Dec. 12, 1961 T. V. FEICHTMEIR 3,012,863

APPARATUS FOR THE PREPARATION OF LABORATORY TEST SAMPLES

Filed Sept. 26, 1958 2 Sheets-Sheet 1

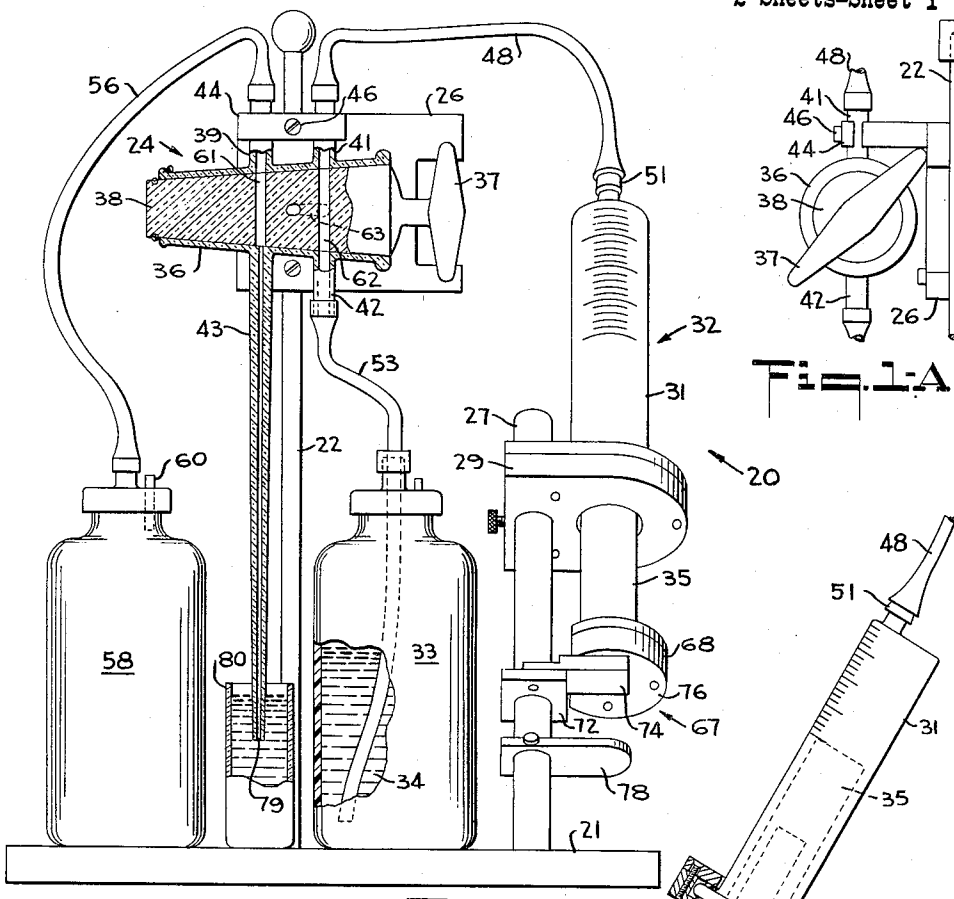


Fig. 1.

Fig. 1-A.

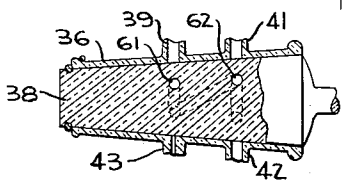


Fig. 2.

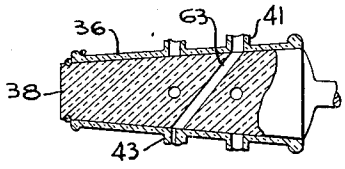


Fig. 3.

