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(54) Title: HYDROGEN PEROXIDE INDICATOR AND METHOD

(57) Abstract: The present invention provides a hydrogen peroxide indicator that includes a substrate on which is disposed an indicator composition that includes at least one of a select group of colorants. As a result of contact with hydrogen peroxide, the colorants change color, and even become colorless, thereby providing an indication of the presence of hydrogen peroxide.

HYDROGEN PEROXIDE INDICATOR AND METHOD

Background of the Invention

Medical instruments, particularly surgical instruments, are typically sterilized prior to use using steam or other sterilizing/disinfecting gases or liquids. A traditional sterilization process uses steam under pressure. Alternative sterilization processes use ethylene oxide or hydrogen peroxide in vapor form as the sterilant.

The use of hydrogen peroxide and other chemical vapor phase sterilization techniques typically involve operating temperatures well below those associated with steam sterilization. These "low temperature" technologies generally operate at temperatures below about 80°C, and often below about 65°C. For hydrogen peroxide sterilization, the sterilized goods are typically available for use shortly after the completion of the sterilization cycle. This is because the decomposition products (e.g., water and oxygen) are nontoxic. The potency of the hydrogen peroxide may be augmented by the presence of electrical energy in the form of an ionizing plasma field.

Sterilization indicators are used to monitor whether a sterilization process has been performed. Sterilization indicators typically include an indicator composition, carried on a substrate, that changes color during the sterilization process. Conventional indicators for hydrogen peroxide, however, often fade upon exposure to light. Thus, there is still a need for a suitable indicator that includes a color change composition for indicating the vapor phase sterilization of an article using hydrogen peroxide.

Summary of the Invention

The present invention is directed to a method and indicator for detecting the presence of hydrogen peroxide in the vapor phase. The method and indicator are particularly well suited for monitoring whether a hydrogen peroxide sterilization process has been performed.

The present invention provides a hydrogen peroxide indicator that includes a substrate and an indicator composition disposed thereon, wherein the indicator composition includes at least one colorant selected from the group consisting of Malachite green oxalate, Crystal violet, Methyl violet 2B, Ethyl violet, New fuchsin, Victoria blue B,

Victoria pure blue BO, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Thionine, Meldolas blue, Methylene green, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red 19, Bromopyrogallol red, and combinations thereof.

Preferably, the colorant is selected from the group consisting of Ethyl violet, New fuchsin, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Quinea green B, Thionine, Meldolas blue, Methylene green, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Mordant red 19, Bromopyrogallol red, and combinations thereof.

In a preferred embodiment the present invention provides a hydrogen peroxide indicator that includes a substrate and an indicator composition disposed thereon, wherein the indicator composition includes a binder, at least one colorant selected from the group consisting of Malachite green oxalate, Crystal violet, Methyl violet 2B, Ethyl violet, New fuchsin, Victoria blue B, Victoria pure blue BO, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Thionine, Meldolas blue, Methylene green, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red

19, Bromopyrogallol red, and combinations thereof, and at least one colorant that does not change color upon contact with hydrogen peroxide vapor.

Methods of monitoring a hydrogen peroxide sterilization process is also provides. These methods include exposing an article to be sterilized and the hydrogen peroxide indicators as described herein to hydrogen peroxide vapor.

Detailed Description of Preferred Embodiments

The present invention provides a hydrogen peroxide indicator that includes a substrate on which is disposed an indicator composition that includes at least one of a select group of colorants. As a result of contact with hydrogen peroxide, the colorants change color, and even become colorless, thereby providing an indication of the presence of hydrogen peroxide.

In particular, the present invention is directed to a system for indicating exposure to a hydrogen peroxide vapor sterilization process. The indicator composition includes at least one component that is transformed (typically, chemically transformed) in the presence of vaporous hydrogen peroxide such that the color of the composition changes. The composition may include one or more components that change color upon contact with hydrogen peroxide, as well as other components that do not change color upon contact with hydrogen peroxide. For example, the composition preferably includes a polymeric binder to aid in applying the composition to a suitable substrate.

Indicators of the present invention are very useful in indicating when an article has been exposed to hydrogen peroxide in the vapor phase. Significantly, indicators of the present invention offer one a simple, yet effective means for indicating when a particular article has been subjected to sterilization using vaporous hydrogen peroxide.

