(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 191 650**
A2

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **86301073.2**

(22) Date of filing: **17.02.86**

(51) Int. Cl.⁴: **B 01 L 3/00**, G 01 N 21/00, G 01 N 33/48

(30) Priority: **15.02.85 JP 29163/85**

(43) Date of publication of application: **20.08.86 Bulletin 86/34**

(84) Designated Contracting States: **DE GB**

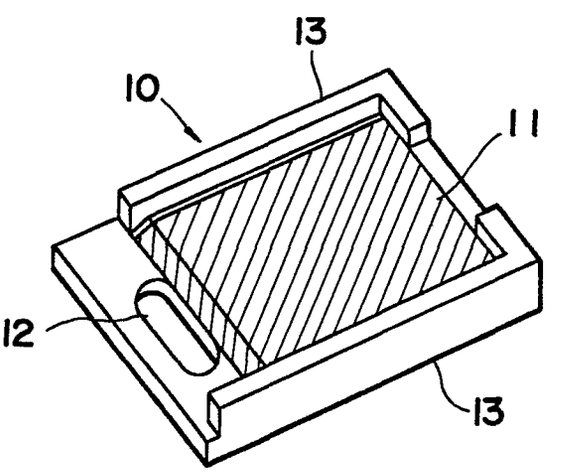
(71) Applicant: **FUJI PHOTO FILM CO., LTD., 210 Nakanuma Minami Ashigara-shi, Kanagawa 250-01 (JP)**

(72) Inventor: **Yaginuma, Nakatsugu, c/o Fuji Photo Film Co. Ltd. 3-11-46 Senzui, Asaka-shi Saitama (JP)**
Inventor: **Hirai, Kikuo, c/o Fuji Photo Film Co. Ltd. 3-11-46 Senzui, Asaka-shi Saitama (JP)**
Inventor: **Sekikawa, Nobuyoshi, c/o Fuji Photo Film Co. Ltd. 3-11-46 Senzui, Asaka-shi Saitama (JP)**
Inventor: **Iwata, Yuzo, c/o Fuji Photo Film Co. Ltd. 3-11-46 Senzui, Asaka-shi Saitama (JP)**
Inventor: **Seto, Shunichi, c/o Fuji Photo Equipment Co. Ltd. 1250, Takematsu, Minami-ashigara-shi Kanagawa (JP)**

(74) Representative: **Arthur, Bryan Edward et al, Withers & Rogers 4 Dyer's Buildings Holborn, London EC1N 2JT (GB)**

(54) Sealing device for analytical slide.

(57) A sealing device for analytical slide encasing a multilayer analytical element within a frame having an opening on each of upper and lower surfaces thereof for use in a process for analysis of a liquid sample comprising steps of applying the liquid sample onto the analytical element, incubating the element and detecting a reaction occurring in the element, said sealing device being to be so arranged adjacently to the analytical slide as to substantially cover the surface of the element on which the liquid sample is applied, for serving to reduce evaporation of the liquid sample from the analytical element during the incubation step, characterised in that at least a part of the surface of the sealing device to face the surface of the element on which the liquid sample is applied is made of an inert material such as a fluorine-containing polymer.



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SEALING DEVICE FOR ANALYTICAL SLIDE

BACKGROUND OF THE INVENTION

Field of the invention

The present invention relates to a sealing device for an analytical slide. More particularly, the present invention relates to an improvement of a sealing device for an analytical slide having a function to reduce the evaporation of a liquid sample from a multilayer analytical element during the incubation process in quantitative analysis of a specific component of the liquid sample employeing an analytical slide.

Description of prior arts

In recent clinical diagnosis, clinical chemical tests including quantitative analysis of a specific component in a body liquid has been paid much attention for the purposes of exact diagnosis and appropriate medical treatments. Photometric determination is frequently employed in the clinical chemical test.

The photometric determination is based on a principle that absorbance or change of absorbance of a specific component(analyte) to be analyzed in a liquid sample or a substance generated by chemical reaction of the analyte including an enzyme reaction is subjected to colorimetry. In the case that an analyte or the generated substance shows neither color nor change of color, an appropriate color-forming reagent which give color formation coupling with the chemical reaction product of the analyte can be employed.

In the clinical chemical test of prior arts, an analysis called wet method has been carried out according to the above principle. For instance, an analysis employing enzyme reaction according to the wet method is performed as follows. A liquid sample containing an analyte such as blood plasma (or diluted solution thereof) and an enzyme-containing solution are placed in a cell and fully mixed. Then, the mixture is placed in an incubator so as to cause enzyme reaction. The incubator employed in the wet method is a tub filled with water and provided with a heating device for keeping the water at a predetermined temperature, for example, 37°C. Incubation process is carried out by putting the cell in the tub for 5 to 10 minutes. After the incubation is completed, the cell is irradiated with rays of predetermined wavelength, for example, near ultraviolet rays (wavelength: 190 to 400 nm) or visible rays (wavelength: 400 to 800 nm) from one side of the cell. Rays having passed through the cell and the solution is photometrically detected by a photodetecter for photoelectric transformation. Th analyte is then quantitatively analyzed using the obtained absorbance.

