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(54) **TEST STRIP FOR DETECTION OF ANALYTE AND METHODS OF USE**

TESTSTREIFEN ZUM ANALYTNACHWEIS UND VERWENDUNGSVERFAHREN

BANDELETTE REACTIVE POUR LA DETECTION D'UN ANALYTE ET PROCEDES D'UTILISATION

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Description

TECHNICAL FIELD

[0001] The present invention relates generally to the fields of test strip devices and methods of detecting analytes. More specifically, the present invention relates to a test strip for the colormetric detection of glucose in whole blood and methods of use.

BACKGROUND

[0002] A variety of test strips for detecting an analyte from a sample are available and described in the literature, notably US 6,284,550 (Home Diagnostics Inc.), EP 0526226 (Ortho Pharmaceutical Corp.), US 5,972,294 (Lifescan Inc.). Of these, many have applications for the detection of glucose from whole blood. However there are many disadvantages to these devices. Some require a large sample volume to be applied to the test strip, others have a wet through problem and still others lead to contamination of the test strip tray. The present invention addresses these problems and provides related benefits.

BRIEF DESCRIPTION OF THE DRAWINGS

[0003]

FIG. 1a and **1**b are a perspective and side view of the preferred embodiment of a test strip of the present invention.
FIG. 2 is a side view of an alternative preferred embodiment of a test strip of the present invention.
FIG. 3 is a block diagram of a preferred embodiment of a method for detecting the presence or concentration of a target using kinetic endpoint measurements.
FIG. 4 is a block diagram of another preferred embodiment of a method for detecting the presence or concentration of a target using kinetic endpoint measurements.
FIG. 5 is a block diagram of a preferred embodiment of a method for detecting the presence or concentration of a target using a fixed time point and kinetic measurements.
FIG. 6 is a block diagram of another preferred embodiment of a method for detecting the presence or concentration of a target using a fixed time point and kinetic measurements.

SUMMARY

[0004] The present invention recognizes that traditional test strip design may be improved such that the wet through problem may be reduced and the contamination problem may be reduced by altering the design of a test strip. The present invention provides such a device and methods of use.

[0005] A first aspect of the present invention is a reagent test strip that includes: a) a top support layer including a sample aperture; b) a membrane that includes a reagent system for indicating the concentration of a target; c) a spreading layer; and d) a bottom support layer including a measuring port in substantial alignment or approximate alignment with the sample aperture. The membrane is affixed to the top support layer and is positioned between the top support layer and the bottom support layer. The spreading layer is positioned above the top support layer and in substantial or approximate alignment with the sample aperture. A fluid applied to the spreading layer, passes through the sample aperture and contacts the membrane.

[0006] A second aspect of the present invention is a method of determining the presence or concentration of a target in a sample that includes the steps of: a) applying a fluid suspected of including a target to the reagent test strip of the present invention; b) detecting the reflectance of the membrane; and c) determining the presence or concentration of the target.

[0007] A third aspect of the present invention is a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) detecting a first reflectance measurement; d) running a preprogrammed kinetic loop instruction; and e) determining the presence or concentration of the target. Preferably the threshold loop instruction includes the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; and repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value. Preferably, a fluid suspected of including a target is applied during the step of running the threshold loop instruction. Preferably the detection loop instruction includes the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the comparison is less than or equal to a predetermined cutoff value; replacing the

value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop.

[0008] A fourth aspect of the present invention is a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) detecting a first reflectance measurement; d) running a preprogrammed kinetic loop instruction; and e) running a consecutive comparison instruction; f) determining the presence or concentration of the target. Preferably, the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; and repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value. Preferably, a fluid suspected of including a target is applied during the step of running the threshold loop instruction. Preferably, the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the comparison is less than a predetermined cutoff value; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop. Preferably, the consecutive comparison instruction comprises the steps of: detecting a third reflectance measurement; comparing the second reflectance measurement to the third reflectance measurement; ending the consecutive comparison instruction if the comparison is less than the predetermined cutoff value; replacing the value of the first reflectance measurement with the value of the third reflectance measurement; and returning to the step of running a kinetic loop instruction.

[0009] A fifth aspect of the present invention is a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) beginning a predetermined time point such that a fixed time point may be reached; d) detecting a first reflectance measurement; e) running a preprogrammed kinetic loop instruction; and f) determining the presence or concentration of the target. Preferably the threshold loop instruction includes the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; and repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value. Preferably a fluid suspected of including a target is applied during the step of running the threshold loop instruction. Preferably the kinetic loop instruction includes the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second measurement; ending the loop if the second reflectance measurement is less or equal to a predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop.

[0010] A sixth aspect of the present invention is a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from a reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) beginning a predetermined time point such that a fixed time point may be reached; d) detecting a first reflectance measurement; e) running a preprogrammed kinetic loop instruction; f) running a consecutive comparison instruction; and g) determining the presence or concentration of the target. Preferably the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; and repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value. Preferably, a fluid suspected of including a target is applied during the step of running the threshold loop instruction. Preferably, the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the second reflectance measurement is less than or equal to a predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop. Preferably, the consecutive comparison instruction comprises the steps of: detecting a third reflectance measurement; comparing the second reflectance measurement to the third reflectance measurement; ending the consecutive comparison instruction if the comparison is less than or equal to the predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the third reflectance measurement; and returning to the step of running a kinetic loop instruction

[0011] A seventh aspect of the present invention is a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) beginning a predetermined time point such that a fixed time point may be reached; and d) detecting the presence or concentration of a target in a sample when the fixed time point is reached. Preferably the threshold loop instruction includes: detecting a threshold comparison value; comparing the threshold comparison value to a predetermined threshold value; and repeating the loop until the threshold comparison value is less than or equal to the predetermined threshold value. Preferably a fluid suspected of including a target is applied during the step of running the threshold loop instruction.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS

[0012] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Generally, the nomenclature used herein and the manufacture or laboratory procedures described below are well known and commonly employed in the art. Conventional methods are used for these procedures, such as those provided in the art and various general references. Terms of orientation such as "up"and "down" or "upper" or "lower" and the like refer to orientation of the parts during use of the device. Where a term is provided in the singular, the inventors also contemplate the plural of that term. The nomenclature used herein and the laboratory procedures described below are those well known and commonly employed in the art. As employed throughout the disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

[0013] The term "wet through" as used herein refers to the tendency of a fluid to migrate around or excessively through a membrane when the membrane is overloaded by fluid. Wet through may cause variations between measurements.

[0014] The term "loop instruction" as used herein refers to a set of programmed commands that a computerized device may repeatedly follow until a condition is met. The condition may be part of the loop instruction such that the number of loops performed vary depending on the sample added to the test strip.

[0015] The term "threshold value" as used herein refers to an absolute raw value such that a threshold comparison measurement may be detected and directly compared. The threshold value is predetermined and preprogrammed in an apparatus and does not require further calculations such as determining reflectance. Once the threshold comparison measurement is less than or equal to the threshold value the threshold loop instruction ends.

[0016] Other technical terms used herein have their ordinary meaning in the art that they are used, as exemplified by a variety of technical dictionaries.

INTRODUCTION

[0017] The present invention recognizes that traditional test strip design may be improved such that the wet through problem may be reduced, and the contamination problem may be reduced by altering the design of a test strip. The present invention provides such a device and methods of use.

[0018] As a non-limiting introduction to the breath of the present invention, the present invention includes several general and useful aspects, including:

1) a reagent test strip that includes: a) a top support layer including a sample aperture; b) a membrane that includes a reagent system for indicating the concentration of a target; c) a spreading layer; d) a bottom support layer including a measuring port in substantial alignment or approximate alignment with the sample aperture;

2) a method of determining the presence or concentration of a target in a sample that includes the steps of: a) applying a fluid suspected of including a target to the reagent test strip of the present invention; b) detecting the reflectance of the membrane; and c) determining the presence or concentration of the target;

3) a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) detecting a first reflectance measurement; d) running a preprogrammed kinetic loop instruction; e) determining the presence or concentration of the target; wherein the threshold loop instruction includes the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the kinetic loop instruction includes the steps of:

detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement;

ending the loop if the comparison is less than or equal to a predetermined cutoff value; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop;

4) A method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) detecting a first reflectance measurement; d) running a preprogrammed kinetic loop instruction; e) running a consecutive comparison instruction; f) determining the presence or concentration of the target; wherein the threshold loop instruction comprises the steps of:

detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold
value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the comparison is less than or equal to a predetermined cutoff value;
replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop; further wherein the consecutive comparison instruction comprises the steps of:

detecting a third reflectance measurement; comparing the second reflectance measurement to the third reflectance measurement; ending the consecutive comparison instruction if the comparison is less than or equal to the predetermined cutoff value; replacing the value of the first reflectance measurement with the value of the third reflectance measurement; and
returning to the step of running a kinetic loop instruction;

5) a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) beginning a predetermined time point such that a fixed time point may be reached; d) detecting a first reflectance measurement; f) running a preprogrammed kinetic loop instruction; e) determining the presence or concentration of the target; wherein the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second measurement; ending the loop if the second reflectance measurement is less than or equal to a predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop;

6) a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) applying a fluid suspected of including a target to the reagent test strip; c) running a preprogrammed threshold loop instruction; d) beginning a predetermined time point such that a fixed time point may be reached; e) determining the presence or concentration of a target in a sample when the fixed time point is reached; wherein the threshold loop instruction includes:

detecting a threshold comparison value; comparing the threshold comparison value to a predetermined threshold value; repeating the loop until the threshold comparison value is less than or equal to the predetermined threshold value; and further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction;

7) A method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from a reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) beginning a predetermined time point such that a fixed time point may be reached; d) detecting a first reflectance measurement; e) running a preprogrammed kinetic loop instruction; f) running a consecutive comparison instruction; g) determining the presence or concentration of the target; wherein the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the second reflectance measurement is less than or equal to a predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and
repeating the loop; further wherein the consecutive comparison instruction comprises the steps of: detecting a third reflectance measurement; comparing the second reflectance measurement to the third reflectance measurement; ending the consecutive comparison instruction if the comparison is less than or equal to the predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the third reflectance measurement; and returning to the step of running a kinetic loop instruction.

[0019] These aspects of the invention, as well as others described herein, can be achieved by using the methods, articles of manufacture and compositions of matter described herein. To gain a full appreciation of the scope of the present invention, it will be further recognized that various aspects of the present invention can be combined to make desirable embodiments of the invention.

I REAGENT TEST STRIP

[0020] Referring to **FIG. 1b,** the present invention includes a reagent test strip **10** that includes: a) a top support layer **11** including a sample aperture **12;** b) a membrane **13** that includes a reagent system for indicating the concentration of a target; c) a spreading layer **14;** d) a bottom support layer **15** including a measuring port **16** in substantial alignment or approximate alignment with the sample aperture **12.** The membrane **13** is affixed to the top support layer **11.** and is positioned between the top support layer **11** and the bottom support layer **15.** The spreading layer **14** is positioned above the top support layer **11** and in substantial or approximate alignment with the sample aperture **12.** A fluid applied to the spreading layer **14,** passes through the sample aperture **12** and contacts the membrane **13.**

[0021] Each element of the reagent test strip **10** is generally manufactured independently then assembled into the desired configuration. Assembly may involve the individual assembly of a singe test strip **10** or may involve assembling a group of test strips **10** then cutting each test strip **10** into the desired size and shape.

