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Ambrose et al.

[11] **3,780,984**

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[54] **APPARATUS AND METHOD FOR FLUID HANDLING AND SAMPLING**

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[21] Appl. No.: **121,147**

Related U.S. Application Data

[62] Division of Ser. No. 753,199, Aug. 16, 1968.

[52] **U.S. Cl.** **251/282,** 251/319

[51] **Int. Cl.** **F16k 1/32**

[58] **Field of Search** 251/319, 282, 322, 251/323, 320, 321

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Primary Examiner—Arnold Rosenthal
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[57] **ABSTRACT**

An apparatus and a method for handling and sampling fluids which comprises principally a nonpumping valve designed so that in operation it moves less than a microliter of fluid, and a pumping valve designed to aspirate a precisely determined amount of fluid into the body of the valve with no more motion than is inherent in the operation of the valve itself and with no change in the physical dimensions of the valve. These valves, when used in combination with a transfer probe and a pump designed to handle minute quantities of fluid, form a precision fluid handling and sampling system which will not contaminate or dilute the fluid to be sampled.

3 Claims, 6 Drawing Figures

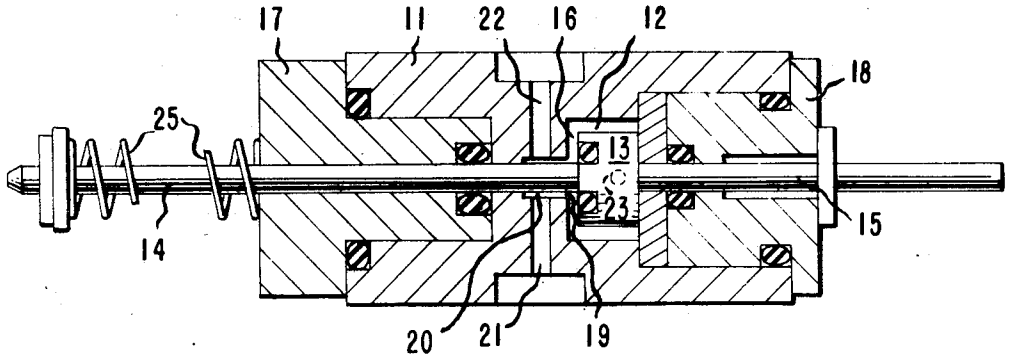


FIG. 1A

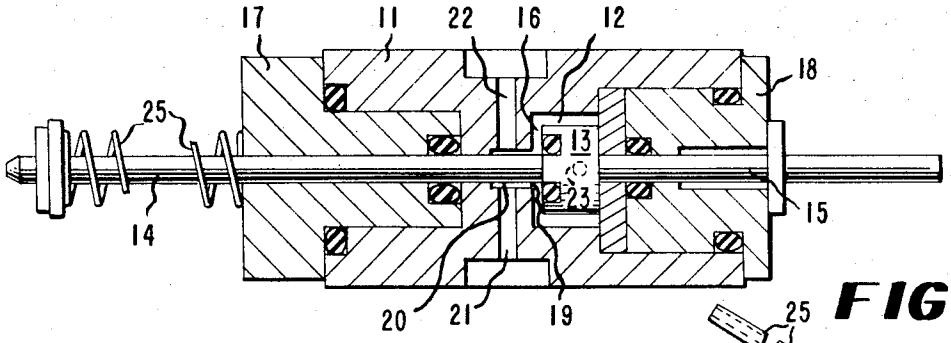


FIG. 1B

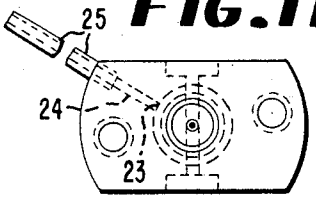


FIG. 2

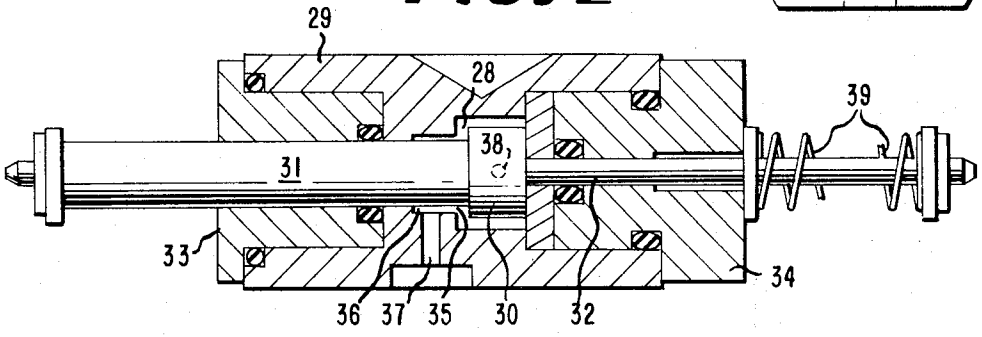


FIG. 3

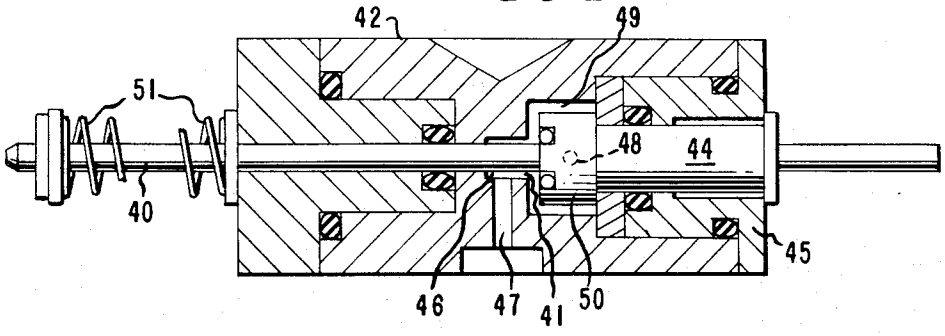


FIG. 4

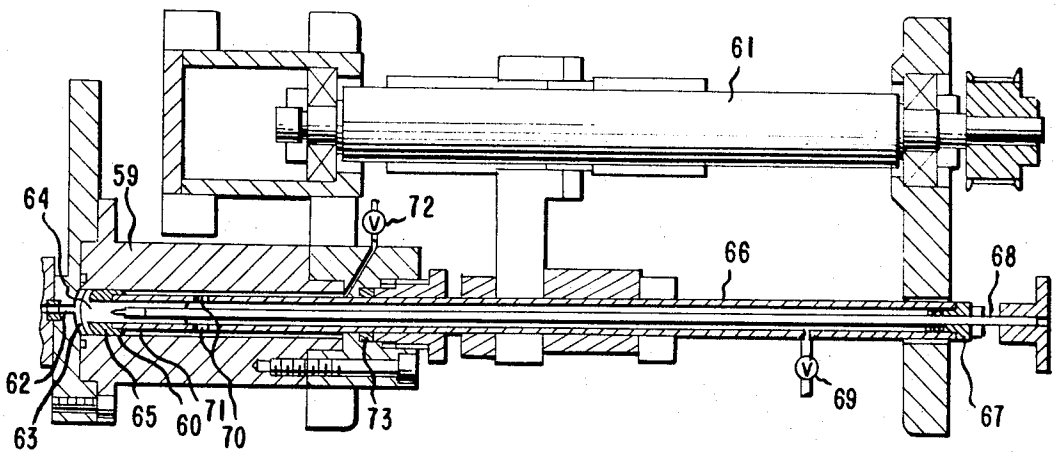
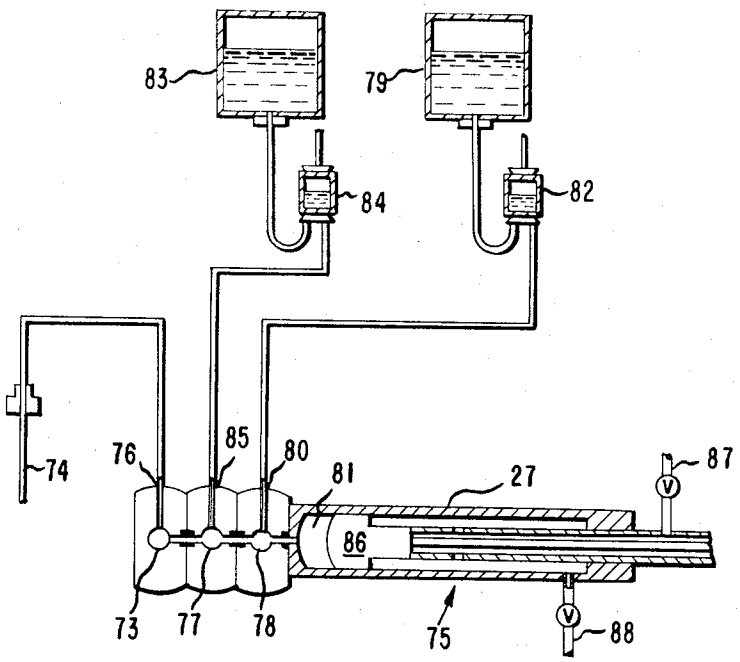

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FIG. 5


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APPARATUS AND METHOD FOR FLUID HANDLING AND SAMPLING

This application is a division of Ser. No. 753,199 filed Aug. 16, 1968 by the same inventors.

