June 1, 1971 D. A. HAMILTON 3,582,285

CHEMICAL PACKAGE

Filed May 19, 1970

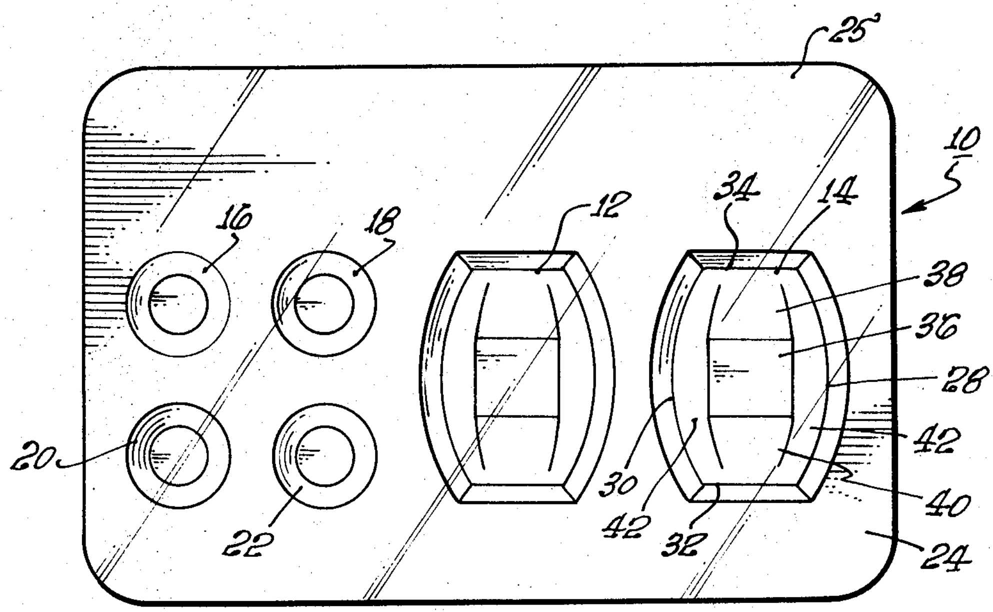

FIG. 1.

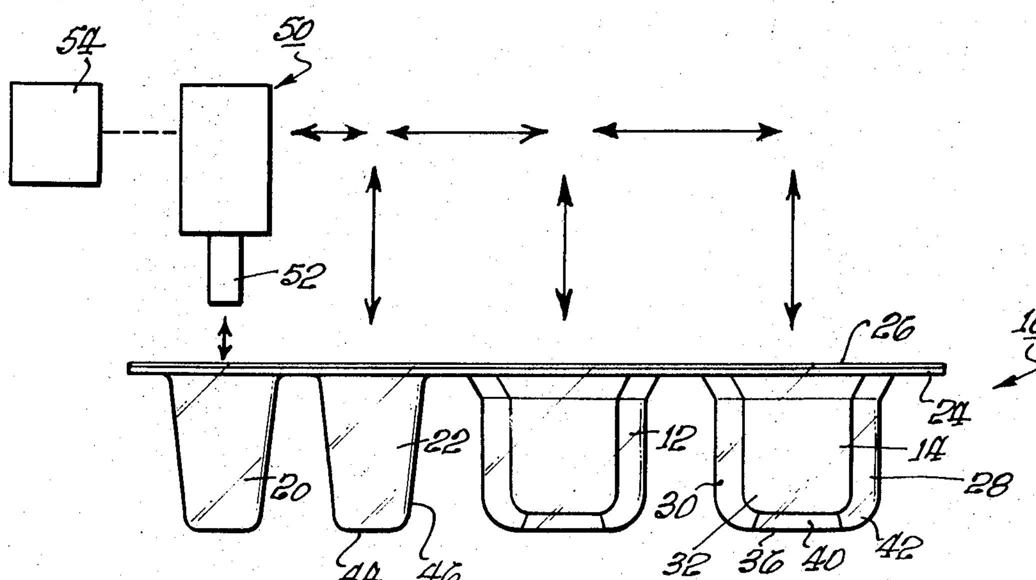

FIG. 2.

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CHEMICAL PACKAGE

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ABSTRACT OF THE DISCLOSURE

A disposable test package comprising a unitary member formed into a plurality of compartments for the admixing and reaction of reagents and sample material added thereto, and a plurality of reagent storage chambers associated with each reaction compartment but not adapted for direct communication therewith; and means overlying said unitary member for preventing the premature dispensing of prepackaged reagents from their storage locations prior to the time of analysis and for maintaining the proper environment with the storage necessary to prolong the storage life of prepackaged reagents.

Since the reagent storage chambers cannot be placed in direct communication with the reaction compartments, means external to the disposable test package are provided to withdraw the prepackaged reagent from its storage chamber and to transfer said reagent to one or more of the reaction compartments and/or another reagent storage chamber.

After incubation, each reaction compartment is utilized as a cuvette for optical analysis, without removal of the reaction mixture therefrom.

BACKGROUND OF THE INVENTION

This invention relates to automatic chemical analysis and, more particularly, to the automatic chemical analysis of body fluids, such as blood, urine, etc.