Preferably, the indicator compositions of the present invention undergo a color change when exposed to an atmosphere above an aqueous solution containing 30 weight percent (wt-%) hydrogen peroxide at 50°C within a period of at least about one hour and/or a color change when exposed to an atmosphere containing about 6 milligrams/liter (mg/l) to about 7 mg/l hydrogen peroxide (in an empty chamber, i.e., without articles to be sterilized) at a pressure of about 8×10^2 Pascals (Pa) to about 13.3×10^2 Pa and a temperature of about 45°C to about 50°C for a period of at least about 50 minutes, which

are typical conditions within an empty commercial hydrogen peroxide plasma sterilizer. More preferably, for use in conventional sterilizers, the indicator compositions of the present invention undergo a color change when exposed to an atmosphere containing about 6 mg/l to about 7 mg/l hydrogen peroxide (in an empty chamber) at a pressure of about 8 x 10^{2} Pa to about 13.3 x 10^{2} Pa and a temperature of about 45°C to about 50°C for a period of at least about 50 minutes. As used herein, a color change includes becoming colorless.

Preferably, the indicator compositions do not significantly fade upon exposure to room lighting, e.g., fluorescent lighting. More preferably, the indicator compositions do not significantly fade, for example, upon exposure to sunlight through a window for one week or room lighting for two months.

Suitable colorants for use in the indicator compositions of the present invention include the following: Malachite green oxalate, Crystal violet, Methyl violet 2B, Ethyl violet, New fuchsin, Victoria blue B, Victoria pure blue BO, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Thionine, Meldolas blue, Methylene green, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red 19, and Bromopyrogallol red. Alternative names and Color Index Numbers for these colorants are listed in Tables 1 and 2 below. Various combinations of these colorants can be used in the indicator compositions of the present invention. Such mixtures or blends would increase the options available in color changes dramatically.

A preferred group of colorants include the following: Ethyl violet, New fuchsin, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Quinea green B, Thionine, Meldolas blue, Methylene green, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast

red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Mordant red 19, Bromopyrogallol red, and combinations thereof.

Another preferred group of colorants include the following: Malachite green oxalate, Methyl violet 2B, New fuchsin, Toluidine blue O, Luxol brilliant green BL, Quinea green B, Thionine, Meldolas blue, Lissamine green B, Alkali blue 6B, Brilliant green, Victoria green S extra, Eriochrome blue black B, Congo red, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Bromopyrogallol red, and combinations thereof.

Suitable colorants become colorless or change to a different color upon exposure to hydrogen peroxide vapor. Preferred are those colorants that show good contrast between the initial color and the color after exposure to hydrogen peroxide vapor. Examples include, Malachite green oxalate, Methyl violet 2B, New fuchsin, Quinea green B, Thionine, Meldolas blue, Lissamine green B, Alkali blue 6B, Congo red, Eriochrome blue black B, Bismarck brown R, Methylene violet 3RAX, and combinations thereof.

Another group of preferred colorants are those that become substantially colorless upon exposure to hydrogen peroxide vapors under conventional sterilization conditions (e.g., 6 mg/l to about 7 mg/l hydrogen peroxide in an empty chamber at a pressure of about 8×10^2 Pa to about 13.3×10^2 Pa and a temperature of about 45°C to about 50°C for a period of at least about 50 minutes) or to the more concentrated hydrogen peroxide vapors in a desiccator. Examples of such colorants include Toluidine blue O, Luxol brilliant green BL, Victoria green S extra, Methylene violet, Bromopyrogallol red, Brilliant green, and combinations thereof.

Such colorants that become substantially colorless after exposure to hydrogen peroxide can also be used in combination with other colorants (e.g., dyes or pigments) that do not change color in the presence of hydrogen peroxide to give a chemical indicator with a suitable contrasting color change. For example, Alkali blue 6B plus a red unreactive dye such as Quinacridone red 19 show a color change from blue (initial) to pink, or a mixture of Brilliant green and Auramine O show a color change from bright green (initial) to bright yellow. In addition to Quinacridone red 19 and Auramine O, other sterilant-immune colored components may include those examples indicated in Tables 3A and 3B below.

Preferably, at least one colorant is present in the indicator composition in an amount sufficient to cause a color change when the composition is exposed to an atmosphere above an aqueous solution containing 30% hydrogen peroxide at 50°C within a period of at least about one hour and/or an amount sufficient to cause a color change when exposed to an atmosphere containing about 6 mg/l to about 7 mg/l hydrogen peroxide (in an empty chamber) at a pressure of about 8×10^2 Pa to about 13.3×10^2 Pa and a temperature of about 45°C to about 50°C for a period of at least about 50 minutes. Generally, the compositions contain about 0.1 wt-% to about 5.0 wt-%, based on the total weight of the composition, of a colorant that changes color upon exposure to hydrogen peroxide.

