[26] • Leachables and extractables: Plastic vessels contain organic compounds that can leach out or be extracted into the drug product. These compounds can contaminate the drug and/or negatively impact the drug's stability.

[27] Clearly, while plastic and glass vessels each offer certain advantages in pharmaceutical primary packaging, neither is optimal for all drugs, biologics or other therapeutics. Thus, there is a desire for plastic vessels, in particular plastic syringes, with gas and solute barrier properties which approach the properties of glass. Moreover, there is a need for plastic syringes with sufficient lubricity properties and a lubricity coating which is compatible with the syringe contents.

[28] Coating plastic vessels with a barrier coating or lubricity coating made by PECVD using organosilicon precursors as described in one of the above cited applications can provide such desired vessels. However, in order to ensure their economic production, an inspection method allowing the inspection of the coating is also required.

[29] A non-exhaustive list of patents of possible relevance includes US Patents 6,068,884 and 4,844,986 and U.S. Published Applications 20060046006 and 20040267194.

SUMMARY ~~OF THE INVENTION~~

[30] The present ~~invention~~disclosure provides a method for inspecting a surface, in particular a coated surface and specifically a plastic surface coated with a PECVD coating made from organosilicon precursors. The inspection is~~in~~ performed by detecting outgassing from the inspected item, in particular outgassing from the coated substrate. The ~~invention~~present disclosure in its main application provides a method for vessel inspection by detecting the outgassing of a vessel wall, e.g. through a barrier layer coated onto the vessel wall. The ~~invention~~present disclosure further pertains to a method encompassing the coating and inspection of a vessel, wherein the inspection is performed by the outgassing method according to present ~~invention~~disclosure. In a particular ~~aspect~~embodiment, the ~~invention~~present disclosure pertains to a method encompassing a PECVD coating step and an inspection step wherein the latter is performed by the outgassing method.

[31] The outgassing method of present ~~invention~~disclosure allows a quick and accurate determination of the properties of an inspected material. For example, it allows the quick and accurate determination whether a coating, e.g. a barrier coating is present on a plastic substrate.

[32] In an aspect, t~~T~~he ~~invention~~present disclosure further pertains to an apparatus (e.g. a vessel processing station of a vessel processing system) configured for performing the above and/or below mentioned method steps. Examples of such processing stations 20, 30, 5501-5504 are depicted in Fig. 1 and 59-61, for example.

[33] The ~~invention~~present disclosure further pertains to a computer-readable medium, in which a computer program for inspection of a surface is stored which, when being executed by a processor of an apparatus, such as a vessel processing system, is adapted to instruct the processor to control the apparatus such that it carries out the above and/or below mentioned method steps.

[33a] In another aspect, the present disclosure pertains to a computer-readable medium, in which a computer program for inspecting the product of a coating process is stored which, when being executed by a processor of a vessel processing system, is adapted to instruct the processor to control the vessel processing system such that it carries out the method as defined above and/or below.

[34] The ~~invention~~present disclosure further pertains to a program element or computer program for inspection of a surface, which, when being executed by a processor of an apparatus, such as a vessel processing system, is adapted to instruct the processor to control the apparatus such that it carries out the above and/or below mentioned method steps.

[34a] In another aspect, the present disclosure pertains to a program element for inspecting the product of a coating process, which, when being executed by a processor of a vessel processing system, is adapted to instruct the processor to control the vessel processing system such that it carries out the method as defined above and/or below.

[35] The processor may thus be equipped to carry out exemplary embodiments of the methods of the present ~~invention~~disclosure. The computer program may be written in any suitable programming language, for example, C++ and may be stored on the computer-readable medium, such as a CD-ROM. Also, the computer program may be available from a network, such as the WorldWideWeb, from which it may be downloaded into image processing units or processors, or any suitable computers.

[36] An ~~aspect~~embodiment of the ~~invention~~present disclosure is a method and system for inspecting a coating or barrier layer on a substrate or other object made of a first material and having a surface, for example an SiO_x coating on a cyclic olefin copolymer ("COC") thermoplastic molded substrate as the object made of the first material, such as a syringe or blood collection tube, by measuring a volatile species outgassed by the coated article, which may be a volatile species originating from the material of the inspected item or originating from a charging material, for example a charging material comprising for example carbon

dioxide, nitrogen, argon, xenon, krypton, a lower hydrocarbon having from 1 to 4 carbon atoms, for example ethylene, ethane, or methane, a lower halogenated hydrocarbon having from 1 to four carbon atoms, for example methyl chloride, methylene chloride, methyl fluoride or trifluoroethane, or a lower hydrocarbon ether having from 1 to four carbon atoms, for example diethylether or dimethylether or ethyl-methyl-ether, which is brought into contact with the inspected item before measuring of the outgassed volatile species takes place ("Outgassing method"). The method can be used for inspecting the product of a coating process wherein a coating has been applied to the surface of a substrate to form a coated surface. The method is carried out under conditions effective to determine, e.g., the presence or absence of a barrier layer. For example, the method can be used as an inline process control for a coating process in order to identify and eliminate coated products not meeting a predetermined standard or damaged coating products.

