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(71) Applicant (for all designated States except US): **SELECTIVE MICRO TECHNOLOGIES, LLC** [US/US]; 66 CHERRY HILL DRIVE, Suite 230, Beverly, Massachusetts 01915 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MERRILL, Landon** [US/US]; 214 Washington Street, Marblehead, Massachusetts 01945 (US). **O'NEILL, Gary** [US/US]; One Trinity Drive, Tyngsborough, Massachusetts 01879 (US). **WARNER, John** [US/US]; 47 Walker Road, Manchester-By-The-Sea, Massachusetts 01944 (US).

(74) Agents: **HANLEY, Elizabeth** et al.; LAHIVE & COCKFIELD, LLP, 28 State Street, Boston, Massachusetts 02109 (US).

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(54) Title: ANTIMICROBIAL GAS DESORBING ARTICLES

(57) Abstract: The present invention provides gas desorbing articles that generally include polymeric materials impregnated with an antimicrobial gas, e.g., chlorine dioxide. Also disclosed are methods of using such articles for remediation of microbial life such as fungi, bacteria and mold. Also disclosed are methods of making such articles and kits related to the same.

WO 2006/078786 A1

ANTIMICROBIAL GAS DESORBING ARTICLES

Related Applications

This application claims priority to U.S. Provisional Application No. 60/645325, filed January 18, 2005, the entire contents of which are hereby incorporated by reference herein.

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Field of the Invention

The invention relates generally to gas desorbing articles, and more specifically to polymeric materials impregnated with an antimicrobial gas, and methods for making and employing the same to remediate microbial life.

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Background of the Invention

The use of gas for retarding, controlling, killing or preventing microbiological contamination (*e.g.*, bacteria, fungi, viruses, mold spores, algae and protozoa); retarding, preventing, or controlling biochemical decomposition; controlling respiration, deodorizing and/or retarding and preventing chemotaxis to name a few, is known. Such gases include, but are not limited to, chlorine dioxide, sulfur dioxide, nitrogen dioxide, nitric oxide, nitrous oxide, carbon dioxide, hydrogen sulfide, hydrocyanic acid, and dichlorine monoxide.

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In particular, chlorine dioxide has been found to be useful as a disinfectant, antiseptic and sanitizer. It is used, *e.g.*, to disinfect drinking water, various water supplies and food items. In addition, chlorine dioxide finds use as a bleaching agent for flour, fats and textiles.

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Despite the advantages of chlorine dioxide, conventional techniques to generate chlorine dioxide often result in unsatisfactory levels of toxic or non-biodegradable by-products or reactants that remain as a residue. For example, conventional techniques to generate chlorine dioxide gas result in residues of the byproduct chlorite on food handling equipment and medical and dental surfaces. Human contact with such residues should be avoided or substantially minimized according to FDA and EPA regulations.

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An additional obstacle to the use of chlorine dioxide is that chlorine dioxide can not be transported commercially as a concentrated gas. An on-site gas generation plant takes up significant space and involves a substantial added expense. For example, it is often impractical to generate chlorine dioxide on farms, where it may be useful to clean raw agricultural products and freshly picked food. Moreover, even when conventional apparatus do not require a separate gas generation component, *e.g.*, those shown in European Patent

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Publication No. 0 571 228 for sulfur dioxide generation, such apparatus can be undesirable because controlling the amount of gas generated, the efficiency of the generation, and the duration of the gas generation has proven difficult.

There exists a need for alternative and convenient means for tapping the properties of chlorine dioxide in a safe, efficient and economical manner without the necessity for a
5 separate generation plant or unwanted by-products.

Summary of the Invention

A novel approach to remediation of microbial life by employing the antimicrobial
10 properties of chlorine dioxide and other antimicrobial gases (e.g., sulfur dioxide), has now been discovered. The present invention involves the impregnation of polymeric materials with an antimicrobial gas for use in a variety of purposes including sterilization, disinfection, deodorization, bleaching and sanitization. In particular, the present invention provides a gas desorbing article including a polymeric material impregnated with an antimicrobial gas and
15 methods of making and using the article. The articles and methods of the present invention are readily applicable to a number of applications where microbial remediation is desired, e.g. in the food industry, where an increase in the shelf life of food of even a few days is a significant commercial advantage and, of course, represents a dramatic reduction in the unnecessary waste of food.

20 In one aspect, the present invention is directed to a gas desorbing article including a polymeric material such as polystyrene impregnated with an antimicrobial gas (for example, chlorine dioxide). In certain embodiments, the article is a container (e.g., a food container) such as a vial, a bottle, or a clam shell. Alternatively, the article is in the form of a packaging material (e.g., a food packaging material), a pellet, a fiber, a liner or a sheet. In a particular
25 embodiment, the article is substantially saturated with the antimicrobial gas and/ or the article is sanitized, disinfected or sterilized. In certain embodiments, the article is impregnated with antimicrobial gas such that it is capable of desorbing antimicrobial gas for at least 10 minutes, 20 minutes, 30 minutes, 2 hours, 1 day or 5 days.

In one embodiment, an item, including, but not limited to, a food item, an agricultural
30 product, a medical instrument, medical waste, a fruit, a vegetable, a flower, a bar sink, a mop bucket, and a dental instrument, is disposed within or exposed to the article. The item may be disinfected, sterilized or sanitized, and, in certain embodiments, may remain as such for at least 10 minutes, 20 minutes, 30 minutes, 2 hours, 1 day or 5 days.

In another embodiment, the article is disposed within a substantially gas impermeable package such that a substantial amount of antimicrobial gas remains impregnated within the polymeric material. In yet another embodiment, the article further includes a gas impermeable material. For example, the article can be formed, at least in part, of a multilayer sheet including a gas impermeable layer and a layer including the impregnated polymeric material. In another aspect, the invention is directed to a package including this multilayer sheet, where the gas impermeable layer impedes the release of antimicrobial gas from the package. In yet another aspect, the invention is directed to methods of remediating microbial life in an environment by enclosing the environment with these articles or packages, such that the gas impermeable material impedes the release of the antimicrobial gas from the environment and microbial life is remediated within the environment.

In a further aspect, the present invention is directed to a method for remediating microbial life by exposing an environment to an article as described herein, such that microbial life is remediated in the environment. The environment may be defined by the article or, alternatively, may be immediately adjacent to the article. In addition, the environment may include an item selected from the group consisting of a food item, an agricultural product, a medical instrument, medical waste, a fruit, a vegetable, a flower, a bar sink, a mop bucket, and a dental instrument. In one embodiment, the environment is sanitized, sterilized, and/or disinfected. In another embodiment, the gas is released over a period of at least about 10 minutes, 20 minutes, 1 hour, or 5 days. In certain embodiments, the gas may be released from the article to maintain a concentration of antimicrobial gas from about 0.10 ppm to about 20 ppm and/or to obtain an initial concentration of antimicrobial gas from about 0.10 ppm to about 20 ppm.

In yet another aspect, the present invention is directed to a method of making an article of the present invention by exposing a polymeric material to the antimicrobial gas (for example, a solution comprising the antimicrobial gas). In certain embodiments, the polymeric material is exposed to the solution for at least about 10 minutes, 20 minutes, 1 hour, 2 hours or 4 hours. Moreover, the solution may have a concentration of antimicrobial gas from about 50 ppm to about 600 ppm chlorine dioxide, from about 50 ppm to about 150 ppm chlorine dioxide, or from about 450 ppm to about 550 ppm chlorine dioxide.

Description Of The Drawings

The advantages of the invention described above, as well as further advantages of the invention, can be better understood by reference to the description taken in conjunction with the accompanying figures, in which:

Figure 1 is a graph illustrating the impregnation of a polystyrene vial with chlorine dioxide gas over time in accordance with the present invention.

Figure 2 is a graph illustrating desorption of chlorine dioxide from a polystyrene vial impregnated with chlorine dioxide in accordance with the present invention.

Figure 3 graphically depicts impregnation of a polystyrene vial with chlorine dioxide over time upon exposure to a 100 ppm chlorine dioxide solution.

Figure 4 graphically depicts the impregnation of a polystyrene vial with chlorine dioxide over time upon exposure to a 500 ppm chlorine dioxide solution.

Figure 5 graphically depicts desorption of chlorine dioxide into water from an impregnated polystyrene vial over time, following impregnation of the polystyrene vial by exposure to a 100 ppm chlorine dioxide solution.

Figure 6 graphically depicts desorption of chlorine dioxide into water from an impregnated polystyrene vial over time, following impregnation of the polystyrene vial by exposure to a 500 ppm chlorine dioxide solution.

Detailed Description Of The Invention

The present invention is based, at least in part, on the discovery that polymeric materials can be impregnated with an antimicrobial gas and can subsequently desorb the gas in a manner that is useful. Such impregnated polymeric material can be employed to remediate microbial life, *e.g.*, to sterilize, disinfect or sanitize desired items, such as food items, raw agricultural products, or medical or dental instruments by desorption of the antimicrobial gas from the polymeric material.