In effect, the colorant concentration should be such as to allow a clear visual indication of a color change. If at least one colorant that does not change color upon exposure to hydrogen peroxide is used in the indicator compositions of the present invention, it is present in an amount sufficient to provide the targeted color intensity, both prior to and subsequent to exposure to hydrogen peroxide vapor. Generally, such compositions contain about 0.1 wt-% to about 5.0 wt-%, based on the total weight of the composition, of a colorant that does not change color upon exposure to hydrogen peroxide.

The indicating composition is generally formulated in the form of a dispersion or solution in water or an organic solvent (preferably, an organic solvent). The composition includes at least one colorant as described above as well as an organic binder. A wide variety of suitable binders can be used. Examples include synthetic or natural polymers or resins. Suitable binders are those that do not interfere with the function of the indicator composition. Examples include cellulose acetate butyrate, shellac, ethyl cellulose, methyl cellulose, acrylic resins, etc. A sufficient amount of binder is included in the compositions to provide adequate binding of the composition to a substrate on which it is disposed, while providing the desired rate of color change. Generally, the compositions contain about 20 wt-% to about 40 wt-% of a polymer binder, based on the total weight of the composition.

Indicator compositions of the present invention can also include other resins that do not necessarily function as a binder. For example, the compositions can include a resin that functions as a dispersing agent, such as Rhoplex I-545, a water based acrylic polymer, available from Rohm and Haas Corp., Philadelphia, PA, that assists in dispersing the ingredients of the composition in the solvent used in application of the composition to a substrate. Indicator compositions of the present invention can also include opacifying agents such as titanium dioxide, surfactants, plasticizers, antifoam agents, and the like. For certain embodiments, a basic material such as an organic amine (e.g., triethanolamine) can be used to enhance sensitivity of the colorant to the low concentration of hydrogen peroxide in a conventional sterilizer. Typically, such additives are used in no more than about 5 wt-% based on the total weight of the indicator composition.

The compositions are typically applied to a substrate out of a solvent as discussed above. Suitable solvents include water and organic solvents such as ketones, esters, alcohols, and the like. Examples of suitable solvents include methyl ethyl ketone, n-propyl acetate, and isopropanol. The solvent is typically used in an amount of about up to about 15 wt-%, based on the total weight of the composition. The indicator composition can be applied to the substrate by a wide variety of techniques, including, for example, printing or coating by flexographic, gravure, screen, or die processes.

The substrate on which the indicator composition is disposed can be any of a wide variety. Typically, suitable substrates include polymeric materials, which may be pigmented or colorless, such as polyester, polyethylene, or polystyrene films, paper, and the like. Preferably, it is a Melinex™ polyester film from E. I. du Pont de Nemours and Company, Wilmington, DE. The substrate may be in the form of a strip of material (e.g., a strip of material having the dimensions 2 cms by 13 cm). Optionally, the composition can be coated as a stripe over the length of the substrate strip.The substrate may also have an adhesive on the surface opposite that on which the indicator composition is disposed. In this way, the indicator may be used as a tape or label for attachment to the article to be sterilized.

The vapor sterilization procedure used is conventional, and is disclosed in, for example U.S. Pat. Nos. 4,756,882, 4,643,876, 4,956,145, and 5,445,792, for example. Preferably, it is a plasma-based sterilization system.

In general, the article to be sterilized is placed in a sterilization chamber, and a dose of hydrogen peroxide, which generally comes pre-measured, is delivered to the chamber. Vapor is generated and allowed to fill the container for an appropriate length of time after which the sterilization is complete. The equipment and the entire procedure is generally controlled electronically. When sterilizing medical instruments, one cycle is often sufficient. The medical instruments are often packaged, with the entire package being placed into the sterilizing compartment. The package allows the hydrogen peroxide to penetrate and effect sterilization of the instruments, while subsequently protecting the instruments from contamination in air. The temperatures used in the process of the present invention are all generally less than 65°C.

The invention will be illustrated in greater detail by the following specific examples. It is understood that these examples are given by way of illustration and are not meant to limit the disclosure or the claims to follow. All percentages in the examples, and elsewhere in the specification, are by weight unless otherwise specified.