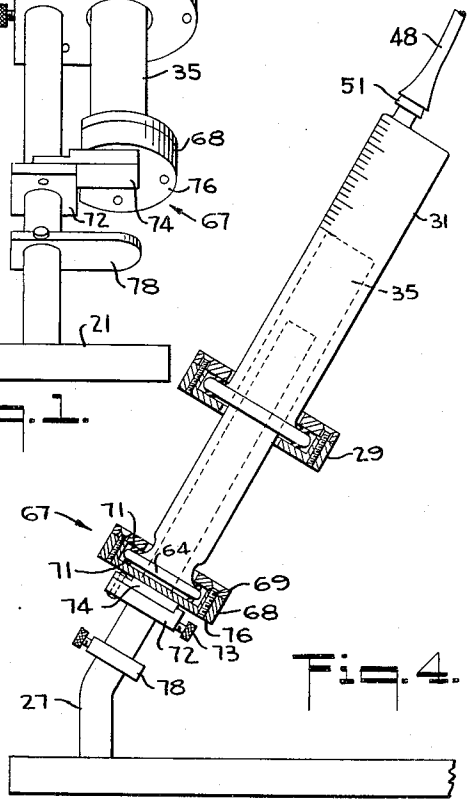


Fig. 4.

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APPARATUS FOR THE PREPARATION OF LABORATORY TEST SAMPLES

Filed Sept. 26, 1958 2 Sheets-Sheet 2

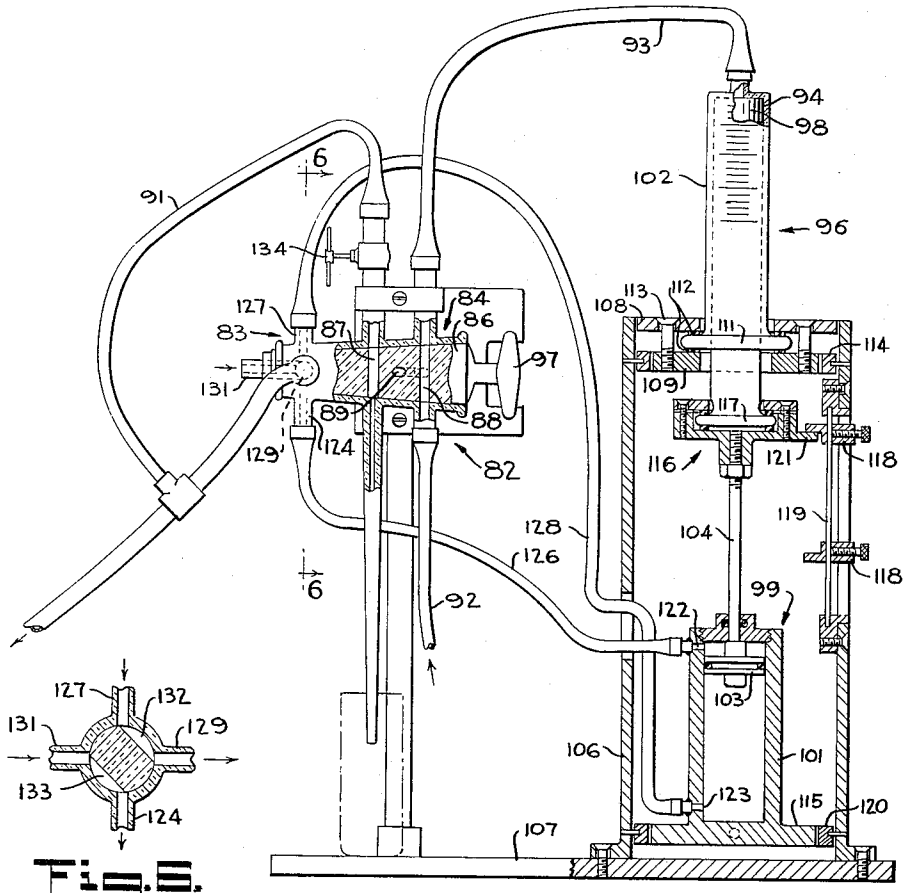


Fig. 5.

Fig. 6.

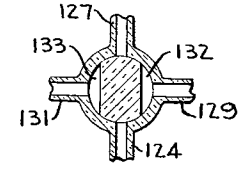


Fig. 8.