According to the process using a cell or test tube, a relatively large amount of a liquid sample and careful handling are required. Therefore, it is difficult to carry out analysis easily and rapidly. Moreover, it is not possible to analyze many samples continuously one after another. To cope with these problems, a dry method using a multilayer analytical element has been proposed and already used in practice in place of the wet method.

A multilayer analytical element has a basic structure comprising a transparent plastic support in the form of a sheet and a reaction layer provided on the suppport which reacts directly or indirectly with an analyte to show formation or change of color. Multilayer analytical elements in various embodiments based on the above basic

structure have been known.

Generally, the multilayer analytical element is encased within a thin plastic frame having an opening on each of upper and lower surfaces thereof so as to take a form of a slide. One of the embodiments of the analytical slide is an integral multilayer analytical element comprising a transparent support, a reagent layer and a porous spreading layer which are superposed in this order as disclosed in Japanese Utility Model Provisional Publication No. 56(1981)-142454 and Japanese Patent Provisional Publication No. 57(1982)-63452. In another embodiment, the integral multilayer analytical element is inserted between an upper frame having an opening for applying a sample liquid at the center thereof and a lower frame having an opening for colorimetry at the center thereof, both ends of the upper and lower frames being combine through fusion.

The process of analysis of a liquid sample employing the above analytical slide can be carried out by steps of applying a liquid sample to the multilayer analytical element through the opening formed on the upper frame, subjecting the element to incubation, for example, at 37°C for 6 minutes after the liquid sample spreads in the element, causing color reaction, irradiating the colored part of the element with rays through an opening formed on the lower frame, and quantitatively analyzing a specific component through colorimetry of reflected rays from the reaction layer.

Operation for analyzing a liquid sample using an analytical slide can be carried out automatically by employing an analytical device involving easy operation and accurate analysis. The analytical device is provided with an application means for applying a liquid sample to the analytical slide, an incubator for heating the slide carrying the applieda liquid sample in order to accelerate a color reaction and a photometric means for opti-

cally detecting the color reaction in the slide. The incubator is a device for incubating the analytical slide at an appropriate temperature and for a period of time which are predetermined depending on the reaction involved.

As mentioned above, an analytical slide is provided with an opening for applying a liquid sample to the multilayer analytical element. Therefore, a liquid sample applied on the element is apt to evaporate during the incubation step. In the case that a reactive gas such as ammonia and carbon dioxide generated in the element by reaction between an analyte and reagent is utilized to cause color reaction, a portion of the gas generated is apt to pass through the opening to the outside and does not contribute to the color reaction. Accordingly, the obtained value is lower than the actual value.

For the purposes of reducing evaporation of the liquid sample, heating the anlytical slide effectively and uniformly and preventing the generated gas from running outside, the incubation step is sometimes carried out employing an analytical slide received within an analytical slide carrier for sealing. The analytical slide carrier moves in unit with the analytical slide received and sealed therein. As desribed in Japanese Patent Provisional Publication No. 58(1983)-21566, an analytical slide carrier can take a form of a housing which is open at a part facing to the lower surface of the multilayer analytical element (a part adjacent to the support surface).

The present inventors have studied the process for quantitative analysis of a component in a liquid sample employing an analytical slide and analytical slide carrier. As the result, it has been found that a known analytical slide carrier disturbs the accuracy of the measurement in the case that a reactive gas such as ammonia generated during the incubation step is used to

cause the color reaction.

In more detail, not a small amount of a reactive gas generated through reaction of an analyte in the analytical element is adsorbed by the inner surface of the analytical slide carrier, particularly in the inner surface facing to the surface of the element on which a liquid sample is applied, without contributing to the desired color reaction. The analytical slide carrier is used repeatedly by liberating an analytical slide which has been subjected to the incubation step, inserting a new analytical slide therein and subjecting to incubation. Accordingly, the reactive gas is adsorbed by the inner surface of the analytical slide carrier during the first incubation step, whereby reduing the color reaction and lowering the obtained value than the actual value. On the contrary, in the incubation steps of the second time and after that, the amount of the reactive gas to be adsorbed by the inner surface of the carrier is remarkably reduced, or the gas is hardly adsorbed by the inner surface. Further, the reactive gas adsorbed by the inner surface during the first incubation step is released to contribute to the color reaction of the analytical slide. These phenomena make the obtained value higher than the actual value.