EXAMPLES

Example 1

Preparation of Indicator Compositions

Indicator compositions were prepared by mixing 70 grams of a shellac binder solution containing 60% weight percent of shellac in isopropanol (commercially available as 5 pound refined shellac in 99 percent isopropanol form Mantrose, Bradshaw and Zinsser Group, Westport, CT), 17.5 grams of dispersing resin (commercially available as Rhoplex I-545 from Rohm & Haas Corp., Philadelphia, PA), in 15 grams of isopropanol, with approximately 0.1 gram or a sufficient amount of colorant (0.1 wt-% to 5 wt-%) to give a good color of the colorants listed in Table 1. The indicator compositions were mixed in glass jars containing marbles. The glass jars were rolled for three hours on a roller mill.

Coating of Indicator Compositions

An indicator composition was coated on a plastic backing (commercially available as "3M Printable Polyester Film Label Stock" from Minnesota Mining and Manufacturing

Co., St. Paul, MN) using a number 16 Meyer bar (commercially available from R. D. Specialties, Webster, NY). The coated ink was dried at 50°C in an oven (commercially available as "Despatch Style V 29" from Despatch Oven Co., Minneapolis, MN) for 2 minutes. The coated film was cut using scissors to obtain indicators of approximately 2 cm by 13 cm.

Test Methods

One indicator composition was placed on an instrument tray lid and exposed to a full cycle of a hydrogen peroxide plasma sterilization procedure at 45-55°C in a STERRAD™ 100SI GMP Sterilizer, obtained from Advanced Sterilization Products Co., Irvine, CA. During the sterilization procedure a vacuum was drawn in the sterilization chamber for 5-6 minutes until the pressure was reduced to 40.0 Pa. A 1.8 ml aliquot of an aqueous solution of 58-60 percent hydrogen peroxide was then injected into the empty sterilization chamber over a period of about 6 minutes, yielding an empty chamber concentration of 6-7 mg/liter hydrogen peroxide. Hydrogen peroxide vapor was allowed to diffuse throughout the chamber for 44 minutes at 8×10^2 to 13.3×10^2 Pa. A vacuum was then drawn, reducing the pressure to 66.7 Pa and removing all detectable hydrogen peroxide vapor from the chamber. A plasma phase was then generated in the chamber by emitting an RF power source at 400 watts and 13.56 MHz for about 15-16 minutes at 66.7 Pa, after which the chamber was vented for 3-4 minutes until atmospheric pressure was reached in the chamber. After exposure to the sterilization procedure the indicators were removed from the tray lid and examined for color change. The results for each indicator composition are described in Table 1.

Some of the colorants were either the same color as they were initially or only slightly lighter, so another set of indicators were exposed to a higher concentration of hydrogen peroxide to determine if changing concentration would effect the results. A set of indicators were taped to a roll of film which was placed in a vented desiccator containing 80 ml of 30 weight percent (wt-%) hydrogen peroxide. The desiccator was placed in an oven (commercially available as "Despatch Style V 29" from Despatch Oven Co.) at 50°C for one hour. The indicators were removed from the desiccator and examined for color change. The results for each indicator composition are also described in Table 1.

Table 1
Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change when in Sterilizer	Color Change When in Desiccator (30% H_2O_2)
1	[1]Malachite green oxalate *(Basic green 4)*	Methane	4200	Blue/ green	Pale green	Pale green
2	[1]Crystal violet *(Gentian violet or Hexamethyl-pararosaniline chloride*	Methane	42555	Very Dark Blue	Slightly Lighter	Lighter
3	[1]Methyl violet 2B *(Basic violet 1)*	Methane	42535	Fuchsia	Lighter	Light lavender
4	[1]Ethyl violet *(Basic violet 4)*	Methane	42600	Blue	No Change	Lighter
5	[1]New fuchsin *(Basic violet 2 or Magenta III)*	Methane	42520	Purple	Slightly lighter	Light pink
6	[1]Victoria blue B *(Basic blue 26)*	Methane	44045	Royal blue	Lighter	Lighter
7	[1]Victoria pure blue BO *(Basic blue 7)*	Methane	42595	Blue	Slightly Lighter	Lighter
8	[1]Toluidine blue O *(BasicbBlue 17 or Tolonium chloride)*	Thiazine	52040	Pale blue	No Change	Colorless
9	[1]Luxol brilliant green BL *(Solvent green 11)*	Methane	None	Blue/ green	Pale green	Almost Colorless
10	[1]Disperse blue 1 *(Solvent blue 18 or Celliton blue extra)*	Anthraquinone	46500	Royal Blue	More gray	Dark gray blue
11	[1]Brilliant blue R *(Acid blue*	Methane	42660	Blue	No Change	Lighter