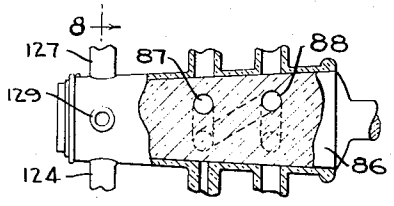


Fig. 7.

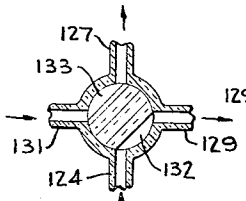


Fig. 10.

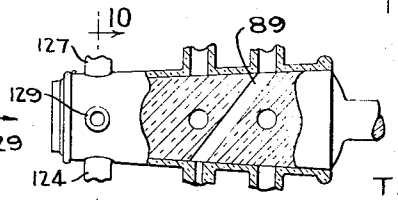


Fig. 9.

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APPARATUS FOR THE PREPARATION OF LABORATORY TEST SAMPLES

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12 Claims. (Cl. 23—253)

My invention relates, in general, to the preparation of laboratory test samples and, more particularly, to apparatus for the apportionment and dilution of fluid samples prior to laboratory analysis.

In many analytical procedures and especially those employed in biochemical, physiological and medical laboratories, a standard or predetermined volume of the sample is taken from a specimen, e.g., blood, plasma, urine or other fluid obtained from a patient or biological source, which sample is diluted or admixed with a reagent or diluent to provide an analytical sample. Customarily these operations are performed manually and are time consuming and tedious, especially when numerous similar specimens are being processed. Moreover, the opportunity for error is considerable and particularly so unless extreme care is taken and skill employed. Similar requirements and problems occur in other fields such as medicinal dose preparation and the like.

In accordance with my invention apparatus is provided wherein the proportionment, measurement and dilution of a sample is accurately and quickly effected and the resultant product easily and quickly ejected with a minimum of manual manipulation. Such apparatus provides for the integrated series of operations including taking of a standard or predetermined volume of the specimen, the taking of a predetermined volume of reagent or diluent from a bulk supply, the mixing of the specimen with the diluent and the discharge of the mixture from the apparatus for immediate use or storage. Manually and mechanically powered versions have been devised as disclosed hereinafter.

Accordingly, it is an object of my invention to provide apparatus wherein the proportionment, measurement and dilution of a fluid sample may be accurately and quickly effected without requiring special care and skill on the part of the operator.

Another object of my invention is to provide apparatus for taking separate measured quantities of diluent and a fluid sample followed by delivery and dilution of the product.

Still another object of my invention is to provide apparatus wherein the operations of measuring, delivering and diluting of fluid samples for analysis are power actuated but each operation manually controlled.

A further object of my invention is to provide apparatus adapted to take a predetermined volume of a fluid sample as well as a predetermined volume of diluent or reagent and dispense and mix same upon the actuation of a simple positive position control.

The invention possesses other objects and features of advantage, some of which, with the foregoing, will be set forth in the following description of the preferred forms of the invention which are illustrated in the drawings accompanying and forming part of the specification. It is to be understood, however, that variations in the showing made by said drawings and description may be adopted within the scope of the invention as set forth in the claims.

With references to said drawings:

FIGURE 1 is front elevational view, partly in section, of a manually powered apparatus constructed in accordance with the invention with the control valve in sample and diluent taking and measuring position.

FIGURE 1*a* is an end view of the control valve as positioned in FIGURE 1.

FIGURE 2 illustrates the control valve of FIGURE 1 in an intermediate position after the sample and diluent volumes have been taken.

FIGURE 3 illustrates the control valve of FIGURE 1 in position to effect discharge of the sample and diluent and mixing of the product.

FIGURE 4 is a side view of the variable volume diluent measuring chamber portion of the apparatus of FIGURE 1, better illustrating preferred details of construction and mounting thereof.

FIGURE 5 is a side elevational view partially in cross-section illustrating a mechanically powered version of apparatus constructed in accordance with the invention.

FIGURE 6 is an enlarged transverse section of the control valve along the plane 6—6 of FIGURE 5.

FIGURE 7 is a longitudinal sectional view of the control valve of FIGURE 5 but with the valve in intermediate position.