[0022] The use of a reagent test strip **10** generally involves inserting the reagent test strip **10** on a test strip tray of a measuring device, detecting a dry strip reading, applying a fluid suspected of including a target to the reagent test strip **10,** and detecting the reflectance of the membrane. The present invention may be utilized with a single drop or multiple drops of a fluid.

TOP SUPPORT LAYER

[0023] The top support layer **11** may prevent a sample from entering the membrane **13** outside of the region accessible through the sample aperture **12** and may provide a structure enabling the user to grasp the reagent test **10.** The top support layer **11** is larger than the sample aperture **12** and is in contact with the membrane **13** outside of the sample aperture **12** thereby eliminating the need for a sink within the test strip **10.** Preferably, the top support layer **11** is larger than the membrane.

[0024] The top support layer **11** may be used in combination with a bottom support layer **15** as demonstrated in **FIG. 1a** or without a bottom support layer **15** as demonstrated in **FIG. 2.** Referring to **FIG. 1a,** when used in combination with a bottom support layer **15,** the membrane **13** is sandwiched between the top **11** and bottom support layers **15.** The top support layer **11** may be affixed to the membrane **13** and to the bottom support layer **15.** When the top support layer **11** is used without a bottom support layer **15** as demonstrated in **FIG. 2,** the membrane **13** is positioned below the top support layer **11** and at least one spacer **17** is affixed to the top support layer **11** such that the membrane **13** is elevated from a test strip tray when the reagent test strip **10** is inserted into a measuring device such as a reflectance meter.

[0025] The top support layer **11** is generally manufactured as a sheet, a roll or a card and subdivided into appropriate size portions. The top support layer **11** may be constructed from any material able to substantially exclude the fluid applied to the test strip **10.** Some examples are polypropylene, polystyrene, polyesters and polymer plastic. Preferably the dimensions are about five centimeters long by about 6.5 millimeters wide however the dimensions may be different depending on the size of a reflectance meter's test strip tray. The thickness of the top support layer **11** may be from about 0.5 mil to about 30 mil, preferably less than about 5 mil and most preferably from about 2 mil to about 3 mil. However the thickness may vary depending on the desired conformation and rigidity of the test strip **10.** For instance, when the top support layer **11** is used in combination with the bottom support layer **15** as demonstrated in **FIG. 1b,** the bottom support layer **15** may provide the majority of the rigidity allowing a thinner top support layer **11** to be utilized. Alternatively, when the top support layer **11** is not used in combination with the bottom support layer **15** as can be seen by comparing **FIG. 1b** and **FIG. 2,** a thicker top support layer **11** may be desired because the top support layer **11** provides the majority of the rigidity.

[0026] The top support layer **11** may be affixed to the membrane **13** using a variety of techniques such as by applying an adhesive. Individual adhesives may be desirable depending on the materials chosen for the top support layer **11,** membrane **13** and bottom support layer **15.** Examples of adhesives that may be utilized with the present invention are acrylic, rubber, ethylene vinyl acetate (EVA) based formulations, hot melt adhesives, and silicon based adhesives.

[0027] Referring to **FIG. 1b,** the sample aperture **12** allows fluid to pass through the top support layer **11** and contact the membrane. The sample aperture **12** should be in substantial alignment or approximate alignment with the measuring port **16** such that a target migrates in a substantially vertical path through the sample aperture **12.** The fluid may migrate through the sample aperture **12** by gravitational forces or by capillary forces.

BOTTOM SUPPORT LAYER

[0028] The bottom support layer **15** may prevent or reduce contact between the membrane **13** and a test strip tray of a measuring device, may add rigidity to the test strip **10** and may provide a structure enabling the user to grasp the reagent test strip **10.** Referring to **FIG. 1b,** the bottom support layer **15** includes a measuring port **16** in substantial alignment or approximate alignment with the sample aperture **12** such that a measuring device such as a reflectance meter may measure a surface of the membrane **13.**

[0029] The bottom support layer **15** may be constructed from any material able to substantially exclude the fluid applied to the test strip **10** such that the sample does not leak through the bottom support layer **15** and contact the user or the test strip tray. Moreover, it may be desirable to construct the bottom support layer **15** from a material sufficiently rigid such that the test strip **10** may be inserted into a measuring apparatus without undue bending or kinking. Some examples of appropriate materials are polypropylene, polystyrene, polyesters, and polymer plastic. The bottom support layer **15** is generally manufactured as a sheet, a roll, or a card then subdivided into appropriate size portions. Preferably the dimensions are about five centimeters long by about 6.5 millimeters wide. The thickness may be from about 1 mil to about 30 mil. The bottom support layer **15** may be affixed such as by adhesive to the membrane **13** or to the top support layer **11** or both. Suitable adhesives are acrylic, rubber, ethylene vinyl acetate (EVA) based formulations, hot melt adhesives and silicon based adhesives.

[0030] The measuring port **16** provides a region whereby a measuring device such as a reflectance meter is able to detect the reflectance from the surface of the membrane **13.** The measuring port **16** should be sufficiently large that the bottom support layer **15** does not interfere with the detection of a reflectance meter when the test strip **10** is correctly inserted into a reflectance meter test strip tray. Preferably, the measuring port **16** is an aperture.

SPREADING LAYER

[0031] The spreading layer **14** distributes the sample uniformly across the sample aperture **12** such that the sample may migrate uniformly towards the membrane. Referring to **FIG. 1b,** the spreading layer **14** is positioned above and in substantial alignment or approximate alignment with the sample aperture **12.** Generally the spreading layer **14** is adhesively affixed to the top support layer **11.** The pores should be sufficiently large to allow the target to flow through the spreading layer **14.** Preferably, the spreading layer **14** is constructed of a material that requires minimum sample volume, absorbs fluids quickly, and distributes fluids uniformly to the membrane **13** through the sample aperture **12.** Some examples of suitable materials for the spreading layer **14** are nylon, paper, glass fibers, polymer fibers, sintered plastics, woven fabrics, non-woven fabrics, and membranes.

MEMBRANE

[0032] A sample migrates through the spreading layer **14,** the sample aperture **12,** and contacts the membrane **13.** As the sample is absorbed into the membrane **13,** the pore size prevents larger particulates from passing through the membrane **13.** The remaining sample continues to migrate through the membrane **13** and contacts the reagent system where the signal is generated. The signal is detected from the surface of the membrane **13** opposite the sample aperture **12.**

[0033] The pore size of the membrane **13** determines the degree of size exclusion and may vary depending on the target of interest and the compounds the user wishes to exclude. Generally when utilizing the present invention with biological samples such as blood and performing an optical glucose detection assay, the pore size should be from about 0.1 um to about 15 um. The membrane **13** may comprise a uniform pore size or variable pore sizes. When the pore size is variable, pores may be configured in either a symmetric gradient or an asymmetric gradient configuration. Some examples of materials suitable for constructing a membrane **13** are polysulfone, polyethersulfone, nitrocellulose, and nylon. Polyethersulfone membranes are particularly well at reducing red blood cell lyses.

[0034] The membrane **13** may be positively charged, negatively charged or may have no charge. The membrane **13** charge may be the net charge after impregnating the membrane **13** with a reagent buffer. For instance, impregnating a neutrally charged membrane **13** with an acidic buffer may result in a net positive charge. When detecting the presence of glucose in whole blood, preferably the membrane **13** is hydrophilic and either positively, negatively, or neutrally charged.

REAGENT SYSTEM

[0035] The reagent system functions as an indicator in the direct or indirect presence of a target such that the target's presence in the sample may be detected. A reagent system must therefore be able to react with the target directly or indirectly and must yield a detectable signal. Typically, the reagent system comprises an enzyme system covalently or non-covalently bound to the membrane. Preferably, the enzyme system selectively catalyzes a primary reation with the

analyte of interest. A product of the primary reaction may be a dye or chromophore which undergoes a change in color that is detectable on the surface of the membrane **13** opposite the sample aperture **12.** Alternatively, the product of the primary reaction may be an intermediate which undergoes another reaction, preferably also enzyme catalyzed, and participates in a secondary reaction which, directly or indirectly, causes a dye or chromophore to undergo a change in color which is detectable on the surface of the membrane **13** opposite the sample aperture **12.** The signal is then detected visually or by a measuring devices such as a reflectance meter, and the presence or concentration of the target may be determined.

[0036] An enzyme system comprises at least one enzyme. In some instances two or more enzymes may be used in combination with one another. In addition, the reagent system may comprise a substrate capable of forming a chromophore. When this configuration is used, the chromophore is indicative of the presence or concentration of the target.

[0037] When the target is glucose, a useful reagent system comprises glucose oxidase and horseradish peroxidase. Glucose oxidase reacts with glucose and oxygen to produce gluconolactone and hydrogen peroxide. Hydrogen peroxide in the presence of a peroxidase such as horseradish peroxidase oxidizes a dye or chromophore and produces a detectable signal. In this configuration, the reflectance may be measured from about 500 nm to about 800 nm, preferably from about 600 nm to about 700 nm, most preferably about 660 nm. Examples of substrates that may be utilized with the present invention are o-dianisidine, o-toluidine, o-tolidine, 2,2'-Azinodi-(3-ethylbenzthiazoline sulphonic acid-(6)), 3-methyl-2-benzothiazolinone hydrazone plus N,N-dimethylaniline, phenol plus 4-aminophenazone, sulfonated 2,4-dichlorophenol plus 4-amino-phenazone, 3-methyl-2-benxothiazoline hydrazone plus 3-(dimethylamino)benzoic acid, 2-methoxy-4-allyl phenol, 4-aminoantipyrine-dimethylaniline, MTBH-DMAB dye couple (3-methyl-2-benzothiazolinone hydrazone hydrochloride and 3-dimethylaminobenzoic acid), AAP-CTA dye couple (4-aminoantipyrene and chromotropic acid), 3-methyl-2-benzothiazoline hydrazone in free form or in acid form (MTBH) and 8-anilino-1-napthalenesulfonate in acid or free form (ANS), 4-aminoantipyrene (AAP) and chromotropic acid, AAP and 8-anilino-1-napthalensulfonate (ANS), AAP and N-ethyl-N-(2 hydroxy-3-sulfopropyl)-m-toludine (TOOS), MTBH combined with its formaldehyde azine, leuco methylene blue, BISMAP, AAP and MAPS, AAP and N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3, 5-dimethylanine, sodium salt, monohydrate (MAOS), SMBTH and MAOS, AAP and 8-anilino-1-natphthalenesulfonate (ANS), MTBH combined with its formaldehyde azine, 3,3,5,5-tertramethylbenzidine (TMB), 4-aminoantipyrine. In addition the following substrates may also be utilized with the present invention. SMBTH and ALPS, MBTH and ALPS, AAP and DAPS, AAP and DAOS, MBTH and DMAB, BISMAP, and combinations thereof.

TARGET

[0038] The present invention is useful in detecting a variety of targets from a variety of samples. Preferably the target is glucose and the sample is whole blood. However, the present invention may be adapted for detecting the concentration or presence of a variety of targets by modifying the membrane **13** to include a reagent system that can detect the desired target. Generally the target is a biological moiety or a chemical moiety. The target may be a protein or a nucleic acid.

