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(54) Title: TIME/TEMPERATURE INDICATORS, THEIR PREPARATION AND USE

(57) Abstract: A time/temperature indicator comprises a dye which undergoes a colour change, for example is bleached, in the presence of a base, in association with a photolabile base.



WO 2006/091465 A1

**TIME/TEMPERATURE INDICATORS, THEIR PREPARATION AND USE**

5           The present invention relates to a novel time/temperature indicator comprising an activated leuco dye or similar dye which undergoes a colour change in the presence of a base, for example can be bleached by a base, in association with a photolabile base.

Many packaged goods, notably foodstuffs and medicines, have a limited shelf life, and such goods commonly have a "use by" date printed on packaging associated  
10 with the goods. However, this is, at best, only a crude indication, as the rate at which such goods deteriorate is a function of the temperature at which they are kept as well as the length of time for which they are kept. Moreover, the temperature may vary considerably during the life of the goods. For example, a product may be bought from a shop, where it is kept in a refrigerator, carried through a sunny car park, where its  
15 temperature rises, stored in a car, where its temperature rises further, and finally stored in a domestic refrigerator, where its temperature is lowered, but may still go up and down as the refrigerator door is opened and closed.

It would, therefore, be desirable to provide an indicator on packaging associated with the goods which will react to changing temperatures over time in the same way as  
20 do the goods themselves. These are referred to as "time/temperature indicators". A number of proposals have been made for such time/temperature indicators. For example, 3M's MonitorMark (trade mark) uses the principle of diffusion along a wick to provide a time/temperature indicator. VITSAB's Time/Temperature Indicator is based on the colour change caused by the controlled enzymatic hydrolysis of a lipid  
25 substrate. Lifelines Inc.'s FreshCheck (trade mark) is based on a polymerisation reaction leading to a coloured polymer, and is suggested for use, *inter alia*, with foodstuffs.

Although all of these are successful in their fields, they are all relatively expensive and add significantly to the cost of the products to which they are applied. They cannot, therefore, be used in practice with lost cost, low margin items, particularly everyday foodstuffs.

5           To meet this requirement, it would be desirable to provide a time/temperature indicator that makes use of relatively cheap components and which can be applied easily, for example by printing at the time that the packaging is printed. Moreover, if the time/temperature indicator is applied to the packaging before the perishable product is packed in it, it is desirable that the indicator should be inactive until a time close to  
10           the time of packaging and then should be activated so that its response closely parallels that of the perishable product.

US Patent No. 4,917,503 discloses a time/temperature indicator which comprises a thermally inactive compound comprising a leuco base and a photosensitive compound that, on exposure to actinic radiation (e.g. ultraviolet), forms an acid that  
15           oxidises the colourless leuco base to a coloured leuco dye at a rate determined by the reaction temperature. The photosensitive compounds suggested for use in this patent include o-nitrobenzaldehyde and derivatives thereof and trihaloalcohols. However, the use of o-nitrobenzaldehyde is restricted in Europe and there are indications that it may be mutagenic. Moreover, certain of the trihaloalcohols are used as anaesthetics. The  
20           compounds proposed also tend to be malodorous. Furthermore, the products of irradiation of these compounds are generally recognised to be harmful to health. For these reasons, it is difficult to use the time/temperature indicator of US Patent No. 4,917,503 in practice in association with foodstuffs or other perishable materials that may be ingested by humans.

25           We have now discovered that the problems with the prior art may be overcome by the use of a dye which undergoes a colour change in the presence of a base, in association with a photolabile base.

Thus, the present invention consists in a time/temperature indicator, comprising a dye which undergoes a colour change in the presence of a base, in association with a photolabile base.

Preferably, the dye is one which can be bleached by a base. However, it is also possible to use a dye which simply changes from one colour to another in the presence of a base. One preferred class of dyes which may be used in the present invention is the class of activated leuco dyes. Leuco dyes are generally synthetic organic colourless powders which, upon oxidation/acidification (collectively referred to herein as "activation") become coloured. More details of such dyes may be found in "Chemistry and Applications of Leuco Dyes", edited by R Muthyala, published in 1997 by Plenum Publishing Corporation, the disclosure of which is incorporated herein by reference.

