolymers, and mixtures thereof.
- 5 25. A method of applying a hydrophilic coating to a substrate surface; a substrate made according to the method; a substrate having a hydrophilic coating substantially as herein described with reference to any one of the embodiments of the invention illustrated in the accompanying examples, but excluding comparative examples.