FIGURE 8 is a transverse sectional view of the control valve along the plane 8—8 of FIGURE 7.

FIGURE 9 is a view similar to FIGURE 7, but with the valve in sample and diluent delivery and mixing position.

FIGURE 10 is a transverse sectional view similar to FIGURE 8 but with the valve in sample and diluent delivery position.

Briefly, the apparatus of the invention includes a calibrated pipette which forms a means into which a predetermined volume of a fluid sample may be drawn, and a variable volume chamber means which may be calibrated or preset to contain a predetermined volume of diluent or of a chemical reagent. Of prime importance, control valve means are provided which in a first position simultaneously connects said chamber with a storage reservoir source so that the predetermined volume of diluent may be introduced into said chamber and the desired volume of sample may be drawn into said pipette. Rotation of said control valve means to a second or intermediate position retains the sample in said pipette and closes off the diluent reservoir. Then upon rotation of said control valve to a third position, the predetermined amount of sample in the pipette and of the diluent in the chamber are expelled and mixed into a container as desired. In the mechanically powered versions, a control means is provided preferably in conjunction with said valve and operating to energize a mechanical motive power means for actuating said variable volume chamber as well as perform the functions indicated above for the manual version.

More particularly, the manually operated apparatus **20** may be assembled simply upon a base plate **21** provided with vertically projecting rod **22** for supporting the control valve **24** by means of a cross plate **26** attached thereto. A similar rod **27** projecting upwardly from base **21** is provided with a clamp member **29** projecting outwardly to engage and support the barrel **31** of a pump or syringe **32**, the latter being provided with a piston plunger **35** reciprocal in the barrel so as to afford a variable volume chamber. The syringe is calibrated and to this end the barrel walls are transparent and provided with graduations so that the amount of liquid contained in the barrel as indicated by the position of the plunger may be determined. A vented glass or plastic bottle **33** may be mounted on base plate **21** or other convenient location to serve as the storage reservoir for diluent or reagent indicated by numeral **34**.

For purposes of illustration the control valve **24** may take the form of a glass or plastic stopcock as illustrated; however, other properly ganged valving means operating substantially as described hereinafter may likewise be employed. The barrel portion **36** of the stopcock is preferably supported as by appropriate blocks (not shown) with the elongated knob handle portion **37** of the stop-

cock plug 38 parallel and adjacent to the outer end of plate 26, the latter being notched and defining upper and lower index portions above and below the notch.

To meet minimum requirements the stopcock control valve means 24 is of a particular design in which a pair of conduit circuits may be sequentially established or cross switched by appropriate rotation of the plug member. Preferably, the barrel 36 of stopcock 24 is provided with upwardly projecting parallel conduit connector stubs 39 and 41 and conduit connector stub 42 projecting downwardly diametrically opposite to stub 41.

Projecting downwardly from a location diametrically opposite to stub 39 there is provided an elongated calibrated pipette 43 which is employed as the sample receiving and measuring chamber means as described more fully hereinafter. In general in hereafter referring to the pipette, the reference is to the calibrated bore of the pipette member. Crosspiece 44 is secured by screw 46 to clamp stopcock 24 to plate 26.

In order to permit filling of the variable volume chamber of syringe 32, conduit stub 41 is coupled to flexible tubing 48 which in turn is coupled to the tip 51 of syringe barrel 31. Also, conduit stub 42 is coupled to tubing 53 which enters reservoir 33 and dips beneath the surface of diluent 34. Conduit stub 39 is similarly coupled to tubing 56 which in turn is connected with a closed polyethylene plastic bottle 58. The bottle is compressible to provide a vacuum, however any suitable evacuation means may be substituted. A check valve 60 is provided on the bottle cap in order to normally prevent ingress of air, but permit egress of air on compression of the bottle.