CROSS REFERENCE TO RELATED APPLICATIONS

This invention is particularly related to the subject matter of U.S. Pat. No. 3,476,515 filed 4/26/66, entitled Analytic Test Pack and Process for Analysis by D. R. Johnson et al. (assigned to the assignee of the present application), since the instant invention may be used to transfer the fluid to be tested from its source to the analytic pack described in that application. It is also related to the subject matter of application Ser. No. 753,197 filed on the same day as this application, entitled Analytic Clinical Analyzer by E. P. Carter (assigned to the assignee of the present application), since the instant invention may be used in the system described and claimed therein to introduce the fluid to be tested into the test packs which are then processed by that system. These cross references are merely intended to illustrate and not to restrict the scope and/or use of any of these inventions.

BACKGROUND

The field of this invention is a fluid handling and sampling system, or more particularly the invention is concerned with the design of a fluid handling and sampling system for use in an analytic instrument. While fluid handling and sampling systems are not restricted to use in analytic research, the demands on such systems are frequently greatest in such research. Technological advances have increased the precision of analytic instruments to the point where chemical analysis can now be performed on minute samples. As a consequence, any fluid handling and sampling system used in such analysis must be designed with care to insure precision in the transfer of the fluids involved and to insure that the sample does not become contaminated or diluted. When the analysis is being performed by hand, the possibility of human error is always present. Recently, however, many analytic tests have been standardized to the point where they can be performed on automatic analytic instruments. Human error is no longer present, but the demands on the instrument to reach the level of manual precision, are exacting.

A typical fluid handling and sampling system for use in analytic research would include a pump which will handle precise quantities of fluid, a valve connected to a transfer probe which is designed to dip into the fluid to be sampled; and a series of secondary valves connected to a series of secondary fluid sources. Such a system would permit the intake of a certain amount of a secondary fluid, such as a buffer solution, the uptake of a certain amount of sample fluid, and the discharge of the sample and secondary fluids into a suitable container. If large amounts of fluid are involved, the requirements for the components of such a system are not particularly stringent. If, however, the amounts of fluid involved are in the microliter range, then the requirements become stringent. In addition, if the sampling system is designed to function in an automatic instrument which operates continuously there are additional requirements on the durability of the components.

The pump for such a system must be capable of handling small quantities of fluid precisely. It is not difficult to design a pump which will do this for a short period of time, but after a few hunored thousand cycles, wear usually causes leakage. This leakage is on the order of microliters. Hence, to insure precision in the microliter range the pumps must be replaced or repaired. This is time-consuming and expensive. This invention includes a novel solution to this problem wherein the pump is designed to compensate externally for variations in its dimensions due to constant wear.

The intake valves for such a system, which are designed to introduce the secondary fluids, are also a source of error. Normally, a valve with moving parts will move fluid as well as control the flow of fluid. The movement of the fluid can be referred to as pumping the fluid. When large quantities of fluid are involved, the small amount of fluid pumped by the valve in its operation will not introduce appreciable error in the amount of fluid passing through the valve. When microliters of fluid are involved, the pumping action of the valve will introduce an appreciable error. If the amount of fluid transferred is constant, this error would be of a type for which compensation can be made. In many applications, however, the amount of fluid transferred is variable and the constant error introduced by the pumping action of the valve is superimposed on a variable volume. This type of error is difficult, if not impossible, to compensate for; and an effort must be made to design a nonpumping valve for use in such situations. A ball valve with its fluid shearing motion is one possible design for such a valve, but for many applications where leakage must be kept to a minimum a positive seating valve is preferable. It is impossible to make a positive seating valve which does not move fluid, but it is possible to make such a valve which moves less than a certain amount of fluid. Since we are dealing with microliters of fluid, a nonpumping valve will be, by definition, one that pumps less than a microliter of fluid. The present invention includes a valve which is designed to be a nonpumping valve.

The pump and the intake valves for secondary fluid comprise the main sources of error in the precision of the sampling system. The other problem is to keep the sampling system from contaminating the sample fluid. This is a particular problem when the sampling system is designed with a transfer probe which dips into the sample fluid. In the operation of such a system there is often a drop of fluid left on the lip of the transfer probe after the discharge of fluids previously handled. Hence, when the transfer probe is dipped into the sample fluid, the drop on the lip of the transfer probe will contaminate the sample system. Part of this problem can be overcome if the transfer probe is cleaned between each use. However, whether the system has been cleaned or not, a drop of fluid still remains to dilute the sample. This problem is particularly acute if the transfer probe is dipped into the sample fluid a number of times, or if the sample volume is small. To overcome this problem, the sampling system must be designed so that no fluid remains on the lip of the transfer probe. This invention relates to a valve or valve assembly designed to aspirate a set amount of fluid from the lip of the transfer probe into the transfer probe so that no contamination or dilution results.

