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[54] **APPARATUS FOR CHEMICAL TESTING**

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[21] Appl. No.: **111,360**

[52] **U.S. Cl.** .....**23/259,** 23/253 R, 206/47 A

[51] **Int. Cl.** **G01n 1/16,** B65d 79/00

[58] **Field of Search**.....23/292, 253, 259, 230; 206/47 A

[56] **References Cited**

UNITED STATES PATENTS

3,446,596	5/1969	Salivar et al.	23/253 X
3,477,822	11/1969	Hamilton	23/292 X
3,480,398	11/1969	Hamilton	23/292 X
3,497,320	2/1970	Blackburn et al.	23/230
3,554,705	1/1971	Johnston et al.	23/292 X

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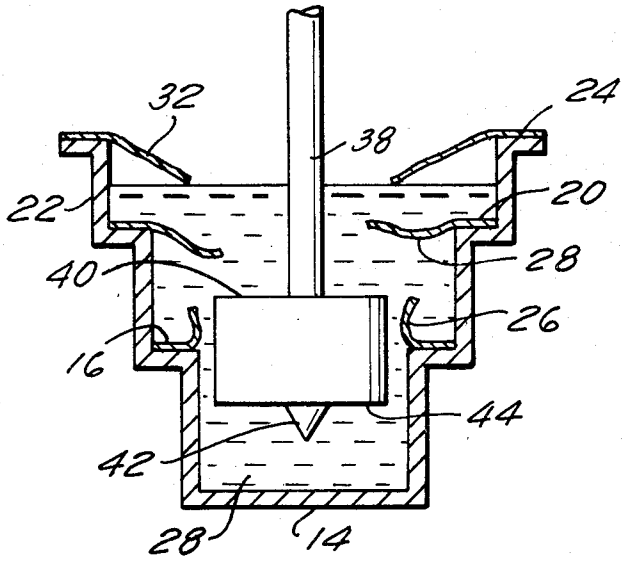
[57] **ABSTRACT**

A reagent container having a series of tiered compartments containing prepackaged reagents for the chemical evaluation of a test sample. A frangible diaphragm seals each compartment from the succeeding compartment. A sample is introduced into the top compartment. After incubation a breaker punctures the seal of the adjacent compartment, allowing the reagents to mix and react. The procedure is repeated for each reagent filled compartment.