WET THROUGH

[0039] The present invention provides improvements relative to currently available technologies. Three problems are common with conventional test strips . First, test strips that do not have a top support layer often have a wet through problem. Secondly, test strips that do not have a bottom support layer and do not have at least one spacer may have contamination problems associated with wet through. Third, test strips that have a spreading layer positioned between two support layers require additional material such as an absorbent sink to capture excess fluid. Referring to **FIG. 1a,** the present invention reduces the wet through problem by utilizing a top support layer **11** with a sample aperture **12** such that the membrane **13** is in contact with the top support layer **11.** The present invention solves the contamination problem by incorporating either a bottom support layer **15** with a measuring port **16** as demonstrated in **FIG. 1b** or by incorporating spacers **17** as demonstrated in **FIG. 2.**

[0040] A wet through problem occurs when excess sample is added to a membrane. The excess sample overloads the membrane and may leak around or through the membrane. A conventional solution to address this problem is the addition of an absorbent sink, see WO 92/15863. However, the absorbent sink configuration does not function well when small sample volumes are applied. A large region houses both the membrane and the sink requiring the user to apply a greater volume of sample than a configuration with a membrane affixed to a top support layer. Importantly, one aim in the design of test strips is to minimize sample volume for the user. Therefore referring to **FIG. 1a,** present invention significantly reduces the wet through problem by contacting the membrane **13** to the top support layer **11** such that the membrane **13** is in substantial alignment or approximate alignment with the sample aperture **12.**

[0041] A problem inherent in test strips that do not have a bottom support layer is contamination of the test device, another test strip, or of another user. Test strips are generally placed in reflectance meters. When a traditional test strip absent a bottom support layer such as the device disclosed in U.S. Patent 5,753,452 is inserted into the meter, the

membrane may contact the measuring device. This may lead to a smearing of the reagent system or fluid containing the target on the test meter and may require the user to frequently clean the test meter. Additionally when a sample is a biological fluid such as whole blood, a portion of the sample may smear on the test strip tray and may come in contact with another user. The present invention overcomes these problems by the presence of a bottom support layer **15** as demonstrated in **FIG. 1b** or spacers **17** as demonstrated in **FIG. 2.** The present invention suspends the membrane 13 from the meter thus preventing contact between the membrane **13** and the meter.

OPTIONAL SPACER

[0042] Referring to **FIG. 2.** in another aspect of the present invention, a reagent test strip **10** is disclosed including a) a top support layer **11** including a sample aperture **12;** b) a membrane **13** including a reagent system for indicating the presence or concentration of a target; c) at least one spacer **17** able to reduce contact between the membrane **13** and a surface; and wherein the membrane **13** is positioned below the top support layer **11** and in substantial alignment or approximate alignment with the sample aperture **12.**

[0043] A spacer **17** functions to elevate the membrane **13** from a surface such as a test strip tray of a measuring device. The spacer may be any constructed from any material able to withstand the weight of the test strip **10.** The size and number of the spacers **17** may be dependent on the configuration of the test strip tray and should elevate the membrane **13** from the test strip tray when inserted into the measuring device. The spacer **17** is generally adhesively affixed to the top support layer **11** on the same surface as the membrane. Some examples of appropriate materials are polypropylene, polystyrene, polyesters, polymer plastic, and paper.

II METHOD FOR DETERMINING PRESENCE OR CONCENTRATION OF A TARGET USING THE TEST STRIP

[0044] The present invention also includes a method of determining the presence or concentration of a target in a sample that includes the steps of: a) applying a fluid suspected of including a target to the reagent test strip **10** of the present invention; b) detecting the reflectance of the membrane; and c) determining the presence or concentration of the target.

[0045] A fluid suspected of including a target may be applied using a variety of techniques such as by directly contacting the fluid to the test strip **10** or by using a dispensing device such as a capillary tube. Directly applying a fluid to the test strip 10 may be preferred by those that monitor target concentration outside of the laboratory such as routine glucose testing in diabetic patients. Diabetic patients generally require multiple measurements of plasma glucose during the day and prick a portion of the body to draw a small amount of whole blood.

[0046] The presence or absence of a target is determined by the change in reflectance of the membrane **13.** The reagent system produces a chromophore that exhibits a color change upon direct or indirect exposure to the target. The reflectance may be detected visually by observing a color change or may be detected using a measuring device such as a reflectance meter. When visually inspecting a color change, a color chart may be provided as a series of standards. The preferred measuring device is a reflectance meter. A reflectance meter has the advantage of higher sensitivity and accuracy. Concentration may be determined directly from the reflectance value. Alternatively, the reflectance may be converted to a K/S value then converted to concentration. The relationship between the K/S value and reflectance has as described in D.B. Judd and G. Wyszeki, Color in Business, Science and Industry (John Wiley & Sons, NY (1975).

III METHOD FOR DETECTING THE PRESENCE OR CONCENTRATION OF A TARGET USING KINETIC ENDPOINT MEASUREMENTS

[0047] The present invention also provides a method of determining the presence or concentration of a target once the reaction between the target and the reagent system is complete or near completion. The assay is complete or near complete when the difference between two reflectance values is equal to or less than a predetermined kinetic endpoint. This method may be utilized with any reagent test strip that undergoes a measurable change in light scatter until a kinetic endpoint is reached. Referring to **FIG. 3**, the method of determining the concentration of a target in a sample includes the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; running a preprogrammed threshold loop instruction; c) detecting a first reflectance measurement; d) running a preprogrammed kinetic loop instruction; e) determining the presence or concentration of the target; wherein the threshold loop instruction includes the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the detection loop instruction includes the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the comparison is less than or equal to a predetermined kinetic endpoint; replacing the value of the

first reflectance measurement with the value of the second reflectance measurement; and repeating the loop.

[0048] A dry strip reading functions as a reference value allowing the first and/or second reflectance measurement to be normalized. A fluid suspected of including the target is applied to the test strip **10** and gravity or capillary force causes the target to migrate through the membrane. Once the surface of the membrane **13** opposite the sample aperture **12** is moistened, the light scatter is reduced. When the detected value drops below a predetermined threshold value, two measurements may be taken at predetermined time intervals. These measurements are the first reflectance measurement and the second reflectance measurement respectively. The second reflectance measurement is compared to the first reflectance measurement. When the comparison is less than or about equal to the predetermined kinetic endpoint, the reaction is complete or near completed and the concentration of the target may be determined. The predetermined kinetic endpoint may be from about 0.2% to about 5 % and preferably from about 0.5% to about 1%. Generally the concentration is determined using the second reflectance measurement, however the first reflectance measurement or a new reflectance measurement may also be used. Alternatively, if the comparison value is greater than the predetermined kinetic endpoint, the value representing the first reflectance measurement may be replaced with the value of the second reflectance measurement and a new second reflectance measurement may be determined and compared to the newly replaced first reflectance measurement. As an alternative to replacing the first reflectance measurement with the second reflectance measurement, the present invention encompasses a loop instruction whereby a third reflectance measurement may be determined and compared to the second reflectance measurement. The present invention also encompasses comparing at least two sets of reflectance measurements such that both sets must be equal to or less than the predetermined kinetic endpoint.

[0049] The method of determining whether the kinetic endpoint is reached may be performed by calculating the change in reflectance measurements and comparing the result to a predetermined value. For instance, ifRl represents a first reflectance measurement, R2 represents a second reflectance measurement, and 1 % represents the predetermined kinetic endpoint (PKE), the comparison (C) may be performed by the following formula: C=((R1-R2)/R2)x 100%. If C is less than or equal to PKE, in this example 1 %, the concentration of the target is calculated. Otherwise the value of R2 becomes R1 and a new R2 is determined and compared to the new R1. The cycle continues until the comparison, C, is less than or equal to the predetermined kinetic endpoint, PKE. The present invention recognizes that the predetermined kinetic endpoint and comparison values are not limited to a percentage but may reflect a variety of units.

[0050] Alternatively a comparison may be desired between at least two sets of reflectance values such that both comparisons are less than or equal to the predetermined kinetic endpoint. Multiple sets of reflectance values may be utilized in this manner. Referring to **FIG. 4**, a method of determining the concentration of a target in a sample is disclosed including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) detecting a first reflectance measurement; d) running a preprogrammed kinetic loop instruction; e) running a consecutive comparison instruction; f) determining the presence or concentration of the target; wherein the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the comparison is less than or equal to a predetermined cutoff value; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop; further wherein the consecutive comparison instruction comprises the steps of: detecting a third reflectance measurement; comparing the second reflectance measurement to the third reflectance measurement; ending the consecutive comparison instruction if the comparison is less than or equal to the predetermined cutoff value; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and returning to the step of running a kinetic loop instruction. For example in addition to the equation above, it may be desirable to obtain third reflectance and fourth reflectance values, R3 and R4. In this instance C1=((R1-R2)/R2) x 100% and C2=((R4-R3)/R4) x 100%. The concentration may be determined once C1 and C2 are less than or equal to PKE. Referring to **FIG. 4**, the present invention also encompasses the condition where C1=((R1-R2)/R2) x 100% and C2=((R3-R2)/R3) x 100%.

[0051] As an alternative to calculating concentration directly from reflectance, the K/S ratio of the membrane 13 may also be utilized with the present invention. Kubelka and Munk derived the K/S ratio and has been described in D.B. Judd and G. Wyszeki, Color in Business, Science and Industry (John Wiley & Sons, NY (1975). The K/S ratio is related to the reflectance by $K/S=(1-R)^2/2R$.

IV Method of Detecting A Target Using A Fixed Time Point and Kinetic Endpoint Measurements

[0052] A hybrid method including a fixed time point method and kinetic endpoint method may also be utilized to determine the presence or concentration of a target in a sample. In this aspect, the kinetic method operates as previously

described however in addition, a fixed time point is also calculated. The fixed time point is the end of a predetermined time point that begins once the threshold value is reached or nearly reached. The method continues so long as either the comparison between the first reflectance reading and the second reflectance reading do not meet the predetermined kinetic endpoint or the fixed time point is reached, whichever is reached first. This method may be utilized with any reagent test strip that undergoes a measurable change in light scatter until a kinetic endpoint is reached.

[0053] Referring to **FIG. 5**, the present invention includes a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip of the present invention; b) applying a fluid suspected of including a target to the reagent test strip; c) running a preprogrammed threshold loop instruction; d) beginning a predetermined time point such that a fixed time point may be reached; e) detecting a first reflectance measurement; and f) running a preprogrammed kinetic loop instruction; g) determining the presence or concentration of the target. Preferably the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; and repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value. Preferably the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second measurement; ending the loop if the second reflectance measurement is less or equal to a predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop.

[0054] Referring to **FIG. 6**, the present invention also discloses a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from a reagent test strip of the present invention; b) running a preprogrammed threshold loop instruction; c) beginning a predetermined time point such that a fixed time point may be reached; d) detecting a first reflectance measurement; e) running a preprogrammed kinetic loop instruction; f) running a consecutive comparison instruction; g) determining the presence or concentration of the target; wherein the threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing the threshold comparison measurement to a predetermined threshold value; repeating the loop until the threshold comparison measurement is less than or equal to the predetermined threshold value; further wherein a fluid suspected of including a target is applied during the step of running the threshold loop instruction; further wherein the kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing the first reflectance measurement to the second reflectance measurement; ending the loop if the second reflectance measurement is less than or equal to a predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and repeating the loop; further wherein the consecutive comparison instruction comprises the steps of: detecting a third reflectance measurement; comparing the second reflectance measurement to the third reflectance measurement; ending the consecutive comparison instruction if the comparison is less than or equal to the predetermined cutoff value or if the fixed time point is reached; replacing the value of the first reflectance measurement with the value of the second reflectance measurement; and returning to the step of running a kinetic loop instruction.