Such systems have been the subject of patents in the past. Specifically, U. S. Pat. No. 2,150,760 issued on

Mar. 14, 1939 to F. Cozzoli describes an apparatus in which the size of the valve cavity is changed by manipulation of a diaphram, which forms a wall of the valve cavity, by an external means coupled to the pump. U. S. Pat. No. 2,185,201 issued on June 2, 1940 to C. Krause, et al. discusses a system in which a vacuum is applied from an external pump at various cycles in the operation of the valve. U. S. Pat. No. 2,619,116 issued on Nov. 25, 1952 to J. D. Ralston discusses a resilient seat which upon springing back from its original position creates suction. And finally U. S. Pat. No. 2,721,008 issued on Oct. 18, 1955 to T. B. Morgan, Jr. discusses a system in which the valve chamber is composed of two cylinders which when moving relative to one another can change the dimensions of the valve chamber to create the desired suction. All of these systems will accomplish the desired result of removing excess liquid from the lip of the transfer probe, but at best they are cumbersome devices requiring external aids or variations in the physical dimensions of the valve cylinder which limit their usefulness. The present invention includes a novel valve which is designed to accomplish the above result simply and efficiently with no more motion than is inherent in the operation of the valve itself and with no change in the physical dimensions of the valve.

SUMMARY OF THE INVENTION

The present invention comprises a nonpumping valve assembly; a pumping valve assembly to aspirate a precise and predetermined amount of liquid from the lip of its intake-output opening into the body of the valve; and a precision pump adapted to handle small quantities of liquid continuously over a long period of time without the introduction of error caused by leakage in the pump due to continuous wear. These three elements can be combined to form an integrated fluid handling and sampling system for use in analytic research.

Specifically, the nonpumping valve assembly comprises: an enclosed valve chamber with at least two orifices; at least one movable support means; and a closing means. The support means and the closing means are disposed within the valve chamber and the support means is adapted to move the closing means to close off at least one of the openings in the valve chamber without obstructing the remaining openings. The support means is further adapted so that the free volume in the valve chamber remains substantially constant when the closing means is moved, so that no fluid is pumped by the motion of the closing means and its associated support means.

The pumping or aspirating valve is composed of the same elements as the nonpumping valve, the difference being that the support means is adapted so that the free volume in the valve chamber changes when the closing means is moved. This causes suction at the intake-output opening of the valve, so the valve can be said to pump. The change in free volume can be carefully controlled in the design of the valve so that the valve can be made to pump the precise amount of fluid desired.

The pump is a piston pump comprising: a cylindrical chamber; a piston disposed within the chamber; and a means for moving the piston. The piston itself is comprised of a support means and a deformable cap supported on the support means in such manner that the deformable cap can be deformed externally to conform to the walls of the cylindrical chamber. In this way, even though constant wear occurs, the effect of this wear can be overcome by externally deforming the cap.

In the sampling system, the aspirating valve, referred to as the intake-output valve, is generally but not necessarily connected to a transfer probe on the intake-output side and to a pump on the opposite side. Optionally, it can be connected to a series of nonpumping valves, referred to as intake valves, which are connected directly to a plurality of secondary fluid sources, containing fluids such as a wash fluid and/or a buffer solution. These intake valves, connected in seriatim, are in turn connected directly to the pump. For convenience in the discussion that follows, we will assume that there are only two intake valves; one connected to a buffer solution, so that a buffer solution can be added to the sample to be tested, and the other connected to a wash fluid, so that the whole system can be cleansed by flushing. This system is meant to be illustrative only. In the case where no buffer solution is required and contamination is not a problem, the system can be composed of a single intake-ouput valve and the pump with no intake valves. In the case where a number of tests are to be performed and a number of different buffer solutions are required, the system can be composed of an intake-output valve, as many intake valves as required, and the pump.

The operation and advantages of the system can best be described with reference to the figures.

FIGS. 1A and 1B illustrate one possible embodiment of a nonpumping valve which can be used as the intake valve of a fluid handling and sampling system.

FIG. 2 illustrates one possible embodiment of a valve which will pump a precisely predetermined volume of fluid and can be used as the intake-output valve of a fluid handling and sampling system.

FIG. 3 illustrates a second possible embodiment of a pumping valve.

FIG. 4 illustrates a possible embodiment of a pump for use in a fluid handling and sampling system.

FIG. 5 is a schematic diagram of one possible embodiment of the fluid handling and sampling system.