The known sealing devices for an analytical slide such as an analytical slide carrier cannot satisfactorily solve the problem of errors in obtained values.

SUMMARY OF THE INVENTION

An object of the invention is to provide an improved sealing device for an analytical slide.

Another object of the invention is to provide a sealing device for an analytical slide characterized in that adsorption of the reactive gas generated through a chemical reaction of an analyte in a multilayer analyti-

cal element received in an analytical slide is reduced.

A further object of the invention is to provide a sealing device for an analytical slide capable of reducing the errors in obtained values.

The present invention resides in a sealing device for analytical slide encasing a multilayer analytical element within a frame having an opening on each of upper and lower surfaces thereof for use in a process for analysis of a liquid sample comprising steps of applying the liquid sample onto the analytical element, incubating the element and detecting a reaction occurring in the element, said sealing device being to be so arranged adjacently to the analytical slide as to substantially cover the surface of the element on which the liquid sample is applied, for serving to reduce evaporation of the liquid sample from the analytical element during the incubation step, characterised in that at least a part of the surface of the sealing device to face the surface of the element on which the liquid sample is applied is made of an inert material such as a fluorine-containing polymer.

Since an inert material such as a fluorine-containing polymer, a metal having a mirror surface or a ceramic having a mirror surface employed for a sealing device for analytical slide of the invention has a small surface energy and is chemically stable, the polymer hardly adsorbs the reactive gas generated from the analytical slide either physically or chemically. Accordingly, the sealing device for an analytical slide of the invention is extremely effective to reduce errors in the obtained values since the sealing device hardly adsorb a substantial amount of the reactive gas generated upon reaction of an analyte in the multilayer analytical element encased in the analytical slide.

Further, the fluorine-containing polymer makes sliding between the analytical slide and the sealing device smooth, which is advantageous in an automatic operation

employing analytical devices. Since the polymer is chemically stable, the polymer gives no influence on the reagents contained in the multilayer analytical element and the layer structure thereof. Accordingly, the sealing device of the invention can be also advantageously employed in an analytical slide wherein no reactive gas is generated.

Moreover, as the fluorine-containing polymer is widely used, the invention can be easily realized.

BRIEF DESCRIPTION OF DRAWINGS

Figs. 1 and 2 are perspective views showing a structure of a carrier for an analytical slide which is one embodiment of a sealing device of the invention.

Fig. 3 is a perspective view showing a structure of a carrier for an analytical slide which is another embodiment of the sealing device of the invention.

DETAILED DESCRIPTION OF THE INVENTION

The sealing device for an analytical slide according to the invention includes various embodiments having functions.

One of the embodiments is one in the form of a housing which is open at a portion facing to the lower surface of a multilayer analytical element and moves in unit with an analytical slide in the incubation process. Concrete examples include a carrier used in an incubator described in Japanese Patent Provisional Publication No. 58(1983)-21566, a combination of an upper cover and a support used in an incubator described in Japanese Patent Provisional Publication No. 58(1983)-21567 and a slide supporting member used in an analytical device described in Japanese Patent Provisional Publication No. 53(1978)-81292. In these embodiments, one analytical slide is

received and sealed in one sealing device so as to move in unit.

In another embodiment, the sealing device in the form of a sheet moves in unit with an analytical slide during the incubation process so that an opening for receiving an analytical element formed on the upper surface of a frame is sealed. The concrete example of the above embodiment includes "a cover for prevention of evaporation of water" employed in a cartridge for analyzing a liquid sample as described in Japanese Utility Model Publication No. 59(1984)-10620, the cover being so designed as to be opened and closed on the upper surface of the analytical slide. The above embodiments include a sealing device whose one end or one side is openably fixed to one end or one side of a frame receiving an analytical element, and a sealing device having side walls provided with a groove at two facing ends along which an analytical slide is inserted.

In a further embodiment of a sealing device which moves in unit with an analytical slide during the incubation process, a sealing device in the form of a belt such as "a sealing guide belt" employed in an incubator for chemical analysis as described in Japanese Utility Model Provsional Publication No. 57(1982)-647 is included.

A still further example of the sealing device includes a sealing device which makes a relative movement against an analytical slide during the incubation process. Such a sealing device is one in the form of a disc provided with a plurality of openings for receiving analytical slides so as to analyze a plurality of slides simulteniously such as "a transporting member" employed in an analyzing device described in Japanese Patent Provisional Publication No. 56(1981)-77746.