4 Claims, 4 Drawing Figures



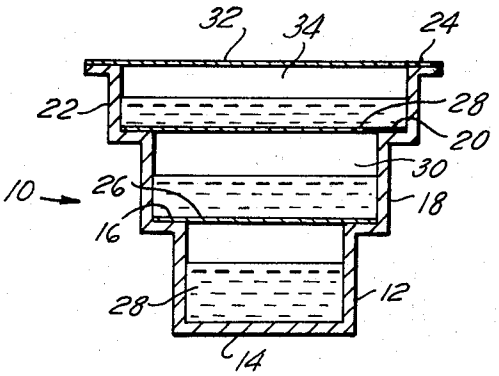


FIG. 1

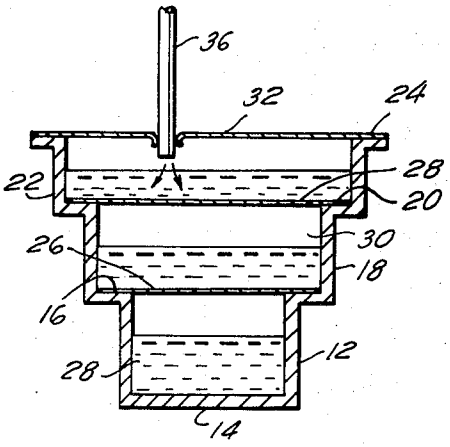


FIG. 2

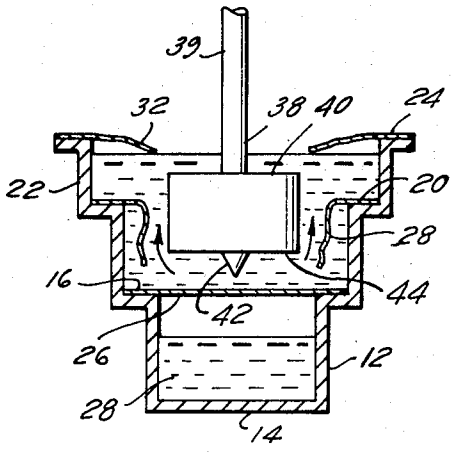


FIG. 3

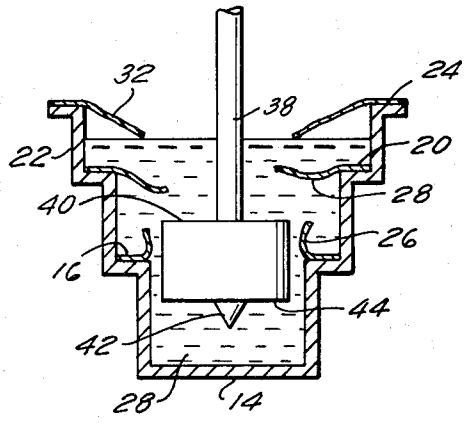


FIG. 4

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APPARATUS FOR CHEMICAL TESTING

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention is directed to an apparatus and method for performing a chemical evaluation of a material employing prepackaged reagents. In particular, it relates to a tiered reagent cup for storing prepackaged reagents and puncturing and mixing means for sequentially exposing a material to be tested to the prepackaged reagents.

2. Description of the Prior Art

In order to perform a chemical evaluation of a serum or other material in the field, it has proven necessary to employ a series of reagent containers. Often a conventional pipetting device is employed to transfer reagents, sequentially, to a reaction chamber in order to test a serum or other material for various properties. This procedure has several major defects. With manual pipetting, reagent volume is always subject to variation. It is also cumbersome to store and clean a series of reagent containers which are to be taken into the field. Prior art compartmented devices for storing reagents have proven, for the most part, unsatisfactory.

In U.S. Pat. Nos. 2,568,029 029 and 2,753,868, a container having a series of compartments is provided for storing ingredients suitable for hypodermic injection. Owing to the narrow-neck compartment design, it is difficult to load the compartments with reagents.

The odd-shaped necks of the compartments have proven difficult to seal, as evidenced by the cumbersome "drop" method for providing septa.

Further, the narrow-necked compartment design prevents adequate mixing of the reagents. Even more important, it is necessary to employ a hypodermic syringe for introducing or removing reagents from the compartments, once the unit is sealed.

Certain prior art devices provide a receptacle for the mixing of reagents prepackaged therein, but do not permit introduction of a material to be tested into the compartments. Such a device is illustrated in U.S. Pat. No. 3,415,360. The non-unitary nature of the receptacle makes it difficult to assemble. The rigid cap prohibits addition of a serum or the like to the top, reagent-containing chamber.

Certain prior art reagent-containing devices are formed wherein a reagent-containing cylindrical insert is spaced within an outer receptacle. Such devices provide various problems in fabrication, since the insert must be correctly positioned and supported by some external support mechanism. In many cases the inserts are sealed by a self-supporting membrane. Such a membrane can be difficult to rupture during mixing of the reagents. Illustrative of such prior art devices is the insulating device disclosed in U.S. Pat. No. 3,359,361.

SUMMARY OF THE INVENTION

It is, therefore, the primary object of the invention to provide a reagent-containing device particularly adapted to evaluate a test sample by the sequential addition of reagents to the test sample.

It is another object of the invention to provide a reagent-containing test device which can be accurately prefilled with reagent and which is of simple design and easily fabricated.

It is an additional object of the invention to provide a device having prepackaged reagents and adapted for the sequential addition of reagents to a test material which also provides enhanced mixing of each of the reagents with the test sample.

It is a further object of the invention to provide a method for introducing a test sample into a reaction chamber containing a prepackaged reagent and thereafter mixing the sample and first reagent with at least one further reagent for further testing.

The above and other objects are met in a unitary tiered reagent cup. The tiered cup has a series of hollow cylinders. The bottom cylinder or base receptacle is closed at one end. The diameter of each cylindrical tier is progressively greater from the bottom to the top of the cup. Each stepped tier is hermetically sealed by a frangible diaphragm which overlies the cylindrical tier and is supported by the step resulting from the diametrical increase of the next larger tier. The frangible diaphragm, therefore, serves to seal the top of one cylindrical tier and becomes the bottom of the cylindrical tier spaced immediately thereabove. The reagent cup may be fabricated with as many tiers, as desired. The top of the reagent cup is hermetically sealed by a frangible diaphragm which is supported by a final step.