V. Method of Detecting A Target Using A Fixed Time Point

[0055] The present invention also provides a method of determining the presence or concentration of a target once a fixed time point is reached. The fixed time point begins once the threshold comparison measurement is less than or equal to the predetermined threshold value. The present invention provides for a method of determining the concentration of a target in a sample including the steps of: a) detecting a dry strip reading from the reagent test strip **10** of the present invention; b) applying a fluid suspected of including a target to the reagent test strip **10;** c) running a preprogrammed threshold loop instruction; d) beginning a predetermined time point such that a fixed time point may be reached; and e) determining the presence or concentration of a target in a sample when the fixed time point is reached. Preferably the threshold loop instruction includes: detecting a threshold comparison value; comparing the threshold comparison value to a predetermined threshold value; repeating the loop until the threshold comparison value is less than or equal to the predetermined threshold value.

EXAMPLES

EXAMPLES I

Demonstration of Decreased Wet Through Problem With a Test Strip of the Present Invention

[0056] The following example illustrates the ability of a test strip 10 of the present invention to reduce the wet through problem associated with alternative test strip 10 configurations.

[0057] The membranes **13** in each of the following configurations were prepared in the same manner. The membrane

13, Biodyne A nylon membrane **13** having a 0.65 um pore size (Pall Corp., Port Washington, NY), was impregnated with a glucose oxidase/horseradish peroxidase exyme system (Toyobo Inc., Tokyo, Japan) and AAP (4-aminoantipyrene, Sigma, St. Louis, MO)/MAOS (N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3,5-dimethylanine, sodium salt, monohydrate, Dojindo Laboratories, Dumamoto, Japan) dye system.

[0058] Configuration A is one aspect of the present invention. Configuration A includes a membrane **13** affixed to the top support layer **11** and positioned above the bottom support layer **15** allowing a reflectance meter to measure light scatter through the measuring port **16.** A hydrophilic, woven, polyester, mesh spreading layer **14** (SaatiTech, Inc., Veniano, Italy) is positioned above the top support layer **11** in substantial and approximate alignment with the sample aperture **12** of the top support layer **11.**

[0059] Alternative configurations for comparison are as follows. Configuration B includes a membrane **13** and a hydrophilic, woven, polyester, mesh spreading layer **14** (SaatiTech, Inc., Veniano, Italy) sandwiched between the top support layer **11** and the bottom support layer **15** such that the spreading layer **14** is positioned between the top support layer **11** and the membrane **13.** Configuration C includes a membrane **13** affixed to the base support layer such that the sample is applied directly to the membrane **13.**

[0060] Whole blood samples with adjusted hematocrit of 42% and treated with sodium heparin as an anticoagulant, were prepared by spiking the sample with a concentrated glucose solution. Whole blood samples having glucose at a concentration of about 100, 250 and 450 mg/dL were prepared. The final glucose concentrations were verified by a YSI 2300 STAT-PLUS Glucose Analyzer (Yellow Springs Instruments Icn., Yellow Springs, OH).

[0061] Samples of 5, 10, 20 and 30 uL were applied to 10 strips of each configuration. Each sample was added to the test strip 10 once the test strip 10 was inserted into a reflectance meter and the reflectance was measured at 660nm. Reflectance readings were converted to glucose concentration values based on a calibration curve, averaged within each test group, normalized to the 5uL test group (Table 1) and the coefficient of variation (CV) was determined (Table 2). The test strips 10 were then visually observed for wet through (Table 3).

TABLE 1

Glucose mg/dL (by YSI)		5μL (% Difference vs. 5μL)	10μL (% Difference vs. 5μL)	20μL (% Difference vs. 5μL)	30μL (% Difference vs. 5μL)
104	Configuration A	0	+4.4	+5.1	+2.8
104	Configuration B	0	+8.0	+11.3	+15.0
104	Configuration C	0	+1.2	+6.5	+10.3
246	Configuration A	0	-2.1	-5.0	-4.0
246	Configuration B	0	+2.1	+20.4	+39.9
246	Configuration C	0	-2.6	+3.8	+20.7
467	Configuration A	0	+1.8	-8.9	-9.7
467	Configuration B	0	+23.8	+54.9	+147.1
467	Configuration C	0	+2.9	+15.3	+38.7

TABLE 2

Glucose mg/dL (by YSI)		5μL (%CV)	10μL (%CV)	20μL (%CV)	30μL (%CV)
104 A	Configuration	5.5	3.4	5.7	5.2
104 B	Configuration	3.3	4.2	2.5	2.7
104 C	Configuration	3.0	2.1	3.5	3.7
246	Configuration A	3.3	3.2	4.7	3.4
246 B	Configuration	3.1	4.1	3.5	3.8
246 C	Configuration	1.8	1.9	6.6	10.1
467 A	Configuration	4.6	3.5	4.4	5.6
467 B	Configuration	5.3	4.1	4.2	9.0
467 C	Configuration	3.7	3.3	6.4	14.8

TABLE 3

Glucose mg/dL		5μL	10μL	20μL	30μL
(by YSI)		Wet Through	Wet Through	Wet Through	Wet Through
104 A	Configuration	No	No	No	No
104 B	Configuration	No	Yes	Yes	Yes
104 C	Configuration	No	No	Yes	Yes
246 A	Configuration	No	No	No	No
246 B	Configuration	No	Yes	Yes	Yes
246 C	Configuration	No	No	Yes	Yes
467 A	Configuration	No	No	No	No
467 B	Configuration	No	Yes	Yes	Yes
467 C	Configuration	No	No	No	Yes

Claims

1. A reagent test strip (10) comprising:

a) a top support layer (11) comprising a sample aperture (12);
b) a membrane (13) comprising a reagent system for indicating the concentration of a target;
c) a spreading layer (14);
d) a bottom support layer (15) comprising a measuring port (16) in substantial alignment or approximate alignment with said sample aperture (12);

wherein said membrane (13) is affixed to said top support layer (11);
further wherein said membrane (13) is positioned between said top support layer (11) and said bottom support layer (15);
further wherein said spreading layer (14) is positioned above said top support layer (11) and in alignment with said sample aperture (12); and
further wherein a fluid applied to said spreading layer (14), passes through said sample aperture (12) and contacts said membrane (13).

2. The reagent test strip (10) according to claim 1, wherein said membrane (13) is hydrophilic.

3. The reagent test strip (10) according to claim 1, wherein said membrane (13) is able to exclude red blood cells.

4. The reagent test strip (10) according to claim 1, wherein said membrane (13) is a symmetric membrane or an asymmetric membrane.

5. The reagent test strip (10) according to claim 1, wherein said membrane (13) comprises polysulfone, polyethersulfone, nylon, or nitrocellulose.

6. The reagent test strip (10) according to claim 1, wherein said reagent system comprises an enzyme.

7. The reagent test strip (10) according to claim 6, wherein said enzyme is glucose oxidase.

8. The reagent test strip (10) according to claim 6, wherein said enzyme is horseradish peroxidase.

9. The reagent test strip (10) according to claim 1, wherein said reagent system comprises glucose oxidase and horseradish peroxidase.

10. The reagent test strip (10) according to claim 1, wherein said reagent system comprises a substrate capable of forming a chromophore

11. The reagent test strip (10) according to claim 10, wherein said substrate is a AAP and MAOS.

12. The reagent test strip (10) according to claim 10, wherein said chromophore is detected by measuring reflectance.

13. The reagent test strip (10) according to claim 12, wherein said reflectance is indicative of the concentration of said target.

14. The reagent test strip (10) according to claim 12, wherein said reflectance is detected directly on said membrane (13).

15. The reagent test strip (10) according to claim 10, wherein said chromophore absorbs light from about 500 nm to about 800 nm.

16. The reagent test strip (10) according to claim 10, wherein said chromophore absorbs light from about 600 nm to about 700 nm.

17. The reagent test strip (10) according to claim 1, wherein said target is a biological moiety or chemical moiety.

18. The reagent test strip (10) according to claim 1, wherein said target is a protein or nucleic acid.

19. The reagent test strip (10) according to claim 1, wherein said target is glucose.

20. The reagent test strip (10) according to claim 1, wherein said spreading layer (14) is hydrophillic.

21. The reagent test strip (10) according to claim 1, wherein said fluid comprises whole blood.

22. The reagent test strip (10) according to claim 1, wherein said reagent test strip (10) reduces wet through of said fluid through said membrane (13).

23. A method of determining the presence or concentration of a target in a sample comprising the steps of:

a) applying a fluid suspected of comprising a target to the reagent test strip (10) of claim 1;
b) detecting the reflectance of said membrane (13) through said measuring port (16); and
c) determining the presence or concentration of said target.

24. The method of determining the presence or concentration of a target in a sample according to claim 23, wherein the step of determining the presence or concentration comprises measuring the absorbance of a chromophore.

25. A method of determining the concentration of a target in a sample comprising the steps of:

a) placing a reagent test strip (10) of claim 1 in a computerized test strip measuring device and detecting a dry strip reading from the reagent test strip (10) of claim 1;
b) applying a fluid suspected of including a target to the reagent test strip;
c) initiating a command program in the computerized device wherein the command is a preprogrammed threshold loop instruction,
wherein said threshold loop instruction comprises the steps of: detecting a threshold comparison measurement; comparing said threshold comparison measurement to a predetermined threshold value;
d) repeating the loop until said threshold comparison measurement is less than or equal to said predetermined threshold value;
e) detecting a first reflectance measurement;
f) running a preprogrammed kinetic loop instruction, wherein said kinetic loop instruction comprises the steps of: detecting a second reflectance measurement; comparing said first reflectance measurement to said second reflectance measurement;
g) ending the loop if said comparison is less than or equal to a predetermined cutoff value;
h) replacing the value of said first reflectance measurement with the value of said second reflectance measurement;
i) repeating the loop; and

j) determining the presence or concentration of the target.

26. The method according to claim 25, wherein the step of determining the presence or concentration of said target comprises calculating the concentration using said second reflectance measurement.

27. The method of claim 25 further comprising the step of:

- running a consecutive comparison instruction after step i);

wherein said consecutive comparison instruction comprises the steps of:

detecting a third reflectance measurement;
comparing said second reflectance measurement to said third reflectance measurement;
ending the consecutive comparison instruction if said comparison is less than or equal to said predetermined cutoff value;
replacing the value of said first reflectance measurement with the value of said third reflectance measurement; and
returning to the step of running a kinetic loop instruction.

28. The method of claim 25 further comprising the steps of:

- beginning a predetermined time point such that a fixed time point may be reached after step c); and
- ending the loop if said second reflectance measurement is less than or equal to a predetermined cutoff value or if said fixed time point is reached in step g.

29. The method of claim 25 further comprising the steps of:

- beginning a predetermined time point such that a fixed time point may be reached after step d);
- ending the loop if said second reflectance measurement is less than or equal to a predetermined cutoff value or if said fixed time point is reached in step g);
- running a consecutive comparison instruction after step i);

wherein said consecutive comparison instruction comprises the steps of:

detecting a third reflectance measurement;
comparing said second reflectance measurement to said third reflectance measurement;
ending the consecutive comparison instruction if said comparison is less than or equal to said predetermined cutoff value or if said fixed time point is reached;
replacing the value of said first reflectance measurement with the value of said third reflectance measurement; and
returning to the step of running a kinetic loop instruction.