There is no limitation on the present invention so far as a sealing device is one for analytical slide encasing a multilayer analytical element within a frame

having an opening on each of upper and lower surfaces thereof for use in a process for analysis of a liquid sample comprising steps of applying the liquid sample onto the analytical element, incubating the element and detecting a reaction occurring in the element, and said sealing device is to be so arranged adjacently to the analytical slide as to substantially cover the surface of the element on which the liquid sample is applied, for serving to reduce evaporation of the liquid sample from the analytical element during the incubation step. As is understood from the above description, the term "sealing" used in the specification does not mean to completely seal an analytical slide from air, but means to seal an analytical slide so as to reduce the evaporation of a liquid sample from a multilayer analytical element during the incubation process, as compared with evaporation of the sample from the slide which is simply exposed to the air.

It is preferred that the sealing device of the present invention is a carrier in the form of a housing which is open at a part facing to the lower surface of a multilayer analytical element and which carries an analytical slide received therein, as shown in the attached Figures 1, 2 and 3.

While the object of the invention can be achieved by forming at least a part of the surface of the sealing device facing to the surface of the analytical element on which a liquid sample is applied, using an inert mateial such as a fluorine-containing polymer, it is preferred that substantially whole surface of the device is formed by an inert material such as a fluorine-containing polymer.

There is no limitation on the fluorine-containing polymer employed in the invention. As a fluorine-containing polymer which is easily obtainable, polytetrafluoroethylene, a copolymer of tetrafluoroethylene and

hexafluoropropylene, polychlorotrifluoroethylene, polyvinylidene fluoride and polyvinyl fluoride can be exemplified. Among the above-mentioned fluorine-containing polymers, fluorine-containing polymer which soften and flow around the melting point threof or a higher temperature such as the copolymer of tetrafluoroethylene and hexafluoropropylene, polychlorotrifluoroethylene, and polyvinylidene fluoride are preferred. The fluorine-containing polymers can be manufactured according to texts such as "Handbook of Polymer Materials" eddited by the Polymer Society of Japan. Fluorine-containing polymers having various properties are manufactured and are commercially available. These polymers can be employed in the invention.

The surface of the sealing device for an analytical slide can be formed of the fluorine-containing polymer in a number of methods. For example, a fluorine-containing polymer as such is molded to produce a sealing device, a fluorine-containing polymer is sintered on a metallic sealing device to form a layer of fluorine-containing polymer, a dispersion or fine powder of a fluorine-containing polymer is applied on the sealing device to form a layer of a fluorine-containing polymer, a fluorine-containing polymer is polymerized on the surface of a sealing device to form a coating layer of the polymer, the surface of the sealing device is coated with a tape or film consisting of a fluorine-containing polymer so as to form a layer of a fluorine-containing polymer, and the flurine-containing polymer as such is melted on the surface of a sealing device. One of preferable embodiments comprises that the surface of a sealing device is first sintered with polytetrafluoroethylene which may contain pigments such as carbon black, titanium dioxide, silica, and then the so coated resin layer is further coated with the fluorine-containing polymer which soften and flow around the melting point threof or a higher

temperature.

The coated fluorine-containg polymer layer preferrably has a thickness in the range of 5 to 50 μm, more preferably 10 to 40 μm.

Examples of the location of the sealing device of the invention where the fluorine-containing polymer is applied will be described with reference to analytical slide carriers shown in the Figs. 1, 2 and 3.

In Figs. 1 and 2, an analytical slide carrier 10 made of a metal is designated by a numeral 10 and so formed as to receive an analytical slide 20 as shown in Fig. 1. In Fig. 2, the analytical slide carrier shown in Fig. 1 is shown with the bottom turned up so that the inside thereof can be seen. The bottom (corresponding to the lower portion in Fig. 1 and upper portion in Fig. 2) and one side portion of the carrier are open. The structure of this nature contributes to perform the incubation process effectively, to supply heat uniformly, and to introduce and discharge the analytical slide easily. The opening 12 which is formed on a part of the cover portion 13 of the carrier (corresponding to the upper portion in Fig. 1 and the lower portion in Fig. 2) for confirming presence of an analytical slide therein functions to easily detect the analytical slide 20 in the carrier in the incubation process.

In the analytical slide carrier shown in Figs. 1 and 2, the approximately center portion of the inside surface of the carrier shown in Fig. 2 faces the surface of the multilayer analytical element on which an liquid sample is applied (through the opening 21 for applying sample). Accordingly, it is effective to coat the fluorine-containing polymer over the surface 11 shown by oblique lines.

Another preferable embodiment of the invention is the analytical slide carrier shwon in Fig. 3 wherein a fluorine-containing polymer is coated on other surfaces

of the carrier as well as the inside surface. In Fig. 3, the carrier 30, opening 32 for confirming an analytical slide and cover portion 33 correspond to the carrier 10, opening 12 and cover portion 13 respectively in Figs. 1 and 2. In the analytical slide carrier shown in Fig. 3, a fluorine-containing polymer is coated all over the inside surface of the carrier (shown by oblique lines).