DISCUSSION OF THE DRAWINGS

The pump illustrated in FIGS. 1A and 1B is a nonpumping valve which will pump less than one microliter of fluid, and can be used as the intake valve of the fluid handling and sampling system. FIG. 1A is a side view of the nonpumping valve. The body of valve **11**, forming the cylindrical valve chamber **12**, is in the shape of a cylinder which has been flattened on its side in two places so that the flat sides are parallel to one another. The closing means is in the form of a cylindrical plug or piston **13** which is disposed concentrically within the valve chamber and supported therein by support rods **14** and **15** which in turn are disposed along the extended axis of the valve cylinder. Support rod **14** passes through the end of the valve chamber **16**, through the body of the valve **11**, and through the end plug **17** to the exterior of the valve. Support rod **15** passes through end plug **18** to the exterior of the valve. The valve chamber **12** has an opening **19** in end **16** through which support rod **14** passes. This opening is expanded into a channel **20** which extends into the valve cylinder and is concentric with support rod **14**. Channel **20** is connected by two other channels, **21** and **22**, to the flattened sides of the valve cylinder. The expanded portion of these channels adjacent to the flat surface of the

valve cylinder are adapted to hold a gasket which will seal one of these, channel **21**, to a similar channel in either another intake valve or the pump, as will be discussed later, and the other channel **22** to a similar channel in the intake-output valve, as will be discussed later. The valve chamber **12** also has an opening **23** in its side with a channel leading to the outside of the valve. This can be seen with reference to FIG. 1B which is a top view of this embodiment of the nonpumping valve. The opening **23** is connected through channel **24** to the outside of the valve and normally to a source of secondary fluid, not shown, through tube **25.** In what follows, this opening **23** and the channel **24** will be referred to collectively as the intake opening. Returning to FIG. 1A, the cylindrical plug **13** has a diameter less than that of the valve chamber **12** so that it can be moved freely within the valve chamber without blocking the intake opening **23.** The diameter of the cylindrical plug **13** is greater than the diameter of the opening **19** so that when the plug is seated at the end of the valve chamber **16** in which the opening is located, the opening will be blocked, effectively closing the valve. The position of the plug **13** in the valve chamber can be manipulated externally either manually or by any suitable device which can be made to operate on the end of either support rod **14** or support rod **15.** The system can optionally be spring loaded as shown in FIG. 1A, where spring **25** will cause the cylindrical plug **13** to return to the closed position when the force is removed from whichever support rod is being used to manipulate the valve. Optionally the spring can be positioned so that the closing means will return to the open position. Mechanisms for spring loading are well known to those skilled in the art so the mechanism is only indicated by the inclusion of a spring in FIG. 1A. Finally all the seals in the valve which can leak are sealed with O-rings or Quad-rings as indicated by the cross hatched area in FIG. 1A; and the positions of the plug and valve body through which the support rods pass are suitably undercut to allow free motion of the support rod. All of these procedures are well known to those skilled in the art of valve construction.

The noval feature of this valve is the fact that in operation it will not pump fluid. The two support rods **14** and **15** are of substantially identical diameters so that, in the motion of the closing means **13,** as one rod moves out of the chamber **12** it is replaced with an equal volume of the other rod. In this way the free volume in the chamber remains constant and no fluid is pumped. Nonpumping has been defined, herein, to be movement of less than one microliter of fluid. There is nothing in the design of the nonpumping valve of FIG. **1** to limit nonpumping of this value, except practicality. In theory the support rods could be made to be exactly equal, so that there would be absolutely no change in the free volume in chamber **12** when the closing means **13** is moved. There would still be some motion of fluid due to the motion of the closing means but this could be minimized by moving the closing means slowly. In practice, however, the support rods can only be made equal to within certain tolerances. A volume change less than one microliter can be achieved. A smaller change could be achieved with greater difficulties and higher cost if desired, but within the requirements of the sampling system it was not deemed necessary.

Once the problem introduced by a valve which inadvertently pumps fluid has been realized, and a nonpumping valve designed, then a valve which will purposely pump a certain desired amount of fluid can be designed. Such a valve is shown in FIG. **2.** The valve in FIG. **2** is almost identical to that in FIG. **1** in that it contains a cylindrical valve chamber **28** in a valve body **29,** and a closing means supported on two support rods **31** and **32.** Support rod **31** extends through the body of the valve **29** and through end plug **33** to the exterior of the valve, and support means **32** extends through end plug **34** to the exterior of the valve. The valve chamber **28** has an opening **35** in one end of the chamber, and this opening expands into a channel **36** which is connected through a second channel **37** to one of the flattened sides of the valve body. In this case there is only one channel **37** leading to one of the flattened surfaces. In other designs, as will be discussed below, there can be two such channels. The end of channel **37** adjacent to the flattened surface is again expanded to house a gasket which will allow sealing either to a pump or to a similar channel, such as channel **22,** in the nonpumping valve of FIG. **1.** The valve chamber **28** also contains an opening **38** in its side which is connected to the outside of the valve by a channel, not shown, in much the same way as that shown in FIG. 1B for the nonpumping valve. Also the valve can be spring loaded with a spring **39** to be normally opened, as shown, or normally closed.