The present invention provides gas desorbing articles generally including polymeric material impregnated with an antimicrobial gas, *e.g.*, chlorine dioxide. The invention provides methods for employing such articles to remediate microbial life, *e.g.*, to extend the life of fruits and vegetables or to remediate medical or laboratory equipment prior to use. The

invention further provides methods of making gas desorbing articles, and kits for making gas desorbing articles, *e.g.*, at the point of use.

One advantage of the present invention is that the articles and polymeric materials of the present invention allow for convenient, efficient and safe remediation using antimicrobial gas. The articles and methods of the present invention provide a means to disinfect, sanitize
5 and/or sterilize an article or its contents, without the production or presence of residual byproducts and/or unused reactants. Additionally, the methods and articles of the present invention provide a convenient means of microbial remediation without additional steps, for example, the need to add any volume to the interior of the article, for example, by the addition
10 of reactants, and, without the need for, for example, an on-site gas generating device. Yet another advantage is that the article can desorb gas over a period of time, thus providing timed release of microbial gas such that microbial life is remediated over time.

In order to more clearly and concisely describe the subject matter of the claims, the following definitions are intended to provide guidance as to the meaning of specific terms
15 used in the following written description, examples and appended claims.

The terms “impregnate,” “impregnating,” “impregnated” and the like, generally refer to the association of a gas with a polymeric material by permeation or diffusion into the polymeric material (*e.g.*, on the surface and/or into openings or interstices of the polymeric material). Without wishing to be bound to any particular theory, it is believed that the gas is
20 soluble in the polymeric material and accordingly, is absorbed by the polymeric material. However, various associations of gas into and onto polymeric material, including, but not limited to, absorption, adsorption, electrostatic and/or ionic, are intended to be encompassed by the teachings of the present invention. Impregnation can be achieved by exposing the polymeric article to the gas (*e.g.*, chlorine dioxide in solution), for a desired length of time.
25 The terms “sorb,” “sorption” and the like, are used interchangeably with “impregnate,” “impregnation” and the like.

As used herein, the terms “desorb,” “desorbing,” “desorption” and the like, refer generally to the removal, release or diffusion of impregnated antimicrobial gas from a polymeric material. Desorption includes removal, release or diffusion of the gas from the
30 polymeric material, whether the gas is associated with the polymeric material by any of a variety of mechanisms, including, but not limited to, absorption, adsorption, electrostatic and/or ionic. Accordingly, a “gas desorbing article” refers to an article capable of desorption of impregnated gas.

As used herein, the terms “remediate,” “remediating” and the like, when used in the context of remediating microbes, refer to reducing, eliminating, retarding, controlling, killing and/or preventing the growth or presence of microbes; retarding, preventing, or controlling biochemical decomposition; controlling respiration, deodorizing and/or retarding and preventing chemotaxis of microbial life and/or growth; and the like. Remediation can include, but is not limited to, sanitization, disinfection and sterilization of the article itself (e.g., for use in laboratory equipment) or its environment (e.g., for use in packing fruits and vegetables or controlling microbial life in a refrigerated case). Remediation also can include antiseptic and germicidal activity.

The terms “microbes” and “microbial life” are used interchangeably to refer generally to all microbial life including bacteria, fungi, viruses, mold, mold spores, algae and protozoa.

As used herein, the terms “sanitize,” “sanitizing” and the like, refer generally to the reduction, but not necessarily the elimination, of microbial life.

The terms “disinfect,” “disinfecting” and the like, refer generally to the destruction or inactivation of microbial life (e.g., infectious fungi and bacteria) but not necessarily the elimination, e.g., viable spores may remain.

The terms “sterilize,” “sterilizing” and the like, refer to the destruction or elimination of microbial life, including vegetative bacteria, bacterial spores, fungi, fungal spores, and viruses. Sterilization is critical to infection control and is widely used in hospitals on medical and surgical instruments and equipment.

“Antiseptic” and “germicide” generally refer to the prevention of infection and/or decay by inhibiting the growth of microorganisms on or in living animals, including humans.

In one aspect, the present invention provides a gas desorbing article that generally includes a polymeric material impregnated with an antimicrobial gas. The articles and/or items with respect to which it is desired to remediate microbial life can include any article including polymeric material capable of impregnation of antimicrobial gas, or item where remediation is desired. This includes any of the articles and/or items disclosed herein, including surfaces (e.g., countertops and lab benches), meat processing and packaging equipment, dental and medical instruments and devices (e.g., syringes, scalpels, implantable devices such as stents and catheters), agricultural products or processed food items (e.g., fruits, nuts, vegetables and the like), food packaging, shipping or storage items (e.g., liners, peanuts, clam shell containers, and spacers), food processing items or utensils, flowers and plants (e.g., cut flowers), bar equipment (e.g., sinks, dishwashers, beer and beverage lines),

cleaning equipment (*e.g.*, mop buckets, sponges, mops and the like), and laboratory systems (*e.g.*, tubing and transfer lines, for example, of water systems).

Commonly used devices made of polymeric material may be imbued with antimicrobial activity so as to, for example, sterilize, disinfect and sanitize its contents. For example, impregnated containers, such as clam shells, or impregnated sheets may be manufactured and sold to farmers for packaging food items or agricultural products. Upon filling the container with the desired contents, the antimicrobial gas would release into the interior volume of the container and serve to remediate, for example, sterilize, disinfect or sanitize, microbial life associated with the contents. The containers can be used in the field upon or after collection of the food items or agricultural products and/or for repackaging prior to sale of the products. The addition of even 1 or 2 days to the shelf life of the food items or agricultural products using the methods of the present invention would provide significant advantages including, for example, a significant cost-saving advantage and reduction of the wasting of food.

Alternatively or in combination, polymeric materials impregnated with an antimicrobial gas such as chlorine dioxide, for example, in the form of one or more pellets, beads, sheets, linings or fibers can serve to remediate microbial life and sanitize, disinfect or sterilize the article and items in the surrounding environment. For example, the articles can be placed within a closed environment, such as a shipping or storage container, such that the gas can desorb into the volume of the container and serve to remediate microbial life and sanitize, disinfect or sterilize the container and/or its contents. In some embodiments, the container is closed or enclosed within further packaging (*e.g.*, shrink wrap) so as to prevent the release of the gas into the external environment, thereby enhancing the antimicrobial effect. For example, the articles can be placed in a closed shipping box or in a refrigerated case, such as a deli case or a refrigerated transport container.

In some embodiments, the container is not enclosed, such as, for example, a cut flower container or a box having openings that is impregnated with gas and/or gas impregnated beads in a cut flower container wherein the gas remediates microbial life thereby increasing the shelf life of the flowers. Another example is fruit and vegetable packing materials shipment, storage and/or display unsealed.

The gas desorbing articles of the present invention can be employed to remediate microbial life, for example, to sterilize, disinfect or sanitize, the article itself, an item exposed to the environment about the article or contained within the article, or an environment

exposed to or contained within the article. The microbe may be present within the article, for example, a container, or alternatively may be adjacent to the article, *e.g.*, fruit packaged with antimicrobial gas-impregnated packing materials. Similarly, the item to be subject to microbial remediation may be contained within an environment defined by the article, for example, within the article itself, or alternatively may be adjacent to or near the article, for example, such that the item is exposed to the article. In particular embodiments, the impregnated polymeric material is placed in an environment that is free or substantially free of the antimicrobial gas, thereby promoting desorption of the gas from the polymeric material into the surrounding environment. Upon release into the environment, the gas can exhibit its antimicrobial properties, for example, by killing mold, microorganisms, pathogens, bacteria or viruses present in the environment or on or in the item. The gas can selectively exhibit antimicrobial properties, as desired, by, for example, varying the original concentration of the antimicrobial solution and/or by varying the exposure time of the contaminated item to the impregnated polymeric material.

The methods and articles of the present invention additionally provide a means for so-called "last-step" antimicrobial remediation, for example, sanitization, disinfection and sterilization. Indeed, the methods of the present invention provide a means for remediating the contents of a package *after* the contents have been packaged.

Additionally, the present invention provides for time release of antimicrobial gas into the surrounding environment or into solution. In some embodiments, the gas desorbs from the polymeric material over time. Accordingly, the present invention provides a time release or residual effect for the antimicrobial gas. This property of continued release renders the present invention particularly suitable for use in various applications including, but not limited to, holding and packaging food items, such as fresh cut fruit and vegetables, raw agricultural products and cut flowers.

In a particular embodiment, the present invention provides an apparatus and method for the controlled release of gas from an environment. For example, the polymeric material can enclose an environment containing a gas, and, optionally a gas generating device, and thereby mediate (*e.g.*, control) the release of the gas from the enclosed environment. As such, gas contained and/or produced in the enclosed environment can be impregnated into the polymeric material, and subsequently desorbed to the external environment. As taught herein, the system can be designed so as to achieve a desired release profile of said gas into the external environment. For example, the nature of the polymeric material, the

concentration of the gas, the rate of gas generation, the volume of the enclosed environment and other factors can be manipulated by one skilled in the art to achieve a desired controlled release profile.