Further, it is possible to provide a fluorine-containing polymer all over the surface of the carrier. In this case, smooth sliding between deposited carriers is secured, which is effective in the analytical operation.

As described in prior arts, the sealing device for analytical slide may be provided in an analytical device used for automatic analyzing operation employing an analytical slide. In this case, a fluorine-containing polymer can be provided on the corresponding area as mentioned above. In more detail, a fluorine-containing polymer is provided on at least a part of the area, preferably a whole portion of the surface corresponding to the surface of the multilayer analytical element in the analytical slide where a sample liquid is applied, thereby reducing adsorption of the reactive gas generated in the analytical element by the sealing device.

There have been already known examples of multilayer analytical element wherein a reactive gas is generated during analyzing operations. Concrete examples include "an integral multilayer analytical element for analyzing ammonia or ammonia-generating substrate" as disclosed in Japanese Patent Provisional Publication No. 58(1983)-77661 and "an integral analytical element" as disclosed in Japanese Patent Publication No. 58(1983)-19062. The sealing device for analytical slide according to the invention is particularly effective when the generated gas is ammonia, that is, an analyte is ammonia or an ammonia-generating substance, because ammonia which is one of the important analytes in analyzing a body liquid

is easily adsorbed by the sealing device. The term "ammonia generating substrate" means a compound or group of compounds which generates ammonia directly upon reaction with a specific reagent or through a plurality of reactions. Examples of the ammonia generating substrate include urea and creatinine.

The present invention will be described more concretely with reference to the following examples. However, the invention is not limited to these examples.

The analytical slide employed in Example 1 receives an integral multilayer analytical element prepared in the following manner.

Preparation of Integral Multilayer Analytical Element for Analyzing Urea-Nitrogen

On a transparent polyethylenetelephthalate (PET) film (thickness: 180 μm) was coated and dried a color forming reagent to form a color-forming reagent layer (thickness of dry basis: 10 μm). A membrane filter (tradename: Fuji Microfilter FM500 manufactured by Fuji Photo Film Co., Ltd.,) having thickness of 140 μm, void ratio of 75 % and mean diameter of 5 μm which had been immersed in a solution of water-repellent silicone resin in hexane and dried was caused to adhere to the reagent layer(which was adhesive under dry condition) to form a barrier layer.

Subsequently, a reaction layer (thickness of dry basis: 20 μm), a light shielding layer (thickness of dry basis: 5 μm) and an adhesive layer were formed by superposing on the barrier layer in this order.

The dry surface of the adhesive layer coated was wet with water. Then a cloth(cotton broad No. 100) was laminated under pressure on the surface to form a spreading layer. Thus, an integral multilayer analytical element for analyzing urea and nitrogen in blood was prepared.

Composition and preparation of coating solutions

employed for forming the reagent layer, reaction layer, light shielding layer and adhesive layer will be shown respectively as follows. These solutions were coated so as to have the dry thickness as mentioned above.

Coating Solution for Reagent Layer

Bromocresol grenn	60 mg.
Copolymer latex of poly(vinyl acetate) and acrylate (solid content: approx. 50 %, pH; 4.4)	5 g.
3,3-Dimethyl glutaric acid	20 mg.
Water	2 mℓ

Coating Solution for Reaction Layer

Gelatin	10 g.
Water	100 mℓ
p-Nonylphenoxypolyglycidol	0.3 g.
Urease	0.8 g.
Ethylenediamine tetraacetic acid· tetrasodium salt	0.4 g.

The coating solution of the above composition was adjusted to have pH 8 by using orthophosphoric acid disodium and sodium hydroxide.

Coating Solution for Light Shielding Layer

Fine powder of titanium dioxide	4 g.
Gelatin	4 g.
p-Nonylphenoxypolyglycidol	0.15 g.
Water	40 mℓ

Coating Solution for Adhesive Layer

Gelatin	2.5 g.
Water	50 mℓ
p-Nonylphenoxypolyglycidol	0.15 g.

Example 1

A multilayer analytical element for analyzing urea-nitrogen prepared in the manner as mentioned above was received in a plastic frame having a circular opening at the center portion of each of upper and lower surfaces to form an analytical slide for analysis of urea-nitrogen as shown by the numeral 20 in Fig. 1.

As shown by oblique lines 11 in Fig. 2, an adhesive tape (thickness: 80 μm) of polytetrafluoroethylene (PTEF) was attached to the surface facing to the sample-applying opening 21 of the analytical slide in the slide carrier made of aluminum (whose surface had been treated with anodizing solution) shown by the numeral 10 in Figs. 1 and 2 (a portion through which a liquid sample is applied to the multilayer analytical element received in the slide).