In copending application Ser. No. 602,025, filed Dec. 15, 1966, and now U.S. Pat. No. 3,504,376, there is disclosed an automated chemical analytical system including a plurality of different disposable reaction containers, a magazine for the storage of the plurality of different reaction containers, a station for the addition of sample material to the reaction container, a mixing and incubation station wherein the reaction mixture is maintained in the disposable container for a period of time sufficient to culminate the chemical reaction, a detection station wherein the analytical data is obtained by monitoring one or more of the physical properties of the reaction mixture, a disposal station wherein the disposable reaction container is eliminated from the system, and means to transport the disposable reaction container from its storage area in the magazine through the system to the disposal station. The heart of the system is the disposable reaction container which, in its broad aspects, has at least one lower compartment for the admixing and reaction of reagents and sample, and an upper section having a plurality of reagent storage chambers in communication with each reaction compartment. At least one wall or end portion of the reaction compartment may be optically transparent so that upon completion of the desired chemical reaction the compartment can be utilized as a cuvette for optical analysis. Optionally, none of the walls need be optically transparent as a probe photometer such as the one disclosed in Gale 3,164,663, may be inserted into the reaction mixture and electromagnetic radiation from a source passed through a radiation conductor, the reaction mixture and back through the radiation conductor to a detection means, without the necessity of passing through the compartment walls.

In U.S. No. 3,497,320 there is disclosed a similar, though conceptually and structually different, analytical apparatus and system. The disposable reaction container in this application has a flexible lower compartment, i.e., one having at least one flexible wall, so that during analysis a radiation source and a detection means can cooperate with the flexible wall or walls of the cuvette to define a fixed optical path length between the radiation source and the detection means through the reaction mixture. The automatic analytical apparatus includes monitoring means having a radiation source and means responsive to the variations in light transmittance or absorbance caused by different concentrations of a tested-for constituent in the reaction mixture. In one embodiment, the light source and the responsive means are pressed against opposite sides of the reaction compartment or cuvette during analysis to define the fixed optical path length through the reaction mixture.

As previously indicated, the heart of each analytical system described above is the disposable reaction container which, in accordance with the disclosures of the aforementioned patents, comprises a test vessel having at least one lower compartment for the admixing and reaction of reagents and samples, and a storage section having a plurality of reagent storage chambers which can be placed in communication with each reaction compartment. Means are provided to hold the analytical reagents, preferably in tablet form, in their respective reagent storage chambers until such time as they are to be dispensed, in accordance with the particular analytical procedure prepackaged therein, into the adjacent reaction compartment. In the most significant embodiment described in the aforementioned patents, a shearable, thin plastic layer is positioned between the reaction compartment section and the reagent storage section. Reagent tablets, predispensed into the reagent storage chambers, are prevented from premature dispensing into the adjacent reaction compartment by this restraining means. During dispensing, the reagent storage chamber is inverted by force applied to the shearable layer through the reagent tablet within the storage chamber. This causes the shearable layer to rupture with the concomitant dispensing of the reagent tablet into the adjacent reaction compartment. With such a design, however, the exacting reagent dispensing goals established for this system by the assignee of the present invention were not obtainable either through failure of the shearable layer to properly rupture or because the reagent tablet was crushed and not totally dispensed from its storage chamber.

Alternate designs, for example as shown by Hamilton in U.S. Nos. 3,477,812; 3,477,822; and 3,480,398; were formulated and tested. Though such packages, as described therein, were more than adequate for those tests which required dispensing of one or two reagent tablets early in the analytical procedure, the extreme hygroscopic nature of the reagent tablets either caused premature dispensing or a failure to dispense for those tablets which would be adjacent a zone of high relative humidity (i.e., the reaction mixture in the adjacent reaction compartment) for any lengthy period of time. Thus, the prepackaged designs described and claimed in the aforementioned patents were not acceptable for all tests which might be conducted in a fully selective, automated chemical analyzer offering a wide test repertoire.

OBJECTS OF THE INVENTION

It is, therefore, an object of this invention to provide a novel disposable reaction container of improved design.

It is a further object of the present invention to provide a novel disposable reaction container suitable for use in an automated analytical system.

It is a further object of the present invention to provide a novel disposable reaction container which eliminates the need to dispense prepackaged reagent tablets through a shearable restraining layer positioned adjacent the upper portion of each reaction compartment.

Yet a still further object of the present invention is to provide a disposable reaction container which eliminates the need for a reagent storage section preformed separately from the reaction compartment section.

These and still further objects, features, and advantages of the present invention will become apparent upon consideration of the following detailed disclosure.