In particular embodiments, the antimicrobial gas is released from the polymeric materials over the course of about 120, 96, 72, 64, 56, 48, 44, 40, 36, 32, 28, 24, 22, 20, 18, 16, 14, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 or 0.5 hours. In a particular embodiment, the antimicrobial gas is released over a period from about 30 minutes to about 5 days. In some embodiments, the polymeric material is impregnated with antimicrobial gas such that it is capable of desorbing antimicrobial gas for at least 10 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 6 hours, 8 hours, 12 hours, 1 day, 2 days or 5 days. Ranges of values and minimum values using a combination of any of the above recited values as upper and/or lower limits are intended to be included as embodiments of the present invention. The ability of an antimicrobial gas such as chlorine dioxide to release over a period of time is dependent on various factors readily known and/or determinable by one skilled in the art, including, but not limited to, the nature of the polymeric material and the concentration of the chlorine dioxide within the polymeric material and the surrounding environment.

The desorption time can be dependent on a number of factors, including the initial concentration desired, the concentration that is desired to be maintained and the length of time over which it is desirable to continue to desorb gas. A number of modifications can be made that are within the scope of the present invention, including for example, employing at least two polymeric materials that have varying sorption and desorption capabilities and rates. In some embodiments, microbial life remains substantially remediated for at least 10 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 6 hours, 8 hours, 12 hours, 1 day, 2 days or 5 days. Ranges of values and minimum values using a combination of any of the above recited values as upper and/or lower limits are intended to be included as embodiments of the present invention.

Additionally, this controlled release property renders the present invention suitable for use with various devices, including bar sinks, mop buckets and humidifiers. For example, a bar sink made of impregnatable polymeric material may be impregnated with chlorine dioxide (for example, by filling the bar sink with a chlorine dioxide solution), thereby allowing for convenient sterilization of the sink and its contents, for example, upon the addition of water. Similarly, a mop bucket may be impregnated with chlorine dioxide, thereby allowing for

convenient sterilization of the mop bucket, and/or for the production of chlorine dioxide solution for cleaning, for example, by the addition of water.

Application of the present invention to a humidifier can involve the impregnation of a separate compartment (of the water tank) made of a gas-desorbing polymeric material. The separate compartment may have a screw cap made of a non-diffusible polymer. Accordingly, the chlorine dioxide impregnated within the polymeric material will desorb through the compartment walls and into the humidifier solution, thereby sanitizing the humidifier solution and/or the humidifier itself. Alternative embodiments, including impregnated filters may be utilized in accordance with the methods of the present invention.

Further embodiments include impregnated trash bags, medical waste bags or liners or packing for trash, medical waste and the like. Such articles can be used, *e.g.*, in remediating microbes, *e.g.*, odor-causing bacteria, mold or viruses, within and/or in the immediate vicinity of the articles.

Other embodiments include laboratory supplies (*e.g.*, vials, pipettes, and syringes), food containers (*e.g.*, baby bottles), and the like (*e.g.*, sponges and wipes) on which microbial life has been remediated by impregnation of antimicrobial gas. Such bottles or other food containers could be shipped with gas impregnated or, alternatively, the article can be impregnated on-site and optionally sealed until used. The invention could be particularly useful where on-site impregnation is not practicable or desired (*e.g.*, a field hospital or in home).

Accordingly, in yet another aspect, the invention provides a method of providing a remediated item, by exposing the item to an article of the present invention, such that the item is remediated, for example, disinfected, sanitized and/or sterilized. For example, the article can be remediated on-site according to the methods of the present invention prior to or after use. For example, a gas impregnated vial can be removed from a gas impermeable package, and used in a non-sterile environment (*e.g.*, a hospital), but remain remediated and/or returned to remediated conditions as a result of gas desorbing from the vial over time. In some embodiments, after use, an item can be placed in a gas impermeable or substantially impermeable container or returned to such a container so as to facilitate or enhance the remediation of microbial life.

Additionally or alternatively, remediated equipment can be packaged in such articles so that they can be shipped, stored and used in remediated condition, *e.g.*, medical devices and equipment such as stents, scalpels, catheters, and the like. Such equipment also could be

returned to the package for remediation as the gas desorbs over time, thus remediating the article for safe disposal or re-use of the article.

In other aspects, the article may include a gas impermeable material in addition to the impregnated polymeric material. In certain embodiments, the article is formed of a first zone including a gas impermeable material and a second zone including an impregnated polymeric material. The article may be of any form, including, but not limited to, a multilayer sheet, film, lining or packaging material, that includes a gas impermeable layer and an impregnated polymeric material layer. Accordingly, the article can be used to remediate an environment, optionally, one that contains an item to be remediated. For example, the article may enclose an environment such that the impregnated polymeric material releases antimicrobial gas into the enclosed environment so as to remediate the interior environment and the contents contained therein. Moreover, the gas impermeable layer would be positioned, for example, disposed on the external surface of the package, so as to impede or prevent the release of gas from the enclosed environment, thereby enhancing the remediating effect.

In another aspect, the invention provides a method for impregnating an article and related systems therefor. Various aseptic packaging systems (for example, from Bosch Inc. (Minneapolis, MN)) can be retrofitted so as to package products, for example, medical or dental instruments or food items, as described herein. For example, a packaging system can be designed or adjusted such that multilayer sheets with a gas impermeable layer and a gas soluble polymeric material are exposed to antimicrobial gas so as to impregnate the gas soluble polymeric material. Immediately upon impregnation, the desired item can be packaged within the article so as to provide a remediated product upon delivery. Accordingly, the present invention provides a method of retrofitting a package system by providing a bath, chamber and/ or a gas generating device. Such features may be activated so as to produce the desired antimicrobial gas and to expose the impregnatable material thereto. Gas generating devices include, but are not limited to, those described in U.S. Patent Application Publication No. 2004/0022676 (Hamilton *et al.*), U.S. Patent Nos. 6,607,696 (Hamilton *et al.*) and 6,602,466 (Hamilton *et al.*), International Publication Nos. WO03/051407 (Hamilton *et al.*), WO04/07375 (Hamilton *et al.*) and WO04/113224 (Warner *et al.*). The invention further provides for assemblies and/or articles for retrofitting packaging systems, such as a bath, chamber, and/or gas generating devices.

In other aspects, the methods and articles of the present invention provide a safe and convenient means for transporting antimicrobial gas. For example, the impregnated

polymeric material may be sealed within a gas impermeable package, which can be conveniently and safely transported without release of the gas into the atmosphere.

In yet another aspect, the methods and articles of the present invention may provide a means for deactivating microorganisms or enzymes in a sample without significant structural damage to cells and microorganisms present within the sample. Accordingly, the present invention provides an improved means of analysis of samples, for example, environmental samples, by creating a sample substantially similar to its natural state while minimizing the changes to the properties of the sample.

In one embodiment, the article of the present invention includes or is formed, at least substantially, of polymeric material. The polymeric material should be gas permeable so as to allow for the impregnation of antimicrobial gas into the polymeric material, and the subsequent desorption of the gas from the polymeric material. Polymeric materials will vary in terms of their ability to be impregnated by an antimicrobial gas such as chlorine dioxide and in terms of their ability to release the gas. Release rates of particular polymeric materials can be readily determined by one skilled in the art, for example, as described in Example 3. One skilled in the art will recognize that various factors may be manipulated to achieve a desired impregnated polymeric material and/ or a desired release profile including, but not limited to, the nature of polymeric material, the solubility of the gas in the polymeric material, the concentration of antimicrobial gas, for example, in solution, to which the material is exposed and the loading time for which the material is exposed. The amount of gas that can be impregnated and desorbed in a polymeric material, and the concentration of the gas in an exposed environment, can be determined by any number of known methods, including those described in the instant application, *e.g.*, in the examples.

The article and polymeric materials of the present invention may be prepared by exposing the polymeric material to the antimicrobial gas, for example, a chlorine dioxide solution, vapor or gas. For example, the polymeric material may be submerged within an antimicrobial gas solution under conditions that promote the impregnation of the gas into the polymeric material. Accordingly, the gas is impregnated into the polymeric material. Upon removal of the external source of gas, the gas will remain sorbed or impregnated in the polymeric material.

The present invention further contemplates use of other gases. Other gases include, but are not limited to, sulfur dioxide, nitrogen dioxide, nitric oxide, nitrous oxide, carbon dioxide, hydrogen sulfide, hydrocyanic acid and dichlorine monoxide. Chlorine dioxide and

other gases may be produced by techniques and devices well known in the art, for example, as described in U.S. Patent Application Publication No. 2004/0022676 (Hamilton *et al.*), U.S. Patent Nos. 6,607,696 (Hamilton *et al.*) and 6,602,466 (Hamilton *et al.*), International Publication Nos. WO03/051407 (Hamilton *et al.*), WO04/07375 (Hamilton *et al.*) and
5 WO04/113224 (Warner *et al.*).