Examples of leuco dyes which may be used in the present invention include the activated forms of known leuco dyes such as triphenylmethane compounds, fluoran compounds, phenothiazine compounds, auramine compounds, spiropyran compounds, indolinophthalide and the like. These leuco dyes may be used alone or in combination. Specific examples of such leuco dyes include the activated forms of the following compounds:

3,3-bis(p-dimethylaminophenyl)phthalide, 3,3-bis(p-dimethylaminophenyl)-6-dimethylaminophthalide (i.e., crystal violet lactone), 3,3-bis(p-dimethylaminophenyl)-6-diethylaminophthalide, 3,3-bis(p-dimethylaminophenyl)-6-chlorophthalide, 3,3-bis(p-dibutylaminophenyl)phthalide, 3-cyclohexylamino-6-chlorofluoran, 3-dimethylamino-5,7-dimethylfluoran, 3-diethylamino-7-chlorofluoran, 3-diethylamino-7-methylfluoran, 3-diethylamino-7,8-benzfluoran, 3-diethylamino-6-methyl-7-chlorofluoran, 3-(N-p-tolyl-N-ethylamino)-6-methyl-7-anilinofluoran, 3-pyrrolidino-6-methyl-7-anilinofluoran, 2-[N-(3-trifluoromethylphenyl)amino]-6-diethylaminofluoran, 2-[3,6-bis(diethylamino)-9-o-chloroanilino]xanthylbenzoic acid lactam, 3-diethylamino-6-methyl-7-(m-trichloromethylanilino)fluoran, 3-diethylamino-7-(o-chloroanilino)fluoran, 3-di-n-butylamino-7-(o-chloroanilino)fluoran, 3-N-methyl-N-n-amyloamino-6-methyl-7-anilinofluoran, 3-N-methyl-N-cyclohexylamino-6-methyl-7-anilinofluoran, 3-

diethylamino-6-methyl-7-anilinofluoran, 3-(N,N-diethylamino)-5-methyl-7-(N,N-dibenzylamino) fluoran, 24-benzoyl leuco methylene blue, 6'-chloro-8'-methoxybenzoindolinospiropyran, 6'-bromo-3'-methoxybenzoindolinospiropyran, 3(2'-hydroxy-4'-dimethylaminophenyl)-3-(2'-methoxy-5'-chlorophenyl)phthalide, 3-(2'-hydroxy-4'-dimethylaminophenyl)-3-(2'-methoxy-5'-nitrophenyl)phthalide, 3-(2'-hydroxy-4'-diethylaminophenyl)-3-(2'-methoxy-5'-methylphenyl)phthalide, 3-(2'-methoxy-4'-dimethylaminophenyl)-3-(2'-hydroxy-5'-chloro-5'-methylphenyl)phthalide, 3-(N-ethyl-N-tetrahydrofurfuryl)amino-6-methyl-7-anilinofluoran, 3-N-ethyl-N-(2-ethoxypropyl)amino-6-methyl-7-anilinofluoran, 3-N-methyl-N-isobutyl-6-methyl-7-anilinofluoran, 3-morpholino-7-(N-propyl-trifluoromethylanilino)fluoran, 3-pyrrolidino-7-m-trifluoromethylanilinofluoran, 3-diethylamino-5-chloro-7-(N-benzyl-trifluoromethylanilino)fluoran, 3-pyrrolidino-7-(di-p-chlorophenyl)methylaminofluoran, 3-diethylamino-5-chloro-7- $\alpha$ -phenylethyl amino)fluoran, 3-(N-ethyl-p-toluidino)-7- $\alpha$ -phenylethylamino)fluoran, 3-diethylamino-7-(o-methoxycarbonylphenylamino)fluoran, 3-diethylamino-5-methyl-7-( $\alpha$ -phenylethylamino)fluoran, 3-diethylamino-7-piperidinofluoran, 2-chloro-3-(N-methyltoluidino)-7-(p-n-butylanilino)fluoran, 3-(N-methyl-N-isopropylamino)-6-methyl-7-anilinofluoran, 3-di-n-butylamino-6-methyl-7-anilinofluoran, 3,6-bis(dimethylamino)fluorenespiro(9,3')-6'-dimethylaminophthalide, 3-(N-benzyl-N-cyclohexylamino)-5,6-benzo-7- $\alpha$ -naphthylamino-4'-bromofluoran, 3-diethylamino-6-chloro-7-anilinofluoran, 3-diethylamino-6-methyl-7-mesidino-4',5'-benzofluoran, 3-N-methyl-N-isopropyl-6-methyl-7-anilinofluoran, 3-N-ethyl-N-isoamyl-6-methyl-7-anilinofluoran, 3-diethylamino-6-methyl-7-(2',4'-dimethylanilino)fluoran, and the like.