In order to properly switch and interconnect the circuits indicated in the foregoing, the stopcock plug 38 is provided with a parallel pair of diametrically disposed passages 61 and 62 which, when oriented in a vertical plane, inter-connect conduit stub 41 with stub 42 and stub 39 to bore of the pipette respectively, provided normal initial position shown in FIGURE 1. Preferably, passages 61, 62 are disposed in a plane which is rotated 45° forwardly of the central longitudinal plane of the upper portion of handle 37 to simplify indexing of the various passages. Accordingly, as shown in FIGURE 1*a*, the upper portion of handle 37, in the position of the valve as indicated in FIGURE 1, is inclined rearwardly 45° from the vertical and bears upon plate 26 as an indexing stop. Stopcock plug 38 is in addition provided with a passage 63 which extends in a plane transversely of that of the passages 61 and 62. Passage 63 also extends obliquely of the axis of the valve and in such manner that in one position of the valve (see FIGURE 3) one end of the passage will be in communication with stub 41 while its opposite end will be in communication with pipette 43. In the position of the valve as shown in FIGURE 1 the passage is closed at both ends.

In practice it has been found that the variable volume chamber when designed with proper cylindrical cavity configuration operates most efficaciously when mounted in an inclined position preferably parallel to an inclined portion of rod 27. An inclination of about 30° from the vertical is suitable. Further, by utilizing a syringe in which the tip 51 is offset to the outer periphery and the barrel 31 is arranged with the tip in the uppermost direction, trapping of air in the chamber is minimized.

As will be clear from FIGURE 4, piston plunger 35 is provided with an external knob 64 contained within a cushioning fixture 67 formed as a cup 68. The knob is secured therein by ring 69 attached to the top of the cup. Flexible gaskets 71 disposed between the knob and a ring 69, as well as between the knob and the bottom of the cup provide cushioning action while preserving alignment of the fixture and the plunger. One or more calibration members such as the stop member 72 are slidably mounted on rod 27 and fitted with thumbscrews 73 for positive positioning at a desired location on the rod.

Member 72 is provided with a projection 74 which is designed to be engaged by the lower face 76 of fixture 67 to thereby limit the downward travel of the plunger. By thus presetting the limit of travel of plunger 35 the volume of diluent which may be introduced into chamber 32 may be predetermined. The projection 74 is pivotally mounted so that it may be swung into registration with the fixture 72 and in this manner permit the plunger to be moved to a position lower than the projection 74 and engage a further stop such as the adjustable member 78. This arrangement as will be evident permits substantially any number of calibration settings or volume of diluent in the chamber 32. Since the syringe walls are transparent not only can the fluid volume be noted but the presence of bubbles readily ascertained.

The bore of the pipette 43 is preferably straight and smooth to insure unimpeded and complete discharge of the fluid contained therein. The pipette 43 is formed to contain an exact amount of fluid between the open end 79 and the surface of the valve plug 38 covering the pipette bore. The specific amount of fluid that the pipette will thus contain may be indicated in suitable manner thereon. The pipette may be removably mounted by means, e.g. of conventional ground glass fittings for inter-changing various size pipettes.

When preparing apparatus 20 for use, stopcock 24 is disposed in the position shown in FIGURE 1 so that tubing 48 is connected with tubing 53. Then the plunger 35 of the syringe is operated reciprocally several times until tubing lines 48, 53 and the chamber are filled with diluent 34 and cleaned of air. Then chamber 32 is filled completely, face 76 of plunger cushioning fixture 67 having been indexed against stop 74 to provide the selected amount of fluid to be drawn into the chamber. In this position of the valve, passage 61 couples conduits 39 and 43 whereby on squeezing bottle 58 slightly and releasing same to create a vacuum the sample will be drawn into pipette 43 from a sample container 80 inserted therebelow. When the sample has been drawn so as to completely fill the pipette, the passage 61 the stopcock handle is rotated 45° to bring the same into alignment with a vertical plane as shown in FIGURE 2 whereupon all passages are closed and the sample container 80 can be withdrawn from beneath the tip. Excess sample adhering to the tip 79 can then be wiped off, and a product reaction vessel then placed under the tip. Thereupon the stopcock handle is rotated to bring the upper portion into a 45° inclination forwardly, with the bottom end of the handle 37 indexed against plate 26. In this position as will be clear from FIGURE 3, diagonal passage 63 couples the syringe chamber to the pipette, so that by simply pressing the plunger inward, the sample and diluent will be expelled through the pipette and into the aforesaid vessel to make available the desired product. At this time bottle 58 may be squeezed and the stopcock rotated to the original position whereby residual diluent is removed from the pipette and discharged into the bottle. Thus the apparatus is now prepared for a new cycle of operation as described above without the need of further cleaning of the pipette and associated passages.