In certain embodiments, the polymeric material is exposed to the gas for 48, 44, 40, 36, 32, 28, 24, 22, 20, 18, 16, 14, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 or 0.5 hours. In a particular embodiment, the polymeric material is exposed to the antimicrobial gas for a period from about 30 minutes to about 5 days. Ranges of values using a combination of any of the
10 above recited values as upper and/or lower limits are intended to be included as embodiments of the present invention. In one embodiment the polymeric material is saturated; in another embodiment, the polymeric material is substantially saturated with antimicrobial gas.

In certain embodiments, the polymeric material is exposed to a gas (*e.g.*, in air or in solution) at a concentration of about 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500,
15 450, 400, 350, 300, 250, 200, 150, 100, 50, 25 and 10 ppm. In a particular embodiment, the polymeric material is exposed to a solution, of about 50 to about 600 ppm, 50 to about 150 ppm, or about 450 to about 550 ppm of, for example, chlorine dioxide solution. Ranges of values using a combination of any of the above recited values as upper and/or lower limits are intended to be included as embodiments of the present invention.

In addition, a polymeric material can be chosen with a desired release profile. Polymeric materials suitable for use in the present invention include, but are not limited to, ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, polylactic acid (PLA), polyethylene, polypropylene, polyvinyl chloride, polyvinyl acetate, methacrylic acid, polyacetylene, polyphenylene, polypyrrole, polythiophene, hydroxyethyl cellulose,
25 hydroxypropyl cellulose, polyethylene glycol (PEG), polyethylene oxide, ethylene oxide-propylene oxide, and co-polymers thereof. In a particular embodiment, the polymeric material is polystyrene. The release profile of any polymeric material or combination of polymeric material can be readily determined, *e.g.*, by using the methods described in the examples.

Accordingly, a desired concentration of released antimicrobial gas, for example, in the exposed environment or solution, can be achieved. In certain embodiments, the article produces a concentration (*e.g.*, produces an initial concentration or maintains a concentration) of antimicrobial gas of about 50, 45, 40, 35, 30, 25, 20, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4,

3, 2, 1, 0.5 or 0.1 ppm in air of antimicrobial gas. In various embodiments, the article produces a concentration of antimicrobial gas of about 0.1 to about 50 ppm, of about 1 to about 40 ppm, of about 5 to about 30 ppm, or about 10 to about 20 ppm in air of antimicrobial gas. In a particular embodiment, the article produces a concentration of antimicrobial gas of about 0.1 to about 20 ppm of chlorine dioxide gas in air. In alternative 5 embodiments, the article can produce a concentration (e.g., produces an initial concentration or maintains a concentration) of antimicrobial gas in solution of about 500, 475, 450, 425, 400, 375, 350, 325, 300, 275, 250, 225, 200, 175, 150, 125, 100, 90, 80, 70, 60, 50, 45, 40, 35, 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, 0.5 or 0.1 ppm. In various embodiments, the article produces a concentration of antimicrobial gas in solution of about 0.1 to about 500 10 ppm, about 0.5 to about 250 ppm, about 1 to about 100 ppm, and about 5 to about 50 ppm. In a particular embodiment, the article produces a concentration of antimicrobial gas of about 0.1 to about 20 ppm of chlorine dioxide gas in solution. Ranges of values using a combination of any of the above recited values as upper and/or lower limits are intended to be 15 included as embodiments of the present invention.

The article of the present invention may be any device that can exhibit the desired antimicrobial activity. For example, the article may be, but is not limited to, a container such as a vial, a bottle or a clam shell container. In a particular embodiment, the article may be a container used to collect and transport food items or agricultural products, such as a clam 20 shell. The device may be of sufficient size to hold and remediate microbial life on the desired item. The article may define a volume capable of holding the desired item. The article may further define an opening, for example into the volume of the article. Moreover, the article may further include a device to enclose the opening, for example, a cap, cover or lid that encloses the opening and the internal volume of the article. The device to enclose the 25 opening may be a separate object, such as a cap, cover or lid, or may be structured as part of the article such that the article is capable of sealing itself. The ability of the article to enclose the opening and the internal volume of the article can serve to enhance the antimicrobial remediating capabilities of the article. Without wishing to be bound to any particular theory, by enclosing and sealing the article, the antimicrobial gas that diffuses into the article will be 30 substantially prevented from escaping the internal volume of the article. Accordingly, the gas will remain in a high concentration, thereby sterilizing, disinfecting or sanitizing the object contained therein.

The article can also be in the form of a packing material, lining, pellets, sheets or fibers. In one embodiment, the polymeric material has a high surface area and/or mass. The polymeric material may be self-sealing by, for example, pressure fit, zip lock, snap fit, tongue and groove or threaded fit techniques, thereby to impede or prevent the escape of antimicrobial gas and to ultimately enhance the sterilizing effect. The article can include packing materials, *e.g.*, for fruits or vegetables.

Alternatively, the polymeric material may be in the form of a pellet. In one embodiment, the pellet may be enclosed within a gas impermeable package, for example, so as to allow for the convenient transportation of chlorine dioxide. In another embodiment, the packaging material, for example, a closed cardboard box, retards permeation of the antimicrobial gas.

In particular embodiments, the polymeric material or article may be enclosed within a gas impermeable or a substantially gas impermeable material so as to impede or prevent the antimicrobial gas from escaping the environment. Accordingly, the gas can serve to remediate microbial life on the contents of the gas impermeable material. For example, the polymeric material may be in the form of a pellet contained within a gas impermeable material. In addition, the article may be a multilayer device with an impregnated polymeric material and an impermeable material, preferably surrounding the impregnated polymeric material, to retard or eliminate release of the gas.

In some embodiments, articles in accordance with the present invention are packed in gas impermeable packaging such that a substantial amount of the gas remains impregnated within the polymeric material. Advantages of this embodiment include that the articles can be prepared, then stored and/or shipped to the point of use, so that the articles are ready to remediate microbial life upon removing the gas impermeable material or packaging. Accordingly, *e.g.*, clam shell containers can be impregnated with chlorine dioxide gas and enclosed in shrink wrap for shipment to where agricultural products are packed. Another exemplary embodiment is the impregnation and packaging of laboratory supplies such as pipettes and vials, so that they are ready for use at a later time without having to take the additional step of sterilizing the item.

Impermeable material, as used herein, refers to a material that substantially hinders or prevents the passage of solids, gases and liquids and/or in which a gas has little to no solubility. Impermeable materials can be constructed from various materials, including polymeric material, glass, metal, metallized polymeric material and/or coated papers.

Suitable impermeable or barrier materials include, but are not limited to, metals, polymeric materials and/or coated papers. Other suitable materials include polymeric layers constructed from, e.g., polyester, polyvinyl chloride, polyvinylidene chloride, acrylobutylstyrene and/or polytetrafluoroethylene, polyacrylate, acrylic, polycarbonate, poly(acrylonitrile, butadiene, styrene), and polyacetal. Also suitable are metallized layers, e.g., any of the above polymeric layers that have been metallized. Also suitable are metallic foils, such as aluminum foils. Various other impermeable materials can be used to form the barrier film as well, such as glass or ceramics. In addition, layers that are composites of the above layers and/or laminates of the above layers, e.g., paper/film/foil composites are also suitable.

As used herein, any item to be, for example, sanitized, sterilized or disinfected may be introduced within the interior volume of the article, may be surrounded by the polymeric material generally, or may be adjacent to the items. In various embodiments, the item may be a food item, including, but not limited, to fruits (such as berries and, in particular, strawberries) and vegetables, raw agricultural products, cut flowers, and medical and dental instruments. In one embodiment, the article is adjacent to the items, such as liners, spacers, or other articles adjacent to the item and used, for example, for storage or shipping. In another embodiment, a sample, such as a biological, environmental or chemical sample, may be exposed to or contained within the article. Accordingly, the sample may be remediated, for example, sanitized, disinfected or sterilized, as necessary to achieve the desired result. For example, an environmental sample may be introduced into an impregnated vial to allow for deactivation of microorganisms or to retain the sterility of the sample. In yet another embodiment, water may be introduced within the article, for example, a spray bottle, to allow for the production of a chlorine dioxide solution for use in various other applications, such as decontamination of medical devices.

In addition, articles of the present invention (for example, containers, packaging material, liners, sheets, pellets, and spacers) may be reused by the methods of the present invention. For example, after initial use, the polymeric material may be exposed to antimicrobial gas such that the gas is re-impregnated within the material, thereby rendering the article suitable for further use.