[36a] In an aspect, the present disclosure pertains to a method for inspecting the product of a coating process wherein a coating has been applied to the surface of a substrate to form a coated surface, the method comprising the steps:

(a) providing the product as inspection object;

(c) in a molecular flow mode of operation, measuring the release of at least one volatile species from the inspection object into the gas space adjacent to the coated surface; and

(d) comparing the result of step (c) with the result of step (c) for at least one reference object measured under the same test conditions, thus determining the presence or absence of the coating, and/or a physical and/or chemical property of the coating.

[37] Generally, the "volatile species" is a gas or vapor at test conditions, and may be selected from the group consisting of a noble gas, carbon dioxide, a hydrocarbon, a halogenated hydrocarbon, an ether, air, nitrogen, oxygen, water vapor, volatile coating components, volatile substrate components, volatile reaction products of the coating, and a combination thereof, optionally is air, nitrogen, oxygen, carbon dioxide, argon, water vapor, or a combination thereof. The volatile species may be charged on the inspected item before inspection, or it may be present in the material without charging (e.g. as volatile substrate components or residual reaction products of the coating). The

method can be used to measure just one or a few volatile species, but optionally a plurality of different volatile species is measured, and optionally substantially all the volatile species released from the inspection object are measured .

[38] Another ~~aspect~~embodiment of the ~~invention~~present disclosure is a method for inspecting an object, e.g. for the presence of a barrier layer, wherein the method encompasses charging the inspected object with a charging material. In this method, an object is provided, made at least in part of a first material, the object having a surface, the object optionally having at least a partial barrier layer between the first material and the surface (in one ~~aspect~~embodiment, the barrier layer forms the surface of the object, i.e. the object is coated with the

barrier layer). Optionally, a charging material is provided that is soluble in, absorbed by, or adsorbed by the first material, and the object is contacted with the charging material. Outgassing is measured from at least a portion of the surface. The method is carried out under conditions effective to determine, e.g., the presence or absence of a barrier layer.

The charging material can enhance the sensitivity of the outgassing method. In particular, it can simplify discrimination between two inspected species, e.g. a substrate which is once coated and once uncoated. The charging material can also allow discrimination between two materialsif it is bound and outgassed by different materials in different amounts.

[39] The discrimination of uncoated versus SiO_x-coated plastic articles relies on the capability of a plastic article to imbibe gases (e.g. a charging material) which can subsequently be outgassed and measured. The solubility of gases in plastics is a key determinant of the amount of gas which can reside in a plastic, and therefore a good estimate of the potential for a particular gas to provide suitable uncoated versus coated article discrimination. It is in one ~~aspect~~embodiment of the ~~invention~~present disclosure advantageous to increase the amount of gas which is absorbed or adsorbed in the plastic by charging the plastic with a charging material. This can result in higher amounts of outgassed volatile species emitted during the outgassing measurement and thus enhance readout.

[40] In a specific ~~aspect~~embodiment of present ~~invention~~disclosure, increased sensitivity of the outgassing measurement can be realized by using a carbon dioxide flush and/or by spiking the substrate with carbon dioxide (e.g. carbon dioxide gas), N_2, Ar, xenon, krypton, a lower hydrocarbon having from 1 to 4 carbon atoms, for example ethylene, ethane, or methane, a lower halogenated hydrocarbon having from 1 to four carbon atoms, for example methyl chloride, methylene chloride, methyl fluoride or trifluoroethane, or a lower hydrocarbon ether having from 1 to four carbon atoms, for example diethylether or dimethylether or ethyl-methyl-ether,. The use of CO_2 is particularly useful when testing COC substrates where the solubility for nitrogen, water and oxygen are low.

[41] Generally, the outgassing method according to present ~~invention~~disclosure comprises the steps:

[42] (a) providing a product as inspection object;

[43] (c) measuring the release of at least one volatile species from the inspection object into the gas space adjacent to a surface of the object; and

[44] (d) comparing the result of step (c) with the result of step (c) for at least one reference object measured under the same test conditions, thus determining the presence or absence of a specific material or a specific component of the inspection object, e.g. of a coating on a substrate.