In order to fill the cup with reagents, a manual or automatic metering device dispenses a pre-selected quantity of reagent into the base receptacle. The receptacle is then sealed by the frangible diaphragm. This procedure is repeated for each succeeding cylindrical tier employing the same or different reagents in each tier. The top tier is sealed by a frangible diaphragm to complete a prepackaged reagent cup.

In use, a test sample is introduced into the top compartment through a hollow needle which is adapted to make a small puncture in the frangible top cover. After a suitable incubation period a breaker means ruptures the seal forming the base of the top compartment, thereby allowing the contents of the top and next succeeding compartment to mix.

After a suitable time the breaker means is employed to rupture the seal forming the base of the second compartment from the top, thereby allowing the contents of the top and next succeeding compartment to mix with the contents of the compartment immediately thereinbelow. This procedure is repeated until all the frangible seals have been broken.

From the above, it is seen that the invention provides a novel apparatus for prepackaging accurate quantities of various reagents in a combination shipping container and reaction cup. The unitary tiered container is readily fabricated by conventional extrusion techniques or the like and does not require specially fabricated and mounted inserts. Since the top of the reagent container has a wide opening, it is possible to employ accurate reagent delivery means to fill each compartment with a carefully predetermined quantity of reagent. By his novel design, applicant has eliminated the necessity of carrying a series of reaction flasks and reagent containers for subjecting a test sample to a sequential addition of reagents. Complete mixing of reagents and test sample is facilitated by the relatively wide openings to the compartments. Further, the action of the breaker as it punctures each succeeding compartment seal, promotes further enhanced mixing.

The invention will be more fully understood when considered in terms of the following description and the accompanying drawing, in which a preferred embodiment of the invention has been illustrated, and in which:

BRIEF DESCRIPTION OF THE DRAWING

FIG. 1 is an axial cross-sectional view of a prepackaged reagent container, constructed in accordance with the invention, showing the prepackaged reagents in separate compartments;

FIG. 2 is a view similar to FIG. 1, with a thin, hollow tube puncturing the top seal, illustrating the introduction of a test sample into the top compartment (as illustrated by the arrows);

FIG. 3 is a view similar to FIG. 1, in which a breaker has punctured the seals of the top and next succeeding compartment of the reagent container, and in which the contents of the second compartment are circulating into the top compartment illustrated by the upwardly disposed arrows): and

FIG. 4 is a view similar to FIG. 3 in which the breaker has punctured the seal of the base receptacle.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The reagent cup, as illustrated in FIG. 1, includes a container **10** having a series of stepped tiers. The container is in the form of a stepped hollow cylinder. At the base of the container is a receptacle **12** enclosed by an integral flat bottom plate **14**.

A flat annular step or shoulder **16** is continuously disposed about the periphery of the top of the base receptacle **12**. In axial alignment with the base receptacle is a cylindrical section **18** upwardly disposed from the outer periphery of shoulder **16**. The radius of cylinder **18** is greater than the radius of base receptacle **12**. The width of shoulder **16** is equal to the difference between the radius of cylinder **18** and receptacle **12**.

Annular shoulder **20** is continuously disposed outwardly from the periphery of the top edge of cylinder **18**. Hollow cylinder **22** has upstanding walls continuously disposed about the periphery of shoulder **20**. The radius of cylinder **22** is greater than the radius of cylinder **18**. Shoulder **20** is equal in length to the difference between the radius of cylinder **22** and the radius of cylinder **18**. Cover seal supporting means **24** is continuously disposed about the top edge of cylinder **22**. As illustrated in FIG. **1**, cover supporting means **24** forms a flat annular shoulder with respect to cylinder **22**.

Container **10** may be formed from rigid, semirigid or flexible materials. Suitable materials include thermosetting and thermoplastic polymers; including polystyrene, polyethylene and polypropylene.