The main difference between this valve and the nonpumping valve is in the relative size of the support rods. Support rod **31** has a larger diameter than support rod **32,** which means that as the closing means **38** is moved to close the valve, the free volume in the valve chamber **28** will be increased because the volume of support rod **32** which moves into the valve chamber is less than the volume of support rod **31** which moves out of the valve chamber. By controlling the relative diameters of the support rods the desired change in the free volume in the valve chamber can be achieved. In the valve shown in FIG. **2** the increase in free volume occurs when the valve is closed. This increase in free volume causes suction in the opening **38** which draws a volume of fluid from the opening, and the channel which connects it to the outside of the valve, into the valve chamber. This aspiration can effectively remove any excess fluid that remains on the exterior lip of the intake-output opening, or on the lip of a probe connected to the opening.

Optionally, the pumping valve could have been designed to pump or aspirate when the closing means was moved to open the valve. A valve designed to operate in this manner is shown in FIG. **3.** This valve is similar to the valve in FIG. **2** except that the position of the support rods has been reversed. The support rod **40** with the smaller diameter extends through the opening **41** in the valve body **42,** and passes through the valve body and through end plug **43** to the exterior of the valve. The support rod **44,** with the larger diameter, passes directly through end plug **45** to the exterior of the valve. Again, the opening **41** is expanded into a channel **46** which is connected to one of the flat sides of the valve by another channel **47.** There is also an opening **48** in the side of the valve chamber **49.** In this case, when the closing means **50** is moved to open the valve, the free volume in the valve cylinder is increased causing suction at opening **48.** A spring **51** is included so that the valve can be spring loaded in the closed position, as shown, or in the opening position.

The body of the pumping valve, such as the one shown in FIG. 3, and the body of the nonpumping valve shown in FIG. 1 differ in another respect. The pumping valve has only one channel 47 leading from the expanded opening 41 in the valve chamber. This means that in normal operation fluid enters the valve through opening 48 and passes through the valve chamber 49 and channels 46 and 47. When the closing means 50 closes the valve, all motion of fluid through the valve ceases. The nonpumping valve of FIG. 1, however, has two channels leading from the expanded opening 19 so that there is a channel formed by channels 22, 20, and 21 which passes directly through the body of the valve. This means that even when the valve is closed there can be a flow of fluid through the body of the valve. When the valve is opened a second stream of fluid is allowed to merge with the first stream of fluid, through opening 23. As designed, then, the nonpumping valve can be used as an internal segment of a transfer line, while the pumping valve must be used as the end segment of a transfer line. This doesn't mean that the valves have to be designed this way. In practice it is often advantageous to construct the valve cylinders of both the pumping and the nonpumping valves so that they are identical. In this case, the valve body 42 of the pumping valve shown in FIG. 3 would have two channels leading from the expended opening 41, instead of just one. In normal operation one of these would be blocked with an end plate of some sort, but at least the valve bodies would be interchangeable. In many instances the blocked passage formed by the extra channel would be disadvantageous because of the difficulty of flushing and because of the ensuing contamination that would result. In practice it is also possible to design the nonpumping valve with just one channel rather than two. These considerations are controlled by the use to which the valves will be put. One such use will be described below.

Both the valves discussed above are to be constructed from suitable material, employing considerations known to those skilled in the art. While the design of the two valves discussed above is similar, this is done merely for convenience. In these embodiments the valves are small, efficient, simple to construct and simple to clean. In addition, they are of a design which makes them readily susceptible to nesting, either with valves of a similar design or with the pump discussed below. When nested with a pump the valves form a fluid handling and sampling system, in which similarly designed valves are convenient; but this does not mean that radically different designs employing the same principals cannot be used.