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Table 1
Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change when in Sterilizer	Color Change When in Desiccator (30% H_2O_2)
	83 or Coomassie brilliant blue R)					
12	[1]Victoria blue R *(Basic blue 11)*	Methane	44040	Royal blue	Slightly Lighter	Lighter
13	[1]Quinea green B *(Acid green 3)*	Methane	42085	Green	Pale green	Very pale green
14	[1]Thionine *(Lauth's violet)*	Thiazine	52000	Blue	No Change	Light gray
15	[1]Meldolas blue	Oxazine	51175	Dark lilac	Slightly Lighter	Pale beige
16	[1]Methylene green	Thiazine	52020	Light blue	None	Very Pale blue
17	[1]Lissamine green B *(Acid Green 50 or Wool Green S)*	Methane	44090	Blue (teal)	Slightly Lighter	Pale blue
18	[2]Alkali blue 6B *(Acid Blue 119)*	Methane	42765	Blue	Light grey blue	Light blue
19	[1]Brilliant Green *(Basic Green 1)*	Methane	42040	Green	Pale green	Colorless

[1]Commercialiy available from Sigma-Aldrich Fine Chemicals, St. Louis, MO.

[2] Commercially available from ICN Biomedicals, Costa Mesa, CA.

Colorants that showed good contrast between the initial color and the color after exposure to hydrogen peroxide vapor are Malachite green oxalate, Methyl violet 2B, New fuchsin, Quinea green B, Thionine, Meldolas blue, Lissamine green B, and Alkali blue 6B.

Another set of preferred colorants for chemical indicators become colorless after exposure in the STERRAD™ Sterilizer or to the more concentrated hydrogen peroxide in a

desiccator. Examples of these colorants include Toluidine blue O, Luxol brilliant green BL, and Brilliant green.

Example 2

Preparation of Indicator Compositions for Screening

A cellulose acetate butyrate binder was prepared by dissolving 15 grams of the cellulose acetate butyrate grade 553-0.4 resin (commercially available from Eastman Chemical Company, Kingsport, TN) in 100 milliliters of methyl ethyl ketone. Indicator compositions were prepared by dissolving a sufficient amount (approximately 0.1 gram or more 0.1 wt-% to 5 wt-% of the colorants listed in Table 2 to give a good color in 15 milliliters of the binder.

The resulting indicator composition was coated as described for Example 1. Each indicator composition was exposed to a full cycle of a hydrogen peroxide plasma sterilization procedure in a STERRAD™ 100SI GMP Sterilizer as described in Example 1. The results for each indicator composition are described in Table 2.

As in Example 1 some of the colorants were either the same color as they were initially or only slightly lighter, so another set of indicators were exposed to a higher concentration of hydrogen peroxide to determine if changing concentration would effect the results. The results for each indicator composition are also described in Table 2.

Table 2
Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change When in Sterilizer	Color Change when in Desiccator (30 % H_2O_2)
20	Spirit soluble HLK BASF			Green	No Change	Slightly Lighter
21	Victoria green S extra			Dark green	Almost Colorless	Very Pale green
22	[1]Acid violet 17	Methane	42650	Purple	No Change	Lighter
23	[1]Eriochrome black T	Monazo	14645	D Brown	Slightly Lighter	None

Table 2
Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change When in Sterilizer	Color Change when in Desiccator (30 % H_2O_2)
24	[1]Eriochrome blue black B	Monazo	14640	Dark lilac	Lighter	Very Pale beige
25	D & C green no. 2			Green/ blue	Pale green	Pale green
26	Spirit soluble fast RR			Purple	Slightly Lighter	No Change
27	Spirit soluble fast red 3B			Fuchsia	Slightly Lighter	Lighter
28	D & C red no. 22			Pink	No Change	Slightly Lighter
29	[1]Nitro red	Monazo	None	Lilac	Lighter	Lighter
30	[1]Congo red	Diazo	22120	Light red	Darker	Blue orange
31	[1]Brilliant cresyl blue ALD	Oxazine		Light blue	No Change	Lighter
32	[1]Arsenazo I	Monazo	None	Very pale pink	No Change	Lighter
33	[1]Basic red 29	Monazo	11460	Dark bold pink	No Change	Lighter
34	[1]Bismarck brown R	Diazo	21010	Brown/ gold	No Change	Significantly Lighter
35	Methylene violet			Light purple	Darker	Colorless
36	[1]Methylene violet 3RAX	Diazine	50206	Fuchsia	No Change	Light pink
37	[1]Mordant brown 1	Diazo	20110	Brown	Lighter	None
38	[1]Reactive black 5	Diazo	20505	Very pale lilac	No Change	Light gray blue
39	[1]Mordant brown 48	Monoazo	11300	Red/ brown	Slightly Lighter	Significantly Lighter
40	[2]Acid brown AX987			Lilac	Light blue	Light blue
41	[2]Acid violet AX990		41001	Dark lavender	Blue	Blue
42	[2]Basic red 15			Red/pink	Lighter	Pale pink
43	Mordant red			Beige	Lighter	Lighter