30. A method of determining the concentration of a target in a sample comprising the steps of:

a) placing a reagent test strip (10) of claim 1 in a computerized test strip measuring device and detecting a dry strip reading from the reagent test strip (10) of claim 1;
b) applying a fluid suspected of including a target to the reagent test strip;
c) initiating a command program in the computerized device wherein the command is a preprogrammed threshold loop instruction,
wherein said threshold loop instruction comprises the steps of: detecting a threshold comparison value; comparing said threshold comparison value to a predetermined threshold value;
d) repeating the loop until said threshold comparison value is less than or equal to said predetermined threshold value;
e) beginning a predetermined time point such that a fixed time point may be reached;
f) determining the presence or concentration of a target in a sample when said fixed time point is reached.

Patentansprüche

1. Ein Reagenz-Teststreifen (10), der umfasst:

   a) eine obere Trägerschicht (11), die eine Probenöffnung (12) umfasst;
   b) eine Membran (13), die ein Reagenzsystem zum Anzeigen der Konzentration eines Targets umfasst;
   c) eine Verteilungsschicht (14);
   d) eine untere Trägerschicht (15), die eine Messöffnung (16) im wesentlichen in Ausrichtung mit oder ungefähr in Ausrichtung mit der Probenöffnung (12) umfasst;

   wobei die Membran (13) an die obere Trägerschicht (11) angebracht ist;
   wobei des Weiteren die Membran (13) zwischen der oberen Trägerschicht (11) und der unteren Trägerschicht (15) positioniert ist;
   wobei des Weiteren die Verteilungsschicht (14) oberhalb der oberen Trägerschicht (11) und in Ausrichtung mit der Probenöffnung (12) positioniert ist; und
   wobei des Weiteren eine Flüssigkeit, die auf die Verteilungsschicht (14) aufgetragen ist, durch die Probenöffnung (12) passiert und die Membran (13) kontaktiert.

2. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei die Membran (13) hydrophil ist.

3. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei die Membran (13) in der Lage ist, rote Blutkörperchen auszuschließen.

4. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei die Membran (13) eine symmetrische Membran oder eine asymmetrische Membran ist.

5. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei die Membran (13) Polysulfon, Polyethersulfon, Nylon oder Nitrocellulose umfasst.

6. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei das Reagenzsystem ein Enzym umfasst.

7. Der Reagenz-Teststreifen (10) gemäß Anspruch 6, wobei das Enzym Glucoseoxidase ist.

8. Der Reagenz-Teststreifen (10) gemäß Anspruch 6, wobei das Enzym Meerrettich-Peroxidase ist.

9. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei das Reagenzsystem Glucoseoxidase und Meerrettich-Peroxidase umfasst.

10. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei das Reagenzsystem ein Substrat umfasst, das ein Chromophor bilden kann.

11. Der Reagenz-Teststreifen (10) gemäß Anspruch 10, wobei das Substrat AAP und MAOS ist.

12. Der Reagenz-Teststreifen (10) gemäß Anspruch 10, wobei das Chromophor durch Messen der Reflexion detektiert wird.

13. Der Reagenz-Teststreifen (10) gemäß Anspruch 12, wobei die Reflexion für die Konzentration des Targets indikativ ist.

14. Der Reagenz-Teststreifen (10) gemäß Anspruch 12, wobei die Reflexion direkt auf der Membran (13) detektiert wird.

15. Der Reagenz-Teststreifen (10) gemäß Anspruch 10, wobei das Chromophor Licht von ungefähr 500 nm bis ungefähr 800 nm absorbiert.

16. Der Reagenz-Teststreifen (10) gemäß Anspruch 10, wobei das Chromophor Licht von ungefähr 600 nm bis ungefähr 700 nm absorbiert.

17. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei das Target eine biologische Einheit oder eine chemische

Einheit ist.

18. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei das Target ein Protein oder eine Nukleinsäure ist.

19. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei das Target Glucose ist.

20. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei die Verteilungsschicht (14) hydrophil ist.

21. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei die Flüssigkeit Vollblut umfasst.

22. Der Reagenz-Teststreifen (10) gemäß Anspruch 1, wobei der Reagenz-Teststreifen (10) das Durchsickern der Flüssigkeit durch die Membran (13) verringert.

23. Ein Verfahren zum Bestimmen des Vorhandenseins oder der Konzentration eines Targets in einer Probe, das die Schritte umfasst:

a) Auftragen einer Flüssigkeit, die in Verdacht steht, ein Target zu umfassen, auf den Reagenz-Teststreifen (10) nach Anspruch 1;
b) Detektieren der Reflexion der Membran (13) durch die Messöffnung (16); und
c) Bestimmen des Vorhandenseins oder der Konzentration des Targets.

24. Das Verfahren zum Bestimmen des Vorhandenseins oder der Konzentration eines Targets in einer Probe gemäß Anspruch 23, wobei der Schritt des Bestimmens des Vorhandenseins oder der Konzentration das Messen des Absorptionsgrads eines Chromophors umfasst.

25. Ein Verfahren zum Bestimmen der Konzentration eines Targets in einer Probe, das die Schritte umfasst:

a) Platzieren eines Reagenz-Teststreifens (10) nach Anspruch 1 in einer computergesteuerten Teststreifen-Messvorrichtung und Detektieren einer Auslesung eines trockenen Streifens von dem Reagenz-Teststreifen (10) nach Anspruch 1;
b) Auftragen einer Flüssigkeit, die in Verdacht steht, ein Target zu beinhalten, auf den Reagenz-Teststreifen;
c) Initiieren eines Befehlsprogramms in der computergesteuerten Vorrichtung, wobei der Befehl eine vorprogrammierte Schwellenwert-Schleifen-Instruktion ist;
wobei die Schwellenwert-Schleifen-Instruktion die Schritte umfasst: Detektieren einer Schwellenwert-Vergleichsmessung; Vergleichen der Schwellenwert-Vergleichsmessung mit einem vorherbestimmten Schwellenwert;
d) Wiederholen der Schleife bis die Schwellenwert-Vergleichsmessung weniger oder gleich dem vorherbestimmten Schwellenwert ist;
e) Detektieren einer ersten Reflexionsmessung;
f) Durchführen einer vorprogrammierten kinetischen Schleifen-Instruktion,
wobei die kinetische Schleifen-Instruktion die Schritte umfasst: Detektieren einer zweiten Reflexionsmessung; Vergleichen der ersten Reflexionsmessung mit der zweiten Reflexionsmessung;
g) Beenden der Schleife wenn der Vergleich weniger oder gleich einem vorherbestimmten Anhaltewert ist;
h) Ersetzen des Wertes der ersten Reflexionsmessung durch den Wert der zweiten Reflexionsmessung;
i) Wiederholen der Schleife; und
j) Bestimmen des Vorhandenseins oder der Konzentration des Targets.

26. Das Verfahren gemäß Anspruch 25, wobei der Schritt des Bestimmens des Vorhandenseins oder der Konzentration des Targets das Berechnen der Konzentration unter Verwendung der zweiten Reflexionsmessung umfasst.

27. Das Verfahren nach Anspruch 25, das Weiter den Schritt umfasst:

- Durchführen einer aufeinanderfolgenden Vergleichs-Instruktion nach Schritt i);

wobei die aufeinanderfolgende Vergleichs-Instruktion die Schritte umfasst:

- Detektieren einer dritten Reflexionsmessung;
- Vergleichen der zweien Reflexionsmessung mit der dritten Reflexionsmessung;

- Beenden der aufeinanderfolgenden Vergleichs-Instruktion wenn der Vergleich weniger oder gleich dem vorherbestimmten Anhaltewert ist;
- Ersetzen des Werts der ersten Reflexionsmessung durch den Wert der dritten Reflexionsmessung; und
- Zurückkehren zu dem Schritt des Durchführens einer kinetischen Schleifen-Instruktion.

28. Das Verfahren nach Anspruch 25, das Weiter die Schritte umfasst:

- Beginnen eines vorherbestimmten Zeitpunkts, so dass ein fixierter Zeitpunkt nach Schritt c) erreicht werden kann; und
- Beenden der Schleife wenn die zweite Reflexionsmessung weniger oder gleich einem vorherbestimmten Anhaltewert ist oder wenn der fixierte Zeitpunkt in Schritt g) erreicht ist.

29. Das Verfahren nach Anspruch 25, das Weiter die Schritte umfasst:

- Beginnen eines vorherbestimmten Zeitpunkts, so dass ein fixierter Zeitpunkt nach Schritt d) erreicht werden kann;
- Beenden der Schleife wenn die zweite Reflexionsmessung weniger oder gleich einem vorherbestimmten Anhaltewert ist oder wenn der fixierte Zeitpunkt in Schritt g) erreicht ist;
- Durchführen einer aufeinanderfolgenden Vergleichs-Instruktion nach Schritt i),

wobei die aufeinanderfolgende Vergleichs-Instruktion die Schritte umfasst:

- Detektieren einer dritten Reflexionsmessung;
- Vergleichen der zweiten Reflexionsmessung mit der dritten Reflexionsmessung;
- Beenden der aufeinanderfolgenden Vergleichs-Instruktion wenn der Vergleich weniger oder gleich einem vorherbestimmten Anhaltewert ist oder wenn der fixierte Zeitpunkt erreicht ist;
- Ersetzen des Werts der ersten Reflexionsmessung durch den Wert der dritten Reflexionsmessung; und
- Zurückkehren zu dem Schritt des Durchführens einer kinetischen Schleifen-Instruktion.

30. Ein Verfahren zum Bestimmen der Konzentration eines Targets in einer Probe, das die Schritte umfasst:

a) Platzieren eines Reagenz-Teststreifens (10) nach Anspruch 1 in einer computergesteuerten Teststreifen-Messvorrichtung und Detektieren einer Auslesung eines trockenen Streifens von dem Reagenz-Teststreifen (10) nach Anspruch 1;
b) Auftragen einer Flüssigkeit, die in Verdacht steht, ein Target zu beinhalten, auf den Reagenz-Teststreifen;
c) Initiieren eines Befehlsprogramms in der computergesteuerten Vorrichtung, wobei der Befehl eine vorprogrammierte Schwellenwert-Schleifen-Instruktion ist;
wobei die Schwellenwert-Schleifen-Instruktion die Schritte umfasst: Detektieren eines Schwellenwert-Vergleichswerts; Vergleichen des Schwellenwert-Vergleichswerts mit einem vorherbestimmten Schwellenwert;
d) Wiederholen der Schleife bis der Schwellenwert-Vergleichswert weniger oder gleich dem vorherbestimmten Schwellenwert ist;
e) Beginnen eines vorherbestimmten Zeitpunkts, so dass ein fixierter Zeitpunkt erreicht werden kann;
f) Bestimmen des Vorhandenseins oder der Konzentration eines Targets in einer Probe wenn der fixierte Zeitpunkt erreicht ist.

Revendications

1. Bandelette réactive (10) comprenant :

a) une couche support supérieure (11) munie d'une ouverture à échantillon (12) ;
b) une membrane (13) comprenant un système réactif destiné à indiquer la concentration d'une cible ;
c) une couche de diffusion (14) ;
d) une couche support inférieure (15) munie d'une ouverture de mesure (16), sensiblement ou approximativement alignée avec ladite ouverture à échantillon (12) ;

dans laquelle ladite membrane (13) est fixée à ladite couche support supérieure (11) ;
dans laquelle, en outre, ladite membrane (13) est positionnée entre ladite couche support supérieure (11) et ladite

couche support inférieure (15) ;
dans laquelle, en outre, ladite couche de diffusion (14) est positionnée au-dessus de ladite couche support supérieure (11) et en alignement avec ladite ouverture à échantillon (12) ; et
dans laquelle, en outre, un fluide appliqué à ladite couche de diffusion (14) traverse ladite ouverture à échantillon (12) et entre en contact avec ladite membrane (13).

2. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite membrane (13) est hydrophile.

3. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite membrane (13) est capable d'exclure des érythrocytes.

4. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite membrane (13) est une membrane symétrique ou une membrane asymétrique.

5. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite membrane (13) comprend du polysulfone, du polyéthersulfone, du nylon, ou de la nitrocellulose.

6. Bandelette réactive (10) selon la revendication 1, dans laquelle ledit système réactif comprend une enzyme.

7. Bandelette réactive (10) selon la revendication 6, dans laquelle ladite enzyme est du glucose oxydase.

8. Bandelette réactive (10) selon la revendication 6, dans laquelle ladite enzyme est de la peroxydase de raifort.

9. Bandelette réactive (10) selon la revendication 1, dans laquelle ledit système réactif comprend du glucose oxydase et de la peroxydase de raifort.

10. Bandelette réactive (10) selon la revendication 1, dans laquelle ledit système réactif comprend un substrat capable de former un chromophore.

11. Bandelette réactive (10) selon la revendication 10, dans laquelle ledit substrat est un AAP et du MAOS.

12. Bandelette réactive (10) selon la revendication 10, dans laquelle ledit chromophore est détecté par mesure de la réflectance.

13. Bandelette réactive (10) selon la revendication 12, dans laquelle ladite réflectance est une indication de la concentration de ladite cible.

14. Bandelette réactive (10) selon la revendication 12, dans laquelle ladite réflectance est détectée directement sur ladite membrane (13).

15. Bandelette réactive (10) selon la revendication 10, dans laquelle ledit chromophore absorbe de la lumière d'environ 500 nm à environ 800 nm.

16. Bandelette réactive (10) selon la revendication 10, dans laquelle ledit chromophore absorbe de la lumière d'environ 600 nm à environ 700 nm.

17. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite cible est un groupe fonctionnel biologique ou un groupe fonctionnel chimique.

18. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite cible est une protéine ou un acide nucléique.

19. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite cible est du glucose.

20. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite couche de diffusion (14) est hydrophile.

21. Bandelette réactive (10) selon la revendication 1, dans laquelle ledit fluide comprend du sang entier.

22. Bandelette réactive (10) selon la revendication 1, dans laquelle ladite bandelette réactive (10) diminue une migration

excessive (*wet through*) dudit fluide à travers ladite membrane (13).

23. Procédé pour déterminer la présence ou la concentration d'une cible dans un échantillon comprenant les étapes consistant à :

a) appliquer un fluide susceptible de comprendre une cible à la bandelette réactive (10) de la revendication 1 ;
b) détecter la réflectance de ladite membrane (13) à travers ladite ouverture de mesure (16) ; et
c) déterminer la présence ou la concentration de ladite cible.

24. Procédé pour déterminer la présence ou la concentration d'une cible dans un échantillon selon la revendication 23, dans lequel l'étape consistant à déterminer la présence ou la concentration comprend la mesure de l'absorbance d'un chromophore.

25. Procédé pour déterminer la concentration d'une cible dans un échantillon comprenant les étapes consistant à:

a) placer une bandelette réactive (10) de la revendication 1 dans un dispositif de mesure de bandelettes réactives informatisé et détecter une lecture de la bandelette sèche pratiquée sur la bandelette réactive (10) de la revendication 1 ;
b) appliquer un fluide susceptible de comprendre une cible à la bandelette réactive ;
c) lancer un programme de commande dans le dispositif informatisé dans lequel la commande est une instruction de boucle à seuil préprogrammé,
dans lequel ladite instruction de boucle à seuil comprend les étapes consistant à : détecter une mesure pour comparaison avec un seuil ; comparer ladite mesure pour comparaison avec un seuil avec une valeur de seuil prédéterminée ;
d) répéter la boucle jusqu'à ce que ladite mesure pour comparaison avec un seuil soit inférieure ou égale à ladite valeur de seuil prédéterminée ;
e) détecter une première mesure de réflectance ;
f) exécuter une instruction de boucle cinétique préprogrammée, ladite instruction de boucle cinétique comprenant les étapes consistant à : détecter une deuxième mesure de réflectance ; comparer ladite première mesure de réflectance à ladite deuxième mesure de réflectance ;
g) terminer la boucle si ladite comparaison est inférieure ou égale à une valeur de coupure prédéterminée ;
h) remplacer la valeur de ladite première mesure de réflectance par la valeur de ladite deuxième mesure de réflectance ;
i) répéter la boucle ; et
j) déterminer la présence ou la concentration de la cible.

26. Procédé selon la revendication 25, dans lequel l'étape consistant à déterminer la présence ou la concentration de ladite cible comprend le calcul de la concentration en utilisant ladite deuxième mesure de réflectance.

27. Procédé selon la revendication 25, comprenant en outre l'étape consistant à :

- exécuter une instruction de comparaison consécutive après l'étape i) ;

dans lequel ladite instruction de comparaison consécutive comprend les étapes consistant à :

détecter une troisième mesure de réflectance ;
comparer ladite deuxième mesure de réflectance à ladite troisième mesure de réflectance ;
terminer l'instruction de comparaison consécutive si ladite comparaison est inférieure ou égale à ladite valeur de coupure prédéterminée ;
remplacer la valeur de ladite première mesure de réflectance par la valeur de ladite troisième mesure de réflectance ; et
revenir à l'étape d'exécution d'une instruction de boucle cinétique.

28. Procédé selon la revendication 25 comprenant en outre les étapes consistant à :

- initialiser un point temporel prédéterminé de sorte qu'un point temporel fixe puisse être atteint après l'étape c) ; et
- terminer la boucle si ladite deuxième mesure de réflectance est inférieure ou égale à une valeur de coupure prédéterminée ou si ledit point temporel fixe est atteint à l'étape g).

29. Procédé selon la revendication 25 comprenant en outre les étapes consistant à :

- initialiser un point temporel prédéterminé de sorte qu'un point temporel fixe puisse être atteint après l'étape d) ;
- terminer la boucle si ladite deuxième mesure de réflectance est inférieure ou égale à une valeur de coupure prédéterminée ou si ledit point temporel fixe est atteint à l'étape g) ;
- exécuter une instruction de comparaison consécutive après l'étape i) ;

dans lequel ladite instruction de comparaison consécutive comprend les étapes consistant à :

détecter une troisième mesure de réflectance ;
comparer ladite deuxième mesure de réflectance à ladite troisième mesure de réflectance ;
terminer l'instruction de comparaison consécutive si ladite comparaison est inférieure ou égale à ladite valeur de coupure prédéterminée ou si ledit point temporel fixe est atteint ;
remplacer la valeur de ladite première mesure de réflectance par la valeur de ladite troisième mesure de réflectance ; et
revenir à l'étape consistant à exécuter une instruction de boucle cinétique.

30. Procédé pour déterminer la concentration d'une cible dans un échantillon comprenant les étapes consistant à :

a) placer une bandelette réactive (10) selon la revendication 1 dans un dispositif de mesure de bandelettes réactives informatisé et détecter une valeur de lecture sur bandelette sèche à partir de la bandelette réactive (10) de la revendication 1 ;
b) appliquer un fluide susceptible de comprendre une cible à la bandelette réactive ;
c) lancer un programme de commande dans le dispositif informatisé dans lequel la commande est une instruction de boucle à seuil préprogrammé ;
dans lequel ladite instruction de boucle à seuil comprend les étapes consistant à : détecter une valeur de comparaison à un seuil ; comparer ladite valeur de comparaison à un seuil à une valeur de seuil prédéterminée ;
d) répéter la boucle jusqu'à ce que ladite valeur de comparaison à un seuil soit inférieure ou égale à ladite valeur de seuil prédéterminée ;
e) initialiser un point temporel prédéterminé de sorte qu'un point temporel fixe puisse être atteint ;
f) déterminer la présence ou la concentration d'une cible dans un échantillon lorsque ledit point temporel fixe est atteint.