The more preferred leuco dyes for use in the present invention include the activated forms of carbazolyl blue, indolyl red, leuco crystal violet, leuco malachite green, bis (p-dimethylaminophenyl)(9-ethylcarbazol-3-yl) methane, bisarylcarbazolylmethane, 3,3-bis(1-N-octyl-2-methyl-indol-3-yl) phthalide, 3-(N,N-diethylamino)-7-(N,N-dibenzylamino) fluoran and crystal violet lactone. A single such dye, or a mixture of any two or more such dyes, may be used.

Another class of dyes which may be used are the vat dyes. Vat dyes are a class of water insoluble dyes, such as indigo and anthraquinone derivatives. These dyes in their reduced and water soluble form, reduced by a base, are colourless or different from their original colour, whilst when oxidised, which may be by an acid, they return to their original colour and their insoluble form. Examples are Vat Blue 3, Blue 5, Vat Green 1, Methylene Violet 3RAX, Light green SF Yellowish, Leuco xylene cyanole FF and Nile Blue A. Vat dyes are especially fast to light and produce brilliant colours with high lightfastness.

A further class of dyes which may be used comprises pH indicators which change colour on going from a neutral or acidic environment to a basic one. Examples of such compounds include: methyl violet, crystal violet, ethyl violet, ethyl orange, malachite green, methyl green, cresol red, thymol blue, bromophenol blue, bromophenol red, Congo red, methyl orange, resorcin blue, alizarin red, methyl red, litmus, bromocresol purple, chlorophenol red, bromothymol blue, phenol red, neutral red, tumeric curcumin, phenolphthalein, thymolphthalein, alizarin yellow R, alizarin yellow GG, clayton yellow, methyl yellow, tropaeolin O sodium salt, bromoxylene blue, bromochlorophenol blue, brilliant green, metanil yellow, benzyl orange, Tashiro's indicator solution, quinaldine red, tetrabromophenol blue,  $\alpha$ -naphthyl red hydrochloride, brilliant yellow, phenol violet, thymol violet, tropaeolin, ethyl orange sodium salt, turmeric, *p*-xylenol blue, bromocresol green sulphone, bromophenol blue sodium salt, *m*-cresol purple sodium salt, *m*-cresolsulphonaphthalein sodium salt, quercetin dihydrate, *o*-cresolphthalein,  $\alpha$ -naphtholphthalein, 2-nitrophenol, 4-nitrophenol, 3-nitrophenol, *p*-rosolic acid, and thymolphthalein.

A single such dye, or a mixture of any two or more such dyes, may be used.

A photolabile base (sometimes called a "photobase generator") is a compound which, in its normal state, is essentially neutral, but which, upon irradiation with ultraviolet light, generates a basic compound. In general, these include classes of compounds such as carbamates, O-acyloximes, O-carbamoyloximes, formamide, amineimide and onium salts. Specific examples of such photolabile bases include:

Quaternary ammonium salts, such as 1-phenacyl-(1-azonia-4-azabicyclo[2,2,2]-octane)bromide; 1,4-dimethyl-1-phenacyl-(1-azonia-4-azabicyclohexane) bromide; and 1-naphthoymethyl-1-phenacyl-(1-azonia-4-azabicyclo[2,2,2]octane)bromide;

Carbamates, such as 1-phenacyl-(1-azonia-4-azabicyclo[2,2,2]octane)-N,N-  
5 dimethylthiocarbamate; 1-methyl-1-phenacyl-(1-azoniacyclohexane)-N,N-  
dimethyldithiocarbamate; 1,4-dimethyl-1-phenacyl-(1-azoniacyclohexane)-N,N-  
dimethyldithiocarbamate; and 1-naphthoymethyl-(1-azonia-4-azabicyclo[2,2,2]octane-  
N,N-dimethyldithiocarbamate;

Amineimides, such as 1,1-dimethyl-1-(2-hydroxy-3-phenoxypropyl)amine-p-  
10 nitrobenzimid, 1,1-dimethyl-1-(2-hydroxy-3-phenoxypropyl)amine-p-cyanobenzimid;  
and 1,1-dimethyl-1-(2-hydroxy-3-phenoxypropyl)amine benzimid.