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Table 2
Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change When in Sterilizer	Color Change when in Desiccator (30 % H_2O_2)
	19					
44	[1]Bromopyrogallol red	Methane	None	Lilac	Pale beige	Colorless

[1]Commercially available from Sigma-Aldrich Fine Chemicals, St. Louis, MO.

[2]Commercially available from Spectra, Kearny, NJ.

[3] Commercially available from ICN Biomedicals, Costa Mesa, CA.

Colorants that showed good contrast between the initial color and the color after exposure to hydrogen peroxide vapor are Eriochrome blue black B, Congo red, Bismarck brown R, and Methylene violet 3RAX.

Another set of preferred colorants for chemical indicators become colorless after exposure in the STERRAD™ Sterilizer or to the more concentrated hydrogen peroxide in a desiccator. Examples of these colorants include Victoria green S extra, Methylene violet, and Bromopyrogallol red.

Comparative Examples

The colorants listed in Table 3A were used to make chemical indicators as described in Example 1. While the colorants listed in Table 3B were used to make chemical indicators as described in Example 2. Each indicator composition was exposed to a full cycle of a hydrogen peroxide plasma sterilization procedure in a STERRAD™ 100SI GMP Sterilizer as described in Example 1. The results for each indicator composition are described in Table 3A or 3B.

As in Example 1, some of the colorants were either the same color as they were initially or only slightly lighter. Thus, another set of indicators were exposed to a higher concentration of hydrogen peroxide to determine if changing concentration would effect

the results. The results for each indicator composition are also described in Table 3A or 3B.

Table 3A
Colorants for Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change in Sterilizer	Color Change in Desiccator (30 % H_2O_2)
1	[1]Brilliant blue G *(Acid Blue 90 or Coomassie Brilliant Blue G 250)*	Methane	42655	Blue	No Change	No Change
2	[1]Acid black 24	Diazo	26370	Grey	No Change	No Change
3	[2]Patent blue violet	Methane		Blue	No Change	No Change
4	[1]Disperse red 13 *(Celliton Scarlet B)*	Monoazo	11115	Purple	No Change	No Change
5	[1]Sudan black B	Diazo	26150	Blue/Black	No Change	No Change
6	[1]Janus green B	Monoazo	11050	Blue	No Change	No Change
7	[1]Acridine orange base *(Solvent Orange 15)*	Acridine	46005	Orange	No Change	No Change
8	[1]Fast green FCF *(Food Green 3)*	Methane	42053	Blue (teal)	No Change	No Change
9	[1]Patent blue VF *(Acid Blue 1)*	Methane	42045	Dark blue		No Change

[1]Commercially available from Sigma-Aldrich Fine Chemicals, St. Louis, MO.

[2] Commercially available from ICN Biomedicals, Costa Mesa, CA.

Table 3B Colorants for Indicator Compositions

Run No.	Colorant	Colorant Class	Color Index No.	Initial Color	Color Change in Sterilizer	Color Change in Desiccator (30 % H_2O_2)
10	[1]Acid red 97	Diazo	22890	Red/orange	No Change	No Change
11	[1]Sulforhodamine B	Xanthene	45100	Dark pink	No Change	No Change
12	Xylenol orange sodium salt			Light pink	No Change	No Change
13	Azure B			Pale blue	No Change	No Change
14	Spirit soluble fast yellow G			Yellow	No Change	No Change
15	[3]Keystone soap fluoro green			Blue/green	No Change	No Change
16	[3]Calco oil blue N		None	Blue	No Change	No Change
17	[3]Oil blue A			Light blue	No Change	No Change
18	[3]Calco oil green			Green	No Change	No Change
19	[3]D & C red no. 33	Monoazo	17200	Pink	No Change	No Change
20	[3]D & C green no. 5	Anthraquinone	61570	Pale blue	No Change	No Change
21	Bordeaux R			Light pink	No Change	No Change
22	[1]Xylenol cyanole FF	Methane	42135	Blue	No Change	No Change
23	Crystal scarlet			Light pink	No Change	No Change
24	Basic blue 41			Dark blue	No Change	No Change
25	[1]Evans blue	Diazo	23860	Blue	No Change	No Change
26	[1]Chicago sky blue	Diazo	24410	Blue	No Change	No Change