BRIEF SUMMARY OF THE INVENTION

These and still further objects of the present invention can be achieved, in accordance therewith, by providing an improved disposable reaction container comprising a unitary member formed into a plurality of compartments for the admixing and reaction of reagents and sample material added thereto, and a plurality of reagent storage chambers associated with each reaction compartment but not adapted for direct communication therewith. Surrounding the openings at the top of each reaction compartment and the adjacent reagent storage chambers is a flange which holds each of the aforesaid elements together as a unitary member and further acts as a barrier to prevent the inadvertent admixing of materials added to adjacent compartments and/or reagent storage chambers. Overlying the openings in the flange, adjacent the top portion of each reaction compartment and each reagent storage chamber, is a thin membrane adapted to prevent the analytical reagents from being prematurely dispensed from their particular storage location and to maintain the proper environment within the storage location necessary to assure prolonged storage life of the prepackaged reagents. During actual use at the time of analysis, this membrane will be punctured to permit the dispensing of the sample material and/or distilled water into one or more of the reaction compartments. Additionally, the membrane will be punctured above those reagent storage chambers having reagents therein which are to be transferred from their respective storage chambers to one or more of the reaction compartments. Since the reagent storage chambers cannot be placed in direct communication with the reaction compartments, means external to the disposable reaction container must be provided to withdraw the prepackaged reagent from the reagent storage chamber and transfer said reagent to one or more of the reaction compartments. In this manner, the need to force a tabletted reagent composition through the shearable layer, referred to above, is eliminated. After appropriate incubation, each reaction compartment is utilized as a cuvette for optical analysis, the optical beam passing through a pair of substantially vertical side wall portions, defining the optical window, and the reaction mixture therebetween.

Sufficient analytical reagents to conduct a single analytical procedure are predispensed into as many of the reagent storage chambers and/or reaction compartments as required by the number of individual reagents utilized. The reagents stored within the storage chambers can be either in solid or liquid form. Liquid storage is not as desirable, however, because there is a greater propensity towards chemical reaction, either with the storage wall or with materials permeating therethrough. Additionally, liquid materials are generally known to be more sensitive to light and other portions of the electromagnetic spectrum and, therefore, degrade faster unless adequate filters are provided to eliminate deleterious radiation. Many analytical procedures, however, are much easier to adapt to a system as herein described if certain chemicals are stored in the liquid form. Nonetheless, it is preferred to store the reagents in solid form whenever possible. When stored in the solid state, the reagents can be in powdered or tabletted form, either singly or in combination with other compatible reagents. A disadvantage of storing two or more powdered reagents together is the extreme amount of surface area available for chemical reaction during storage. Even though the materials are relatively nonreactive with respect to each other or to other degrading factors, prolonged storage under such conditions may have a deleterious effect on the reagent mixture. In such cases it would be best to package the materials separately or to package them in tablet form. Tabletting significantly reduces the surface area available for reaction with degrading factors. The actual form of the tablet is not critical but selection of a proper shape, for example to give minimum contact with other reagent tablets, may prove advantageous in increasing the storage life of the prepackaged reagents. Additionally, tabletting provides a feasible method for accurately prestoring the proper amount of chemical reagent within a particular storage chamber. Severe dust and contamination problems may exist when a plurality of different powdered chemicals are being deposited into storage chambers which are but a fraction of an inch apart. When the tabletting form of reagent addition is utilized, these problems are, at least, eliminated from the packaging line and placed in their own environment where they can be dealt with separately. It is, of course, necessary to use only those materials in the tabletting process which will not have a deleterious effect on the analytical procedure. In any case, the reagents, whether stored in liquid or dry form, must be put into the reagent storage chambers in a measured amount, the tolerance of which is determined by the given analytical procedure.

Since it is presently preferred to store the predispensed reagents in tablet form, the use to which the disposable reaction container of the present invention is put will be discussed with reference thereto. Initially the membrane is punctured to permit the dispensing of the sample material and/or distilled water into one or more of the reaction compartments. Additionally, the membrane is punctured above each reagent storage chamber to permit access to the reagents stored therein. Distilled water is added to each of the reagent storage chambers and all reagent tablets dissolved at the same time to give corresponding liquid solutions. If reagent powders are utilized, in place of reagent tablets, the procedure up to this point is essentially the same. If, however, liquid reagent solutions are prestored in the reagent storage chambers, the need to add an aliquot of distilled water may be unnecessary, if the liquid reagent is not in concentrated form. From this point on, however, the procedure for transferring the analytical reagent from its storage chamber to the reaction compartment is the same since all reagents are now in the liquid state. If necessary, the reagents can be suitably agitated after distilled water addition to provide homogeneous reagents suitable for their intended use.

At the appropriate time in the analytical procedure, liquid reagent transfer means is lowered into the reagent storage chamber, an aliquot of liquid reagent withdrawn therefrom, the liquid transfer means indexed upwardly out of the reagent storage chamber, traversed to a position over an adjacent reaction compartment, lowered into the reaction compartment and caused to dispense the aliquot of liquid reagent material into the reaction compartment. The liquid transfer means is then indexed upwardly and traversed to a dwell position awaiting the next liquid transfer operation. Alternatively, the liquid transfer means can be reciprocated vertically, with the package brought into the proper position for liquid transfer, either to or from the reagent storage chambers and/or reaction compartments, by the associated transport mechanism.

Optionally, the liquid transfer means can withdraw a macro-aliquot of liquid reagent and dispense smaller portions thereof into each of a plurality of reaction compartments. Or the liquid transfer means can be a pluralpronged mechanism adapted to enter into more than one reagent storage chamber, withdraw appropriate liquid reagent material therefrom, and dispense the plurality of liquid reagents into one or more adjacent reaction compartments after transportation thereto. The use of these optional features will depend, to a great extent, upon the complexity of the analytical procedures, in terms of the number of individual reagents required and the different times at which they must be transferred from their storage chambers to the reaction compartments, undertaken with an analytical system utilizing the disposable test package of the present invention. After appropriate incubation, each reaction compartment is utilized as a cuvette for optical analysis, without removal of the reaction mixture therefrom.