In order to provide discrete reagent compartments within container **10** frangible seals are provided. The seals are supported by the respective annular shoulders of the container. Suitable frangible materials for the seal include thin metal foils and heat-sealable materials, including polymeric films, such as cellophane and laminates. The seals should be inert to the reagents employed and impermeable to the liquid reagents employed. The thickness of the seal will, of course, vary to some extent with the diameter of different sized devices. As a practical matter the seal should rupture on the application of an axial force of less than about three pounds. Once ruptured, the seal should tear easily to accommodate the pointed breaker which is preferably employed to rupture the seal. To facilitate assembly the seal may have impregnated at the outer periphery thereof a suitable adhesive material capable of forming a liquid impermeable bond with the container. If desired, a heat activatable seal may be employed and suitable heating means applied to the periphery of the seal to form a suitable bond with the container.

As illustrated in FIG.**1**, a thin plastic diaphragm **26** overlies base receptacle **12** to form a base compartment **28** in the container. Diaphragm **26** acts as a cover for base compartment **28** and as a base for the compartment of cylinder **18**. Diaphragm **28** overlies cylinder **18** forming compartment **30**, a second reagent chamber in the container.

Shoulder **20** forms a seal supporting means for diaphragm **28**. Shoulder **16** forms a seal supporting means for diaphragm **26**.

Cover seal **32** overlies cylinder **22** to form top reagent compartment **34**. Container seal **32** is supported by top shoulder **24**.

In order to fill the tiered container with suitable reagents, the container is supported by suitable supporting means. Such supporting means includes a bracket of complementary configuration with container **10**, test tube holder means, or an apertured test tube bracket capable of accepting and retaining in a perpendicular position, the container wherein the container is supported across an aperture by top shoulder **24**. A first reagent is metered into compartment **28** in base receptacle **12**. Conventional manual or automated reagent delivery means may be employed. Thereafter, plastic diaphragm **26** is placed on shoulder **16** and adhesively sealed to the shoulder. Next, a second reagent is introduced into compartment **30** by suitable delivery means. Thereafter, diaphragm **28** is emplaced on shoulder **20** and adhesively adhered to the shoulder. Finally, a third reagent is introduced into compartment **34** and cover diaphragm **32** is bonded to shoulder **24** to form a completed reagent cup.

Of course, the quantity of reagent in each of the respective compartments will be dependent, in part, upon the nature of the material being tested and of the quantity of material added to the reagent cup. In order to prevent overflow and to provide enhanced mixing, it is generally preferred that the top and middle reagent compartments are filled to no greater than about one half their respective capacity.

The bottom receptacle may be filled to virtually its full capacity, if necessary. Although the drawings illustrate the use of a reagent cup with liquid reagents, solid reagents may be employed in one or more compartments. The quantity of solid reagent which may be added to the top and middle compartments is dependent, in part, on the physical properties of the plastic diaphragm forming the base of these compartments.

Turning now to FIGS. **2–4**, there is illustrated a method for the sequential addition of prepackaged reagents to a sample of material to be tested, whereby a chemical evaluation of the material may be performed. Initially, as illustrated in FIG. **2**, a liquid test material is

introduced into the top reagent compartment by means of a thin tube **36**. A micropipette or syringe needle may be employed for this purpose. Turning now to FIG. **3**, after an appropriate incubation or reaction period, a breaker **38** descends and punctures the diaphragm **28** separating the top and middle reagent compartments. As the breaker descends, it forces the reagent out of the second compartment up into the first compartment, thereby promoting mixing. The breaker then retracts and is washed. The procedure is repeated for as many reagents as are present. In FIG. **4** washed breaker **38** punctures the diaphragm **26** between the middle and bottom reagent compartments, thereby effecting mixing of the entire contents of the container.

It will be obvious to those skilled in the art that various breaker designs are possible. A preferred breaker design is illustrated in FIG.**3**. Breaker **38** includes a thin gripping tube **39** which may be knurled or scored to facilitate handling. Cylinder **40** is concentrically disposed about tube **39**. For best mixing results, the diameter of cylinder **40** should be less than the diameter of base receptacle **12**. The diameter of cylinder **40** should be preselected such that upon introduction into base receptacle **12**, the contents therein are forced upwardly about the outer periphery of cylinder **40** and intimately mixed with the contents of compartments **30** and **34**.

Puncture tip **42** in axial alignment with tube **38** is centrally disposed on the lower face **44** of cylinder **40**. The breaker may be readily fabricated, employing a sharp pointed needle and a cylinder with a hollow core, wherein the diameter of the core is slightly smaller than the diameter of the needle. The cylinder is heated, and while in its expanded state, is slipped over the needle such that the needle point is exposed below the bottom face of the cylinder. Thereafter, the cylinder is cooled in order to form a shrink fit about the needle.