N-substituted 4-(o-nitrophenyl)dihydropyridines, optionally substituted with  
alkyl ether and/or alkyl ester groups, such as N-methyl nifedipine (Macromolecules  
1998, 31, 4798), N-butyl nifedipine, N-butyl 2,6-dimethyl-4-(2-nitrophenyl) 1,4-  
15 dihydropyridine 3,5-dicarboxylic acid diethyl ester, and N-methyl 2,6-dimethyl 4-(4,5-  
dimethoxy-2-nitrophenyl)-1,4-dihydropyridine 3,5-dicarboxylic acid diethyl ester;

Quaternary organo-boron photoinitiators such as those disclosed in GB-A-2 307  
473, the disclosure of which is incorporated herein by reference;

$\alpha$ -Aminoacetophenones, such as 4-(methylthiobenzoyl)-1-methyl-1-  
20 morpholinoethane (IrgacureR 907 ex Ciba Specialty Chemicals) and (4-  
morpholinobenzoyl)-1-benzyl-1-dimethylaminopropane (IrgacureR 369 ex Ciba  
Specialty Chemicals); and

The  $\alpha$ -ammonium ketones, iminium ketones or amidinium ketones in the form  
of their tetraaryl- or triarylalkylborate salts as disclosed in US 6,551,761 B1, the  
25 disclosure of which is incorporated herein by reference.

The amounts of dye and photolabile base in the time/temperature indicator  
composition of the present invention may vary depending on the required properties.

However, in general, we prefer to employ from 0.01 to 10.0% by weight, more preferably from 1.0 to 3.0% by weight, of the leuco dye and from 0.01 to 10.0% by weight, more preferably from 0.05 to 2.0% by weight, of the photolabile base, based on the weight of the whole composition. However, these amounts are not critical to the invention and amounts outside these ranges may be used, if desired. In particular, for a greater intensity of coloration, higher amounts may be used.

The dye and the photolabile base may be employed in a single composition and printed to form a single layer on a substrate, or they may each be used as a separate composition and printed to form two layers, one on top of the other, on the substrate.

In addition to the dye and the photolabile base, the composition may contain other components to render the composition printable. Such other components may include, for example, resins, solvents and binders [such as polyvinyl butyral (PVB), nitrocellulose, polyurethanes (PU), polyesters, cellulose acetate propionate (CAP), polyacrylates, polyamides and polyvinyl alcohol].

The compositions may be printed using many conventional printing techniques, of which the flexographic and gravure printing techniques are preferred. The compositions of the present invention will, of course, be formulated in accordance with the specific requirements of the printing technique used, as is well known in the art.

There is no restriction on the nature of the substrate on which the composition of the present invention is printed. Examples include paper, cardboard, cellophane and various plastics films. Any plastic materials commonly used in the industry, especially for food wrapping, may be used as the plastics film. Examples of such materials include synthetic and semi-synthetic organic polymers, such as cellulose acetate, cellulose acetate butyrate (CAB), cellophane, polyvinyl chloride (PVC), polyvinyl fluoride, polyvinylidene chloride (PVDC), polyethylene, polypropylene (PP), polyamides, polyesters, polyphenylene oxide, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polymethyl methacrylate, poly(methyl pentene (TPX), polyvinyl acetal, polystyrene, acrylonitrile-butadiene-styrene (ABS), acrylonitrile-styrene-acrylate (ASA), polycarbonate, polystyrene, polyether sulphone,



polyether ketones, polyimides, and copolymers and/or mixtures thereof. If desired, films made from any of these polymers may be coated with coating materials well known in the art, and/or may be laminated to a film or films made of the same or different polymers. Further examples of such plastic materials may be found in  
5 standard reference texts, such as "Plastic Films", 3<sup>rd</sup> Edition, by J. H. Briston, published by Longman Group in 1989.