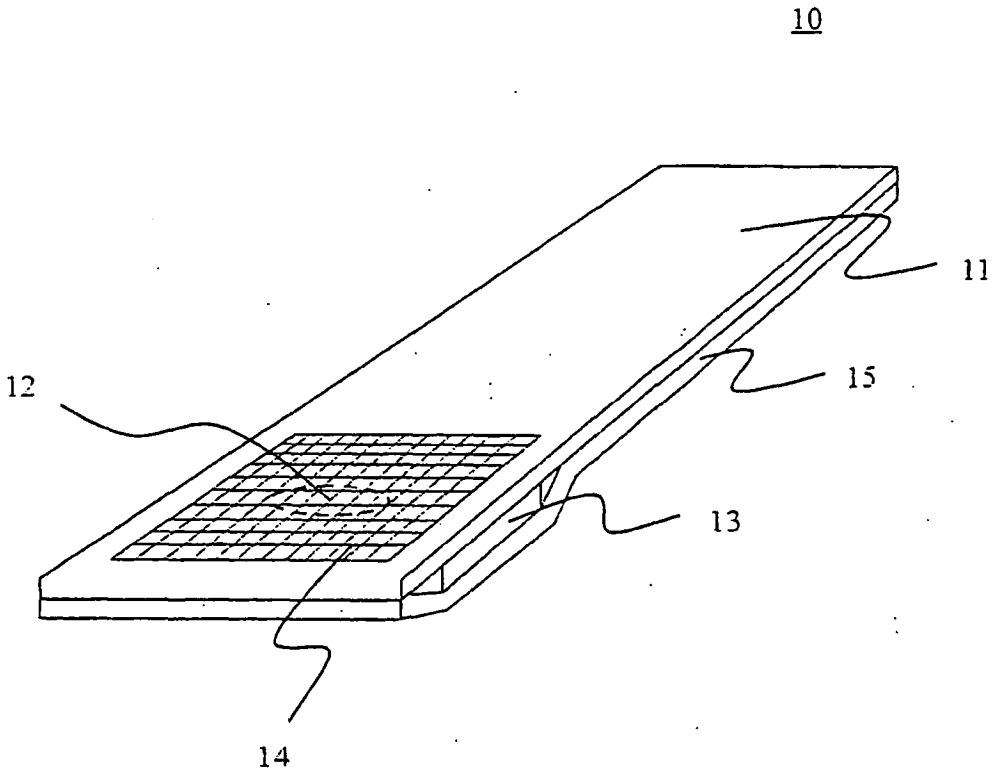

FIG. 1a

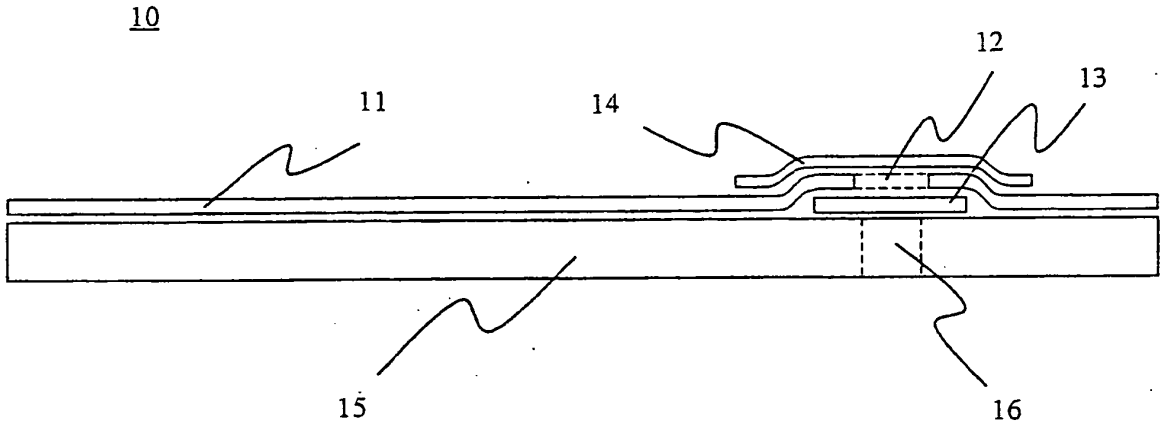

FIG. 1b

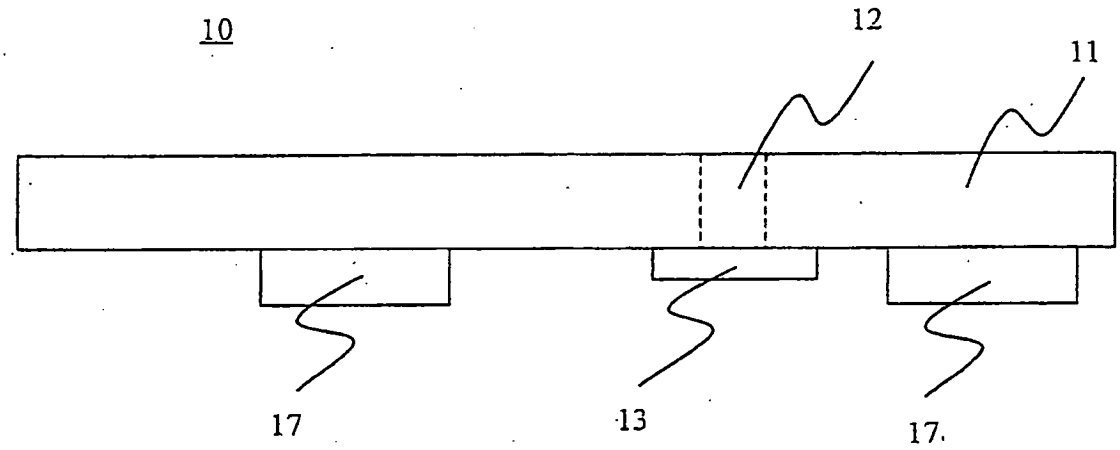

FIG. 2

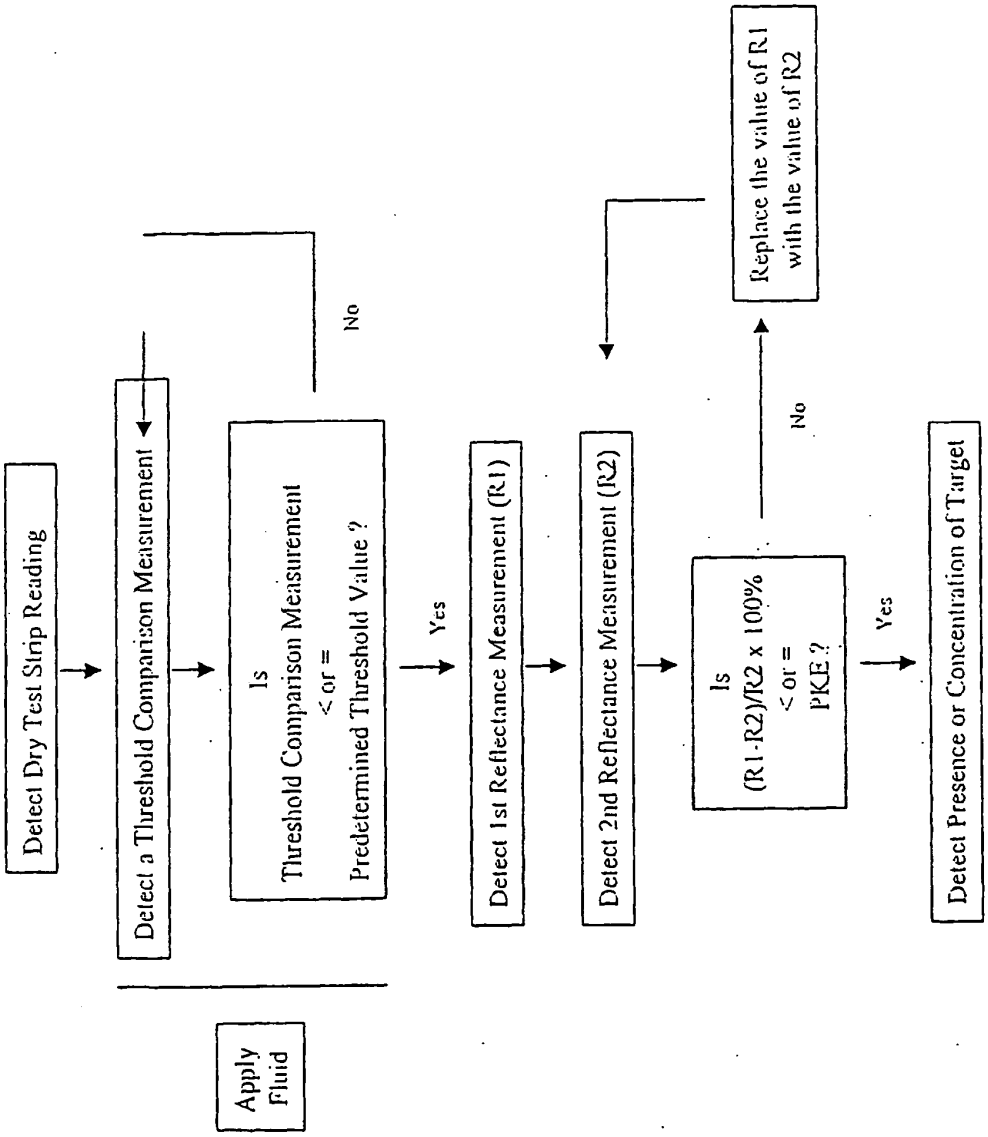
Detect Dry Test Strip Reading
Apply Fluid
Detect a Threshold Comparison Measurement
Is Threshold Comparison Measurement < or = Predetermined Threshold Value ?
No
Yes
Detect 1st Reflectance Measurement (R1)
Detect 2nd Reflectance Measurement (R2)
Is (R1-R2)/R2 x 100% < or = PKE ?
No
Yes
Replace the value of R1 with the value of R2
Detect Presence or Concentration of Target

FIG. 3

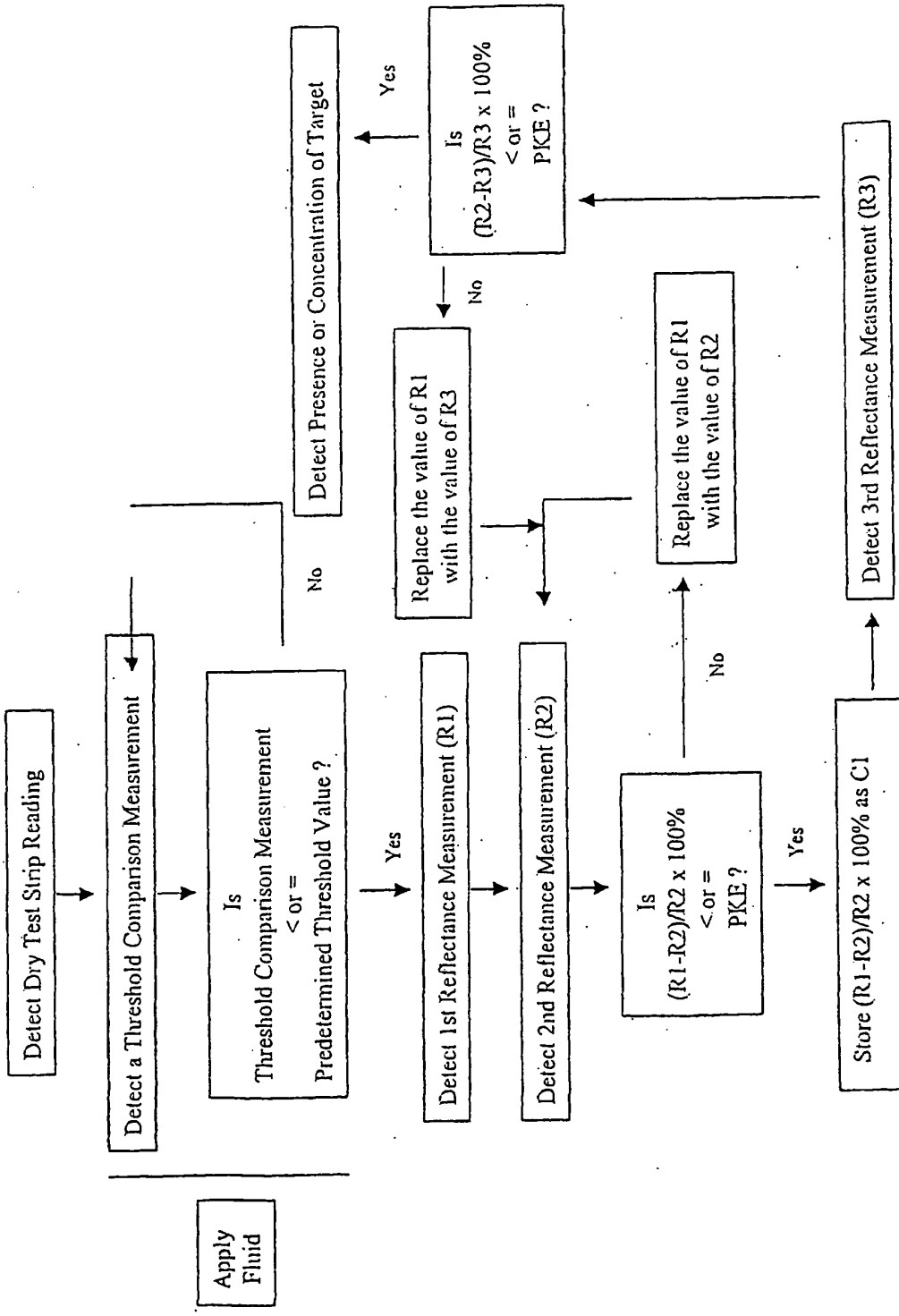
Detect Dry Test Strip Reading
Apply Fluid
Detect a Threshold Comparison Measurement
Is Threshold Comparison Measurement < or = Predetermined Threshold Value ?
No
Detect Presence or Concentration of Target
Yes
Detect 1st Reflectance Measurement (R1)
Detect 2nd Reflectance Measurement (R2)
Is (R1-R2)/R2 x 100% < or = PKE ?
No
Replace the value of R1 with the value of R2
Yes
Store (R1-R2)/R2 x 100% as C1
Detect 3rd Reflectance Measurement (R3)
Is (R2-R3)/R3 x 100% < or = PKE ?
No
Replace the value of R1 with the value of R3
Yes