BRIEF DESCRIPTION OF THE DRAWINGS

The nature of the invention will be more easily understood when it is considered in conjunction with the accompanying drawings wherein:

FIG. 1 is a side view of an exemplary disposable reaction container of the present invention, showing a schematic regent transfer means and the path along which such reagent transfer means traverses in transferring analytical reagents from their storage chambers to an adjacent reaction compartment; and

FIG. 2 is a top view of the disposable reaction container of FIG. 1, with the membrane removed.

Referring to FIGS. 1 and 2, there is seen a disposable reaction container **10** having two reaction compartments **12** and **14** and a plurality of reagent storage chambers **16**, **18**, **20** and **22** associated therewith. Adjacent the upper portion of the reaction compartments and the reagent storage chambers is a flange **24** which holds the unit together as a unitary member and further acts to prevent the inadverent mixing of materials held in different compartments and/or chambers. Overlying flange **24**, and thereby sealing the interior of the reaction compartments and the reagent storage chambers from the ambient environment, is membrane **26**. Flange **24** and membrane **26** are wider along one portion **25** thereof which is adapted for the storage of information thereon. Any suitable type of information coding can be placed on this code area to indicate or record any information which desirably should be known during a chemical analysis, such as the actual test which has been pre-stored in the particular disposable reaction container, the patient number, instructions for the associated automated analytical apparatus and system, analytical results, etc. Typical codes include binary coding in the form of light and dark areas, magnetic coding, etc. which can either be in machine- and/or human-readable form.

As shown, each reaction compartment has a small flat portion **36** at the bottom thereof which is adapted to couple ultrasonic energy from an adjacent ultrasonic generating means to the materials previously added to the reaction compartment. From the edges of each flat portion **36**, the walls defining the lower portion of each reaction compartment are slightly rounded and/or substantially flat surfaces diverging upwardly toward the adjacent side walls. Substantially vertical side wall portions **32** and **34** are connected, respectively, to flat portion **36** by substantially flat portions **40** and **38**. The actual connections between substantially flat portions **38** and **40** and substantially vertical side wall portions **32** and **34** are slightly rounded connections naturally caused by the process by which this unitary member is formed. Rounded wall portions **42** connect bottom wall portions **36**, **38** and **40** with curved side walls **28** and **30**. Thus, flat wall portion **36** is defined as the lowest part of each compartment such that when it is properly positioned over an adjacent ultrasonic generating means, the ultrasonic energy produced by such means is effectively coupled with the materials previously dispensed into the reaction compartment. This is particularly advantageous where tabletted materials have been prestored in the reaction compartments, as opposed to their initial prestorage in one or more of the reagent storage chambers. Curved side walls **28** and **30** prevent a tabletted material from finding a static ultrasonic energy zone of limited magnitude in which it can reside and thus avoid agitation and subsequent dissolution. Since the tablet no longer remains trapped in such a low energy zone, its movement through the reaction mixture is continuous and the agitation caused by the ultrasonic generating means is sufficient to bring the tabletted formulation into solution.

To the extent that tabletted materials are not predispensed into either of the reaction compartments, the need to provide the uniquely configured reaction compartments, as described above, may be unnecessary. Accordingly, other reaction compartment designs can be utilized; for example, as shown in application Ser. No. 860,140, filed Aug. 14, 1969, the disclosure of which is incorporated herein by reference to the extent necessary to complete the disclosure, or understanding, of the present application. In one embodiment described therein, a small circular compartment is provided in the lower portion of each reaction compartment for the storage of a magnetic stirring bar which can be rotated to thoroughly mix the materials added to the reaction compartment. In a further embodiment described therein, the bottom wall of the reaction compartment is flat. A common feature of all the embodiments so far described is the provision of a pair of opposed, substantially vertical side wall portions through which optical analysis can be made. It is this feature which makes the reaction compartments suitable for use as optical cuvettes without need for removal of the reaction mixture therefrom.

The side wall portions of compartments **12** and **14** terminate in a horizontal flange **24** which encircles the upper perimeter of the two compartments and holds them together as a distinct unit. Each flat bottom wall portion **36** is parallel or substantially parallel with horizontal flange **24**. As shown, the side walls do not extend vertically all the way to flange **24** but, instead, diverge outwardly just prior to the intersection thereof with flange **24**. Optionally, the side walls, whether curved or straight, can extend completely to the horizontal flange thereby eliminating the need for the outwardly diverging upper side wall portions. In such a design, the upper portion of the substantially vertical side walls, such as **34** and **36**, define positive aligning surfaces which can be utilized, for example, to position the disposable reaction container during reagent prestorage and for manipulating the disposable container during transportation thereof through an automated analytical system.

The reagent storage chambers can be of any suitable configuration though, preferably, they should be of uniform dimension and of such configuration as to eliminate problems associated with the storage therein, and the removal therefrom, of analytical reagents. As shown in FIGS. 1–2, each reagent storage chamber **16**, etc. has a bottom wall **44** and a side wall **46** thereby defining an inverted, truncated cone having a larger opening at the upper portion thereof than that defined by the bottom wall thereof. It should be understood, however, that a cylindrical configuration, for example, would be an equally suitable design for the reagent storage chambers.