It is important to note that when the fluid is being discharged from the apparatus as aforesaid, the fluid in the pipette as well as that in the fluid line connecting the pipette and syringe chamber 32, is under the direct influence of the force exerted by the plunger. In this manner even if the bore of the pipette is relatively small, the fluid therein will be readily expelled. Thus, the apparatus may be effectively utilized for quickly and accurately supplying extremely small amounts of diluted product.

As will be now understood, in the arrangement illustrated in FIGURES 1 to 4, in order to supply the pipette with specimen or diluent the bottle 58 must be manually operated, and correspondingly in order to expel the

diluent and the specimen from the apparatus, the syringe plunger must likewise be manually operated. In FIGURES 5 to 10 inclusive, there is illustrated an embodiment of the invention in which the operation of drawing liquid specimen and diluent into the apparatus is automatically effected simply upon placing the valve in the position permitting passage of said liquids thereto, and likewise the discharge of the two fluids is effected on placing the valve in position permitting such discharge. Movement of the liquids into and out of the chambers or passages is preferably effected by vacuum operated means controlled by a composite valve unit **82** serving to control the flow of such liquids as well as the fluid medium for the vacuum operated means.

The unit **82** is comprised of a valve portion **84** for controlling the liquids, and a portion **83** for the control of the vacuum operated means, the valve portion **84** being substantially similar to the valve member **24** previously described, and provided with a plug **86** having diametrical passages **87** and **88**, and diagonal passage **89** corresponding to the passages **61**, **62** and **63** respectively. Passages **87** is designed to connect the pipette and tube **91** leading to a vacuum source (not shown). Passage **88** provides for communication between the diluent supply pipe **92** and tube **93** operatively connected with variable volume chamber **94** of syringe or pump **96**. As will be understood, diagonal passage **89** is for connection of tube **93** and the pipette. A valve handle **97** provides for manipulation of the valve plug in a manner correspondingly to handle **37**.

Diluent is drawn into and expelled from chamber **94** by piston-plunger **98**, and as here shown movement of the plunger is arranged to be effected by vacuum operated means **99** which as above noted is designed to be controlled by the valve portion **83** of unit **82**. Means **99** includes a cylinder **101** axially aligned with the barrel **102** of the syringe and containing a reciprocal piston **103** mounted in the cylinder and operatively connected with the plunger **98** by a piston rod **104**.

The syringe and cylinder **101** are as illustrated in FIGURE 5, mounted in a supporting frame **106** positioned adjacent the valve unit **82** and supported therewith on a base plate **107**. Desirably, the syringe is held in position on the frame **106** by means of upper and lower rings **108** and **109** between which is clamped the flanged end **111** of the barrel. The flange **111** is maintained in spaced relation between the rings by means of gaskets **112** and the rings are secured together with the flange cushioned therebetween by means of screws **113**. In order to avoid any strain or bind on the syringe in case of any misalignment in the connection or assembly of the syringe and cylinder, such connection is preferably made with a universal type of joint. Accordingly as here shown, the lower ring **109** is pivotally attached to an outer ring **114** which is in turn pivotally secured directly to the frame, the pivotal axis of the two rings being at right angles to one another. Attachment of the piston rod **104** to the piston-plunger **98** is effected by means of spaced plates **116** between which is reliently held a flange **117** of plunger **98**. A universal connection is also provided between the frame and the bottom of cylinder **101**, such connection being conveniently in the form of the universal connection of the barrel and frame and comprising the pair of concentric members **115** and **120** pivotally connected to each other on one axis, and to the frame on a normal axis.