FIG. 4

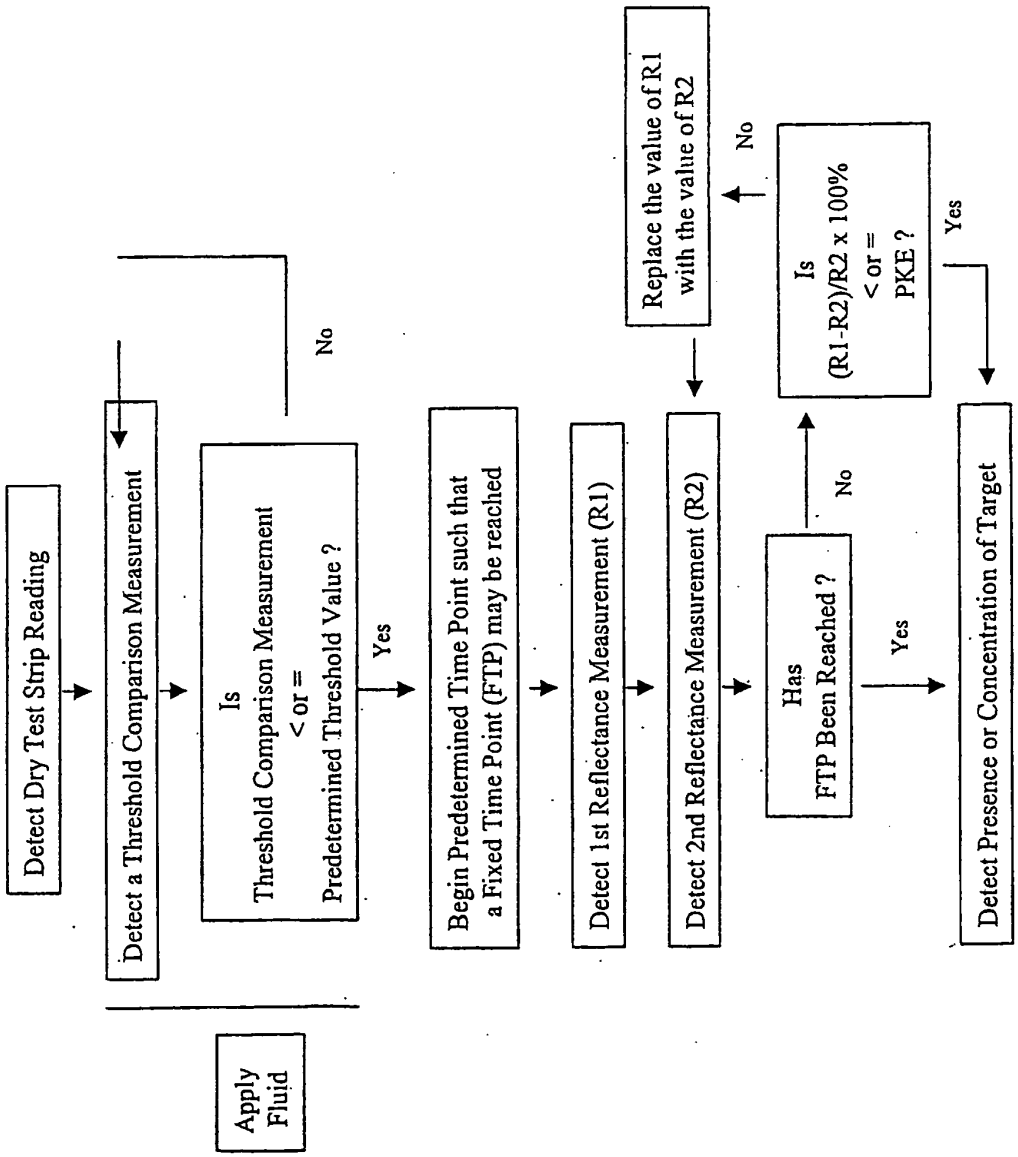
Detect Dry Test Strip Reading
Apply Fluid
Detect a Threshold Comparison Measurement
Is Threshold Comparison Measurement < or = Predetermined Threshold Value ?
No
Yes
Begin Predetermined Time Point such that a Fixed Time Point (FTP) may be reached
Detect 1st Reflectance Measurement (R1)
Detect 2nd Reflectance Measurement (R2)
Has FTP Been Reached ?
No
Yes
Is (R1-R2)/R2 x 100% < or = PKE ?
No
Yes
Replace the value of R1 with the value of R2
Detect Presence or Concentration of Target

FIG. 5

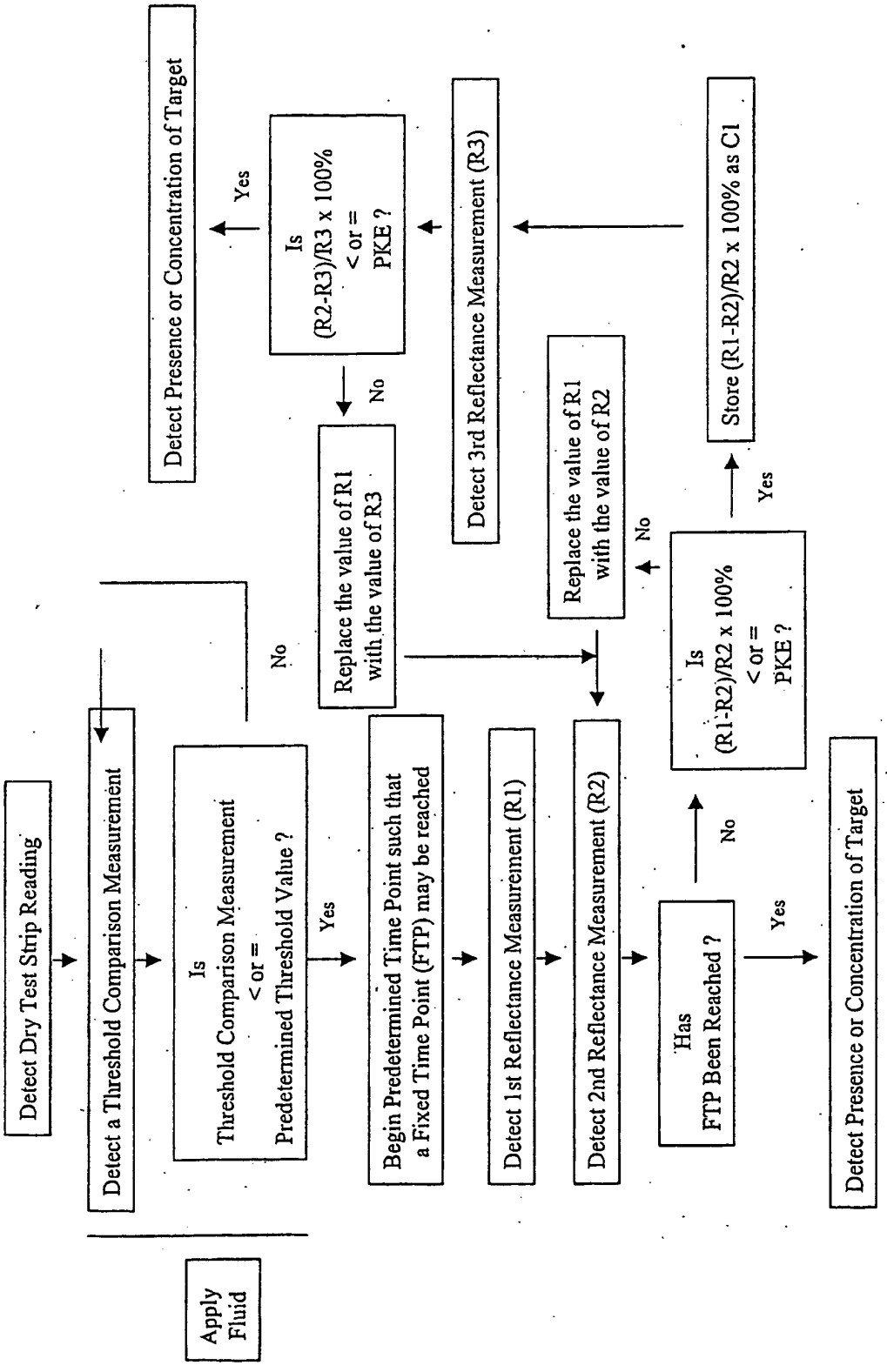
Apply Fluid
Detect Dry Test Strip Reading
Detect a Threshold Comparison Measurement
Is Threshold Comparison Measurement < or = Predetermined Threshold Value ?
No
Yes
Begin Predetermined Time Point such that a Fixed Time Point (FTP) may be reached
Detect 1st Reflectance Measurement (R1)
Detect 2nd Reflectance Measurement (R2)
Has FTP Been Reached ?
No
Yes
Is (R1-R2)/R2 x 100% < or = PKE ?
No
Yes
Store (R1-R2)/R2 x 100% as C1
Replace the value of R1 with the value of R2
Detect 3rd Reflectance Measurement (R3)
Is (R2-R3)/R3 x 100% < or = PKE ?
No
Yes
Replace the value of R1 with the value of R3
Detect Presence or Concentration of Target
Detect Presence or Concentration of Target

FIG. 6

REFERENCES CITED IN THE DESCRIPTION

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- **D.B. Judd ; G. Wyszeki.** Color in Business, Science and Industry. John Wiley & Sons, 1975 **[0046] [0051]**

专利名称(译)	用于检测分析物的测试条和使用方法		
公开(公告)号	EP1532267A4	公开(公告)日	2006-06-14
申请号	EP2003760340	申请日	2003-06-13
[标]申请(专利权)人(译)	艾康实验技术公司		
申请(专利权)人(译)	ACON Laboratories公司.		
当前申请(专利权)人(译)	ACON Laboratories公司.		
[标]发明人	LIN JINN NAN WANG CHIA LING		
发明人	LIN, JINN-NAN WANG, CHIA-LING		
IPC分类号	C12Q1/54 G01N33/52 C12Q1/00 C12Q1/28 G01N33/53		
CPC分类号	G01N33/525 C12Q1/54 Y10S435/968 Y10S435/97		
代理机构(译)	庆祝活动，JENTSCHURA & PARTNER		
优先权	10/173457 2002-06-15 US		
其他公开文献	EP1532267B1 EP1532267A2		
外部链接	Espacenet		

摘要(译)

本发明的一个方面是试剂测试条，其包括：a）包括样品孔的顶部支撑层; b）膜，其包括用于指示靶标浓度的试剂系统; c）扩散层; d）底部支撑层，其包括与样品孔基本对齐或近似对齐的测量端口。优选地，膜固定到顶部支撑层。优选地，膜位于顶部支撑层和底部支撑层之间。优选地，扩散层位于顶部支撑层上方并且与样品孔基本对齐或近似对齐。优选地，施加到扩散层的流体穿过样品孔并接触膜。

TABLE 1

Glucose mg/dL (by YSI)		5μL (% Difference vs. 5μL)	10μL (% Difference vs. 5μL)	20μL (% Difference vs. 5μL)	30μL (% Difference vs. 5μL)
104	Configuration A	0	+4.4	+5.1	+2.8
104	Configuration B	0	+8.0	+11.3	+15.0
104	Configuration C	0	+1.2	+6.5	+10.3
246	Configuration A	0	-2.1	-5.0	-4.0
246	Configuration B	0	+2.1	+20.4	+39.9
246	Configuration C	0	-2.6	+3.8	+20.7
467	Configuration A	0	+1.8	-8.9	-9.7
467	Configuration B	0	+23.8	+54.9	+147.1
467	Configuration C	0	+2.9	+15.3	+38.7