In another aspect, the present invention provides kits and methods for using kits that can be employed to make and use gas desorbing articles. In a particular embodiment according to the invention, a kit includes a reactant and/or device for the production of an antimicrobial gas (e.g., chlorine dioxide in solution). In one embodiment, the kit includes

instructions or other useful information (e.g., a chart providing guidance for generating desired concentrations of chlorine dioxide solutions). Optionally, the kit may further include at least one of a polymeric material, an article including a polymeric material, or a gas impermeable membrane. In some embodiments, the kit includes a substantially gas impermeable packaging material for use in retaining the antimicrobial gas impregnated or substantially impregnated within the polymeric material.

Exemplification of the Invention

The following examples are expected to be illustrative of the invention and in no way limit the scope of the invention.

Example 1: Administration of a Contaminated Solution to an Impregnated Vial

16 ml of tap water plated on R2A Agar and determined to have approximately about 3.7 log cfu/ml heterotrophic bacteria was added to a 16 ml vial impregnated with chlorine dioxide by exposure of the vial to 500 ppm chlorine dioxide gas for 120 minutes. Samples were extracted at 1 min, 5 min, 15 min, 30 min and 1 hour to determine whether there was any growth. Analysis of samples extracted at 1 min, 5 min, 15 min and 30 min exhibited no detectable microbial life. The sample extracted at 1 hr showed growth of one colony. It is believed that this was a result of experimental contamination.

Example 2: Impregnation of Polystyrene with Chlorine Dioxide

Polystyrene vials and glass containers (as a control) were each exposed to chlorine dioxide solutions in water having a concentration of about 193 ppm. The concentration of the gas in the solution did not significantly change upon exposure of the glass vials to the solution.

The drop in concentration of the chlorine dioxide in solution exposed to the polystyrene vials was attributed to the impregnation of the vial with chlorine dioxide. Figure 1 is a graph depicting the amount of gas impregnated in a 6.45 g polystyrene vial over time. As shown in Figure 1, in 8 hrs, a 6.45 g vial of polystyrene was impregnated with 1.77 mg of chlorine dioxide.

Example 3: Release of Chlorine Dioxide from Impregnated Polystyrene

Three polystyrene vials were filled with 715-ppm chlorine dioxide solution with water and allowed to sit in a dark area for 24 hrs. After 24 hrs the vials were emptied of their solution and placed in an airtight 2.5 liter glass chamber. The vials were not sealed. A
5 PortaSens II gaseous chlorine dioxide sensor (Analytical Technology, Inc., Collegeville, PA) monitored the release of chlorine dioxide gas from the tubes into the chamber for 22 hrs. The release of chlorine dioxide from the vials is shown in Figure 2.

Example 4: Impregnation of Common Containers and Packing Materials

10 Certain containers and packing materials, including polystyrene clamshell containers, PLA clamshell containers, expanded polystyrene or expanded polyethylene pack materials, were impregnated with chlorine dioxide by exposure to chlorine dioxide solution. Each of the containers, upon exposure to chlorine dioxide exhibited a greenish tinge, indicating the impregnation of chlorine dioxide within the walls of the materials.

Example 5: Impregnation of Polystyrene with Chlorine Dioxide

Four categories of vials were filled with chlorine dioxide solution as follows:

- 1) three 15 ml polystyrene vials were filled with 100 ppm chlorine dioxide solution;
- 2) three 15 ml glass vials (as a control) were filled with 100 ppm chlorine dioxide
20 solution;
- 3) three 15 ml polystyrene vials were filled with 500 ppm chlorine dioxide solution;
and
- 4) three 15 ml glass vials (as a control) were filled with 500 ppm chlorine dioxide
solution.

25 A vial from each category was exposed to the appropriate chlorine dioxide solution for 2, 3 or 4 hours. The amount of chlorine dioxide sorbed by the vial was calculated as the difference in the concentration of chlorine dioxide solution initially upon exposure to the vial and at the 2, 3 or 4 hour time points. Specifically, the amount of chlorine dioxide was calculated using the following formula:

30 $([\text{ClO}_2 \text{ (in control)}] - [\text{ClO}_2 \text{ (in polystyrene vial)}]) \times .015 = \text{mg sorbed by polystyrene vial}$

Accordingly, the concentration of the chlorine dioxide solution was measured initially upon exposure to the vial and subsequently at the 2, 3 or 4 hour time point, as appropriate, using a spectrophotometer LaMatte 420 nm (Chestertown, MD). As the polystyrene vials were not

optically clear upon exposure to the chlorine dioxide solution, the solution was transferred to a glass vial prior to measurement of the concentration. The results of the trials run upon exposure to 100 ppm chlorine dioxide are shown in Figure 3. As indicated therein, the concentration of the chlorine dioxide solution to which the glass vial was exposed exhibited minimal change. By contrast, the concentration of chlorine dioxide solution to which the polystyrene vial was exposed diminished over time.

The results of the trials run upon exposure to 500 ppm chlorine dioxide are shown in Figure 4. As above, the concentration of the chlorine dioxide solution to which the glass vial was exposed exhibited minimal change while the concentration of chlorine dioxide solution to which the polystyrene vial was exposed diminished over time.

Example 6: Desorption of Chlorine Dioxide from Impregnated Polystyrene

Chlorine dioxide solution was removed from each vial prepared in Example 5. After the vials were allowed to air dry, the vials were filled with deionized water to allow for desorption of the chlorine dioxide from the vial into the water. In order to determine the amount of chlorine dioxide desorbed from the vials over time, the concentration of the chlorine dioxide for a sample from each category of vial was measured at 30, 60 and 90 minutes. The desorption of ClO_2 over time from polystyrene vials previously exposed to 100 ppm chlorine dioxide solution is shown in Figure 5. As expected, the ClO_2 concentration in solution increased over time and was greater for those vials with greater initial exposure times to ClO_2 .

Further calculation indicates that at 90 minutes, chlorine dioxide eluted from the vials as indicated in Table 1. The amount of chlorine dioxide desorbed from the polystyrene vial at 90 minutes was calculated as follows:

$$([\text{ClO}_2 \text{ (in polystyrene vial)}] - [\text{ClO}_2 \text{ (in control vial)}]) \times .015 = \text{mg desorbed from polystyrene vial}$$

Accordingly, the percent ClO_2 recovered is calculated as follows:

$$(\text{ClO}_2 \text{ desorbed} / \text{ClO}_2 \text{ sorbed}) \times 100 = \% \text{ ClO}_2 \text{ recovered}$$

Table 1: Recovery of ClO₂ from impregnated vials after 90 minutes

| | Vial exposed to ClO ₂ solution for 2 hours | Vial exposed to ClO ₂ solution for 3 hours | Vial exposed to ClO ₂ solution for 4 hours |
|------------------------------------|---|---|---|
| ClO ₂ desorbed (µg) | 24.9 | 35.3 | 635 |
| Percent ClO ₂ Recovered | 39% | 41% | 40% |

The desorption of ClO₂ over time from polystyrene vials previously exposed to 500 ppm chlorine dioxide solution is shown in Figure 6. As above, the ClO₂ concentration in solution increased over time and was greater for those vials with greater initial exposure times to ClO₂.

Further analysis indicates that chlorine dioxide desorbed from the vials as indicated below in Table 2.

Table 2: Recovery of ClO₂ from impregnated vials after 90 minutes

| | Vial exposed to ClO ₂ solution for 2 hours | Vial exposed to ClO ₂ solution for 3 hours | Vial exposed to ClO ₂ solution for 4 hours |
|------------------------------------|---|---|---|
| ClO ₂ desorbed (µg) | 141 | 141 | 195 |
| Percent ClO ₂ Recovered | 44% | 33% | 27% |

The results demonstrate that the percent recovery from polystyrene vials exposed to 100 ppm solution was relatively consistent despite variation in exposure time to the ClO₂ solution. However, the percent recovery from polystyrene vials exposed to 500 ppm solution varied significantly. Indeed, the greater the amount of chlorine dioxide sorbed into the vial, the lower the percent recovery of the resulting chlorine dioxide into solution. Without wishing to be bound to any particular theory, it is believed that the mass transfer of chlorine dioxide through the polystyrene to the polystyrene/ water interface may be the rate limiting step for desorption of chlorine dioxide from the polystyrene.

Utilizing the information provided in this application and the techniques and data provided by the foregoing examples, one skilled in the art will be able to design a polymeric

material exhibiting a desired release profile, *i.e.*, a release of a desired concentration of antimicrobial gas over a desired time period.