Since it is contemplated that tabletted formulations can be prestored in the reagent storage chambers, it may be desirable to form the bottom wall of each reagent storage chamber in the non-planar configuration, described herein with respect to reaction compartments **12** and **14**, so as to enable the more rapid and complete solution of the tabletted reagents in the liquid material subsequently added to the reagent storage chamber.

The bottom walls of the reaction compartments and the reagent storage chambers should be at the same level so that all portions of the disposable test package can be placed over an adjacent ultrasonic mixer, in a mixing station, to thereby dissolve the non-liquid reagent material, or thoroughly mix liquid reagent materials, no matter where they reside in the disposable test package. By providing the bottom walls at the same level, such mixing can be accomplished in one station with one ultrasonic mixer. Such mixing would be the primary mixing associated with the formation of analytical reagents suitable for use in the analytical procedure, but it should be understood that additional mixing may be found desirable after an aliquot of the liquid reagent has been transferred from its storage chambers to one or more reaction compartments.

An alternate, though not presently preferred, design of the disposable test package has the plurality of reaction compartments in the center of the test package, with the plurality of reagent storage chambers disposed adjacent thereto but between the reaction compartments and either or both of the longitudinal edges of the test package. To enable direct readout through the lower portion of the reaction compartments, the bottom walls of the reagent storage chambers must be at a higher level so that an unobstructed optical path through the reaction mixture is defined.

In operation, test package **10** is taken from a supply magazine and passed to a prepunch station where access holes are made through the membrane above each reaction compartment and at least those reagent storage chambers which will be entered during the course of the analytical procedure. The test package is then passed to a sample addition station where the proper amount of sample is aliquoted into at least one of the reaction compartments. This addition is accomplished, for example, by injecting the sample aliquot through a needle which has been inserted through an access hole in membrane **26**. Preferably, a diluent flush through the aliquoter needle follows the injection of the concentrated sample solution into one or more of the reaction compartments. If non-liquid reagents or concentrated reagents are predispensed into the reaction compartments, it may be desirable to add an aliquot of distilled water to the reagent-containing reaction compartment prior to sample addition. If the reagents are in solid form or in concentrated liquid form, an aliquot of distilled water, is added to each of such reagent-containing storage chambers. If necessary, the reagent mixture is thoroughly mixed to provide a homogeneous solution suitable for transfer during the course of the analytical procedure. The sample-holding container is then passed to one or more reagent addition stations where the liquid reagent is appropriately withdrawn from its reagent storage chamber and transferred to one or more of the adjacent reaction compartments. This manner of reagent transfer is schematically shown in FIG. 1 where liquid transfer means **50** having aliquoting probe **52** on the lower end thereof is lowered into reagent storage chamber **20**; caused to withdraw an aliquot of liquid reagent therefrom; returned to its initial, or transfer level; indexed to a position over one or more of the reaction compartments, such as reaction compartment **12**; lowered into the underlying reaction compartment; caused to dispense the aliquot, or at least a portion of the aliquot, therefrom into the reaction compartment; returned to its initial, or transfer, level; and indexed to a rest position awaiting further commands from control means **54**.

Variations of this liquid transfer sequence can be preprogrammed into control means **54** and caused to be conducted by the information stored on the disposable test package, such as along wider portion **25** of flange **24**, and which is read by a suitable code reader shortly after the test package is transferred into the automated analytical system.

Reagent addition can be done in one operation, or it can be done sequentially as dictated by the particular analytical procedure being conducted. If done sequentially, the addition can be done before, during, or after incubation. In essence, reagents can be added any time prior to final detection as determined by the particular analytical procedure utilized. Reagent transfer is generally followed by a further distilled water flush to clean the transfer mechanism thereby reducing and/or eliminating cross-contamination, especially where non-wettable materials are used for the transfer probes. If desired, the liquid reaction mixture within the reaction compartments can be agitated, at a mixing station, after each reagent addition. The container next passes to an incubation station where appropriate reaction conditions are imposed upon the materials within the reaction compartments for a time sufficient to complete the desired reaction or, at least, to bring it to the desired state for analysis. It is not necessary that the mixing and incubation stations be separate and distinct as it is contemplated that these operations may be performed in a single station. The test package is passed to a detection station where light of appropriate wavelength is passed from a light source through the reaction mixture to detection means situated on the opposite side of the reaction mixture from the light source. The amount of light transmitted (or, conversely, the amount of light absorbed) at the testing wavelength will be representative of the amount of the constituent undergoing analysis in the sample aliquot.

By providing a plurality of distinct reaction compartments, the disposable reaction container of the present invention can be utilized for conducting a primary test and, concomitantly therewith, at least one secondary analysis. Normally, the secondary analyses are in the form of a blank, either a sample blank, a reagent blank, or a sample plus reagent blank, under addition conditions which cause a difference in a particular physical property to result from that obtained with the primary test. Appropriate correlation of the date obtained with the primary test and each secondary test will yield analytical data of greater clinical value. As indicated above, the difference in the physical properties of the reaction mixtures within the reaction compartments, is usually determined by passing light of appropriate wavelength through the various reaction mixtures. In one embodiment, the optical path through the reaction mixture is defined by the distance between the substantially vertical side walls through which optical analysis is made. In a separate embodiment, light from the light source and light which is passed through the reaction mixture can be conducted to, and from, the substantially vertical side walls of the reaction compartment through light conduits which cooperate with the relatively flexible walls of the reaction compartment to define a fixed optical path-length therebetween. Either embodiment is suitable for use in the practice of the present invention.