Alternatively, the cylinder may be force-fit over the needle. Further, a unitary breaker may be formed or extruded from plastic materials by employing a suitable die or mold. The container may be fabricated by conventional extrusion processes employing a tiered die.

The following example is given to further illustrate the novel method for the sequential addition of reagents which have been prepackaged within the tiered reagent cup of the invention for the purpose of performing a chemical evaluation of a test material and is not limitative of scope.

EXAMPLE I

One drop of pyridine is introduced into the bottom receptacle of the tiered reagent cup of the invention. The bottom receptacle is thereafter sealed by an impervious frangible diaphragm. Two drops of a solution made by dissolving 1 gram of ferric chloride in 100 ml of chloroform is introduced into the compartment immediately above the bottom receptacle. An impervious frangible plastic diaphragm is then adhesively sealed above the compartment. One milliliter of chloroform is introduced into the top compartment. The compartment is hereafter sealed in the manner described hereinabove.

One drop of a liquid suspected of containing phenols or enols is then introduced into a thin hollow glass tube by capillary action. An opened end of the capillary tube is forced through the top frangible diaphragm of the reagent container and the unknown liquid is forced into the top compartment. After about a minute, a pointed breaker is pushed through the top and next succeeding frangible seal, thereby mixing the contents of the top and the next succeeding compartment. The breaker is removed and thoroughly washed, thereafter the washed breaker is forced through the frangible seal covering the bottom receptacle, thereby agitating and mixing the contents of the reagent cup. The breaker is removed and the contents of the cup are examined for a color change typical of phenols and/or enols.

It will be obvious that the above test procedure is applicable to reagent cups having more than one compartment. If desired, the reagent cup can be fabricated from transparent material so that precipitates, color changes and other physical properties may be observed through the walls of the cup. A suitable transparent material is the polycarbonate identified by the trademark Lexan. In any event, the cup material must be nonreactive to the reagents employed therein. Further, the seal material should be inert to and impervious to the vapors of any liquid reagents employed therein. It will be obvious to those skilled in the art that serum or other organic materials may be evaluated employing suitable reagents in a predetermined sequence of addition, as provided by the invention.

Having thus described the invention it is not intended to be limited, except as set forth in the following claims.

I claim:

1. A unitary tiered reagent container adapted for the chemical evaluation of a material by the sequential addition of pre-packaged reagents thereto comprising:

a plurality of tiered cylinders in abutting axial alignment and having a bottom cylinder of smallest diameter and each succeeding cylinder having a greater diameter than the preceding cylinder;

each cylinder having a radially disposed annular shoulder means for sealingly mounting a frangible partition means dividing the cylinders into individual compartments.

each of said partition means being supported on said shoulder means and frangible cover means enclosing the cylinder of greatest diameter and means permanently enclosing the end of the cylinder of smallest diameter whereby a tiered reagent container is formed adapted to house sequentially a reagent in each cylinder in tiered abutting axial alignment.

2. The invention in accordance with claim **1**, wherein each compartment contains a predetermined quantity of a preselected reagent, whereby a sample may be introduced into the compartment sealed by the frangible cover means and sequentially exposed to the balance of the reagents in the container by sequentially puncturing the succeeding frangible partitions.

3. A unitary tiered container for chemically evaluating a test sample, having discreet compartments, each compartment having a predetermined amount of a preselected liquid reagent, comprising:

a cylindrical hollow base receptacle permanently enclosed at one end;

a plurality of hollow cylinders in integral, abutting axial alignment therewith, each successive cylinder having a greater diameter than the preceding;

a continuously disposed annular shoulder joining the abutting ends of each successive cylinder;

a plurality of frangible, inert, impermeable diaphragms dividing the cylinders into individual compartments, each of said diaphragms supported and adhesively affixed to an annular shoulder and one of said diaphragms overlying the cylinder of greatest diameter and forming a cover for the container.

4. The invention in accordance with claim 3, in combination with puncture means for successively rupturing each of said frangible partition means, said puncture means comprising an elongated gripping tube having a needle point and a cylinder fixedly secured thereto and in axial alignment therewith, spaced adjacent said needle point, wherein the diameter of the cylinder is less than the diameter of the base receptacle.

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