FIG. 4 illustrates one embodiment of a pump which can be used in a precision fluid handling and sampling system. In this instance it cosists of a cylinder 59, a piston 60 and a means 61 of driving that piston. The pump cylinder 59 can be made to nest with the intake valve (or the intake-output valve if no intake valve is included) by having the channel 62, leading to the pump chamber 63, mate with one of the channels in the intake valve such as channel 46 in FIG. 3. At the rear of the cylinder is a packing gland 73 to seal the piston rod. In one embodiment, the end of the pump cylinder forming the forward wall of the pump chamber 63 is rounded so that no liquid will be trapped in the square corners inherent in a flat front wall. In another, the forward wall is conically shaped for the same purpose. The piston 60 consists of a deformable cap 64, a forward end plug 65, a hollow shaft 66, a rear end plug 67 and a screw shaft 68 running through the rear end plug 67, concentrically through hollow shaft 66, and into the deformable cap 64. The purpose of such a construction is to allow the shape of the deformable cap to be changed by external means - the screw 68 - to conform to the forward and side walls of the pump chamber. The deformable cap 64, made from any suitable deformable material, e.g. Teflon, can be shaped like a mushroom with its stem protruding through the forward plug 65 into the hollow shaft 66. When the screw 68 is turned the stem of the deformable cap 64 is drawn further into the hollow shaft 66 and the hood of the mushroom is forced into contact with the forward plug 65. This pressure changes the shape of the deformable cap, and forces the sides of the deformable cap into contact with the walls of the cylinder 59. This is advantageous, since with repeated use the cap will wear to the point where it no longer fits snugly within the cylinder. When this happens, leakage occurs which can cause errors limiting the precision of the instrument. In this embodiment, such constant wear can be compensated for, externally, by deforming the deformable cap to the point where it once again fits snugly with the walls of the cylinder. The fact that this can be done externally eliminates costly and time consuming dismantling of the device. The fact that the cap is made from a deformable material has a second advantage in that when the piston is brought into contact with the rounded forward wall it is desirable that that portion of the cap furthest from the outlet channel makes contact with the forward wall first. Then, as the piston is further driven forward the cap deforms slightly until it mates fully with the forward wall. In this way, fluid left at the bottom of the forward wall will be forced up into the channel, completely emptying the pump chamber 63.

The means 61 used to drive the piston can be any suitable means. Many are known to those skilled in the art. In this embodiment, the hollow support rod 66 is linked to a ball screw by a pair of ball nuts. The ball nuts are threaded onto the ball screw, back to back, and are adjusted to take up all lost motion between the ball nuts and the ball screw. The ball screw is driven through a set of pulleys and a timing belt from a stepping motor. One step of the motor moves the piston a distance equivalent to a 20 microliter volume, such that the error in this step is less than 0.5 microliter.

Since the system described above can be used to perform precise analytic tests, it is important that it be kept clean at all times. When the pump draws in fluid, the cylinder walls are exposed to that fluid. When the fluid is discharged, a molecular film of fluid remains on the walls even when the tightest fitting piston is used. This film would contaminate the next, fluid taken into the pump, beyond the 0.02% to 0.03% required in some tests. To overcome this, the pump must be designed to cleanse itself. The portion of the cylinder in front of the piston can be cleansed by drawing a cleansing fluid through channel 62, in a manner which will be described below. Some method, however, must be provided for cleansing the portion of the cylinder behind the piston. This can be done by providing an inlet port 69 to allow a cleansing liquid to pass through the hollow shaft 66 and through outlet 70 into the area 71 behind the piston. Movement of the piston forward will automatically draw the cleansing fluid through inlet

port 69 into the area 71, and movement of the piston backwards will force the cleansing fluid out through outlet port 72. At both inlet port 69 and outlet port 72, suitable one way valves must be provided. Since the requirements on a valve used for this purpose are not stringent, any suitable valve known to one skilled in the art will suffice. Optionally both inlet and outlet ports could be in the valve cylinder.

FIG. 5 is a schematic diagram of the elements described above as they can be combined to form a fluid handling and sampling system. This system can be part of a fully automatic analytic instrument such as the one described in patent application Ser. No. 753,197 wherein the operational steps of the sampling system are programmed by some sequencing circuit which in itself operates in response to a coded input, or it can be a simple manually operated system. The operation would be much the same. For purposes of convenience, it will be assumed that the sampling system comprises: a single intake-output valve 73; and intake valve 77 connected to a source of cleansing fluid; an intake valve 78 connected to a source of buffer solution; and a pump. The system can best be described in operation. Initially the intake-output valve 73 is opened and both intake valves 77 and 78 are closed. The operation begins with the closing of intake-output valve 73 and the opening of intake valve 78. By suction, provided by the pump 75, the buffer solution is drawn from its source 79 into the intake valve 78 through intake orifice 80, and into the pump chamber 81. In an operation where precise amounts of fluid are to be transferred from the source to a reaction chamber of some sort, it is usually necessary to keep the transfer system free from gas bubbles so that the pump will deliver an accurate amount of fluid. In such a system a de-bubbler 82 can be provided for this purpose; but this is optional. The design of the de-bubbler is standard and known to those skilled in the art.