The disposable test package of the present invention tures within the reaction compartments, is usually detertion mechanism, such as a double-beam detection mechanism, or with a photometer which is rapidly indexed to bring each reaction compartment, with the reaction mixture therein, into the optical path between the light source and the detection means.

With the embodiment shown in the figures, a four-pronged transfer mechanism could be utilized to transfer liquid reagents from their respective storage chambers to the pair of reaction compartments **12** and **14**. For example, the transfer mechanism would be lowered such that one probe would enter into each of the storage chambers. A certain amount of distilled water would be added to each storage chamber followed by movement of the transfer mechanism, without withdrawal of liquid reagent from the storage chambers, to a position where it would be lowered into the reaction compartments (two probes per compartment) and a certain amount of distilled water added thereto. After appropriate formation of the liquid reagent material, such as by mixing, liquid transfer could be effected with all, or any combination, of the probes being utilized to transfer liquid reagent material from a particular storage chamber to one or more of the reaction compartments and/or other reagent storage chambers. After all reagent addition, mixing, incubation, etc. has been accomplished in accordance with the particular analytical procedure being conducted, the difference in physical properties of the reaction mixtures in the reaction compartments would be monitored to yield data from which the final analytical result would be derived.

In such a system as contemplated for use with the disposable test package of the present invention, where the liquid transfer mechanism is utilized to repeatedly transfer different materials, cross-contamination is a problem which must be given adequate consideration. It has previously been found that if, for example, the sample aliquot is separated from the diluent flush by an air bubble, dispensed, and then followed by a diluent flush equivalent to the amount of the sample aliquot, cross-contamination is minimized to well within acceptable limits. Such a technique can be utilized with the system herein contemplated not only for the sample aliquot but for the transfer of liquid reagents as well. Additionally, if found desirable, an additional diluent flush between package dispensing operations can be made into an appropriate waste receptacle, to thoroughly protect against inadvertent cross-contamination.

In this multi-probed embodiment, it should be understood that each probe can be designed to operate independently of the operation of the other probes. With such a design, great flexibility is achieved in the types of analytical procedures which can be conducted by means of the automated analytical system contemplated hereby.

In one embodiment of the present invention, membrane **26** is heat sealed to flange **24**, adjacent the upper portions of the reaction compartments and reagent storage chambers, to maintain the predispensed reagents in their particular storage locations and to provide the proper environment necessary for prolonged storage life. The membrane is punctured at the time of analysis to permit access to the reaction compartments and the storage chambers. In a further embodiment, however, it is contemplated that the membrane can be peeled or otherwise removed from flange **24** immediately prior to conducting the analytical procedure. Such removal can be either manually- or machine-achieved. If the membrane is peeled from its position adjacent the flange, the need to puncture the membrane prior to the addition, or transfer, of materials to and from the various compartments and chamber is eliminated. Also, the flap caused by such a puncture is eliminated thereby eliminating the possibility of flap interference with subsequent operations, such as mixing, reagent and/or sample addition and transfer, photometric monitoring, etc.

The test package described herein can be protected, during storage, by its own individual envelope which functions as a primary barrier to limit access of deleterious factors to the disposable test package and the analytical reagents stored therein. Since the barrier now performs the primary function of maintaining proper environmental control, the membrane fulfills that function to the extent that the primary barrier is prematurely broken during storage. Additionally, the membrane retards access of deleterious factors to the prepackaged reagents since such factors must also pass through the membrane (or the walls of the storage chamber) before they can adversely affect the prepackaged reagents. By proper selection of the primary barrier, a greater degree of freedom in selection of materials for the membrane is obtained since one function thereof, in a primary sense, has been shifted from the membrane to the barrier material. For example, in place of a plastic membrane, aluminum foil can be used. The membrane herein described can also be provided by one portion of the aforementioned primary barrier, such that, at the time of analysis, the membrane is removed from the test package so as to give access thereto. In this event, the membrane fulfills both primary functions of maintaining the reagent tablets in proper position within the test package as well as maintaining the proper environmental control necessary for prolonged storage life.

It is also contemplated that the reagent storage chambers can be of such configuration as to hold reagent tablets securely in place therein. For example, ribs or

detents as shown in Hamilton U.S. Nos. 3,477,821 and 3,477,822 can be provided to properly position one or more reagent tablets within certain of the reagent storage chambers. While the membrane no longer performs the primary function of holding the reagent tablet within its storage chamber, it does fulfill that function to the extent that the tablet is jarred loose from its primary restraining means and/or portions of the tablet are broken loose from the main tablet during storage prior to actual use.

The disposable test package of the present invention is also amenable to in situ lyophilization of liquid reagents added, during initial manufacture of the test package, to the individual storage locations. In such a process, the liquid reagents are frozen under high vacuum whereby the water associated therewith is removed by sublimation. It is expected that dissolving of the lyophilized material, at the time of analysis, will be much easier than the corresponding step where reagent tablets are utilized.

The manner of producing the disposable test packages of the present invention is not considered part of this invention. In general, however, any suitable method can be used which will produce a test package having the desired characteristics. For example, thermoforming operations, such as pressure forming or vacuum forming, can be used to produce the lower portion of the test package herein described which has a relatively intricate design, as compared to the membrane. Pressure forming, however, is preferred because it is possible by using high pressure air to get the plastic material into areas where it cannot be drawn by vacuum.