[45] Typically, an outgassing method for inspecting a coated substrate according to present ~~invention~~disclosure comprises the steps:

[46] (a) providing a product comprising a coating as inspection object;

[47] (c) measuring the release of at least one volatile species from the inspection object into the gas space adjacent to the coated surface; and

(d) comparing the result of step (c) with the result of step (c) for at least one reference object measured under the same test conditions, thus determining the presence or absence of the coating, and/or a physical and/or chemical property of the coating or of the coated substrate.

[48] In the outgassing method, the physical and/or chemical property of the coating to be determined can be selected from the group consisting of its barrier effect, its wetting tension, and its composition, and optionally is its barrier effect.

[49] Advantageously, step (c) is performed by measuring the mass flow rate or volume flow rate of the at least one volatile species in the gas space adjacent to the coated surface.

[50] Optionally, the reference object (i) is an uncoated substrate; or (ii) is a substrate coated with a reference coating. This depends on, e.g., whether the outgassing method is used to determine the presence or absence of a coating (then the

reference object can be an uncoated substrate) or to determine the properties of the coating, e.g. in comparison to a coating with known properties, or e.g. of the inspected material in general in comparison to a known material. For determining the coating's identity with a specific coating, a reference coating will also be a typical choice.

[51] The outgassing method can also comprise as an additional step between steps (a) and (c) the step of (b) changing the atmospheric pressure in the gas space adjacent to the coated surface such that a pressure differential through the coated surface is provided and a higher mass flow rate or volume flow rate of the volatile species can be realized than without the pressure differential. In this case, the volatile species will migrate into the direction of the lower side of the pressure differential. If the coated object is a vessel, the pressure differential is established between the vessel lumen and the exterior in order to measure the outgassing of the volatile species from the coated vessel wall. The pressure differential can e.g. be provided by at least partially evacuating the gas space in the vessel. In this case, the volatile species can be measured which is outgassed into the lumen of the vessel.

[52] If a vacuum is applied to create a pressure differential, the measurement can be performed by using a measurement cell interposed between the coated surface of the substrate and a source of vacuum.

[53] In another ~~aspect~~embodiment, the inspection object can be contacted with a volatile species in step (a), optionally a volatile species selected from the group consisting of air, nitrogen, oxygen, water vapor, carbon dioxide, a noble gas, and a combination thereof, optionally in order to allow the adsorption or absorption of the volatile species onto or into the material of the inspection object. Then, the subsequent release of volatile species from the inspection object is measured in step (c). As different materials (like, e.g., the coating and the substrate) have different adsorption and absorption characteristics, this can simplify the determination of the presence and characteristics of a coating.

[54] The substrate can be a polymeric compound, optionally is a polyester, a polyolefin, a cyclic olefin copolymer, a polycarbonate, or a combination of these. The

outgassing method of the ~~invention~~present disclosure is of particular interest for the inspection of COC, polyethylene terephtalate and polypropylene.

[55] In the context of present ~~invention~~disclosure, the coating characterized by the outgassing method may be any coating, but is typically a coating prepared by PECVD from, e.g., an organosilicon precursor as described herein and in the applications cited in paragraphs 1 to 3 of this description, to which applications explicit reference is made herewith in order to point out coatings on which present ~~invention~~disclosure can be applied. For example, the coating can be a barrier layer, optionally is a SiO_x layer wherein x is from about 1.5 to about 2.9. For another example, the coating can be a lubricity layer, characterized as defined in the Definition Section or in the cited applications and/or a hydrophobic layer, characterized as defined in the Definition Section or in the cited applications.

[56] When the coating process whose product is inspected by the outgassing method is a PECVD coating performed under vacuum conditions, the subsequent outgassing measurement can even be conducted without breaking the vacuum used for PECVD.

[57] The volatile species measured can be a volatile species released from the coating, a volatile species release from the substrate, or a combination of both. In one ~~aspect~~embodiment, the volatile species is a volatile species released from the coating, optionally is a volatile coating component, and the inspection is performed to determine the presence, the properties and/or the composition of the coating. In another ~~aspect~~embodiment, the volatile species is a volatile species released from the substrate and the inspection is performed to determine the presence of the coating and/or the barrier effect of the coating.