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Table 3B Colorants for Indicator Compositions

Run No.	Colorant 6B	Colorant Class	Color Index No.	Initial Color	Color Change in Sterilizer	Color Change in Desiccator (30 % H_2O_2)
27	[1]Acid blue 113	Diazo	26360	Blue	No Change	No Change
28	[1]Acid blue 120	Diazo	26400	Grey/blue	No Change	
29	Acid red 88			Dark pink	No Change	No Change
30	Acid red 151			Red/pink	No Change	No Change
31	[1]Acid violet 5	Monoazo	18125	Dark lavender	No Change	No Change
32	[1]Disperse red 1	Monoazo	11110	Red/orange	No Change	No Change
33	Direct red 81			Pale pink	No Change	No Change
34	[1]Disperse red 19	Monoazo	11130	Dark orange	No Change	No Change
35	[1]Sudan red 7B	Diazo	26050	Dark pink	No Change	No Change
36	[2]Basic red 73			Light red	No Change	No Change
37	[3]Acid green AX986			Lime green	No Change	No Change

[1]Commercially available from Sigma-Aldrich Fine Chemicals, St. Louis, MO.

[2]Commercially available from Spectra, Kearny, NJ.

[3] Commercially available from ICN Biomedicals, Costa Mesa, CA.

Example 4

A preferred composition was prepared as described in Example 1 using the components and the amounts given in Table 4. The resulting indicator composition was coated as described for Example 1. Each indicator composition was exposed to a full cycle of a hydrogen peroxide plasma sterilization procedure in a STERRAD™ 100SI GMP Sterilizer as described in Example 1.

Table 4	
Indicator Composition	Weight Percent
Shellac Binder	70.2
Rhoplex I-545 Water based Acrylic Polymer Resin	23.0
Alkali Blue 6B	00.6
Quinacridone red 19 available as Sunfast Red 19	00.3
Triethanolamine	02.0
Isopropanol	03.9

Colorants that become colorless after exposure in the STERRAD™ Sterilizer or to the more concentrated hydrogen peroxide in a desiccator can be used in combination with dyes or pigments which are stable to hydrogen peroxide to give a chemical indicator with a suitable contrasting color change. For example, Alkali blue 6B plus a red unreactive dye such as Quinacridone red 19 (commercially available as Sunfast Red 19 from Sun Chemical Corporation, Cincinnati, OH) showed a color change from blue (initial) to pink after exposure in the STERRAD™ Sterilizer. Another example was made by combining Brilliant green and Auramine O (commercially available from Sigma Aldrich Fine Chemicals, St. Louis, MO) which showed a color change from bright green (initial) to bright yellow after exposure in the STERRAD™ Sterilizer.

The complete disclosures of the patents, patent documents, and publications cited herein are incorporated by reference in their entirety as if each were individually incorporated. Various modifications and alterations to this invention will become apparent to those skilled in the art without departing from the scope and spirit of this invention. It should be understood that this invention is not intended to be unduly limited by the illustrative embodiments and examples set forth herein and that such examples and embodiments are presented by way of example only with the scope of the invention intended to be limited only by the claims set forth herein as follows.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference to any prior art in this specification is not, and should not be taken as, an acknowledgment or any form of suggestion that that prior art forms part of the common general knowledge in Australia.

The claims defining the invention are as follows:

1. A hydrogen peroxide sterilization indicator comprising a substrate and an indicator composition disposed thereon, wherein the indicator composition comprises at least one colorant that changes color as a result of contact with hydrogen peroxide selected from the group consisting of Ethyl violet, New fuchsin, Victoria blue B, Victoria pure blue BO, Toluidine blue 0, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Meldolas blue, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Erichrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red 19, Bromopyrogallol red, and combination thereof.

2. A hydrogen peroxide sterilization indicator comprising a substrate and an indicator composition disposed thereon, wherein the indicator composition comprises a binder, at lease one colorant that changes colour as a result of contact with hydrogen peroxide selected from the group consisting of Ethyl violet, New fuchsin, Victoria blue B, Victoria pure blue BO, Toluidine blue 0, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Meldolas blue, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red 19, Bromopyrogallol red, and combinations thereof, and at least one colorant that does not change upon contact with hydrogen peroxide vapor.

3. A method of monitoring a hydrogen peroxide sterilization process, the method comprising exposing an article to be sterilized and the hydrogen peroxide indicator of claim 2 to hydrogen peroxide vapor.