Equivalents

5 Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

CLAIMS

We claim:

1. A gas desorbing article comprising a polymeric material impregnated with an antimicrobial gas.
5
2. The article of claim 1, wherein the article is a container such as a vial, bottle, or clam shell.
- 10 3. The article of claim 1, wherein the article is in the form of a packaging material, a pellet, a fiber, a liner or a sheet.
4. The article of any one of the preceding claims, wherein the article is a food container or a food packaging material.
- 15 5. The article of any one of the preceding claims, wherein the article is substantially saturated with the antimicrobial gas.
- 6 6. The article of any one of the preceding claims, wherein the article is impregnated with antimicrobial gas such that it is capable of desorbing antimicrobial gas for at least 10 minutes, 20 minutes, 30 minutes, 2 hours, 1 day or 5 days.
- 20 7. The article of any one of the preceding claims, wherein the article is sanitized, disinfected or sterilized.
- 25 8. The article of any one of the preceding claims, wherein the gas is chlorine dioxide.
9. The article of any one of the preceding claims, wherein the polymeric material comprises a polystyrene.
- 30 10. The article of any one of the preceding claims, further comprising an item disposed within or exposed to the article.

11. The article of claim 10, wherein the item is disinfected, sterilized or sanitized.
12. The article of claim 10, wherein the item is selected from the group consisting of a food item, an agricultural product, a medical instrument, medical waste, a fruit, a vegetable, a flower, a bar sink, a mop bucket, and a dental instrument.
13. The article of claim 11 or 12, wherein the item remains substantially disinfected, sterilized or sanitized for at least 10 minutes, 20 minutes, 30 minutes, 2 hours, 1 day or 5 days.
14. The article of any one of the preceding claims, wherein the article is disposed within a substantially gas impermeable package such that a substantial amount of antimicrobial gas remains impregnated within the polymeric material.
15. The article of any one of the preceding claims, wherein the article further comprises a gas impermeable material.
16. The article of claim 15, wherein the article comprises a multilayer sheet comprising a gas impermeable layer and a layer comprising the impregnated polymeric material.
17. A package comprising the multilayer sheet of claim 16, wherein the gas impermeable layer impedes the release of antimicrobial gas from the package.
18. A method of remediating microbial life in an environment comprising enclosing the environment with the article of claim 15 or 16 or the package of claim 17, such that the gas impermeable material impedes the release of the antimicrobial gas from the environment and where microbial life is remediated within the environment.
19. A method for remediating microbial life comprising exposing an environment to the article of any one of claims 1-16, such that microbial life is remediated in the environment.
20. The method of claim 19, wherein the environment is defined by the article.

21. The method of claim 19, wherein the environment is immediately adjacent to the article.

22. The method of any one of claims 19-21, wherein the environment includes an item
5 selected from the group consisting of a food item, an agricultural product, a medical instrument, medical waste, a fruit, a vegetable, a flower, a bar sink, a mop bucket, and a dental instrument.

23. The method of any one of claims 19-22, wherein the environment is sanitized,
10 sterilized, and/or disinfected.

24. The method of any one of claims 19-23, wherein the gas is released over a period of at least about 10 minutes, 20 minutes, 1 hour, or 5 days.

25. The method of any one of claims 19-24, wherein the gas is released from the article to
15 maintain a concentration of antimicrobial gas from about 0.10 ppm to about 20 ppm.

26. The method of any one of claims 19-25, wherein the gas is released from the article to
20 obtain an initial concentration of antimicrobial gas from about 0.10 ppm to about 20 ppm.

27. A method of making the article of any one of claims 1-16, comprising exposing a polymeric material to the antimicrobial gas.

28. The method of claim 27, wherein the polymeric material is exposed to a solution
25 comprising the antimicrobial gas.

29. The method of claim 28, wherein the polymeric material is exposed to the solution for at least about 10 minutes, 20 minutes, 1 hour, 2 hours or 4 hours.

30. The method of claim 28 or 29, wherein the solution has a concentration of
30 antimicrobial gas from about 50 ppm to about 600 ppm chlorine dioxide, from about 50 ppm to about 150 ppm chlorine dioxide, or from about 450 ppm to about 550 ppm chlorine dioxide.