By employing the above analytical slide carrier provided with PTEF tape and analytical slide for analyzing urea-nitrogen, automatic analysis of urea-nitrogen in a control serum, Monitrol I•X (manufactured by Daide Corp.: U.S.A.) was carried out repeatedly. The automatical analysis operation was carried out by employing an automatic analyzing device of Fuji drychem system (manufactured by Fuji Photo Film Co., Ltd) provided with an incubator disclosed in Japanese Patent Provisional Publication No. 58(1983)-21566. Incubation was carried out at a temperature of 37°C for 6 minutes.

Comparison Example 1

Analysis of urea-nitrogen was carried out in the same manner as in Example 1 except that a carrier which was provided with no PTFE tape so that the anodized aluminum surface was exposed was employed.

The results of Example 1 and Comparison Example 1

are shown in the following Table 1.

Table 1
Obtained Values of Analysis of Urea-Nitrogen
(Sample: Monitrol I•X)

	Obtained Values (mg/dℓ)		
	first time	second time	third time
Example 1	15.0	14.9	15.0
Comparison Example 1	14.1	15.0	15.0

As is clear from Table 1, substantially same values were obtained in Example 1 and reproducibility of the obtained value is high. On the contrary, in Comparison Example 1, the obtained value at the first time was lower than those at the second and third times. It is thought that this is because the obtained value of the first time is influenced by the adsorption of ammonia gas by the surface of the carrier.

Example 2

An analytical slide for analyzing ammonia was prepared in the same manner as in Example 1 except that the following changes were made on the integral multilayer analytical element for analyzing urea-nitrogen used in Example 1.

(1) Bromphenol blue was employed instead of bromocresol green as the color-forming reagent to be contained in a color-forming reagent layer.

(2) Urease was removed from the reaction layer and

pH of the coating solution was adjusted to be 10.0 in order to increase sensitivity.

Analysis of ammonia was carried out in the same manner as in Example 1 employing the above analytical slide for analyzing ammonia and analytical slide carrier prepared in Example 1. Subsequently, the amount of ammonia gas adsorbed and left in the carrier was measured.

Comparison Example 2

The amount of ammonia gas adsorbed and left in a carrier was measured in the same manner as in Example 2 except that a carrier having an anodized aluminum (aluminium oxide) coated surface exposed was employed, the surface facing to a liquid sample applying surface of the similar multilayer analytical element to one used in Comparison Example 1.

The results of Example 2 and Comparison Example 2 are shown in Table 2.

Table 2

	Material of Surface	Amount of Ammonia existed
Example 2	PTEF	0.0009 µg
Comparison Example 2	aluminum oxide	0.3 µg

As shown in Table 2, ammonia gas hardly was present in the carrier of Example 2. On the contrary, a large amount of ammonia gas existed by adsorption of the carrier of Comparison Example 2.

Example 3

Analysis of urea-nitrogen was carried out using an analytical slide, analytical slide carrier and automatic analyzing device similar to those used in Example 1 under the same conditions as in Example 1 except that an aqueous albumin containing 7 % of human blood serum and approx. 100 mg/dμ of urea-nitrogen as used as a sample liquid to be dropped in place of the commercially available control serum Monitrol I•X.

Analysis was repeated 15 times.

Comparison Example 3

Analysis of urea-nitrogen was carried out in the same manner as in Example 3 except that a carrier having an anodized aluminum (aluminium oxide) coated surface exposed was employed, the surface facing to the liquid sample applying surface of the similar multilayer analytical element to one used in Comparison Example 1.

The results of Example 3 and Comparison Example 3 are shown in Table 3.

Table 3

	Amount of Urea & Nitrogen	CV Value
Example 3	100.5 mg/dℓ	1.1 %
Comparison Example 3	96.5 mg/dℓ	1.4 %

As shown in Table 3, anmonia gas was hardly adsorbed by the surface of the carrier of Example 3 (according to the invention). Therefore, the obtained value was higher

than that of Comparison Example 3 and fluctuation of the obtained value (CV value) was decreased.

Example 4

A multilayer analytical element for analyzing urea-nitrogen prepared in the manner as mentioned above was received in a plastic frame having a circular opening at the center portion of each of upper and lower surfaces to form an analytical slide for analysis of urea-nitrogen as shown by the numeral 20 in Fig. 1.

On the inner surface of the same sealing device as employed in Example 1, polytetrafluoroethylene(PTEF) containing carbon black was sintered to form a layer of approx. 10 μm thick and the sintered layer was coated with a tetrafluoroethylene-hexafluoropropylene copolymer (FEP) through fusion.