The time/temperature indicator composition may be activated by exposure to UV radiation or similar energising radiation, including electron beam. The nature and amount of radiation used is similar to that used for the photoinitiation of UV-curable  
10 printing inks and is well known to those skilled in the art. The dye and photolabile base are, of course, preferably inert with respect to each other until activation.

The invention is further illustrated by the following non-limiting Examples. The ketonic resin used in the Examples was a neutral, unsaponifiable, hydrogenated ketonic resin supplied by Huls as Synthetic Resin SK.

15 **EXAMPLE 1**

(a) Pergascript Black I-2R\* (3-dibutylamino-6-methyl-7-anilino-2-fluoranthrene, a leuco dye, supplied by CIBA Speciality Chemicals) (0.5 g) was dissolved in a solution of ketonic resin in ethyl acetate at ratio of 40:60 (5 g), by gentle heating and stirring over a magnetic stirrer. The resulting clear and colourless solution was left to cool down and  
20 to this, a solution of 5% citric acid in isopropyl alcohol was added slowly until the colour of the solution turned dark green-black.

(b) Benzyl carbamate (0.1 g), a photolabile base generating material Supplied by Aldrich, was dissolved in a solution of ketonic resin in ethyl acetate at ratio of 40:60 (10 g), by gentle heating and stirring over a magnetic stirrer to give a clear colourless  
25 solution.

(c) Solution (a) was coated on a LENETA (N2A) chart using a No. 1 K Bar and left to dry. This produced a dark green image.

- (d) Solution (b) was coated over the print (c) using a No. 1 K Bar and left to dry. The colour of the print still remained dark green.
- (e) Print (d) was irradiated using a UV rig running at 15m/minute. The dark green colour instantly faded to a greyish colour.
- 5 (f) Print (e) was placed under different temperature conditions of 0°C, 27° and 50°C. After 2 days, only the print at 50°C started to fade further.

### **EXAMPLE 2**

- (g) Pergascript Black I-2R solution was prepared according to Example 1(a).
- (h) Benzyl carbamate was prepared according to Example 1(b).
- 10 (i) Solution (h) was coated on a LENETA (N2A) chart using a No. 1 K Bar and left to dry. This produced a clear and colourless print.
- (j) Solution (g) was coated over the print (i) using a No. 1 K Bar and left to dry. The colour of the print still remained dark green.
- (k) The print (j) was irradiated using a UV rig running at 15m/minute. The dark  
15 green colour instantly faded to a greyish colour.
- (l) Print (k) was placed under different temperature conditions of 0°C, 27° and 50°C. After 2 days, only the print at 50°C started to fade further.

### **EXAMPLES 3 TO 9**

- Using the procedure described in Example 1, coating mixes were prepared by  
20 blending together a leuco dye and a photolent base generating material. The coating mixes were coated on LENETA (N2A) charts using a No. 1 K Bar, according to Example 1. All prints were irradiated using a UV rig running at 15m/minute. The examples and results are illustrated in Table 1.

**Table 1**

Examples	Leuco Dye	Photol latent	Colour prior to UV irradiation	Colour after UV irradiation
3A	1	A	Green	Light grey
3B	2	A	Green	Light grey
3C	3	A	Dark Green	Light green
3D	4	A	Green	Green/beige
3E	5	A	Pink	Pink/beige
4A	1	B	Green	Light beige
4B	2	B	Green	Light beige
4C	3	B	Dark Green	Light green
4D	4	B	Green	Green/beige
4E	5	B	Light pink	Beige
5A	1	C	Green	Light beige
5B	2	C	Green	Light beige
5C	3	C	Dark Green	Light green
5D	4	C	Green	Green/beige
5E	5	C	Pink	Pink/beige
6A	1	D	Green	Light beige

6B	2	D	Green	Light beige
6C	3	D	Dark Green	Light green
7A	1	E	Green	Light beige
7B	2	E	Green	Light beige
7C	3	E	Dark Green	Light green
8A	1	F	Green	Light beige
8B	2	F	Green	Light beige
8C	3	F	Dark Green	Light green
9A	1	G	Green	Light beige
9B	2	G	Green	Light beige
9C	3	G	Dark Green	Light green

**EXAMPLE 10****Preparation of 1-phenyl- (1-azonia-4-azabicyclo [2,2,2]-octane) N,N-dimethyl-dithiocarbonate, photolabile base material**

- 5           A sample of the title compound was synthesised according to the reference in "J. Polymer Science; part A; Polymer Chemistry; Vol. 39, 1329-1441 (2001).