4. The indicator of claim 2 or the method of claim 3, wherein the binder is shellac.

5. The indicator or method of any of the preceding claims, wherein the colorant that changes colour as a result of contact with hydrogen peroxide is selected from the group consisting of New fuchsin, Quinea green B, Meldolas blue, Lissamine green B, Alkali blue 6B, Congo red, Eriochrome blue black B, Bismarck brown R, Methylene violet 3RAX, and combinations thereof.

6. The indicator or method of any of claims 1-4, wherein the colorant that changes colour as a result of contact with hydrogen peroxide is selected from the group consisting of Toluidine blue 0, Luxol brilliant green BL, Victoria green S extra, Methylene violet, Bromopyrogallol red, Brilliant green, and combinations thereof.

7. A method of monitoring a hydrogen peroxide sterilization process, the method comprising exposing an article to be sterilized and a hydrogen peroxide sterilization indicator to a sterilant vapor consisting essentially of hydrogen peroxide, wherein the hydrogen peroxide sterilization indicator comprises a substrate and an indicator composition disposed thereon, wherein the indicator composition comprises at least one colorant that changes colour as a result of contact with hydrogen peroxide selected from the group consisting of Malachite green oxalate, Crystal violet, Methyl violet 2B, Ethyl violet, New fuchsin, Victoria blue B, Victoria pure blue BO, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Thionine, Meldolas blue, Methylene green, Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D & C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29,

Bismarck brown R, Methylene violet, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red 19, Bromopyrogallol red, and combinations thereof.

8. The indicator or method of any of claims 1, 3-5 and 7, wherein the indicator composition further comprises at least one colorant that does not change colour upon contact with hydrogen peroxide vapor.

9. The indicator or method of claim 7, wherein the colorant that does not change colour upon contact with hydrogen peroxide vapor is selected from the group consisting of Quinacridone red 19, Auramine 0, Brilliant blue G, Acid black 24, Patent blue violet, Disperse red 13, Sudan black B, Janus green B, Acridine orange base, Fast green FCF, Patent blue VF, Acid red 97, Sulforhodamine B, Xylenol orange sodium salt, Azure B, Spirit soluble fast yellow G, Keystone soap fluoro green, Calco oil blue N, Oil blue A, Calco oil green, D & C red no. 33, D & C green no. 5, Bordeaux R, Xylenol cyanole FF, Crystal scarlet, Basic blue 41, Evans blue, Chicago sky blue 6B, Acid blue 113, Acid blue 120, Acid red 88, Acid red 5, Acid red 151, Acid violet 5, Disperse red 1, Direct red 81, Disperse red 19, Sudan red 7B, Basic red 73, Acid green AX986, and combinations thereof.

10. A hydrogen peroxide sterilization indicator comprising a substrate and an indicator composition disposed thereon, wherein the indicator composition consists essentially of a binder, an optional colorant that does not change colour upon contact with hydrogen peroxide, an optional dispersing agent, an optional opacifying agent, an optional surfactant, an optional plasticizer, an optional antifoam agent, an optional basic material, and at least one colorant that changes colour as a result of contact with hydrogen peroxide selected from the group consisting of Malachite green oxalate, Ethyl violet, New fuchsin, Victoria blue B, Victoria pure blue BO, Toluidine blue O, Luxol brilliant green BL, Disperse blue 1, Brilliant blue R, Victoria blue R, Quinea green B, Thionine, Meldolas blue,

Lissamine green B, Alkali blue 6B, Brilliant green, Spirit soluble HLK BASF, Victoria green S extra, Acid violet 17, Eriochrome black T, Eriochrome blue black B, D & C green no. 2, Spirit soluble fast RR, Spirit soluble fast red 3B, D, C red no. 22, Nitro red, Congo red, Brilliant cresyl blue ALD, Arsenazo 1, Basic red 29, Bismarck brown R, Methylene violet, Methylene violet 3RAX, Mordant brown 1, Reactive black 5, Mordant brown 48, Acid brown AX987, Acid violet AX990, Basic red 15, Mordant red 19, Bromopyrogallol red, and combinations thereof.

11. The indicator or method of any of the preceding claims, wherein the substrate is a polyester film.

12. Hydrogen peroxide sterilization indicators comprising a substrate and an indicator composition disposed thereon and/or uses thereof substantially as herein described with reference to the Examples (excluding the Comparative Examples).

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3M INNOVATIVE PROPERTIES COMPANY
by its Patent Attorneys
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