By employing the above analytical slide carrier provided with the FEP layer on the top and analytical slide for analyzing urea-nitrogen, automatic analysis of urea-nitrogen in a control serum, Monitrol I•X (manufactured by Daide Corp.: U.S.A.) was carried out repeatedly. The automatical analysis operation was carried out by employing an automatic analyzing device of Fuji drychem system (manufactured by Fuji Photo Film Co., Ltd) provided with an incubator disclosed in Japanese Patent Provisional Publication No. 58(1983)-21566. Incubation was carried out at a temperature of 37°C for 6 minutes.

Comparison Example 4

Analysis of urea-nitrogen was carried out in the same manner as in Example 4 except that a carrier which was provided with no FEP & PTFE layers so that the anodized aluminum surface was exposed was employed.

The results of Example 4 and Comparison Example 4

are shown in the following Table 4.

Table 4
Obtained Values of Analysis of Urea-Nitrogen
(Sample: Monitrol I•X)

	Obtained Values (mg/dℓ)		
	first time	second time	third time
Example 4	15.0	14.9	15.0
Comparison Example 4	14.0	15.0	15.1

As is clear from Table 4, substantially same values were obtained in Example 4 and reproducibility of the obtained value is high. On the contrary, in Comparison Example 4, the obtained value at the first time was lower than those at the second and third times. It is thought that this is because the obtained value of the first time is influenced by the adsorption of ammonia gas by the surface of the carrier.

Example 5

An analytical slide for analyzing ammonia was prepared in the same manner as in Example 1 except that the following changes were made on the integral multilayer analytical element for analyzing urea-nitrogen used in Example 1.

(1) Bromphenol blue was employed instead of bromocresol green as the color-forming reagent to be contained in a color-forming reagent layer.

(2) Urease was removed from the reaction layer and

pH of the coating solution was adjusted to be 10.0 in order to increase sensitivity.

Analysis of ammonia was carried out in the same manner as in Example 1 employing the above analytical slide for analyzing ammonia and analytical slide carrier prepared in Example 1. Subsequently, the amount of ammonia gas adsorbed and left in the carrier was measured.

Comparison Example 5

The amount of ammonia gas adsorbed and left in a carrier was measured in the same manner as in Example 5 except that a carrier having an anodized aluminum (aluminium oxide) coated surface exposed was employed, the surface facing to a liquid sample applying surface of the similar multilayer analytical element to one used in Comparison Example 1.

The results of Example 5 and Comparison Example 5 are shown in Table 5.

Table 5

	Material of Surface	Amount of Ammonia existed
Example 5	PTFE-FEP	0.0005 µg
Comparison Example 5	aluminum oxide	0.3 µg

As shown in Table 5, ammonia gas hardly was present in the carrier of Example 5. On the contrary, a large amount of ammonia gas existed by adsorption of the carrier of Comparison Example 5.

Example 6

Analysis of urea-nitrogen was carried out using an analytical slide, analytical slide carrier and automatic analyzing device similar to those used in Example 1 under the same conditions as in Example 1 except that an aqueous 7 % human blood serum containing approx. 66 mg/dμ of urea-nitrogen was used as a sample liquid to be dropped in place of the commercially available control serum Monitrol I•X.

Analysis was repeated 15 times.

Comparison Example 6

Analysis of urea-nitrogen was carried out in the same manner as in Example 6 except that a carrier having an anodized aluminum (aluminium oxide) coated surface exposed was employed, the surface facing to the liquid sample applying surface of the similar multilayer analytical element to one used in Comparison Example 1.

The results of Example 6 and Comparison Example 6 are shown in Table 6.

Table 6

	Amount of Urea & Nitrogen	CV Value
Example 6	66.0 mg/dℓ	1.7 %
Comparison Example 6	61.2 mg/dℓ	2.0 %

As shown in Table 6, anmonia gas was hardly adsorbed by the surface of the carrier of Example 6 (according to the invention). Therefore, the obtained value was higher

than that of Comparison Example 6 and fluctuation of the obtained value (CV value) was decreased.

Example 7

The analysis of Example 4 was repeated except that the slide carrier having the inner surface directly coated with a tetrafluoroethylene-heptafluoropropyl tetrafluoro vinyl ether copolyme (HFP) through fusion.

Comparison Example 7

The amount of ammonia gas adsorbed and left in a carrier was measured in the same manner as in Example 7 except that a carrier having an anodized aluminum (aluminium oxide) coated surface exposed was employed, the surface facing to a liquid sample applying surface of the similar multilayer analytical element to one used in Comparison Example 1.

The results of Example 7 and Comparison Example 7 are shown in Table 7.

Table 7

	Material of Surface	Amount of Ammonia existed
Example 7	melted HFP	0.0014 µg
Comparison Example 7	aluminum oxide	0.3 µg

As shown in Table 7, ammonia gas hardly was present in the carrier of Example 7. On the contrary, a large amount of ammonia gas existed by adsorption of the carrier of Comparison Example 7.