Polyethylene, polyvinylchloride, polystyrene, and cellulose propionate are suitable materials for use in the fabrication of the membrane and the reaction compartment-reagent storage chamber portion of the test package. Also, fluorocarbons can be utilized as the reaction compartment-reagent storage chamber portion, especially where strong liquid materials are intended to be stored in the disposable test package.

In addition to eliminating the problems of membrane rupture or tablet hang-up associated with prior disposable test package designs, the disposable reaction container described herein has many unique advantages which make it particularly suitable for use with an automated analytical system. Since the reagent storage chambers are not, during reagent dispensing, placed in actual communication with the reaction compartment, duplication of reagents can be eliminated since a single reagent can be withdrawn from one storage chamber and dispensed into as many reaction compartments as desired. This implies that essentially the same reagent will be utilized in all reaction compartments to which aliquots thereof are dispensed. Additionally, somewhat greater freedom in the choice of analytical procedures is also obtained because of the potential ability of transferring a reagent solution from one storage chamber to another prior to actual dispensing thereof into one or more reaction compartments. Further, since the reagent tablets can be predissolved in their own storage chamber, and not dispensed directly into the reaction compartment and then dissolved therein, there are no concentration gradients at the surface of the dissolving tablets, and no heat of solution problems, which might adversely affect the rate of the chemical reactions leading to the measured optical absorbance of the reaction mixture.

From a machine point of view, less means must be provided to ensure complete dissolution of the reagent tablets since all such tablets (or powders) can be dissolved at one station, followed by the easier mixing of solutions after each aliquoting or liquid transfer operation. By eliminating the concept of dispensing a tabletted reagent through a shearable layer, less force is required to dispense the reagent material into the reaction compartment, with greater dispensing reliability expected to be attendant thereto.

While the invention has been described with reference to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and detail may be made without departing from the true spirit and scope of the invention. Accordingly, all modifications to which the present invention is readily susceptible, without departing from the spirit and scope of this disclosure, are considered part of the present invention.

I claim:

1. A disposable test package comprising a unitary member formed into a plurality of distinct compartments for the admixing and reaction of materials added thereto, and a plurality of reagent storage chambers associated with each reaction compartment, each of said reaction compartments being of greater volume than each of said reagent storage chambers and adapted to receive during analysis an aliquot of sample material and/or an aliquot of liquid and sufficient reagents to conduct a predetermined analysis therein without loss of material therefrom, said reagent storage chambers not being adapted for direct communication with any of said reaction compartments; a plurality of reagents stored within said reagent storage chambers and/or said reaction compartments of said unitary member; and means overlying said unitary member for preventing the premature movement of said prepackaged reagents from their storage locations prior to the time of analysis and for maintaining the proper environment within said storage locations necessary to prolong the storage life of said prepackaged reagents within said disposable test package.

2. The disposable test package of claim **1** wherein said means overlying said unitary member comprises a thin plastic membrane.

3. The disposable test package of claim **2** wherein said membrane is adapted to be removed from said unitary member at the time of analysis.

4. The disposable test package of claim **1** wherein each of said reaction compartments has side walls and a bottom wall, at least one pair of opposed side walls being substantially vertical and sufficiently optically transparent for optical analysis therethrough.

5. The disposable test package of claim **4** wherein said substantially vertical side walls are disposed parallel to the longitudinal axis of said disposable test package.

6. The disposable test package of claim **4** wherein said substantially vertical side walls of each reaction compartment are connected to each other by curved wall portions.

7. The disposable test package of claim **1** wherein said unitary member and said membrane are bonded together.

8. The disposable test package of claim **1** wherein said unitary member and said membrane are heat sealed together.

9. The disposable test package of claim **1** further including a flange about the upper perimeter of said reaction compartments and said reagent storage chambers, adjacent ones of said reaction compartments and said reagent storage chambers being separated by portions of said flange which act as a barrier to prevent the inadvertent admixing of materials added to adjacent compartments and reagent storage chambers.

10. The disposable reaction container of claim **9** wherein said flange is wider along one longitudinal portion thereof, the area circumscribed by said flange being substantially rectangular and substantially equal to the area circumscribed by said means overlying said unitary member, the portion of said means overlying said unitary member above said wider flange portion being adapted for the storage of information thereof.

11. The disposable test package of claim **1** wherein the bottom wall of each reaction compartment is flat.

12. The disposable reaction container of claim **1** wherein the bottom wall of each reaction compartment is of non-planar configuration and adapted to effectively couple the transducing action of an ultrasonic mixer adjacent thereto whereby materials added to each reaction compartment can be thoroughly mixed.

13. The disposable test package of claim **1** wherein each reagent storage chamber comprises a bottom wall and at least one side wall, the bottom wall of each reagent compartment being flat.

14. The disposable test package of claim **1** wherein each reagent storage chamber comprises a bottom wall and at least one side wall, the bottom wall of each reagent storage chamber being of non-planar configuration and adapted to effectively couple the transducing action of an ultrasonic mixer adjacent thereto whereby materials added to each reagent storage chamber can be thoroughly mixed.