In this embodiment the capacity of the sampling system is 5 milliliters. At this point the pump draws in 1 milliliter of buffer solution. Intake valve 78 closes, intake-output valve 73 opens, and the pump discharges the buffer solution into a drain through sample probe 74. This is the buffer flush. Intake-output valve 78 opens again, and pump 75 draws in a volume of buffer solution equal to 5 milliliters, less the volume of the sample fluid which will be required. In this embodiment the sample size usually can be varied from 20 to 500 microliters, in increments of 20 microliters. Intake valve 78 closes, intake-output valve 73 opens, the sample transfer probe 74 moves from the drain the dips into the sample. It is important to note that, upon opening, intake-output valve 73 has aspirated any excess fluid remaining on the lip of the transfer probe 74 into the transfer probe, so that no fluid remains on the lip of the transfer probe to contaminate or dilute the sample. The pump then draws in the required sample volume to make up the total 5 milliliter volume. The sample probe then moves from the sample container to a position over the receptacle which is to receive the sample and buffer fluids. The system can be adapted to deliver this mixture in any way desired. One possibility is to inject the mixture into the analytic pack described in application Ser. No. 545,494. If this is the case, the transfer probe 74 can be a hypodermic needle so that it can be inserted through the rubber dam which forms the seal on the analytic pack. However, the application of this system is not intended to be limited to use with such an analytic pack. This system can be used to transfer fluid from a container, to any location, by any means desired by and known to those skilled in the art.

In the operation described above, the sample and buffer solution are usually discharged into the receptacle in two steps. This facilitates the use of a separation column in the receptacle; if such a column is desired. In this embodiment most of the buffer solution is contained in the pump 81. The sample is generally separate from the buffer solution, and of a volume small enough to be contained within the transfer probe and the associated transfer lines leading up to the pump chamber. In effect, this means that there is no mixing of the sample fluid and the buffer solution within the sampling system, even though the two fluids are in contact with one another. Upon discharge, which is caused by reversing the action of the pump 75, the sample fluid is discharged first, followed by the buffer solution. This means that, if a separation column is used, the sample fluid will be washed through the separation column by the buffer solution in a manner consistent with good laboratory practice.

The sample probe 74 is then positioned over the drain. Intake-output valve 73 closes, intake valve 77 opens and 1 milliliter of a washing fluid, which can be water, any solvent, or any fluid which will produce the desired flushing effect, is drawn from its source 83, optionally through a de-bubbler 84, through the intake orifice 85 in intake valve 77 and into the pump chamber 81. Intake valve 77 closes, intake-output valve 73 opens, and the pump discharges the flushing fluid into the drain. This is the water flush, which can be repeated as many times as desired. At the end of the water flush the fluid handling system is cleaned and ready for intake of the buffer solution for the next operation. Actually, when only one buffer is being used, it is not necessary to use a water flush step. The use of a water flush becomes necessary when a number of buffer solutions are used. The water flush is included in this simple single buffer situation merely to illustrate the operation of the system.

The pump 75 shown in FIG. 5 is a piston pump such as that described in FIG. 4. This is a convenient pumping system for the application described above, but it is not the only pumping system which can be used. As described above, the pump shown in FIG. 5 can be constructed so that it can automatically cleanse the portions of the pump behind the piston 86. This is done by drawing some cleansing fluid into port 87 as the volume of the pump chamber 81 is decreased, and forcing this cleansing fluid out through port 88 as the volume of the mixing chamber is increased. This double cleansing decreases contamination and insures the desired precision.

What is claimed is:

1. A nonpumping valve assembly comprising: an enclosed cylindrical valve chamber having two opposed ends separated by a tubular side wall, said valve chamber having at least one connecting orifice in one of its ends, a second orifice in its other end and at least one orifice for admitting a first fluid into said valve chamber; a cylindrical channel having two opposed ends separated by tubular side walls, said channel being connected to said valve chamber, at one of its ends, through said connecting orifice and having third and fourth orifices in its side walls to provide a throughput

passage through said channel for a second fluid; a valve seat associated with said connecting orifice; an essentially cylindrical movable closing means disposed within said valve chamber and adapted to cooperate with said valve seat to close off said connecting orifice without obstructing the remaining orifices in said valve chamber; a movable support means comprising two cylindrical support rods of substantially equal diameter connected to said closing means for moving said closing means into and out of contact with said valve seat, said closing means and said cylindrical support rods being disposed concentrically within said valve chamber so that one of said support rods extends through one of said connecting orifices and the other of said support rods extends through said second orifice, and being constructed so that when said closing means is in contact with said valve seat, the volume within said valve chamber occupied by said closing means and said support means, and therefore unavailable to fluid, remains substantially constant when said closing means is moved.

2. The valve of claim **1** wherein said support rods are constructed in a manner such that the volume within said valve chamber occupied by said closing means and said support rods changes by no more than one microliter when said closing means is moved.

3. The valve of claim **2** wherein the orifice associated with said valve seat is connected to a source of second fluid which can be added to said first fluid by opening said valve.

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