Impregnation of Polystyrene Via I

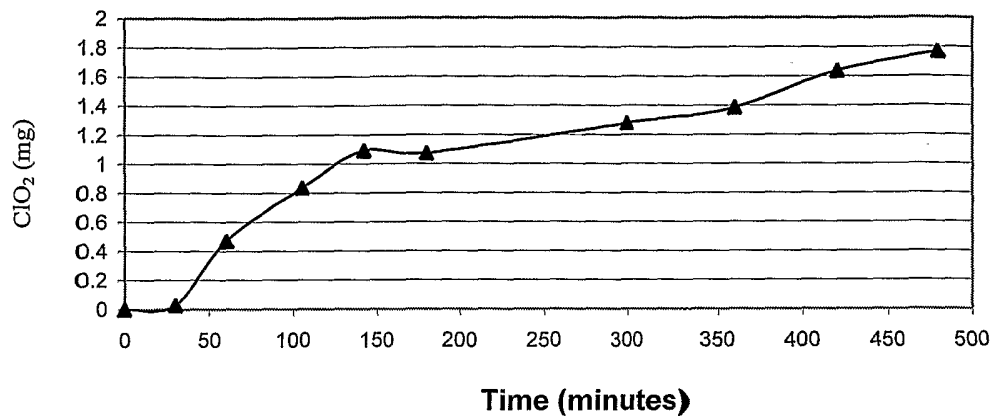


Figure 1

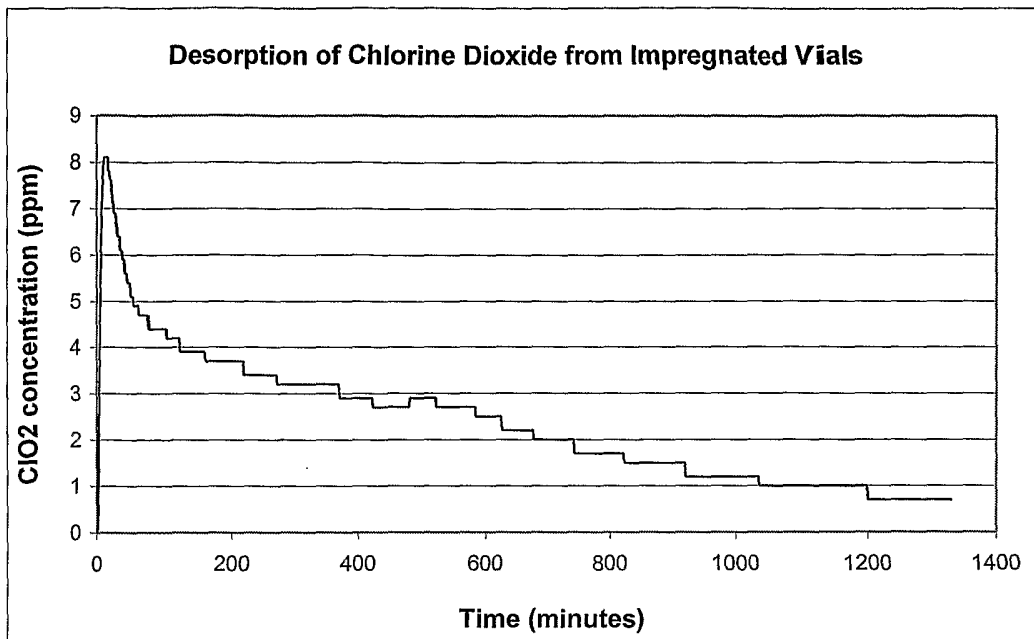


Figure 2

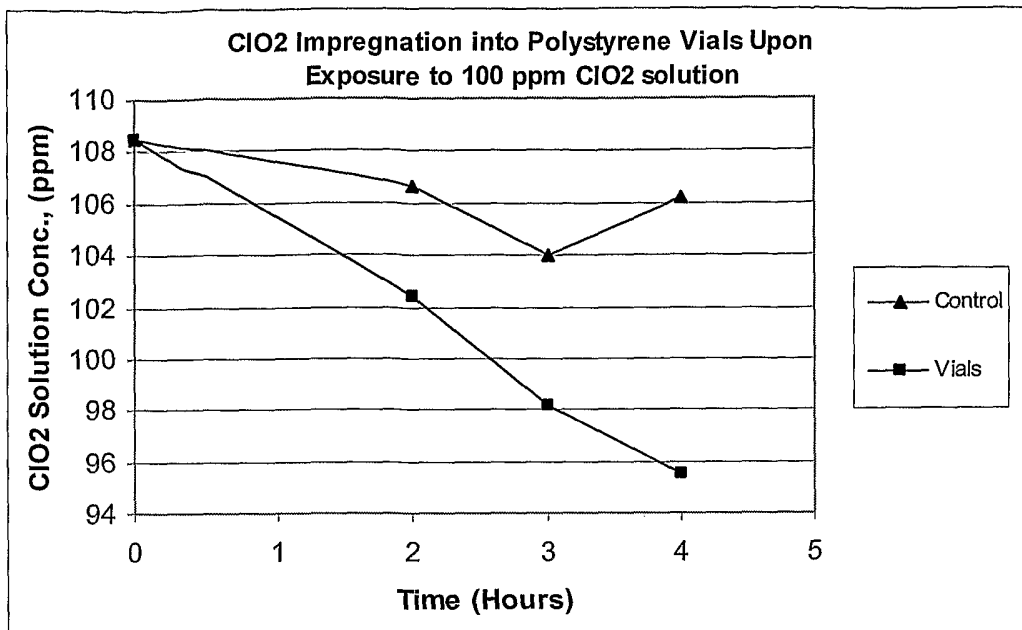


Figure 3

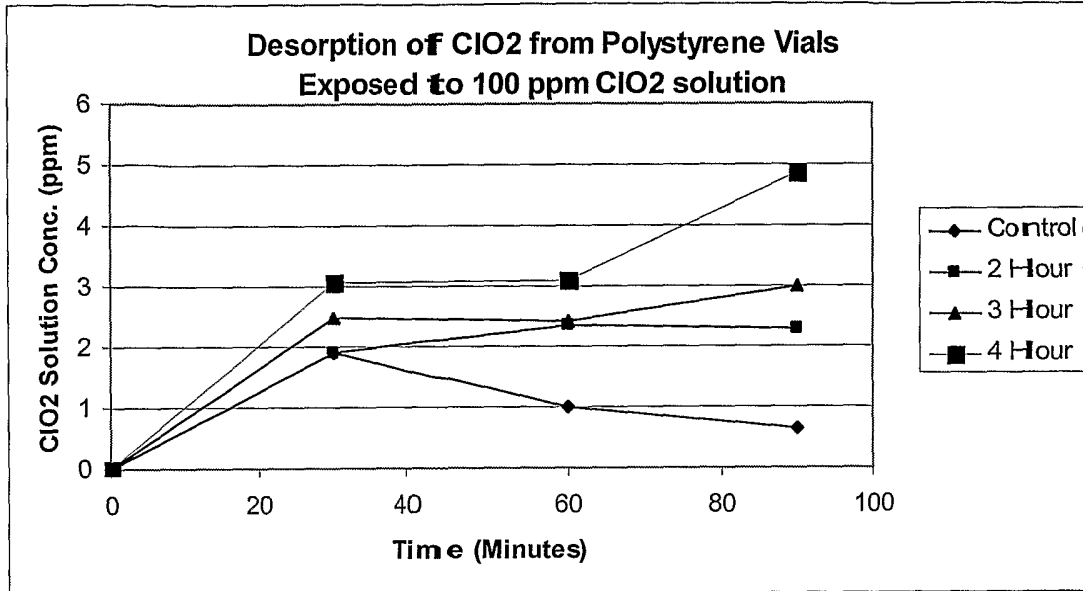


Figure 4

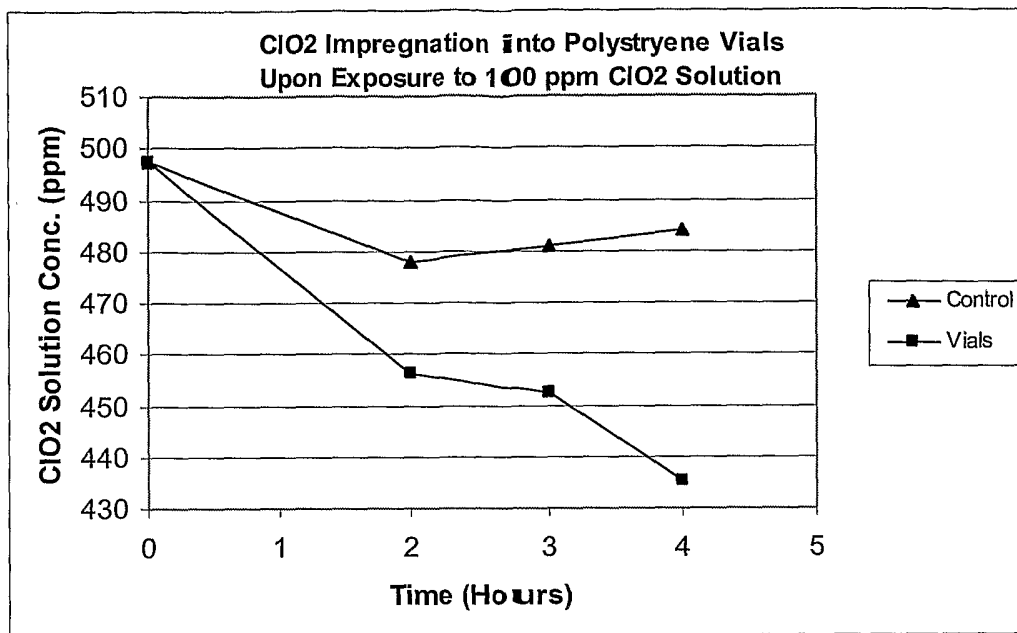


Figure 5

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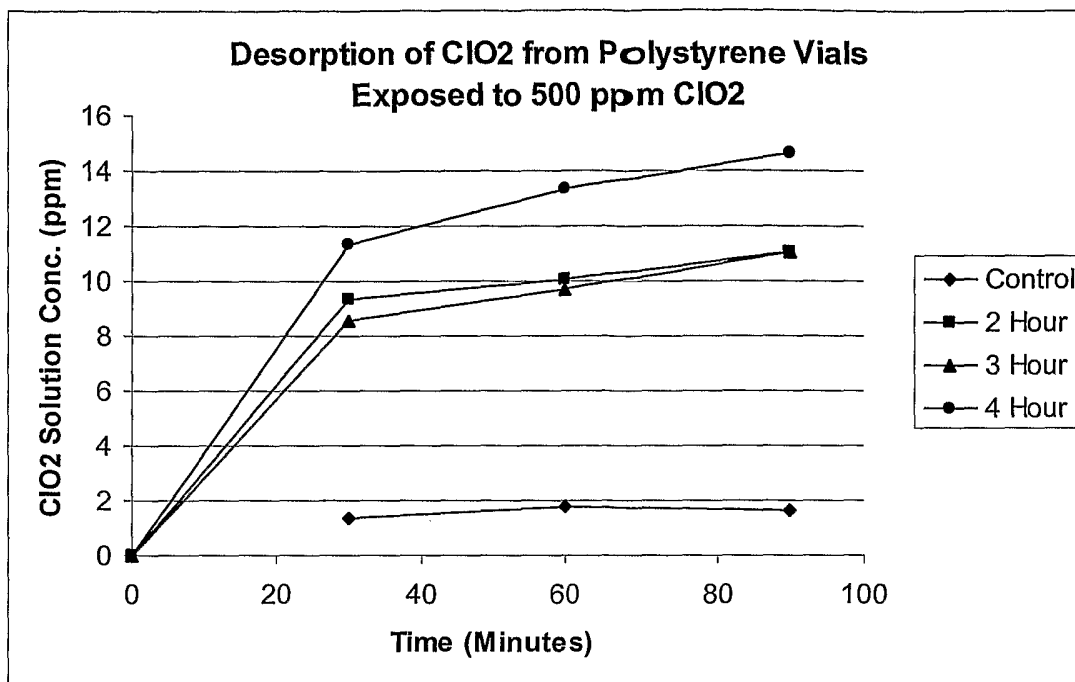


Figure 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/001847

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A01N25/10 A01N25/18 A01N59/00 A01P1/00 A61L2/20

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)
 A01N A61L

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 practical, search terms used)
 EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| X | WO 96/20019 A (BAXTER INTERNATIONAL INC) 4 July 1996 (1996-07-04) page 1, paragraph 1 page 3, line 24 - page 5, line 19 page 7, line 6 - page 11, line 9 examples 1-10 claims 1-30 | 1-30 |
| P, X | ----- WO 2005/037327 A (WATER TECHNOLOGIES LIMITED) 28 April 2005 (2005-04-28) page 1, paragraph 1 page 4, paragraph 1-5 page 5, paragraph 3 - page 7, paragraph 5 examples 1-4 claims 1-49 ----- -/-- | 1-30 |

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents :

| | |
|--|--|
| <p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p> | <p>*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</p> <p>*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</p> <p>*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.</p> <p>*&* document member of the same patent family</p> |
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| Date of the actual completion of the international search | Date of mailing of the international search report |
| 5 May 2006 | 16/05/2006 |

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| Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Authorized officer Marie, G |
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/001847