15. The disposable test package of claim **1** wherein each reagent storage chamber comprises a bottom wall and at least one side wall, the bottom walls of said reagent storage chambers and the bottom walls of said reaction compartments being substantially at the same level whereby materials added thereto can be thoroughly mixed at the same time by a single external mixing means.

16. The disposable test package of claim **1** wherein all of said reagent storage chambers are disposed to one side of all of said reaction compartments in a direction parallel to the extensions of said substantially vertical side walls along the longitudinal axis of said disposable test package, the center points of said reagent storage chambers falling within the area circumscribed by the near edge of the adjacent reaction compartment, said parallel extensions of said substantially vertical side walls and the edge of said disposable test package on the opposite side of said reagent storage chambers from said edge of said adjacent reaction compartment.

17. The disposable test package of claim **1** wherein said plurality of reaction compartments are disposed along the longitudinal axis of said disposable test package, and said plurality of reagent storage chambers associated with each of said reaction compartments are disposed between said reaction conpartments and the longitudinal edges of said disposable test package, the bottom walls of said reaction compartments being lower than the bottom walls of said reagent storage chambers whereby there is an unobstructed optical path through the reaction mixture within each reaction compartment.

18. A disposable test package comprising a unitary member formed into a plurality of distinct compartments for the admixing and reaction of materials added thereto, and a plurality of reagent storage chambers associated with each of said reaction compartments, each of said reaction compartments being of greater volume than each of said reagent storage chambers and adapted to receive during analysis an aliquot of sample material and/or an aliquot of liquid and sufficient reagents to conduct a predetermined analysis therein without loss of material therefrom, said reagent storage chambers being incapable of being brought into communication with said reaction compartments or any of said other reagent storage chambers, such that to transfer a reagent stored within any one of said reagent storage chambers to another of said reagent storage chambers or to any of said reaction compartments, means external to said disposable test package must be provided to withdraw the reagent from its storage location and to transfer the withdrawn reagent to another of said reagent storage chambers or at least one of said reaction compartments; a plurality of reagents stored within said reagent storage chambers and/or said reaction compartments of said unitary member; and means overlying said unitary member for preventing the premature movement of said prepackaged reagents from their storage locations prior to the time of analysis and for maintaining the proper environment within said storage locations necessary to prolong the storage life of said prepackaged reagents within said disposable test package.

19. A disposable test package comprising a unitary member formed into a plurality of distinct compartments for the admixing and reaction of materials added thereto, each of said reaction compartments having a plurality of side walls and a bottom wall, said side walls disposed parallel to the longitudinal axis of said disposable test packaging being substantially vertical and sufficiently optically transparent for optical analysis therethrough, a plurality of reagent storage chambers associated with each of said reaction compartments, and a flange about the upper perimeter of said reaction compartments and said reagent storage chambers, adjacent ones of said reaction compartments and said reagent storage chambers being separated by portions of said flange which act as a barrier to prevent the inadvertent admixing of materials added to adjacent compartments and reagent storage chambers, said reagent storage chambers being incapable of being brought into communication with said reaction compartments or any of said other reagent storage chmbers, whereby to transfer a reagent stored within any one of said reagent storage chambers to another of said reagent storage chambers or to any of said reaction compartments, means external to said disposable test package must be provided to withdraw the reagent from its storage location and to transfer the withdrawn reagent to another of said reagent storage chambers and/or said reaction compartments; a plurality of reagents stored within said reagent storage chambers and/or said reaction compartments of said unitary member; and means overlying said unitary member for preventing the premature movement of said prepackaged reagents from their storage locations prior to the time of analysis and for maintaining the proper environment within said storage locations necessary to prolong the storage life of said prepackaged reagents within said disposable test package.

20. The disposable test package of claim **19** wherein said means overlying said unitary member comprises a thin plastic membrane.

21. The disposable test package of claim **19** wherein each reagent storage chamber comprises a bottom wall and at least one side wall, the bottom walls of said reagent storage chambers and the bottom walls of said reaction compartments being substantially at the same level whereby materials added thereto can be thoroughly mixed at the same time by a single external mixing means.

22. The disposable test package of claim **21** wherein all of said reagent storage chambers are disposed to one side of all of said reaction compartments in a direction parallel to the extensions of said substantially vertical side walls along the longitudinal axis of said disposable test package, the center points of said reagent storage chambers falling within the area circumscribed by the near edge of the adjacent reaction compartment, said parallel extensions of said substantially vertical side walls and the edge of said disposable test package on the opposite side of said reagent storage chambers from said edge of said adjacent reaction compartment.

23. The disposable test package of claim **1** wherein said means overlying said unitary member comprises a thin membrane of aluminum foil.

24. The disposable test package of claim **1** wherein said reagent storage chambers are adapted to hold at least one reagent tablet securely in place therein.

25. The disposable test package of claim **1** further including a primary envelope in which said disposable test package is stored, said envelope serving to maintain the proper environment immediately adjacent said disposable test package to prolong the storage life of the prepackaged reagents therein.

26. The disposable test package of claim **25** wherein said means overlying said unitary member is defined by a portion of said envelope.

References Cited

UNITED STATES PATENTS

3,476,515	11/1969	Johnson et al.	23—253X
3,480,398	11/1969	Hamilton	23—253
3,497,320	2/1970	Blackburn	23—292X

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