Control of reciprocal movement of the plunger **98** to afford the desired amount of diluent in the chamber **94**, is effected by means of a set of stops **118** adjustably secured to a rod **119** on the frame for different vertical positions. The plate assembly **116** is provided with a lateral extension **121**, and the stops may be rotated so as to be in or out of the path of the projection as the plunger is reciprocated. It will thus be evident the stops may be positioned in relation to the calibrations on the barrel so that the exact amount of diluent to be delivered will be indicated and assured.

As will be clear, on downstroke of the piston **103**, diluent will be drawn into the chamber **94**, and correspondingly, on the upstroke of the piston the diluent will be discharged from the chamber. In order to provide for such movement of the piston the walls of the cylinder are provided with ports **122** and **123**, and are so located as to lie above and below the piston in all of the positions thereof. By means of the valve portion **83**, each of the ports may be alternately vented and connected to a source of vacuum, and in such manner that when either port is connected to the source of vacuum the other is being vented.

In accordance with the foregoing, connection is made to the valve portion **83** by each of the ports **122** and **123**, and for this purpose there is provided in the body of such portion a stub **124** which is connected to port **122** by a tube **126**, and a stub **127** connected by a tube **128** to port **123**. Stubs **129** and **131** also provided on the body, are connected to the source of vacuum and open to the atmosphere respectively. Passages **132** and **133** are provided on the plug and so arranged that in one position (see FIGURE 6) of the latter, passage **132** will connect vacuum stub **129** to stub **127** leading to port **123**. At the same time passage **133** will be connecting vent stub **131** to stub **124** communicating with port **122**. It will thus be clear that in said position of the valve, passage **88** will connect the diluent supply with chamber **94**, and thus as piston **103** is retracted, diluent is drawn into chamber **94**. Since passage **87** to the pipette is also now open, sample or specimen fluid may be drawn from the specimen vessel into the pipette, and then as soon as the pipette is filled the valve may be turned to the intermediate position indicated in FIGURES 7 and 8, wherein all passages in the entire valve **82** will be closed. Desirably, a needle valve **134** is provided in the sample bleed line **91** so that the amount of vacuum may be varied in accordance with viscosity of the fluid being treated. After the vessel is removed and an empty container for the product inserted under the pipette, the valve is turned to the position shown in FIGURES 9 and 10 wherein the diagonal passage **89** will establish connection between chamber **94** and the pipette, and at the same time passage **133** will communicate vent stub **131** to port **123**, and passage **132** will connect port **122** to vacuum stub **129**. In this manner piston plunger **98** will force the diluent from chamber **94**, thereby expelling the fluid in the pipette and discharging together therewith into the product container.

What is claimed is:

1. An apparatus for the proportionment and dilution of a fluid comprising in combination means including a calibrated pipette for measuring out a predetermined volume of said fluid, means including a variable volume chamber adapted for presetting to a predetermined volume, and unitary fluid flow control means operative in one position to simultaneously couple said pipette to a vacuum source in order to draw the predetermined volume of said fluid therein and said variable volume chamber to a diluent supply, and in another position to discharge diluent from said variable volume chamber through said pipette, said fluid being thereby washed from and admixed with the predetermined volume of diluent.

2. An apparatus for the proportionment and dilution of a liquid comprising in combination means including a calibrated pipette for measuring out a predetermined volume of said fluid, means including a variable volume chamber adapted for presetting to a predetermined volume, diluent storage means, vacuum source means, and unitary control valve means operative in one position to simultaneously couple said pipette to said vacuum source for drawing said fluid therein and said variable volume chamber to said diluent storage, and in a second position to close off said vacuum supply, and to couple said variable volume chamber for discharge of the predetermined

volume of diluent to wash and mix with the predetermined volume of said fluid, said pipette in a final position.

3. Apparatus as described in claim 2 wherein said control stopcock valve means comprises a valve provided with a pair of circuits which simultaneously couple said pipette to said vacuum source and said chamber to said diluent storage in said first position, and said valve being provided with an independent passage coupling said chamber to discharge through said pipette in said final position.

4. Apparatus as described in claim 3 wherein said variable volume chamber comprises a calibrated syringe with a plunger therein, and in which adjustable means are provided to limit the travel distance of the syringe plunger to predetermine the volume of diluent delivered, said plunger being operative in said final position to force the fluid from the chamber through said independent passage and pipette.