[58] The outgassing method of the present ~~invention~~disclosure is suitable to determine the presence and characteristics of a coating on a vessel wall. Thus, the coated substrate can be a vessel having a wall which is at least partially coated on its inner or outer surface during the coating process. For example, the coating is disposed on the inner surface of the vessel wall.

[59] The conditions effective to distinguish the presence or absence of the coating, and/or to determine a physical and/or chemical property of the coating can include a test duration of less than one hour, or less than one minute, or less than 50 seconds, or less than 40 seconds, or less than 30 seconds, or less than 20 seconds, or less than 15 seconds, or less than 10 seconds, or less than 8 seconds, or less than 6 seconds, or less than 4 seconds, or less than 3 seconds, or less than 2 seconds, or less than 1 second.

[60] In order to increase, e.g., the difference between a reference object and the inspection object with regard to the release rate and/or kind of the measured volatile species, the release rate of the volatile species can be modified by modifying the ambient pressure and/or temperature, and/or humidity. The use of a charging material *according to present* ~~*invention*~~*disclosure serves the same purpose.*

[61] The measurement may, e.g., be carried out using a microflow technique.

[62] In an ~~aspect~~embodiment, the outgassing is measured using a microcantilever measurement technique. E.g., the measuring can be carried out by

[63] (i) (a) providing at least one microcantilever which has the property, when in the presence of an outgassed material, of moving or changing to a different shape;

[64] (b) exposing the microcantilever to the outgassed material under conditions effective to cause the microcantilever to move or change to a different shape; and

[65] (c) detecting the movement or different shape, optionally by reflecting an energetic incident beam, e.g. a laser beam, from a portion of the microcantilever that changes shape, before and after exposing the microcantilever to outgassing, and measuring the resulting deflection of the reflected beam at a point spaced from the cantilever; or by

[66] (ii) (a) providing at least one microcantilever which resonates at a different frequency when in the presence of an outgassed material;

[67] *(b) exposing the microcantilever to the outgassed material under conditions* effective to cause the microcantilever to resonate at a different frequency; and

[68] (c) detecting the different resonant frequency, e.g. using a harmonic vibration sensor.

[69] An apparatus for performing the outgassing method is also considered, for example an apparatus comprising a microcantilever as described above.

[70] Using the outgassing method of the present ~~invention~~disclosure, for example a barrier layer on a material that outgasses a vapor can be inspected, wherein the inspection method has several steps. A sample of material that outgasses a gas and has at least a partial barrier layer is provided. In an ~~aspect~~embodiment of the ~~invention~~present disclosure, a pressure differential is provided across the barrier layer, such that at least some of the material that outgasses is on the higher-pressure side of the barrier layer. The outgassed gas passing through the barrier layer is measured. If a pressure differential is present, the measurement typically is performed on the lower-pressure side of the barrier layer.

[71] Other ~~aspects~~embodiments of the ~~invention~~present disclosure will be apparent from this disclosure and the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[72] FIG. 1 is a schematic diagram showing a vessel processing system according to an embodiment of the disclosure.

[73] FIG. 2 is a schematic sectional view of a vessel holder in a coating station according to an embodiment of the disclosure.

[74] FIG. 3 is an exploded longitudinal sectional view of a syringe and cap adapted for use as a prefilled syringe.

[75] FIG. 4 is a schematic sectional view of another embodiment of the invention for processing syringe barrels and other vessels.

[76] FIG. 5 is an enlarged detail view of the processing vessel of FIG. 4.

[77] FIG. 6 is a schematic view showing outgassing of a material through a coating.

and

(c) detecting the movement or different shape, preferably by reflecting an energetic incident beam, e.g. a laser beam, from a portion of the microcantilever that changes shape, before and after exposing the microcantilever to outgassing, and measuring the resulting deflection of the reflected beam at a point spaced from the cantilever; or by

(ii) (a) providing at least one microcantilever which resonates at a different frequency when in the presence of an outgassed material;

(b) exposing the microcantilever to the outgassed material under conditions effective to cause the microcantilever to resonate at a different frequency; and

(c) detecting the different resonant frequency, e.g. using a harmonic vibration sensor.

30. An apparatus for performing the method according to any of claims 1 to 29.

31. A computer-readable medium, in which a computer program for inspecting the product of a coating process is stored which, when being executed by a processor of a vessel processing system ~~(20)~~, is adapted to instruct the processor to control the vessel processing system such that it carries out the method of one of claims 1 to 29.

32. A program element for inspecting the product of a coating process, which, when being executed by a processor of a vessel processing system ~~(20)~~, is adapted to instruct the processor to control the vessel processing system such that it carries out the method of one of claims 1 to 29.