CLAIMS:

1. A sealing device for analytical slide encasing a multilayer analytical element within a frame having an opening on each of upper and lower surfaces thereof for use in a process for analysis of a liquid sample comprising steps of applying the liquid sample onto the analytical element, incubating the element and detecting a reaction occurring in the element, said sealing device being to be so arranged adjacently to the analytical slide as to substantially cover the surface of the element on which the liquid sample is applied, for serving to reduce evaporation of the liquid sample from the analytical element during the incubation step, characterised in that at least a part of the surface of the sealing device to face the surface of the element on which the liquid sample is applied is made of an inert material.

2. The sealing device as claimed in claim 1, wherein the inert material is a fluorine-containing polymer.

3. The sealing device as claimed in claim 1, wherein the inert material is a fluorine-containing polymer selected from the group consisting of polytetrafluoroethylene, copolymer of tetrafluoroethylene and hexafluoropropylene, polychlorotrifluoroethylene, polyvinylidene fluoride and polyvinyl fluoride.

4. The sealing device as claimed in claim 1, wherein the inert material is a fluorine-containing polymer which softens and flows around the melting point threof or a higher temperature.

5. The sealing device as claimed in any one of claims 1 to 4, wherein the sealing device moves in unit with the analytical slide during the incubation process.

6. The sealing device as claimed in any one of claims 1 to 4, wherein the device is in the form of a housing which is open at a portion facing the lower surface of a multilayer analytical element.

7. The sealing device as claimed in any one of claims 1 to 4, which is in the form of a sheet and so designed as to seal the opening of the upper surface of the frame.

8. The sealing device as claimed in any one of claims 1 to 4, wherein the device is made of a metal material and the fluorine-containing polymer is superposed in layer on the surface of the metal material.

9. The sealing device as claimed in any one of claims 1 to 4 wherein the device moves relatively to the analytical slide during the incubation process.

10. The sealing device as claimed in claim 1 or 2, wherein the multilayer analytical element is for use of analysis of ammonia or ammonia-generating substrate.

11. The sealing device as claimed in claim 1 or 2, wherein substantially whole surface of the sealing device coreesponding to the surface of the multilayer analytical element on which the liquid sample is applied is made of a fluorine-containing polymer.

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FIG. 1

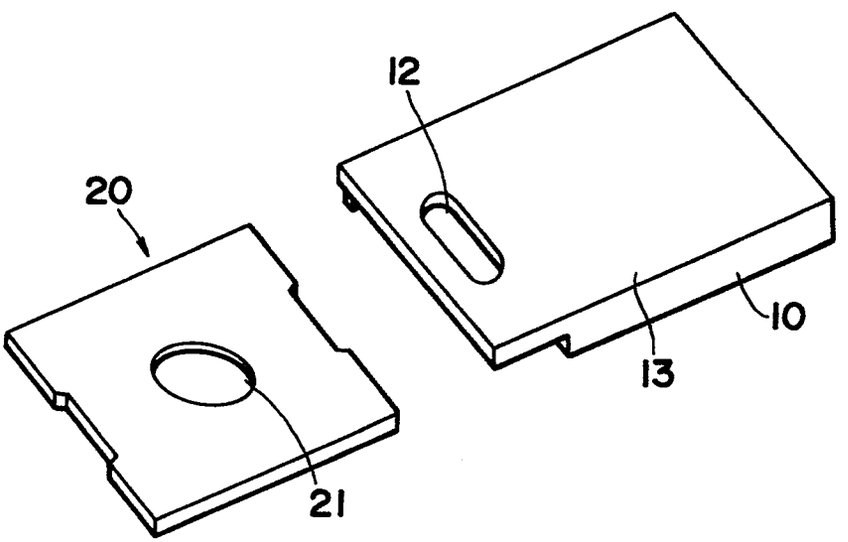

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FIG. 2

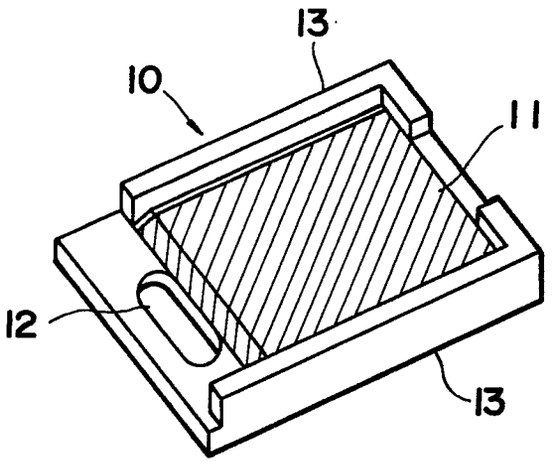

FIG. 3