5. Apparatus for the apportionment and dilution of a liquid specimen to provide a sample product comprising in combination means including a calibrated pipette for measuring out a predetermined volume of said specimen, means providing a variable volume chamber and including a reciprocally operating member, vacuum powered reciprocating motor means arranged to actuate said member to vary the volume of said chamber, and unitary fluid flow control means adapted for positioning in a first position to simultaneously couple said pipette to a vacuum source, couple said chamber to a diluent supply and energize said vacuum motor means to actuate said member to increase the volume of said chamber, whereby specimen will be drawn into said pipette and said chamber will be filled with diluent, for positioning in a second position to close all circuits and for positioning in a third position to simultaneously couple said chamber for discharge through said pipette and energize said vacuum motor to actuate said member to discharge said diluent through said pipette.

6. Apparatus as described in claim 5 wherein said control means comprises a valve provided with a pair of passages arranged so that said valve in one position thereof will simultaneously couple said pipette to said vacuum source, couple said chamber to said diluent supply, said valve also including a section for switching vacuum power to said motor to actuate said member to draw diluent into said chamber in the first position, and said valve including a cross-switching passage arranged in said third position to communicate said chamber with said pipette while vacuum is applied to said motor to actuate said member to discharge diluent from the chamber and through said pipette.

7. Apparatus for the apportionment and dilution of a fluid specimen to provide an analytical sample comprising in combination, means providing a variable volume chamber including a reciprocating member, a reciprocating vacuum piston motor operatively connected to said member and arranged to drive said chamber means, a unitary control valve with a calibrated pipette attached directly thereto and provided with a pair of conduit circuits which in a first position is arranged to simultaneously couple said pipette to a vacuum source and said chamber to a diluent supply, said valve including a switching section simultaneously operative in said first position to apply vacuum power to said motor to operate said member to increase the volume of and thereby draw a predetermined volume of diluent into said chamber, said valve being positionable in a second position to close all circuits, and said valve being further provided with a diagonal circuit which in a third position of the valve simultaneously connects said chamber to said pipette and said switching section to apply said vacuum power to said motor to actuate said member to discharge the fluid in said chamber to wash said specimen from said pipette and be admixed therewith.

8. Apparatus as described in claim 7 wherein said variable volume chamber including said member and said vacuum motor means operatively connected together are supported upon a universal mounting to provide compliant vertical alignment.

9. Apparatus as described in claim 8 wherein adjustable stops are provided to limit the travel distance of the member and thereby predetermine the volume of diluent drawn in the chamber.

10. Apparatus as described in claim 7 wherein auxiliary vacuum regulating means are included in the pipette vacuum supply circuit.

11. Apparatus as described in claim 7 wherein said valve is constructed with said first circuits being disposed in a plane of about 45° inclination to the handle thereof, said diagonal circuit being in a plane normal to said circuit plane and said control switching section includes quadrantally oriented passages in parallel alignment with said handle for switching vacuum power and air vent circuits to actuate said vacuum motor.

12. In an apparatus for supplying an admixture of a predetermined amount of sample and a selected amount of diluent, unitary stopcock valve means having first and second pairs of opposing conduit connecting stub means lying in a single longitudinal plane on the barrel portion thereof being provided with a pair of parallel passages in the plug portion thereof simultaneously communicating opposing members of said pairs of conduit connecting stubs in a first position of said stopcock plug said stopcock plug being provided with a third diagonally oriented passage arranged to cross connect one of said first pair of conduit stubs with the opposing stub of the second pair of stubs in a second position, said passages being closed simultaneously in an intermediate position, a conduit for coupling to a vacuum source communicating with a conduit connecting stub of said first pair, a calibrated pipette formed as a continuation of the second stub of said first pair and depending directly therefrom, conduit means for communicating with a diluent reservoir coupled to the conduit connecting stub of the second pair on the same side of the stopcock barrel as said pipette, a variable volume chamber provided with calibrated volume stop means, and conduit means coupling the other of said second pair of conduit connecting stubs to said variable volume chamber.

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