**EXAMPLE 11**

- 10           Using the procedure described in Example 1, coating mixes were prepared by blending together an oxidised leuco dye and the photolabile base generating material prepared as described in Example 10 or a sample of the photolabile base CGI277

supplied by CIBA. The coating mixes were coated on LENETA (N2A) charts using a No. 1 K Bar, according to Example 1. All prints were irradiated using a UV rig running at 15m/minute. The examples and results are illustrated in Table 2.

**Table 2**

Example	Leuco Dye	Photoinitiator	Start Colour after irradiation	Colour after prolonged time and temperature
1	4+6	Example 10	Light green	Light beige
2	4+6	CGI277	Green	Light beige

5

**EXAMPLES 12-14**

Using the procedure described in Example 1, coating mixes were prepared by blending together the photolabile base CGI277 supplied by CIBA and a number of dyes.

- 10 The selected dyes (0.3g) were dissolved in a solvent mixture of propylene carbonate (PC) and isopropyl alcohol (IPA) (5g). To enhance the solubility of the dyes, a few drops of water were added to the solvent mix. The dye solutions were added to a solution of cellulose acetate propionate (CAP) resin in ethyl acetate at a ratio of 40:60 (20 g). The dye/resin mixes were coated on LENETA (N2A) charts using a No. 2 K
- 15 Bar, according to Example 1. All prints were irradiated using a UV rig running at 15m/minute. The examples and results are illustrated in Table 3.

**Table 3**

Example	Dye	Photoinitiator	Start Colour after irradiation	Colour after prolonged time and temperature
12	7	CGI277	Purple	Pink

13

13	8	CGI277	Dark green	Green
14	9	CGI277	Dark purple	Pink

The leuco dyes used in the above Examples were:

- 1 Black N102 (2-Anilino-6-diethylamino-3-methylfluoran, supplied by Yamamoto)
- 5 2 ODB-2 (2-Anilino-6-dibutylamino-3-methylfluoran, supplied by Yamamoto)
- 3 ODB-7 [6-Diethylamino-3-methyl-2-(3-toluidino) fluoride, supplied by Yamamoto]
- 4 Pergascript Black- 2IR (Diaminofluoran), supplied by Ciba Speciality Chemicals
- 10 5 Pergascript Red I-6B\* (Bisindolyl phthalide compound), supplied by Ciba Speciality
- 6 Pergascript Blue SRB (Bisarylcarbazolylmethane compound), supplied by Ciba Speciality Chemicals
- 7 Eriochrom Black T
- 15 8 Brilliant Green
- 9 Nile Blue A

The photolatents used were:

- A 4-Methoxybenzyloxycarbonyl azide (supplied by Aldrich)
  - 20 B 1-Benzylimidazole (supplied by Aldrich)
- DOCSNY.182727.1

- C Benzyl-4-oxo-1-piperidinecarboxylate (supplied by Aldrich)
- D 1- Fluorenylmethoxycarbonyl-4-piperidone (supplied by Aldrich)
- E Benzyloxycarbonyl-Glycinamide (supplied by Aldrich)
- F N-(Benzyloxycarbonyl)-1-H-pyrazole-1-carboxamidine (supplied by Aldrich)
- 5 G N-(Benzyloxycarbonyl)-2-aminoacetonitrile (supplied by Aldrich)
- H Benzyl carbamate (supplied by Aldrich)
- I CGI277 supplied by CIBA

#### **EXAMPLE 15**

Coating mixes were prepared by blending together an oxidised leuco dye and the  
10 photolent base CGI277 supplied by Ciba, a photolent base generating material. The  
oxidised dye was prepared from Pergascript Black I-2R\* (3-dibutylamino-6-methyl-7-  
anilino-fluoran, a leuco dye, (0.5 g), which was dissolved in a solution of ketonic resin in  
ethyl acetate at ratio of 40:60 (5 g), by gentle heating and stirring over a magnetic  
stirrer. The resulting clear and colourless solution was left to cool down and to this, a  
15 solution of 5% citric acid in isopropyl alcohol was added slowly until the colour of the  
solution turned dark green-black. The leuco dye solution was then blended with a 2%  
solution of the photolent base CGI277 in propylene carbonate (PC) and isopropyl  
alcohol (IPA). The coating mixes were coated on LENETA (N2A) charts using a No. 2  
K Bar, according to Example 1. All prints were irradiated using a UV rig running at  
20 15m/minute. The dark green colour on irradiation turned to greyish colour, which over  
period of time turned to lighter grey colour.