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | US 4 829 129 A (KELLEY ET AL) 9 May 1989 (1989-05-09) column 1, paragraph 1 column 3, paragraphs 4,6,8 examples 1-18 claims 1-21 ----- | 1-30 |
| X | US 6 451 253 B1 (PITOCHELLI ANTHONY R ET AL) 17 September 2002 (2002-09-17) the whole document ----- | 1-30 |
| X | WO 03/051406 A (SELECTIVE MICRO TECHNOLOGIES, LLC) 26 June 2003 (2003-06-26) cited in the application paragraphs [0009] - [0028] paragraphs [0062] - [0088] paragraphs [0172], [0248] examples 1,3-16 claims 1-49 ----- | 1-30 |
| X | WO 01/60750 A (SELECTIVE MICRO TECHNOLOGIES, LLC) 23 August 2001 (2001-08-23) claims 1-58 page 31, line 7 - page 33, line 7 ----- | 1-30 |
| X | WO 2004/045654 A (SELECTIVE MICRO TECHNOLOGIES, LLC; HAMILTON, RICHARD, A; WARNER, JOHN,) 3 June 2004 (2004-06-03) page 2, line 1 - page 3, line 24 page 4, line 22 - page 9, line 25 page 10, lines 17-25 page 11, line 12 - page 12, line 8 page 13, lines 9-24 page 20, lines 5-13 page 28, lines 12-29 claims 1-37 ----- | 1-30 |
| X | WO 96/39029 A (SOUTHWEST RESEARCH INSTITUTE) 12 December 1996 (1996-12-12) page 3, line 13 - page 5, line 24 page 25, line 9 - page 29, line 7 examples 1-16 claims 1-38 ----- | 1-30 |
| X | US 5 639 295 A (WELLINGHOFF ET AL) 17 June 1997 (1997-06-17) claims 1-39 ----- | 1-30 |
| P,X | WO 2005/041660 A (AVERY DENNISON CORPORATION; HARTMAN, WILLIAM, G; KO, CHAN, U) 12 May 2005 (2005-05-12) page 3, line 17 - page 4, line 18 ----- | 1-30 |
| | -/-- | |

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/001847

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | EP 0 611 163 A (WELLINGHOFF, STEPHEN T; SOUTHWEST RESEARCH INSTITUTE) 17 August 1994 (1994-08-17) page 3, lines 7-31 page 6, line 36 - page 7, line 13 claims 1-17 ----- | 1-30 |
| X | WO 96/41526 A (BERNARD TECHNOLOGIES, INC; SOUTHWEST RESEARCH INSTITUTE) 27 December 1996 (1996-12-27) claims 1-47 examples 1-4 ----- | 1-30 |
| X | EP 0 423 817 A (BRISTOL-MYERS SQUIBB COMPANY) 24 April 1991 (1991-04-24) the whole document ----- | 1-30 |
| X | EP 0 611 162 A (WELLINGHOFF, STEPHEN T; SOUTHWEST RESEARCH INSTITUTE) 17 August 1994 (1994-08-17) claim 12 ----- | 1-30 |
| X | EP 1 454 594 A (MICROFLEX CORPORATION) 8 September 2004 (2004-09-08) claims 1-11 ----- | 1-30 |
| X | US 4 654 208 A (STOCKEL ET AL) 31 March 1987 (1987-03-31) claims 1-23 ----- | 1-30 |
| X | US 4 499 077 A (STOCKEL ET AL) 12 February 1985 (1985-02-12) claims 1-5 ----- | 1-30 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/001847

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date | | | |
|--|------------------|-------------------------|---|---|------------|-----------------------------|
| WO 9620019 | A | 04-07-1996 | AT 214620 T 15-04-2002 | | | |
| | | | AU 713632 B2 09-12-1999 | | | |
| | | | AU 4422496 A 19-07-1996 | | | |
| | | | BR 9506910 A 16-09-1997 | | | |
| | | | CA 2182265 A1 04-07-1996 | | | |
| | | | CN 1142193 A 05-02-1997 | | | |
| | | | DE 69525938 D1 25-04-2002 | | | |
| | | | DE 69525938 T2 21-11-2002 | | | |
| | | | DK 748233 T3 08-07-2002 | | | |
| | | | EP 0748233 A1 18-12-1996 | | | |
| | | | JP 9509876 T 07-10-1997 | | | |
| | | | JP 3741443 B2 01-02-2006 | | | |
| | | | TW 482651 B 11-04-2002 | | | |
| | | | WO 2005037327 | A | 28-04-2005 | US 2005079230 A1 14-04-2005 |
| US 4829129 | A | 09-05-1989 | AU 1934388 A 21-12-1988 WO 8809176 A1 01-12-1988 | | | |
| US 6451253 | B1 | 17-09-2002 | NONE | | | |
| WO 03051406 | A | 26-06-2003 | AU 2002357278 A1 30-06-2003 | | | |
| | | | BR 0215019 A 10-05-2005 | | | |
| | | | CA 2470434 A1 26-06-2003 | | | |
| | | | CN 1627963 A 15-06-2005 | | | |
| | | | EP 1467774 A1 20-10-2004 | | | |
| | | | JP 2005512769 T 12-05-2005 | | | |
| | | | MX PA04005961 A 01-11-2004 | | | |
| WO 0160750 | A | 23-08-2001 | AU 4316701 A 27-08-2001 | | | |
| | | | BR 0108486 A 22-04-2003 | | | |
| | | | CA 2399245 A1 23-08-2001 | | | |
| | | | CN 1400912 A 05-03-2003 | | | |
| | | | EP 1255572 A2 13-11-2002 | | | |
| | | | JP 2003522640 T 29-07-2003 | | | |
| | | | MX PA02007993 A 05-04-2004 | | | |
| | | | US 2001038805 A1 08-11-2001 | | | |
| WO 2004045654 | A | 03-06-2004 | AU 2003290924 A1 15-06-2004 | | | |
| | | | AU 2003295499 A1 15-06-2004 | | | |
| | | | WO 2004045655 A2 03-06-2004 | | | |
| WO 9639029 | A | 12-12-1996 | AU 698032 B2 22-10-1998 | | | |
| | | | AU 6160296 A 24-12-1996 | | | |
| | | | BR 9606416 A 14-10-1997 | | | |
| | | | CA 2196782 A1 12-12-1996 | | | |
| | | | DE 69626466 D1 10-04-2003 | | | |
| | | | DE 69626466 T2 11-03-2004 | | | |
| | | | DK 774898 T3 23-06-2003 | | | |
| | | | EP 0774898 A1 28-05-1997 | | | |
| | | | ES 2193244 T3 01-11-2003 | | | |
| | | | HK 1013215 A1 26-09-2003 | | | |
| | | | JP 10504844 T 12-05-1998 | | | |
| | | | NZ 310748 A 27-04-1998 | | | |
| | | | US 5639295 | A | 17-06-1997 | NONE |
| | | | WO 2005041660 | A | 12-05-2005 | NONE |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/001847

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|--|------------|------------------|-------------------------|------------------|
| EP 0611163 | A | 17-08-1994 | AT 185681 T | 15-11-1999 |
| | | | CA 2115484 A1 | 13-08-1994 |
| | | | DE 69421199 D1 | 25-11-1999 |
| | | | DE 69421199 T2 | 20-04-2000 |
| | | | DK 611163 T3 | 27-12-1999 |
| | | | ES 2139709 T3 | 16-02-2000 |
| | | | GR 3032180 T3 | 27-04-2000 |
| | | | HK 1013216 A1 | 16-06-2000 |
| | | | JP 2837345 B2 | 16-12-1998 |
| | | | JP 8165207 A | 25-06-1996 |
| | | | PT 611163 T | 28-04-2000 |
| | | | SG 43915 A1 | 14-11-1997 |
| WO 9641526 | A | 27-12-1996 | AU 713284 B2 | 25-11-1999 |
| | | | AU 5988396 A | 09-01-1997 |
| | | | BR 9606515 A | 15-12-1998 |
| | | | EP 0774899 A1 | 28-05-1997 |
| | | | JP 2002515021 T | 21-05-2002 |
| | | | NZ 309662 A | 24-09-1998 |
| | | | US 5922776 A | 13-07-1999 |
| EP 0423817 | A | 24-04-1991 | AU 629701 B2 | 08-10-1992 |
| | | | AU 6470690 A | 26-04-1991 |
| | | | CA 2027713 A1 | 21-04-1991 |
| | | | JP 3164403 A | 16-07-1991 |
| | | | NZ 235624 A | 23-12-1993 |
| | | | US 5126070 A | 30-06-1992 |
| EP 0611162 | A | 17-08-1994 | AT 173377 T | 15-12-1998 |
| | | | CA 2115483 A1 | 13-08-1994 |
| | | | DE 69414616 D1 | 24-12-1998 |
| | | | DE 69414616 T2 | 15-04-1999 |
| | | | DK 611162 T3 | 02-08-1999 |
| | | | ES 2126705 T3 | 01-04-1999 |
| | | | GR 3029414 T3 | 28-05-1999 |
| | | | JP 2994199 B2 | 27-12-1999 |
| | | | JP 8081580 A | 26-03-1996 |
| | | | SG 43357 A1 | 17-10-1997 |
| | | | US 5360609 A | 01-11-1994 |
| | | | EP 1454594 | A |
| JP 2004270128 A | 30-09-2004 | | | |
| US 2004170671 A1 | 02-09-2004 | | | |
| US 4654208 | A | 31-03-1987 | NONE | |
| US 4499077 | A | 12-02-1985 | NONE | |