**CLAIMS:**

1. A time/temperature indicator, comprising a dye which undergoes a colour change in the presence of a base, in association with a photolabile base.
2. A time/temperature indicator according to Claim 1, in which said dye is an activated leuco dye.
3. A time/temperature indicator according to Claim 2, in which the activated leuco dye is the activated form of carbazoyl blue, indolyl red, leuco crystal violet, leuco malachite green, bis (p-dimethylaminophenyl)(9-ethylcarbazol-3-yl)methane, bisarylcarbazolylmethane, 3,3-bis(1-N-octyl-2-methyl-indol-3-yl)phthalide, 3-(N,N-diethylamino)-7-(N,N-dibenzylamino)fluoran or crystal violet lactone.
4. A time/temperature indicator according to Claim 1, in which said dye is a vat dye.
5. A time/temperature indicator according to Claim 4, in which said vat dye is Vat Blue 3, Blue 5, Vat Green 1, Methylene Violet 3RAX, Light green SF Yellowish, Leuco xylene cyanole FF or Nile Blue A.
6. A time/temperature indicator according to any one of the preceding Claims, in which the photolabile base is a quaternary ammonium salt, a carbamate, an O-acyloxime, an O-carbamoyloxime, a formamide, an amineimide or an onium salt.
7. A time/temperature indicator according to any one of the preceding Claims, in which the photolabile base is 4-methoxybenzyloxycarbonyl azide, 1-benzylimidazole, benzyl-4-oxo-1-piperidinecarboxylate, fluorenylmethoxycarbonyl-4-piperidone, N-(benzyloxycarbonyl)glycinamide, N-(benzyloxycarbonyl)-1-H-pyrazole-1-carboxamidine, or N-(benzyloxycarbonyl)-2-aminoacetonitrile.
8. A time/temperature indicator according to any one of the preceding Claims, in which the dye and the photolabile base are employed as a mixture.
9. A time/temperature indicator according to Claim 8, in which the mixture also comprises a resin.



10. A time/temperature indicator according to Claim 9, in which the dye and the photolabile base are suspended in the resin.
11. A time/temperature indicator according to any one of the preceding Claims, in which the dye and the photolabile base are printed on a substrate.
12. A packaged perishable product where the packaging bears a time/temperature indicator according to any one of the preceding Claims.
13. A product according to Claim 12, in which the perishable product is a food.
14. A product according to Claim 12, in which the perishable product is a drug.
15. A method of activating a time/temperature indicator in which a product according to any one of Claims 12 to 14 is exposed to ultraviolet radiation sufficient to convert said photolabile base to a base form.

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/005445

## A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N31/22

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)  
G01N

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, 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	US 4 917 503 A (BHATTACHARJEE ET AL) 17 April 1990 (1990-04-17) column 1, line 50 - column 2, line 20 column 2, line 51 - column 3, line 12 column 5, line 65	1-6,8-15
X	GB 1 506 401 A (BIO MEDICAL SCIENCES INC) 5 April 1978 (1978-04-05) pages 2-3 claim 1	1,6
X	US 4 737 463 A (BHATTACHARJEE ET AL) 12 April 1988 (1988-04-12) columns 1-4	1-6,8-15
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☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

\* Special categories of cited documents:

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

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

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

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

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

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Date of the actual completion of the international search

16 June 2006

Date of mailing of the international search report

23/06/2006

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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/005445

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 544 925 B1 (PRUSIK THADDEUS ET AL) 8 April 2003 (2003-04-08) column 4, line 37 column 7, lines 6-20 column 8, lines 23-67 examples 1,10	1-6,8-15
Y	US 5 053 339 A (PATEL ET AL) 1 October 1991 (1991-10-01) column 4, lines 22-55 column 11, lines 48-55 table 6	1-6,8-15

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